medical nutrition & disease

A CASE-BASED APPROACH

fifth edition

Lisa Hark, PhD, RD
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WILEY Blackwell

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Preface

The development of *Medical Nutrition & Disease* began in 1990 as a self-instructional, case-based textbook for medical students and was first published by Wiley-Blackwell in 1995. The 5th edition now includes 13 chapters and 26 cases, all of which continue to be co-written by a multidisciplinary team of registered dietitians and physicians. Medical students and medical residents have also been invited to contribute to several 5th edition chapters and cases, offering an opportunity to educate these trainees about nutrition and target our audience. This new edition also recognizes the increasingly important role of team-based care and interprofessional education. During the development of the 5th edition, the Interprofessional Education Collaborative (IPEC) was formed which aims to promote and encourage interprofessional learning experiences to better prepare future clinicians for team-based care of patients. The national organizations included in the IPEC are the Association of American Medical Colleges, American Association of Colleges of Nursing, American Association of Colleges of Osteopathic Medicine, American Association of Colleges of Pharmacy, American Dental Education Association, and the Association of Schools of Public Health. These groups

represent higher education in allopathic and osteopathic medicine, dentistry, nursing, pharmacy, and public health and have created core competencies for interprofessional collaborative practice that can guide curricula development at all health professions schools. *Medical Nutrition & Disease* is designed so that medical, physician assistant, dietetic, nursing, public health, and pharmacy students and practitioners can enhance their nutrition knowledge, skills, and attitudes to provide effective counseling to patients with or at risk for a variety of chronic conditions – essentially the ideal text for interprofessional learning.

Over the past 20 years, the role of a healthy lifestyle in preventing and treating the most common chronic diseases, such as obesity, cancer, heart disease, hypertension, and diabetes continues to mount. Each chapter and case is based on strong scientific evidence supporting nutrition and physical activity interventions and provides practical advice on how to counsel patients to make positive behavior and lifestyle changes. All cases include "before and after" diets and over 50 references are included at the end of each chapter. The 5th edition also includes six new cases, covering emerging nutrition issues for macular degeneration, menopause, celiac disease, polycystic ovarian syndrome, colon cancer, and lead poisoning in children.

Registered dietitians and dietetic technicians can earn **48 pre-approved continuing education credits** from the Academy of Nutrition and Dietetics by successfully completing the multiple choice questions included in the book. There are no additional fees and all forms and directions are inserted inside the back cover.

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Part I
Fundamentals of Nutrition Assessment

1
Overview of Nutrition Assessment in Clinical Care

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Objectives

Recognize the value of nutrition assessment in the comprehensive care of ambulatory and hospitalized patients.

Obtain an appropriate patient history, including medical, family, social, nutrition/dietary, physical activity, and weight histories; use of prescription and over-the-counter medicines, dietary and herbal supplements; and consumption of alcohol and other recreational drugs.

Demonstrate how to interpret physical findings that reflect nutritional status,

including body mass index, waist circumference, growth and development, and signs of nutritional deficiency.

Describe the diagnosis, prevalence, health consequences, and etiology of obesity and malnutrition.

Identify the most common physical findings associated with vitamin/mineral deficiencies or excesses.

List the laboratory measurements commonly used to assess the nutritional status of patients.

Source: Objectives for chapter and cases adapted from the *NIH Nutrition Curriculum Guide for Training Physicians*. (www.nhlbi.nih.gov/funding/training/naa)

Nutrition Assessment in Clinical Care

Nutrition assessment is the evaluation of an individual's nutritional status based on the interpretation of clinical information. Nutrition assessment is important because obesity and malnutrition are common in the clinical setting. The purpose of nutrition assessment is to:

accurately evaluate an individual's dietary intake and nutritional status,

determine if medical nutrition therapy and/or counseling is needed,

monitor changes in nutritional status, and

evaluate the effectiveness of nutritional interventions.

Accurate nutritional assessment leads to correct diagnosis and treatment. Many patients can benefit from medical nutrition therapy (MNT) using established evidence-based protocols.

Integrating Nutrition into the Medical History and Physical Examination

The following illustrates how nutrition can be integrated into all components of the clinical assessment, including the medical history, diet history, review of systems, physical examination, laboratory data, and treatment plan.

Medical History

Past Medical History

Standard past medical history including immunizations, hospitalizations, surgeries, major injuries, chronic illnesses, and significant acute illnesses may have nutritional implications. Detailed information should be obtained about current or recent medication

use including vitamins, minerals, laxatives, topical medications, over-the-counter medications, and products such as nutritional or herbal supplements which patients frequently fail to report as medications. Nutritional supplements include any products that may alter caloric, vitamin, or protein intake. Whether the patient has any known food allergies (i.e., peanut, gluten) or suffers from lactose (milk) intolerance is also important.

Family History

In assessing risk for future diseases, patients are asked to identify their parents, siblings, children, and partner, give their respective ages and health status, and indicate familial occurrences of disease or cause of death of any deceased family members. Family history of diabetes, cancer, heart disease, thyroid disease, obesity, hypertension, osteoporosis, food allergies, eating disorders, or alcoholism should be ascertained. Food sensitivity may be based on inherited immune system characteristics and family history of food intolerance should be assessed.

Social History

The diet history is typically obtained as part of the patients' social history because socioeconomic factors such as who the patient lives with and what resources they have available influence food selection and

preparation. Pertinent non-medical information recorded in the social history includes the patient's occupation, daily exercise pattern, and marital and family status. Information should be solicited regarding the patient's education, economic status, residence, emotional response and adjustment to illness, and any other information that might influence the patient's understanding of his or her illness and adherence to a nutritional therapy. Details concerning the duration and frequency of the patient's use of substances such as alcohol, tobacco, illicit drugs, and caffeine are also documented. These data can be extremely useful when formulating the treatment plan. Economic limitations that influence access to an adequate diet, difficulties shopping for or preparing food, participation in feeding programs (e.g. Women, Infants, and Children (WIC), Meals on Wheels) are relevant aspects of the nutritional assessment.

The Importance of Taking a Diet History

The purpose of obtaining dietary information from patients is to assess their nutritional intake and establish a baseline from which to negotiate changes. Infants, children, adolescents, pregnant women, older adults, and patients with a family history of or who have diabetes, hypertension, heart disease, hyperlipidemia, obesity, eating disorders, alcoholism, osteoporosis, gastrointestinal or

renal disease, cancer, or weight loss or gain should consistently be asked about their eating habits, even during routine visits. Relative strengths for each method of collecting dietary information are described in this section. In addition, patients' past and/or current dietary patterns, such as vegetarian or kosher diet practices, cultural background, and social situations should be considered during the interview. Family members who purchase and prepare foods should be invited for the interview process whenever possible. Diet-related questions may take a few minutes, if properly directed (See Table 1-1). Registered dietitians typically collect more detailed information from a diet history and make this information available to the physician, nurse practitioner, or physician assistant. This history may include information on food preferences, portion sizes, frequency of eating out, and emotional responses to eating. The detailed intake information can be used to determine calories, fat, protein, sodium, and fiber intake along with adequacy of vitamin and mineral intake can serve as a basis for counseling.

Table 1-1 Key Diet History Questions for Brief Intervention

Source: Lisa A. Hark, PhD, RD. 2014. Used with permission.

Questions for All Patients

How many meals and snacks do you eat every day? Do you feel that you eat a healthy balanced diet? Why or why not? What do you like to drink during the day, including alcohol? How many glasses? How often do you eat fruits and vegetables? How often do you eat dairy products? Low-fat or regular type? How often do you eat out? What kinds of restaurants? Do you usually finish what is on your plate or leave food? How often do you exercise, including walking?
In addition to the questions above: **Questions for Patients with Hyperlipidemia (Chapter 6)** How often do you eat fatty meats? (hot dogs, bacon, sausage, salami, pastrami, corned beef) How often do you eat fish? How is it prepared? What types of fats do you use in cooking and baking? What do you spread on your bread? What type of snacks and desserts do you eat?
Questions for Patients with Hypertension (Chapter 6)

Do you use a salt shaker at the table or in cooking? Do you read food labels for sodium content? (<400 mg/serving permitted) How often do you eat canned, smoked, frozen, or processed foods?
Questions for Patients with Diabetes (Chapter 8) What times do you take your diabetes medication (including insulin)? What times do you eat your meals and snacks? Do you ever skip meals during the day? How many servings of starchy foods such as breads, cereals, rice, pastas, corn, peas, or beans do you eat during a typical day?

24-Hour Recall

Purpose This informal, qualitative, questioning method elicits all foods and beverages the patient has consumed in the preceding 24 hours. This method is recommended for follow-up visits for patients with diabetes because of the ability to assess the timing of meals, snacks, and insulin injections.

Questions "Starting with the last thing you ate please describe everything that you ate or drank within the past 24 hours (meals and snacks),

including quantities, and how you prepared these foods." Family members are usually consulted if the patient is a child or unable to convey adequate detail. Patients can be asked to write down what they ate the day before while they are waiting to be seen. Hospitalized patients can be monitored through calorie counts reported by the nursing or dietary staff, who can record the daily amounts of food and drink the patient consumes. Keep in mind that the 24-hour recall method, when used alone, may underestimate or overestimate a person's usual caloric intake because the patient's recollection may not reflect long-term dietary habits. It may be helpful to add the question, "Is this fairly typical or was there something unusual about yesterday?" Use caution generalizing this information.

Usual Intake/Diet History

Purpose Similar to the 24-hour recall, a usual intake/diet history is a retrospective method to obtain dietary information by asking the patient to recall his or her normal daily intake pattern, including amounts of foods consumed. This method is suggested for older adults who may frequently skip meals, or for interviewing pediatric patients whose diets may not be varied. This approach provides more information about usual intake patterns than others and tends to reflect long-term dietary habits with greater accuracy.

Questions “Please tell me what you usually eat and drink during the day for meals and snacks?” As a busy clinician, this question may be all that you will have time to ask, but it can serve as a screening mechanism to identify patients who need further screening with a registered dietitian. When using this approach it is important to be flexible. Begin by asking patients to describe their usual intake and if they cannot recall their usual diet, ask what they ate and drank the day before (a switch to the 24-hour recall method). You can then ask if these 24 hours are typical. Also bear in mind that some patients tend to report having eaten only those foods that they know are healthy. It is also important to ask patients if they have changed their diet for health reasons or because of a health professional's advice.

Food Frequency Questionnaire

Purpose The food frequency questionnaire is another retrospective approach used to determine trends in a patient's usual consumption of specific foods.

Questions Patients are usually asked several key questions regarding the frequency of intake of particular foods. Frequencies have been created to identify daily, weekly, or monthly consumption patterns and are especially good for specific nutrients (e.g., fiber, iron, or saturated fat). Patients can be asked these questions during the history, or these items can

be added to the written form for new patients that can be mailed to them prior to their visit or completed while they are in the waiting room. For the clinician, questions can be geared toward the patient's existing medical conditions, which is why this method is effective for patients with diabetes, heart disease, hypertension, or osteoporosis and can be used for evaluating current intake of, for example, fruits, vegetables, dairy products, or processed foods.

Three-Day Food Record

Purpose Unlike the retrospective tools mentioned earlier, a food record is ideally completed prospectively and daily as patients consume their usual diet and reviewed by the clinician at the medical visit. More accurate results can be obtained by collecting data over a longer period (e.g., 7 days).

Questions Patients are asked to record information on meals, food items, quantity consumed, preparation methods, etc., and details such as activities while eating, mood, hunger level, etc., can also collected. This method is preferred for active patients who may be trying to adhere to a new dietary regimen (e.g., a weight loss diet). Three-day records are the most accurate reflection of patients' diets but it is difficult for most patients to keep a written log, including portion sizes, of everthing they ate and drank over three days.

Review of Systems

This subjective reexamination of the patient's history is organized by body systems. It differs from the past medical history by concentrating on symptoms, not diagnoses, and by emphasizing current more than past information. All positive and negative findings are listed. Nutrition questions vary according to the patient's age. One goal of this part of the history is to determine whether any dietary changes have occurred in the patient's life, either voluntarily or as a consequence of illness, medication use, or psychological problems. Examples within the review of systems that may have nutritional implications (and their potential significance) include weakness and fatigue (anemia), clothes tighter or looser (weight gain or weight loss), post-meal cramping or diarrhea (lactose intolerance), chronic headaches, fatigue, gastrointestinal symptoms (gluten sensitivity), constipation (low fluid or fiber intake), amenorrhea (anorexia nervosa), or changes in appetite.

Physical Examination

The physical examination begins with the patient's vital signs (blood pressure, heart rate, respiration rate, temperature), height, weight, body mass index (BMI), and general appearance. For example, “On examination, she is a well-developed, athletic woman.” When

terms such as obese, overweight, undernourished, thin, well-nourished, well-developed, or cachectic (profound, marked state of ill health and malnutrition) are used, they should be supported by findings in the physical examination and noted in the problem list.

Body Mass Index (BMI)

To calculate BMI using the metric system:

$$\text{BMI} = \frac{\text{weight (kg)}}{\text{height (m}^2\text{)}}$$

To calculate BMI using English units:

$$\text{BMI} = \frac{\text{weight (lbs)}}{\text{height (in}^2\text{)}} \times 703$$

Body mass index provides a more accurate measure of total body fat (adiposity) than body weight alone. The BMI is also more accurate than the older height–weight tables, which were based on a homogeneous population, primarily Caucasian, with higher than average socioeconomic status. BMI has also been shown to more estimate obesity than bioelectrical impedance tests. BMI values associated with the lowest mortality increase slightly as people age. However, BMI may overestimate body fat in very muscular people and underestimate body fat in some underweight people who have

lost lean tissue, such as the elderly. Classifications of underweight, normal weight, overweight, and obesity are shown in Table 1-2. Health professionals should routinely assess height, weight, and BMI, and evaluate growth and development in infants, children, and adolescents.

Table 1-2 Classifications of BMI

Source: National Heart, Lung, and Blood Institute, NIH. *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*. 1998. Used with permission.

Underweight	<18.5 kg/m^2
Normal weight	18.5–24.9 kg/m^2
Overweight	25–29.9 kg/m^2
Obesity (Class 1)	30–34.9 kg/m^2
Obesity (Class 2)	35–39.9 kg/m^2
Extreme obesity (Class 3)	≥40 kg/m^2

Diagnosis and Assessment of Overweight and Obesity

Body Mass Index (BMI)

According to the National Heart Lung and Blood Institute's (NHLBI) *Clinical Guidelines*,

many people with a BMI of 25 kg/m^2 or greater begin to experience negative health effects, such as elevated low-density lipoprotein cholesterol (LDL-C) and total cholesterol levels, high blood pressure, and glucose intolerance. These guidelines define overweight individuals as those with a BMI of 25 to 29.9 kg/m^2 and obese individuals as those with a BMI of 30 kg/m^2 and above. The NHLBI *Clinical Guidelines* classify BMI as shown in Table 1-2. BMI values can be determined from height and weight measurements as shown in Figure 1-1.

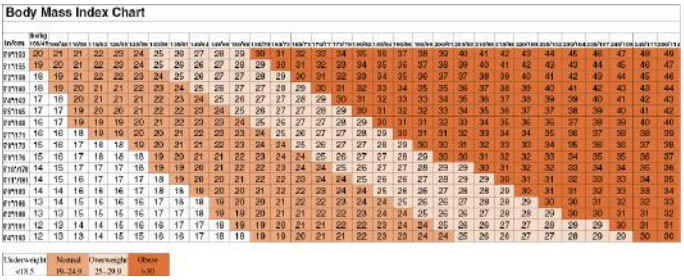


Figure 1-1 BMI Values Based on Height and Weight

Waist Circumference

Waist circumference is an independent measure of risk in normal weight and overweight individuals. Excess fat located in the abdominal area (termed visceral adipose tissue) is reflected by waist circumference measurement. Waist circumference is a predictor of morbidity, and is considered an

independent risk factor for diabetes, dyslipidemia, hypertension, and cardiovascular disease when BMI is not markedly increased. In patients with a BMI greater than 35 kg/m^2, there is little additional risk from elevated waist circumference, as severe risk is already present. Therefore, measuring waist circumference is recommended in patients with a BMI less than 35 kg/m^2. The waist circumference measurement is particularly important for patients with a family history of diabetes and those who may be borderline overweight.

In order to obtain an accurate waist circumference measurement, patients should be standing in only their underwear. A horizontal mark should be drawn just above the uppermost lateral border of the right iliac crest, which should then be crossed with a vertical mark in the midaxillary line. The measuring tape is placed in a horizontal plane around the abdomen at the level of this mark on the right side of the trunk. The plane of the tape should be parallel to the floor and the tape should be snug but not tight. Patients should be advised to breathe normally while the measurement is taken. Waist circumference values greater than 102 cm (40 inches) in men and greater than 88 cm (35 inches) in women are considered indicators of increased risk, although these values may differ for different ethnic groups. Waist circumference is one of the diagnostic

criteria of metabolic syndrome (Chapter 1: Case 1). In patients trying to lose weight by exercising, waist circumference may decrease without significant weight loss.

Percent Weight Change

Weight loss is very common in hospitalized patients and those residing in chronic care facilities. Weight loss is also frequently seen in older adults or those with decreased changes due to chronic illnesses such as cancer, gastrointestinal problems, or secondary to surgery, chemotherapy, or radiation therapy. If weight loss is identified in the medical history or review of systems, it is essential to take a diet and weight history and determine the percent weight change over that period of time using the patient's current body weight and usual weight. Severity of weight loss is defined by percent change in a defined period of time (Table 1-3).

$$\text{Percent weight change} = \frac{\text{Usual Weight} - \text{Current Weight}}{\text{Usual Weight}} \times 100$$

Table 1-3 Interpretation of Percent Weight Change

Time	Significant Weight Loss	Severe Weight Loss
1 week	1–2%	>2%

Time	Significant Weight Loss	Severe Weight Loss
1 month	5%	>5%
3 months	7.5%	>7.5%
6 months	10%	>10%
1 year	20%	>20%

Physical Examination Findings

Nutrition-oriented aspects of the physical examination focus on the skin, hair, eyes, mouth, nails, extremities, abdomen, skeletal muscle, and fat stores. Areas to examine closely for muscle wasting include the temporalis muscles, thenar, hypothenar, and interosseous muscles on the hands. The skeletal muscles of the extremities are a less sensitive indicator of malnutrition. Subcutaneous fat stores should be examined for losses due to a sudden decrease in weight or for excess accumulation in obesity. Isolated vitamin deficiencies such as scurvy or pellagra are rarely seen in modern clinical practice. At the present time, the most commonly encountered nutritional problem seen in clinical practices in the United States and many developed countries is obesity and its associated complications. Specific clinical signs that are attributable to nutrient deficiencies and

significance on physical examination are shown in Table 1-4. Combined nutrient deficiencies are still seen in those with disordered intake such as alcoholics or patients receiving chemotherapy.

Table 1-4 Physical Examination Findings with Nutritional Implications

Source: Lisa A. Hark, PhD, RD and Darwin Deen, MD, MS. 2014. Used with permission.

Exam	Nutritional implications
Vital signs	Blood pressure, height, weight, BMI, percent weight change
General	Wasted, cachectic, overweight, obese, muscle weakness, anorexic, waist circumference

Exam	Nutritional implications
Skin	Acanthosis nigricans (obesity, metabolic syndrome, insulin resistance, diabetes)
	Ecchymosis (vitamin K, C deficiency)
	Dermatitis (marasmus, niacin, riboflavin, zinc, biotin, EFA deficiency)
	Follicular hyperkeratosis (vitamin A deficiency)
	Petechiae (vitamin A, C, K deficiency)
	Pigmentation changes (niacin deficiency, marasmus)
	Pressure ulcers/delayed wound healing (kwashiorkor, diabetes, vitamin C, zinc deficiency)
	Psoriasiform rash, eczematous scaling (zinc deficiency)
	Purpura (vitamin C, K deficiency)
	Scrotal dermatosis (riboflavin deficiency)
	Pallor (iron, folic acid, vitamin B_{12}, copper, vitamin e deficiency)

Exam	Nutritional implications
Hair	Thickening and dryness of skin (linoleic acid deficiency)
	Dyspigmentation, easy pluckability (protein), alopecia (zinc, biotin deficiency)
Head	Temporal muscle wasting (marasmus and cachexia)
	Delayed closure of fontanelle (pediatric undernutrition or growth retardation)
Eyes	Night blindness, xerosis, bitot spots, keratomalacia (vitamin A deficiency)
	Photophobia, blurring, conjunctival inflammation, corneal vascularization (riboflavin deficiency), macular degeneration

Exam	Nutritional implications
Mouth	Angular stomatitis (riboflavin, iron deficiency)
	Bleeding gums (vitamin C, K, riboflavin deficiency)
	Cheilosis (riboflavin, niacin, vitamin B_6 deficiency)
	Dental caries (fluoride deficiency)
	Hypogeusia (zinc, vitamin A deficiency)
	Glossitis (riboflavin, niacin, folic acid, vitamin B_{12}, vitamin B_6 deficiency)
	Nasolabial seborrhea (vitamin B_6 deficiency)
	Papillary atrophy or smooth tongue (riboflavin, niacin, iron deficiency)
	Fissuring, scarlet or raw tongue (niacin, folate, B_{12}, B_6 deficiency)
Neck	Goiter (iodine deficiency)
	Parotid enlargement (marasmus, bulimia)
Thorax	Thoracic achitic rosary (vitamin D deficiency)

Exam	Nutritional implications
Abdomen	Abdominal obesity (metabolic syndrome, diabetes, heart disease)
	Diarrhea (niacin, folate, vitamin B_{12} deficiency, marasmus)
	Hepatomegaly/ascites (kwashiorkor, alcoholism)
Cardiac	Heart failure (thiamin, selenium deficiency, anemia)
Genital/ urinary	Delayed puberty (marasmus, eating disorder, celiac disease)
	Hypogonadism (zinc deficiency)

Exam	Nutritional implications
Extremities	Ataxia (vitamin B_{12} deficiency, vitamin B_6 toxicity)
	Bone ache, joint pain (vitamin C deficiency)
	Bone tenderness, kyphosis (vitamin D deficiency)
	Edema (thiamin or protein deficiency)
	Growth retardation, failure to thrive (energy deficiency)
	Hyporeflexia (thiamin deficiency)
	Bone tenderness, kyphosis (calcium, vitamin D deficiency)
	Muscle wasting and weakness (vitamin D, magnesium deficiency, marasmus)
	Tenderness at end of long bones (vitamin D deficiency)
	Squaring of shoulders—loss of deltoid muscles (kwashiorkor)
Nails	Spooning (koilonychias) (iron deficiency)
	Transverse lines (kwashiorkor, hypochacemia)

Exam	Nutritional implications
Neurological	Dementia, delirium, disorientation (niacin, thiamin, vitamin E deficiency)
	Loss of reflexes, wrist drop, foot drop (thiamin deficiency)
	Ophthalmoplegia (vitamin E, thiamin deficiency)
	Peripheral neuropathy (thiamin, vitamin E, vitamin B_{12} deficiency)
	Tetany (vitamin D, calcium, magnesium deficiency)

Laboratory Data Used to Diagnose Nutritional and Medical Problems

No single blood test or group of tests accurately measures nutritional status. Therefore clinical judgment is important in deciding what tests to order based on the individual's history and physical findings. The following tests are grouped according to medical condition.

Alcoholism: Aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), thiamin, folate, and vitamin B_{12}.

Anemia: Complete blood count (CBC), serum iron and ferritin, total iron binding capacity (TIBC), transferrin saturation, mean corpuscular volume (MCV), reticulocyte count, red blood cell folate, and serum vitamin B_{12}.

Diabetes: Fasting serum glucose, hemoglobin A1C, insulin levels, C-reactive protein (CRP), serum, and urinary ketone bodies.

Eating Disorders: Potassium, albumin, serum amylase, thyroid studies, beta carotene aspartate amino transferase (AST), alanine aminotransferase (ALT), and anemia.

Fluid, Electrolyte, and Renal Function: Sodium, potassium, chloride, calcium, phosphorus, magnesium, blood urea nitrogen (BUN), creatinine, urine urea nitrogen, urinary and serum, oxalic acid, and uric acid.

Hyperlipidemia: Cholesterol, triglyceride, low density lipoprotein-cholesterol (LDL-C), high density lipoprotein-cholesterol (HDL-C), LPa, homocysteine, and thyroid stimulating hormone (TSH) (secondary cause).

Musculoskeletal pain, weakness: 25(OH) vitamin D, phosphate, parathyroid hormone (PTH).

Malabsorption: 24-hour fecal fat, barium imaging studies, electrolytes, albumin, serum triglycerides, and hydrogen breath test.

Metabolic Syndrome: Fasting serum glucose, lipid panel, and uric acid.

Refeeding Syndrome: Albumin, calcium, phosphorous, magnesium, and potassium.

Malnutrition:

Protein Status

Clinically, visceral protein status may be depleted by increased protein losses in the stool and urine as a result of wounds involving severe blood loss, or by poor dietary protein intake. The following serum protein levels may prove useful in conjunction with other nutrition assessment parameters. Once again, however, each of these tests has limitations because serum protein levels are affected not only by nutrition and hydration status, but by disease states, surgery, and liver dysfunction.

The half-life ($t_{1/2}$) of each protein is given because it allows use of these tests to monitor changes in protein nutrition over time:

Serum albumin Serum albumin has a half-life of 18 to 20 days and reflects nutritional status over the previous 1 to 2 months. Levels may decrease with acute stress, overhydration, trauma, surgery, liver disease, and renal

disease. False increases occur with dehydration. This test is not a good indicator of recent dietary status or acute changes in nutritional status (less than 3 weeks) given its long half-life. Significantly reduced levels of serum albumin (<3.5 mg/dL) have been associated with increased morbidity and mortality in clinical studies.

Serum transferrin Serum transferrin has a half-life of 8 to 9 days. Changes in serum transferrin levels are influenced by iron status, as well as by protein and calorie malnutrition. Results of this test reflect intake over the preceding several weeks.

Serum prealbumin With a half-life of 2 to 3 days, serum prealbumin reflects nutritional status as well as protein and calorie intake over the previous week. Prealbumin levels may be falsely elevated with renal disease or, as with albumin, reduced with severe liver disease.

Assessment and Problem List: Medical Nutrition Therapy

The healthcare professional clinically assesses the individual patient based on his/her history, review of systems, physical examination, and laboratory data.

Active problems are listed in order of their importance. Inactive problems are also recorded. Evidence of a nutrition disorder

should be considered primary if it occurs in patients with no other etiology that explains signs and symptoms of malnutrition. A primary nutrition problem is usually the result of imbalances, inadequacies, or excesses in the patient's nutrient intake. Manifestations may include obesity, weight loss, malnutrition, or poor intake of vitamins or minerals such as iron, calcium, folate, vitamin D, or vitamin B_{12}.

Patients having normal weight and no other risk factors should be encouraged to maintain their weight. Overweight patients with co-morbidities, such as diabetes, hypertension, or heart disease, should be advised to lose weight by increasing their physical activity level and reducing their total calorie and saturated fat intake, using smaller portion sizes, and selecting healthier foods. Referral to a registered dietitian for additional counseling and support has been shown to be effective.

Secondary nutrition problems occur when a primary pathologic process results in inadequate food intake, impaired absorption and utilization of nutrients, increased loss or excretion of nutrients, or increased nutrient requirements. Common causes of secondary nutritional disorders include anorexia nervosa, malabsorption, trauma, acute medical illness, and surgery. Malnutrition may occur as a result of a chronic condition or an acute episode complicating an underlying disease. After

assessing each problem, medical nutrition therapy should be recommended that includes both a diagnostic component and a treatment plan. Patient education is an essential part of medical nutrition therapy. Key dietary issues by age and disease are summarized in Table 1-5.

Table 1-5 Key Dietary Issues by Age and Disease

Source: Lisa A. Hark, PhD, RD and Darwin Deen, MD, MS. 2014. Used with permission.

Age/Disease	**Key Dietary Issue**
Infants	Fluoride, iron, calories, protein, fat for growth and development
Children	Fluoride, iron, calcium, calories, protein, fat for growth and development
Teenagers	Iron, calcium, calories, protein for pubertal development (screen for eating disorders)
Pregnancy	Folate, iron, calcium, vitamin D, protein, appropriate weight gain
Alcoholism	Folate, thiamin, vitamin B_{12}, calories
Anemia	Iron, vitamin B_{12}, folate
Ascites	Sodium, protein
Beriberi	Thiamin

Age/Disease	Key Dietary Issue
Cancer	Adequate protein, calories, and fiber
Celiac Disease	B complex, vitamins, vitamin D
COPD, Asthma	Vitamin D, calcium, weight loss, calories
Diabetes	Carbohydrates, saturated fat, cholesterol, calories, fiber
Heart Disease	Saturated fat, monounsaturated fat, cholesterol, sugar, fiber
Hyperlipidemia	Saturated fat, monounsaturated fat, cholesterol, sugar, fiber
Heart Failure	Sodium
Hypertension	Sodium, calcium, potassium, alcohol, sugar, total calories
Kidney Stones	Calcium, oxalate, uric acid, protein, sodium, fluid
Liver Disease	Protein, sodium, fluid
Malabsorption	Vitamins A, D, E and K
Obesity	Total calories, portion sizes, saturated fat
Osteoporosis	Vitamin D and calcium
Pellegra	Niacin

Age/Disease	Key Dietary Issue
Renal Failure	Protein, sodium, potassium, phosphorous, fluid
Rickets	Vitamin D and calcium
Scurvy	Vitamin C
Vegetarian diet	Protein, vitamin B_{12}, iron, calcium

Estimating Energy and Protein Requirements

Resting Energy Expenditure (REE)

The amount of energy required to maintain vital organ function in a resting state over 24 hours is referred to as the resting energy expenditure (REE). Basal metabolic rate (BMR) is the minimum calorie requirement for an individual at a neutral environmental temperature while fasting. BMR is generally impractical to measure. REE is approximately 10 percent above BMR. Thus, the REE is used clinically for estimation of BMR. REE accounts for approximately 65 percent of total daily energy expenditure and varies considerably among individuals with different height, weight, age, body composition, and gender. REE significantly correlates with lean body mass. Regular physical activity, especially weight-bearing exercises, can increase muscle

mass, and thus increase REE. Since REE decreases as people age due to the loss of lean body mass over time, regular exercise can play a significant role in maintaining REE, especially in older adults. The energy produced by the oxidation of dietary macronutrients is shown in Table 1-6. The Mifflin–St. Jeor equation to estimate energy requirement is shown in Table 1-7. Activity factors are added to the REE as necessary to calculate total daily caloric needs, which vary for active and inactive patients. Total energy expenditure (TEE) is equal to the REE times the appropriate physical activity factor. The physical activity factor for hospitalized patients or those confined to bed is 1.2; for non-hospitalized, sedentary patients, 1.3.

Table 1-6 Definition of Energy/Calorie

Energy is expressed in kilocalories (kcal) and is produced by the oxidation of dietary protein, fat, carbohydrate, and alcohol.
One gram of **protein** yields approximately 4 kcal. One gram of **carbohydrate** yields approximately 4 kcal. One gram of **fat** yields approximately 9 kcal. One gram of **alcohol** yields approximately 7 kcal.

A calorie is the amount of heat required to raise the temperature of 1 gram of water by 1 degree Celsius. A kilocalorie is the amount of heat required to raise the temperature of 1 kilogram of water by 1 degree Celsius.

Table 1-7 Mifflin-St. Jeor Equation to Estimate Energy Requirement

Adults 19 years and older
Estimated Energy Requirement (kcal/day) = Total Energy Expenditure **Men** 10 × weight (kg) + 6.25 × height (cm) – 5 × age (y) + 5 **Women** 10 × weight (kg) + 6.25 × height (cm) – 5 × age (y) – 161

Source: Mifflin, MD, St. Jeor ST, Hill LA, Scott, BJ, Daughtery SA, Koh YO. A new perspective equation for resting energy expenditure in healthy individuals. *Am J Clin Nutr*. 1990;(2):1241–-1247.

Protein Needs of Hospitalized or Critically Ill Patients

Protein requirements in a critically ill patient depend on the degree of catabolic stress the patient is experiencing. Guidelines are as follows:

In unstressed well-nourished individuals, protein needs range from 0.8 to 1.0 g/kg body weight per day.

In post-surgical patients protein needs range from 1.5 to 2.0 g/kg body weight per day.

In highly catabolic patients (burns, infection, fever), protein needs can be over 2 g/kg body weight per day.

Malnutrition

According to the World Health Organization (WHO), malnutrition affects all age groups across the entire lifespan, from conception to older adults. Health consequences range from intrauterine brain damage and growth failure to reduced physical and mental capacity in childhood to an increased risk of developing diet-related chronic diseases later in life.

Insufficient food intake results in loss of fat, muscle, and ultimately visceral tissue. This reduction in tissue mass is reflected in weight loss. The smaller tissue mass reduces nutritional requirements, likely reflecting more efficient utilization of ingested food and reduction in work capacity at the cellular level. The combination of decreased tissue mass and reduction in work capacity impedes homeostatic responses, including responses to illness or surgery. The stress of critical illness inhibits the body's conservation response to

malnutrition. In addition, undernourished individuals experience nutrient deficiencies and imbalances that exacerbate the reduction in cellular work capacity. Malnutrition is also associated with a decrease in the inflammatory response and immune function. These alterations result in increased morbidity and mortality among undernourished patients. Adequate nutrition is essential for reversing these physiological effects. Aggressive nutritional support, instituted early in critical illness, may reduce the adverse effects of malnutrition in the critically ill patient.

Etiology/Causes of Malnutrition

Decreased Oral Intake Poverty, poor dentition, gastrointestinal obstruction, abdominal pain, anorexia, dysphagia, depression, social isolation, and chronic pain are some of the many possible causes of decreased oral intake.

Increased Nutrient Loss Glycosuria, proteinuria, gastrointestinal bleeding, diarrhea, malabsorption, a draining fistula, or protein-losing enteropathy can result in nutrient losses.

Increased Nutrient Requirements Hypermetabolism state or excessive catabolic processes can result in increased nutrient requirements. Common examples of situations that can dramatically affect nutrient

requirements include surgery, trauma, fever, burns, hyperthyroidism, severe infection, malabsorption syndromes, cancer, chronic obstructive pulmonary disease (COPD), cardiac cachexia, critical illness, and HIV/AIDS. Pregnant women and children also experience increased nutritional requirements during growth and development.

Diagnosis of Malnutrition

Malnutrition is defined as a suboptimal or deficient supply of nutrients that interferes with an individual's growth, development, general health, or recovery from illness. A BMI of less than 18.5 kg/m^2 defines adults who are consistently underweight and at risk for malnutrition. Infants and children who fall below the 5th percentile for weight-for-age or BMI-for-age on the growth chart should also be evaluated further and followed closely. In acute malnutrition, a child's weight-for-age percentile on the growth chart falls first, followed by a decline in height growth. In extreme cases of malnutrition or starvation, a child's head circumference growth may also plateau. The importance of plotting pediatric growth parameters over time is paramount, as poor weight gain and/or weight loss are key to diagnosing malnutrition, failure to thrive, and other medical conditions associated with poor weight gain in the pediatric population, such as

cystic fibrosis. Crossing growth percentile lines should always prompt close follow-up.

Marasmus results when the body's requirements for calories and protein are not met by dietary intake. Marasmus is characterized by severe tissue wasting, excessive loss of lean body mass and subcutaneous fat stores, and weight loss. Decreased protein intake is usually associated with decreased calorie intake, but can occur independently.

Kwashiorkor describes a predominant protein deficiency. Kwashiorkor is characterized by lethargy, apathy, irritability, retarded growth, changes in skin (dermatitis) and hair pigmentation, edema, and low serum albumin. Both marasmus and kwashiorkor are associated with weakness, weight loss, decline in functional status (increased difficulties with activities of daily living), impaired immune function with increased susceptibility to infection, and increased risk of morbidity and mortality.

Prevalence of Malnutrition

Children, older adults, and hospitalized and nursing home patients are particularly prone to malnutrition. According to WHO, 99 million children (17 percent) under 5 years of age were underweight in developing countries in 2011. This number is estimated to have declined from

28 percent in 1990. Fifty percent of deaths among children less than 5 years of age in developing countries are associated with malnutrition. One in three people are affected by vitamin and mineral deficiencies and one in four pre-school children suffer from malnutrition. One in six infants are born at low birth weight in developing countries.

Some degree of malnutrition occurs during most hospitalizations regardless of the type of injury or illness. The prevalence of malnutrition in the out-patient population has not been clearly determined. Risk factors for malnutrition include chronic diseases, use of multiple prescription medications, poverty, inadequate nutritional knowledge, homebound and/or non-ambulatory status, poor social support structure, major psychiatric diagnosis, and alcoholism. Malnutrition in nursing home patients has been reported in up to 50 percent of residents.

Food insecurity is defined by the United States Department of Agriculture (USDA) as lack of access to enough food to fully meet basic needs at all times due to lack of financial resources. Households that are insecure, even when hunger is not present, have such limited resources that they may run out of food or cannot afford balanced meals. Hungry households have been defined as those that lack adequate financial resources to the point where

family members, especially children, are hungry on a regular basis and the food intake of adults is severely reduced.

According to the USDA, an estimated 17 million (15 percent) of American households experienced food insecurity for at least some time during 2011. This represented 33.5 million adults and 16.7 million children. Approximately 8.6 million children (11.5 percent) lived in households in which one or more child was food insecure. Nationally, food insecurity was significantly higher for households with incomes near or below the Federal poverty line (35 percent), households headed by a single woman (37 percent) or man (24.9 percent), Black, non-Hispanic (25 percent) and Hispanic (26.2 percent) households, all households with children (21 percent) and households with children under age 6 (22 percent). Households with WIC-eligible incomes experience food insecurity more than those with higher income levels. Studies have shown that the federally funded WIC program is an effective means of decreasing rates of food insecurity while positively influencing nutrient intakes.

Unfortunately, with the shift from welfare to work, many low-income working families who are eligible for Federal assistance do not participate, leaving children more vulnerable to food insecurity than ever before. In 2011, 57 percent of food insecure households received

assistance from one or more of the three largest Federal food and nutrition assistance programs. The Supplemental Nutrition Assistance Program (SNAP), formerly known as the Food Stamp Program, provided benefits to 44.7 million people in the UnitedStates in 2011. This accounted for 40.1 percent of food insecure households.

Food insecurity and poor diet quality exist at unsettling levels throughout the United States despite attempts to create a food and nutrition safety net. Studies show that specific populations, including low-income women with children living in rural areas, are at increased risk for experiencing food insecurity. Providing nutrition education to all food assistance program participants, including information regarding the benefits associated with the recommended intake of fruits and vegetables as well as the availability and affordability of fresh produce, should be a priority.

Overweight and Obesity

Health Consequences of Overweight and Obesity

Obesity is a complex, multi-factorial disease that is becoming increasingly common among adults and children worldwide. Once considered a problem only in developed countries, overweight and obesity are now

dramatically on the rise in developing countries as well, particularly in urban settings. Obese individuals have an increased risk of diabetes, coronary heart disease, hyperlipidemia, hypertension, stroke, gallbladder disease, sleep apnea, osteoarthritis, respiratory problems, and certain types of cancers (endometrial, breast, prostate, and colon), all of which increase their risk of mortality. According to the Centers for Disease Control and Prevention (CDC), seven out of ten deaths among Americans each year result from chronic diseases. Obesity-related conditions such as heart disease, type 2 diabetes, stroke, and certain types of cancer account for more than 50 percent of preventable deaths each year.

Recent studies show that overweight (BMI = 25.0–29.9) or class I obesity (BMI = 30.0–34.9) are not associated with excess mortality compared to normal BMI individuals (BMI = 18.5–24.9). However, class II/III obesity (BMI ≥ 35.0) is associated with significantly higher mortality, ranging from 40 percent among females to 62 percent among males relative to individuals with normal BMI. In considering attributable mortality risk, class II/III obesity (BMI ≥ 35.0) is responsible for approximately 4 percent of deaths among females and 3 percent among males. Obesity accounts for approximately 5 to 7 percent of national health expenditures in the United States. Recent studies demonstrate that across

all payers, public and private, per capita medical spending for the obese was $1,723 higher per year (42 percent) than for an individual of normal weight and $266 higher per year for overweight individuals. The aggregate national cost of overweight and obesity was approximately $114 billion dollars in 2012. Other studies indicate that obesity-related expenditures are expected to increase to 16 to 18 percent of healthcare spending by 2030.

Etiology of Overweight and Obesity

The etiology of obesity is believed to be due to a combination of biological and environmental factors. Biological factors that have been identified include an individual's genetic predisposition, the size and number of adipose cells, and REE. Environmental factors that have been identified as contributory to overweight and obesity include excessive caloric intake and inadequate physical activity. These are the most likely environmental factors associated with the significant increase in overweight and obesity seen in the United States. and developed countries over the past several decades. Recent research is examining the role of exposure to environmental toxins and the contribution of gut bacteria.

Genetics In humans, 426 variants of 127 different genes have been associated with obesity. According to the Human Obesity Gene

Map, single mutations in 11 genes were strongly implicated in 176 cases of obesity worldwide. Additionally, 50 chromosomal locations have been mapped that contain genes that may be related to obesity. According to the CDC, "several independent population-based studies reported that a gene of unknown function, referred to as fat mass and obesity-associated gene (FTO), may be responsible for up to 22 percent of all cases of obesity. Interestingly, the FTO gene also shows a strong association with diabetes. The mechanism by which FTO operates is currently under investigation."

Family history reflects genetic susceptibility and environmental exposures shared by close relatives. Genetic studies over the past several decades investigating adopted twins and their biological and adoptive parents show that adoptees' weight correlates most strongly with their biological parents' weight. Additional research has shown that children with one overweight parent have a 40 percent chance of becoming overweight as adults. This risk increases to 80 percent if both parents are overweight. Regardless of the strong evidence for genetic influences on human obesity, genetics accounts for no more than one-third of the variance in body weight. Experts agree that since there has been no change in the gene pool over the past three decades, the dramatic increase in the prevalence of obesity in both

children and adults in the United States. likely reflects environmental influences (epigenetic).

Adipose Cell Size and Number The size and number of fat cells have been studied for many years and vary between normal, overweight, and obese individuals. During infancy, adolescence, and pregnancy, fat cells normally increase in number. With modest weight gain, fat cells increase in size, and with significant weight gain, fat cells increase in both size and number. With weight loss, fat cells decrease in size but not in number. The lack of reduction in fat cell number may help explain why it is difficult for obese individuals to maintain weight loss for an extended period of time after a significant weight loss.

Excess Caloric or Energy Intake Humans require energy (calories) to support normal metabolic functions, physical activity, and growth and repair of tissues. According to the latest National Health and Nutrition Examination Survey III (NHANES), Americans are eating 220 more calories per day compared to 20 years ago. This increase in calories can be partially attributed to a combination of increased portion sizes or “super-size” servings and the increased frequency of eating outside the home, especially at fast-food restaurants. This calorie increase may also be secondary to increased body weight, which increases energy requirements.

Decreased Physical Activity The dramatic increase in sedentary activities and labor-saving devices (sitting at the computer, watching television, using the remote control, taking escalators, elevators, or moving sidewalks, using drive-through windows to pick up food, and using garage door openers as examples) have reduced the amount of energy we expend as a society. According to the CDC, less than half (48 percent) of all adults met the 2008 Physical Activity Guidelines. Gender differences indicate that men (52 percent) were more likely than women (42 percent) to meet guidelines for aerobic activity. Ethnic differences also exist. More non-Hispanic white adults (23 percent) met the standard guidelines than non-Hispanic black adults (17 percent) and Hispanic adults (14 percent). Americans living in the South were more likely to be less physically active than individuals living in other United States regions. Less than 30 percent of high school students got at least 60 minutes of physical activity every day. In addition, the Behavioral Risk Factor Surveillance System indicates that participation in physical activity declines as people age.

Because regular physical activity modestly contributes to caloric expenditure, reduced abdominal fat, and increased cardio-respiratory fitness, it should be strongly encouraged, along with a reduced calorie diet, to improve the health of overweight and obese individuals.

Recent studies from the National Weight Control Registry have indicated that regular physical activity is the single best predictor of long-term weight control in overweight and obese individuals who have lost weight.

Prevalence of Overweight and Obesity

According to the CDC, more than one-third of United States adults or 78 million Americans were obese in 2009–2010. Approximately 12.5 million (17 percent) United States children and adolescents were obese. Although obesity prevalence has not measurably increased in the past few years, levels are still high at 36 percent of United States adults aged 20 and over. Over the past decade obesity prevalence among men and boys in the United States has increased significantly but not among women and girls overall. Adults over the age of 60 were more likely to be obese than younger adults. Worldwide, obesity prevalence has more than doubled from 1980 to 2008. In 2008, the WHO estimated that more than half a billion adults worldwide were obese, approximately 205 million men and 297 million women. The prevalence of overweight and obesity were highest in the WHO Regions of the Americas (62 percent for overweight and 26 percent for obesity) and lowest in the WHO Region for South East Asia (14 percent overweight and 3 percent obesity). The CDC's Behavioral Risk Factor Surveillance System (BRFSS) shown in

Figure 1-2 illustrates that during the past 25 years there has been a dramatic increase in United States obesity rates. This United States map demonstrates this trend by mapping the increased prevalence of obesity across each of the states. In 1985, there were 13 states that had 10 percent or less prevalence of obesity; in 2010 no states had less than 20 percent prevalence of obesity. In 1985, no states had more than a 14 percent increase in prevalence of obesity. In 2010, 12 states had a prevalence of obesity equal to or greater than 30 percent. No state in the United States met *The Healthy People 2010* objective to lower obesity prevalence to 15 percent among adults and 5 percent among children.

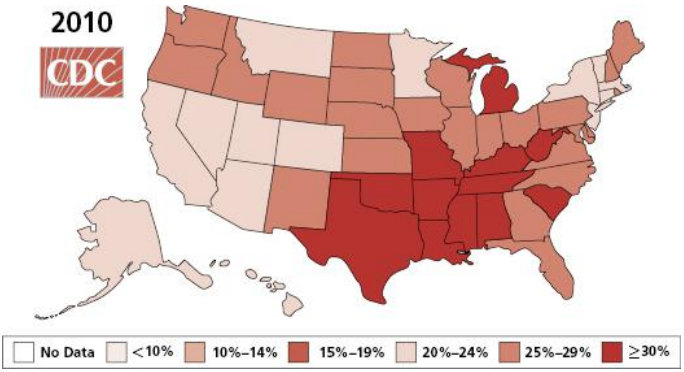
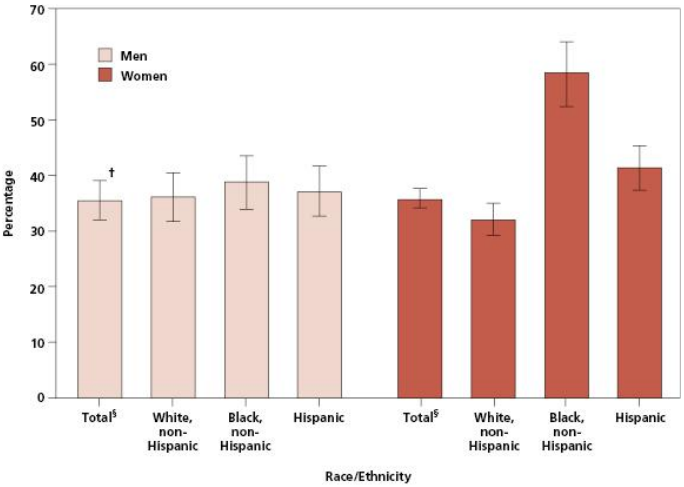


Figure 1-2 Prevalence of Overweight and Obesity Rates in the United States by State (2010)

Available from http://www.cdc.gov.

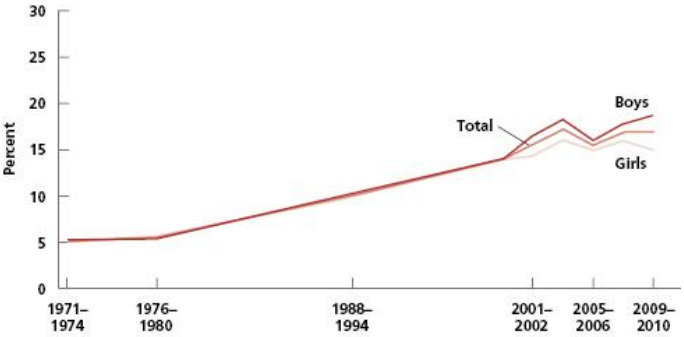
Among women, the age-adjusted prevalence of overweight or obesity among racial and ethnic minorities is higher among non-Hispanic black and Mexican-American women than among non-Hispanic white women. For men, the difference is less pronounced, as shown in Figure 1-3. While *Healthy People 2020* has identified obesity reduction among children and adolescents as a chief objective, inadequate progress has been made toward this goal. For children and adolescents, overweight is defined as BMI above the 85th percentile and obesity is greater than the 95th percentile-for-age. Figure 1-4 demonstrates the increase in obesity that has occurred among children and adolescents since 1976. Figure 1-4 also shows how over the last decade obesity prevalence among boys in the United States has increased more significantly than among girls. More recent studies of smaller geographic regions (e.g., New York City) are showing some declines in rates of childhood obesity.



* Defined as a body mass index (weight [kg] / height [m]2) ≥30.
† 95% confidence interval.
§ Includes other races (i.e., Asians and American Indians/Alaska Natives) not shown separately because of small sample sizes, which affect reliability of estimates.

Figure 1-3 Prevalence of Obesity in Adults by Race/Ethnicity: 2009–2010

Source: Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity in the United States, 2009–2010. NCHS data brief no. 82. Hyattsville, MD: US Department of Health and Human Services, CDC, National Center for Health Statistics. 2012.



NOTE: Obesity is body mass index greater than or equal to the 95th percentile of the sex- and age-specific 2000 CDC growth charts.
SOURCES: CDC/NCHS. National Health and Nutrition Examination Surveys (NHANES) I–III: and NHANES, 1999–2000, 2001–2002, 2003–2004, 2005–2006, 2007–2008, and 2009–2010.

Figure 1-4 Trends in Obesity Among Children and Adolescents Aged 2–19 Years, by Sex: United States, 1971–1974 through 2009–2010

Source: Fryar, CD, Carroll MD, Ogden CL. Prevalence of obesity among children and adolescents: United States, Trends 1963–1965 through 2009–2010.

Treatment (Case 1.1 and 1.2)

There is strong evidence that a weight loss of 10 percent of body weight will result in a reduction in blood pressure, fasting glucose, and lipid levels. This level of weight loss can also reduce an individual's risk of cancer. Treatment is particularly important for obese individuals who have three or more of the following risk factors: cigarette smoking, hypertension, high LDL-C levels, low HDL-C levels, elevated fasting glucose levels, and/or family history of diabetes, coronary heart disease, or cancer, and

age over 45 and 55 years for men and women, respectively.

The USDA has developed My Plate based on the *Dietary Guidelines for Americans* (www.choosemyplate.gov). Nutritional guidelines originally were aimed at preventing malnutrition; recent guidelines have evolved to support overall good nutrition, and to prevent obesity. The MyPlate guidance system is intended to provide a framework for adults and children for determining what and how much to eat each day using the familiar image of a place setting for a meal. The ChooseMyPlate.gov website provides a multitude of well-organized information to help Americans make the best food choices. It also allows for the development of individualized dietary and physical activity plans.

Effective Counseling for Lifestyle and Behavior Change

Lifestyle and behavior changes often require many attempts, large and small, over many years. The first principle of behavior change is to understand the long-term nature of the needed changes, to encourage those who have not met goals or have relapsed, and for healthcare providers to not become discouraged with apparent lack of immediate success.

In making a change, people move through a series of steps: Precontemplation, Contemplation, Preparation, Action, Maintenance, and Relapse (Prochaska Stage of Change Model). This model is often used to clarify for people and their providers their readiness for change. Healthcare providers can provide information and motivational counseling to help patients move from one stage to another. Providers can help patients by considering their behavioral beliefs, such as personal perceived risk of negative outcome from the behavior, normative beliefs (similar behavior by family members and individuals important to them), and efficacy expectations (they believe the change will make a difference and is personally achievable). People often need skills (e.g., label reading and menu planning) to help turn their intention to action. Providers who model or perform a specific behavior are more likely to help patients perform this behavior. Reviewing barriers to a change, the circumstances of previous behavior change and relapse, and motivations to change can also provide useful insights to patients.

Important questions that allow healthcare providers to assess patients' level of change include:

How have you changed your diet or exercise since the last visit?

What problems did you encounter in making these changes?

How confident are you about sustaining these changes you have made?

What additional changes would you like to make in your diet or exercise pattern to improve your health?

How can I help you with these changes?

What one behavior could you change that would result in the most significant change in your health?

What one or two behaviors would you be unlikely to change now?

In conclusion, the value of nutrition assessment in the clinical care of both ambulatory and hospitalized patients cannot be overemphasized. Nutrition assessment during the medical history and physical examination to evaluate growth and development in children and documentation of signs of nutrient excess or deficiencies in children and adults should be routine in clinical care. Development of a realistic treatment plan that includes lifestyle counseling can help patients change their behaviors and lead healthier lives.

Case 1 Obesity and Metabolic Syndrome

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Objectives

Identify methods to diagnose obesity and metabolic syndrome appropriately.

Describe the metabolic and health consequences associated with being overweight or obese.

Assess the patient's risk for metabolic complications associated with excess weight gain given the anthropometric and laboratory data, and usual diet of the patient.

Describe the components of a successful weight management program, including specific nutrition, physical activity, and behavioral recommendations.

Describe the efficacy of medications (over-the-counter and prescription) and surgical approaches to the treatment of obesity.

RS is a 44-year-old African–American woman who works as a management consultant. She presents to her family physician with elevated blood pressure and obesity. She has a history of dieting but has been unable to maintain a healthy weight. This is approximately the

twelfth time in the past 15 years she has tried a weight-loss diet. RS states her weight problems began when she had her first child 18 years ago. Although she understands the medical consequences associated with being overweight, she is primarily motivated to lose weight for cosmetic reasons.

Past Medical History

RS has no past medical history of cardiovascular or gallbladder disease. (She has not had an EKG for the past 5 years). She takes no medications, vitamins, or herbal supplements although she states that she should be taking calcium. When asked about sleep disturbances, she admits to snoring at night, but denies waking up in the middle of the night or falling asleep during daytime activities.

Family History

The family history is positive for overweight and obesity. RS's brother and sister are overweight. Her father and another sister are normal weight. Her mother is obese, hypertensive, and had a myocardial infarction at the age of 67. RS states that her mother does not have diabetes although her blood glucose was elevated in a recent blood test.

Social History

RS does not smoke. She averages two to three 4-ounce glasses of wine per week. She eats three meals per day and admits to nibbling whenever food is available at work or when she is bored. She states she has no time to exercise due to her work and family schedule. RS is currently at her highest adult weight.

Obstetrical History

RS delivered three healthy, full-term children, who are now 18, 13, and 10 years old. She gained 35 to 40 pounds (16 to 18 kg) with each pregnancy and lost about 20 pounds (9 kg) after each birth. RS has never been able to reach her pre-pregnancy weight.

Review of Systems

Skin: No history of rashes or unusual skin pigmentation.

HEENT: No visual complaints.

Neurologic: No headaches, tremors, seizures, or depression.

Endocrine: Normal menstrual cycle; denies abnormal heat or cold intolerances.

Cardiovascular: Normal rate and rhythm; no orthopnea, or dyspnea.

Joints: No swelling, heat, or redness.

Physical Examination

Vital signs

Temperature: 98.4 °F (36.9 °C)

Heart rate: 88 BPM

Blood pressure: 135/88 mm Hg

Height: 5′3″ (160 cm)

Current weight: 208 lb (94.5 kg)

BMI: 36.8 kg/m^2

Waist circumference: 38 inches (96.5 cm)

Weight history: Her highest adult weight is her current weight while her lowest adult weight of 150 lb (68 kg) was before she had children at age 25. Her weight has averaged 175 lb (79.4 kg).

Exam

General: Obese woman in no acute distress; no cushingoid features, negative for hirsutism, no dorsal, cervical, or supraclavicular fat

Skin: No striae, no acanthosis nigricans

HEENT: Unremarkable

Neck: Nonpalpable thyroid

Chest: Clear

Heart: S_1 and S_2 normal rate and rhythm

Abdominal: Obese, no organomegaly

Extremities: No edema

Laboratory Data

Patient's Fasting Values	**Normal Values**
Glucose: 116 mg/dL	70–99 mg/dL
Potassium: 3.8 mEq/L	3.5–5.0 mEq/L
Cholesterol: 216 mg/dL	desirable <200 mg/dL
Triglycerides: 175 mg/dL	desirable <150 mg/dL
HDL-C: 42 mg/dL	desirable for female ≥50 mg/dL
Calculated LDL-C: 139 mg/dL	desirable <130 mg/dL

RS provides vague information on serving sizes particularly when she feels guilty about them. The following represents her usual diet:

Breakfast (home)	
Coffee	8 ounces (240 mL)
Half and half cream	1 ounce (30 mL)
Bagel	1 large

Breakfast (home)	
Cream cheese	2 Tbsp.
Orange juice	8 ounces (240 mL)
Lunch (office)	
Chef salad	2 cups
(Turkey, ham, cheese, boiled egg)	
French dressing	3 Tbsp.
Bread sticks	2 small
Iced tea (presweetened)	12 ounces (360 mL)
Snack (office)	
Pretzels	1.5 ounce bag
Diet soda	12 ounces (360 mL)
Dinner (home)	
Spaghetti	2 cups
Tomato sauce	½ cup
Beef meatballs	3 ounces (85 g)
Garlic bread	1 piece
Red wine	5 ounces (150 mL)
Snack (home)	
Vanilla wafers	10 small

Breakfast (home)	
Lemonade	12 ounces (360 mL)

Total calories: 2691 kcal

Protein: 94 g (14% of calories)

Fat: 90 g (30% of calories)

Saturated fat: 33 g (11% of calories)

Monounsaturated fat: 21 g (7% of calories)

Cholesterol: 334 mg

Carbohydrate: 355 g (53% of calories)

Dietary fiber: 13 g

Sodium: 4800 mg

Calcium: 601 mg

Case Questions

How are overweight and obesity clinically assessed in this patient?

What are the medical risks associated with obesity in this patient?

Does RS meet the criteria to diagnose metabolic syndrome?

What are the appropriate treatment goals for RS?

RS is interested in trying a high-protein, low-carbohydrate diet. Describe the

biochemical and metabolic effects of high protein, low carbohydrate diets.

Is this popular diet appropriate for RS based on her medical history?

What dietary and exercise guidelines would you recommend for RS considering her diagnosis of metabolic syndrome and her current diet?

On a subsequent visit, RS is interested in medication for weight loss. Discuss the current criteria and options for pharmacologic therapy.

Answers to Questions: Case 1

Part 1: Assessment and Diagnosis

1. How are overweight and obesity clinically assessed in this patient?

Body mass index (BMI) is a useful clinical calculation for documenting obesity because it assesses the relative risk of excess weight. BMI is defined as weight/height^2 (kg/m^2) (Figure 1-1). The amount of intra-abdominal adipose tissue, independent of BMI, correlates strongly with increased risk of cardiovascular disease, stroke, dyslipidemia, hypertension, and type 2 diabetes in both men and women. Abdominal obesity can be assessed by measuring patient's waist circumference, in the horizontal plane

around the abdomen at the level of the iliac crest.

RS is clinically assessed as having Class 2 obesity since she has a BMI of 36.8 kg/m^2. In addition, she has excess adipose tissue located in her abdomen, as indicated by her waist circumference of 38 inches (96.5 cm), increasing her risk for heart disease and diabetes.

2. What are the medical risks associated with obesity in this patient?

Obesity increases a person's risk of developing cardiovascular disease, dyslipidemia, hypertension, type 2 diabetes, osteoarthritis, gallstones, respiratory disease, cholecystitis, and certain types of cancer. Obesity also increases patient's risk during surgical procedures because increased subcutaneous fat can make surgery technically more difficult and prolongs the procedure. Post-operative complications are more common in obese patients.

Evidence exists to indicate that RS is experiencing some signs of physical stress related to obesity which include the following:

RS complains of snoring, which combined with obesity, places her at risk for sleep apnea in the future.

Borderline high LDL-C according to the Adult Treatment Panel (ATP III) Guidelines from the National Cholesterol Education Program (NCEP) (Chapter 6).

Elevated fasting glucose level, indicating impaired fasting glucose and suggesting impaired glucose tolerance and insulin resistance, although not frank diabetes. RS is at risk for type 2 diabetes due to the constellation of risk factors: obesity, abdominal fat distribution, sedentary lifestyle, and impaired glucose tolerance.

Elevated blood pressure adding to her risk of disease according to the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) (Chapter 6).

Elevated triglyceride level and a low HDL-C level for a woman.

3. Does RS meet the criteria to diagnose metabolic syndrome?

Recent attention regarding risk for coronary heart disease has focused on a cluster of metabolic abnormalities that arise primarily out of obesity. According to the NCEPATP III Guidelines, patients can be diagnosed with metabolic syndrome if they exhibit any three of the five conditions shown in Table 1-8. (Note differences in low normal ranges for HDL-C

cholesterol for men and women.) RS has all five of the criteria for metabolic syndrome.

Table 1-8 Diagnosing Metabolic Syndrome: 3 or More of the Following 5 Criteria

Source: Adult Treatment Panel (ATP) III Guidelines. NCEP Report.

Abdominal obesity	Waist circumference Men >40 inches Women >35 inches
Pre-hypertension	BP > 130/>85 mm Hg
Glucose intolerance	FBG > 110 mg/dL
High triglycerides	>150 mg/dL
Low HDL-C	Men <40 mg/dL
	Women <50 mg/dL

Part 2: Medical Nutrition Therapy

4. What are the appropriate treatment goals for RS?

The first line of treatment for patients with obesity and the metabolic syndrome is weight reduction and increased physical activity. However, one does not need to lose a lot of weight to be successful.

Weight Reduction Clinical research has demonstrated that obese individuals who achieve and maintain a 10 percent reduction in body weight, regardless of initial BMI, are likely

to lower their blood pressure, serum glucose, and LDL-C and triglyceride levels, thereby reducing their risk of developing diabetes and cardiovascular disease. The Diabetes Prevention Program (DPP), a national study comparing lifestyle changes to medication, found that type 2 diabetes can be prevented or delayed with just a 5 to 7 percent weight loss due to lifestyle changes. For a more complete review of the DPP (see Chapter 8: Case 8.2).

Lifestyle modifications may also prevent the onset of hypertension as well as reduce elevated blood pressure. RS has a blood pressure of 135/88 mm Hg. According to JNC-7, she should begin an aggressive lifestyle modification program to lower her blood pressure to reduce the risk of cardiovascular disease.

A linear association has been demonstrated between excess body weight (BMI > 27 kg/m^2) and severity of hypertension. A mean weight loss of 20 pounds (9.2 kg) is associated with a 6.3 mm Hg reduction in systolic BP and a 3.1 mm Hg reduction in diastolic BP. In addition, weight loss enhances the blood pressure lowering effect of anti-hypertension medications.

The incidence of other health problems associated with obesity, such as sleep apnea and osteoarthritis, also decrease with moderate weight loss. Thus, if RS were to lose 20 pounds (9.2 kg) or about 10 percent of her weight, it is

likely that the clinical abnormalities associated with the metabolic syndrome will improve.

Increased Physical Activity Exercise has been shown to be the single best predictor of long-term weight maintenance and therefore should always be encouraged for weight loss. Patients who participate in regular exercise have lower blood pressure levels as well as a reduced risk of cardiovascular disease and osteoporosis compared to those who do not exercise. The CDC recommend a minimum of 30 minutes a day of physical activity, 5 days a week for adults. The Institute of Medicine (IOM) recommends adults to reach 1 hour a day of exercise, which is consistent with the CDC's recommendations for physical activity for children and teenagers. Current research indicates that this level of physical activity can be accumulated throughout the day. Both observational and interventional studies suggest that even brisk walking 3 hours per week can reduce the risk of cardiovascular disease and type 2 diabetes by at least 30 percent.

An active lifestyle has also been shown to prevent or delay the development of type 2 diabetes, since both moderate and vigorous exercise decrease the risk of impaired glucose tolerance and type 2 diabetes. It is likely that the beneficial effects of exercise on the prevention of cardiovascular disease are

associated with improvements in the metabolic syndrome. In hypertensive patients with hyperinsulinemia, regular exercise has consistently demonstrated a reduction in blood pressure levels. Regular exercise has also been shown to reduce levels of triglyceride-rich very low density lipoprotein (VLDL) particles, and raise HDL-C levels.

5. RS is interested in trying a high-protein, low-carbohydrate diet. Describe the biochemical and metabolic effects of high-protein, low-carbohydrate diets.

High-protein, low-carbohydrate diets remain popular today: the most controversial being those that exclude almost all carbohydrate (<5 percent of total calories). These extremely low-carbohydrate diets, such as the Atkins diet, may consist of greater than 150 grams of protein, 100 grams of total fat (much of which is saturated fat), 500 mg cholesterol, and less than 28 grams of carbohydrate per day during the induction phase of the diet.

These diets cause the body to go into ketosis. Ketosis can be defined as an increased level of ketones in the blood. Ketones are acetoacetic acid and beta-hydroxybutyric acid, which form from the breakdown of free fatty acids. Ketosis also occurs during starvation, but due to lack of calories and protein, significant lean body mass is lost. In the weight-loss diets that try to

promote ketosis, the dietary protein is excessive and therefore, lean body mass seems to be preserved (although research is sparse).

When ketone bodies build up in excessive amounts in the blood (ketonemia), they spill into the urine (ketonuria) and are excreted as sodium or potassium salts, resulting in a net loss of these two minerals. In addition, excess dietary animal protein may also lead to hyperuricemia (increased uric acid in the blood) and hyperuricosuria (increased excretion of uric acid in the urine). This increases the patient's risk of developing gout, uric acid kidney stones, and possibly bone loss. It is therefore critical to drink at least 64 ounces (1920 mL) of water per day on such a high-protein diet, and maintain an adequate electrolyte intake.

The question then is why do people lose weight on high-protein, low-carbohydrate diets? Most experts agree that when patients adhere to any weight-loss program, plan their meals, and focus on what and how much they are eating, they lose weight. In addition, when entire food groups, such as carbohydrates, are avoided, caloric intake is significantly reduced.

The rationale given for this low-carbohydrate, high-protein diet is that high-carbohydrate diets promote insulin resistance and cause obesity, but there is little convincing data for this. Insulin resistance does occur as a result of increased body weight, lack of exercise, or

medical conditions such as type 2 diabetes. Protein also stimulates insulin secretion. Consuming more calories than your body requires from any food source potentially leads to weight gain if not balanced with increased exercise.

6. Is this popular diet appropriate for RS based on her medical history?

Given the cardiovascular concerns and the lack of data from well-controlled studies, a ketogenic weight-loss diet does not seem to be appropriate for RS. If she feels that she is eating too many carbohydrates from starches and simple sugars, suggest she become more aware of serving sizes, eat more vegetables and fruit, and ingest her carbohydrates from predominantly whole grains.

On a ketogenic diet, when carbohydrates are reduced to 28 grams per day, fat and protein intake are significantly increased. Depending on the choice of protein-containing foods, a high saturated fat diet may result. It is well established from epidemiological data and clinical trials that a high saturated fat intake increases serum LDL-C levels and therefore the risk of cardiovascular disease. The current ATP III Therapeutic Lifestyle Changes Diet advocates less than 7 percent of the total calories coming from saturated fat, less than 200 milligrams of cholesterol and up to 20

percent of calories from monounsaturated fat per day (Chapter 6).

In addition, in order to keep carbohydrates low enough so that ketosis occurs, fruits, fruit juices, grains and dairy products are severely limited or avoided. Therefore these diets may be lacking in vitamins (A, B, C, D) and minerals (calcium, magnesium). Patients are advised in these ketogenic diet books to take many vitamin and mineral supplements.

7. What dietary and exercise guidelines would you recommend for RS considering her diagnosis of metabolic syndrome and her current diet?

Considering the fact that RS has tried unsuccessfully to diet twelve times over the past 15 years, it is important to assess what RS feels is her biggest vulnerability and also what lifestyle changes she is willing to incorporate. RS needs to focus on decreasing her total caloric intake and increasing her level of physical activity to lose weight and improve her metabolic syndrome.

Dietary Goals Specifically, RS would benefit from decreasing her consumption of saturated fat, simple carbohydrates, sodium and low-fiber foods intake. The current IOM report recommends 45 to 65 percent of total calories coming from carbohydrates and 20 to 35 percent from fat.

Because of the beneficial effects of increasing monounsaturated fat (MUFA) on triglyceride and HDL-C levels, RS could replace saturated fat with MUFA by using olive oil on her salad instead of French dressing and substituting low-fat cream cheese for the full-fat varieties. Snacking on hummus and raw carrots rather than pretzels, crackers, or cookies should also be suggested. She could also choose carbohydrate-containing, high-fiber foods such as fresh fruits, vegetables, and whole grain breads instead of bagels and pasta. RS needs to be counseled on reducing her serving size of pasta. She can add cooked frozen vegetables to her spaghetti to fill her up at dinner. Water and other non-caloric drinks should be substituted for sugar-sweetened drinks or fruit juice, as these drinks are contributing a significant number of empty calorie carbohydrates to her diet.

As shown in the revised menu, we recommend that RS substitute a small amount of peanut butter, a good source of MUFA and protein, rather than butter or cream cheese at breakfast. We also suggest she skip the cheese and egg yolk on the Chef's salad at lunch. Turkey, boiled ham, and egg whites are good sources of lean, low fat protein. If RS skips the garlic bread with dinner and limits her pasta to one cup cooked, she will be successful in decreasing calories, carbohydrate, saturated fat, and cholesterol. By adding vegetables, RS will improve the

nutritional value of her diet while keeping total calories low. Finally, RS should be advised to take a calcium supplement (500 mg per day) since her calcium intake is far below her daily requirement of 1200 mg per day.

An alternate diet would be the Dietary Approaches to Stop Hypertension (DASH) diet. It is an excellent diet evaluated in a multi-center randomized, controlled trial which assessed the effects of dietary patterns on blood pressure, supports eating plenty of fruits, vegetables, and dairy foods for patients with high blood pressure. This trial enrolled 459 adults with mean base-line blood pressure levels of 131.3/84.7 mm Hg. Subjects were randomized to the control diet rich in fruits and vegetables with an average fat content or a combination diet with low-fat dairy and reduced total and saturated fat. Results showed a 5.5 mm Hg greater decrease in systolic pressure and 3.0 mm Hg greater decrease in diastolic pressure with the intervention diet as compared to the control diet. The average sodium intake was 3000 mg/day. Reduction in blood pressure began within 2 weeks and was maintained for the duration of the study. Further blood pressure reductions were achieved with sodium restriction (see Chapter 6: Case 6.2).

Physical Activity Goals

RS states that she does not have time to exercise due to her work and children's schedule. She currently works as a management consultant and travels several times a month. Therefore, in order to realistically encourage RS to increase her activity, it would be helpful to address these time barriers and to help her identify strategies to achieve increased physical activity. When she is traveling and does not have child care responsibilities, she could walk if she brings her exercise clothes and sneakers. When she is at home, she might be able to take a walk at night after dinner, or she could walk during her lunch break at work. In RS's case, she can benefit from using a pedometer that measures the number of steps taken each day. Metabolic fitness goals could be set at 5000 steps (or 30 minutes) per day, which can be gradually achieved over time. Keeping a record of her exercise may help RS stick with her commitment.

Realistic Weight Goals

The healthcare provider should discuss the appropriate rate of weight loss. A safe rate of weight loss is 1 to 2 pounds or 1 percent of body weight per week. RS's current weight is 208 pounds (94.3 kg), and she is 63 inches (160 cm) tall. If RS is able to adhere to these dietary recommendations and increase her physical

activity, she should be able to reduce her weight by 10 to 20 pounds (4.5 to 9.0 kg) over a period of 6 months. Studies have shown that weight loss slows or stops after about the 24th week of most diets. This “plateau” occurs because the calories consumed and energy expended are now sufficient to maintain, rather than allow for additional weight loss.

After attaining this goal, a new weight goal can be negotiated. Since RS would like to lose more, it is helpful to reiterate how much healthier she will be when she meets her first goal, and the fact that she is very successful if she maintains that weight loss. A potential next goal of 175 pounds (79.4 kg) can be set.

Recommended revised diet for weight loss:

Breakfast (home)	
Coffee	8 ounces (240 mL)
Whole grain bread	1 slice
Peanut butter	1 Tbsp.
Low fat milk (1%)	4 ounces (120 mL)
Banana	1 small
Lunch (office)	
Chef salad (no cheese)	2 cups

Breakfast (home)	
(turkey, ham, egg whites, tomato, raw broccoli)	
Olive oil	2 Tbsp.
Balsamic vinegar	2 Tbsp.
Diet soda or water	12 ounces (360 mL)
Snack (office)	
Hummus	4 Tbsp.
Raw carrots	2 ounces (57 g)
Water	8 ounces (240 mL)
Dinner (home)	
Spaghetti	1 cup
Mixed vegetables	10 ounces (283 g)
Lean beef meatballs	3 ounces (85 g)
Water	8 ounces (240 mL)
Snack (home)	
Fat-free yogurt	8 ounces (240 mL)

Total calories: 1506 kcal

Protein: 78 g (20% of calories)

Fat: 59 g (34% of calories)

Saturated fat: 11 g (7% of calories)

Monounsaturated fat: 29 g (17% of calories)

Carbohydrate: 178 g (46% of calories)

Dietary fiber: 34 g

Sodium: 1934 mg

Calcium: 785 mg

Part 3: Pharmacotherapy Options

8. On a subsequent visit, RS is interested in medication for weight loss. Discuss the current criteria and options for pharmacologic therapy.

Pharmacological interventions to facilitate weight loss include enhancing satiety, decreasing fat absorption, and decreasing appetite. Three medications for weight loss are currently approved by the FDA for long-term use: Xenical (orlistat), Qsymia (topiramate and phentermine) and Belviq (lorcacerin). It is important to note that although most people consider stopping the drug after weight loss has resulted, this generally precipitates a regain of weight. Similarly, it would be inappropriate to stop a cholesterol lowering medication after blood cholesterol has been reduced or to discontinue a hypertension medication because blood pressure has normalized.

However, weight reduction with these medications is modest (7 to 11 pounds or 3 to 5 kg) over a 1-year period. Orlistat can be obtained over-the-counter under the name Alli, in a 60-mg dose. Other over-the-counter weight-loss dietary supplements are available but their safety and efficacy are not assured by clinical trials.

Xenical (orlistat) Orlistat's activity occurs in the small intestine and promotes weight loss by inhibiting gastric and pancreatic lipases, thus partially blocking the hydrolysis of triglycerides. Thirty percent of ingested fat is unabsorbed and excreted in the stool. Patients are required to follow a low-fat diet (≤30 percent) in order to minimize side effects, specifically steatorrhea, associated with fat malabsorption. Orlistat is prescribed at a dose of 120 mg TID with meals containing fat. Because fat-soluble vitamins may also be malabsorbed, a multivitamin should be prescribed once per day to be taken at least two hours before or after the medication. Xenical is contraindicated for pregnant and lactating women and those with chronic malabsorption syndromes and cholestasis. In a 2-year study, patients given Xenical lost more weight, maintained more weight loss and reduced serum cholesterol, LDL-C, and blood pressures compared with those subjects taking a placebo. In a meta-analysis of 15 studies, orlistat reduced weight by 2.9 kg more than placebo.

It is incumbent upon the physician to bring the patient back for a follow-up visit within a month in order to assess the effectiveness of the medication as well as any side effects. One criterion of success for either medication is a 4 pound (1.8 kg) weight loss in the first month. If this has not occurred it is important for the physician and patient to re-evaluate the effectiveness of the medication for improvement in behavior, adherence, etc.

Qsymia (topiramate and phentermine) This is a fixed-dose combination of the sympathomimetic amine phentermine and the antiepileptic drug topiramate. It suppresses appetite and promotes satiety. Phentermine is a sympathomimetic amine and topiramate is an anti-epileptic drug whose mechanism of action in the appetite/satiety chain is unclear. Patients in a randomized controlled study for 1 year lost 5.1% on low dose and 10.9% in high dose as compared to placebo loss of 2.1 percent (LOCF). The drug can cause fetal harm and should not be taken during pregnancy. The drug is contraindicated also in glaucoma, hyperthyroidism, and known sensitivity to sympathomimetic amines. The most commonly observed side effects include paresthesia, dizziness, dysgeusia, insomnia, constipation, and dry mouth. Depression and suicidal thoughts can occur, in which cases the drug should be stopped. Phentermine has known potential for abuse.

Belviq (lorcacerin) This is a selective agonist of the serotonin (5-hydroxytyptamine) 2C (5-HT2c) receptor. Weight loss in a 2-year randomized controlled trial was 5.8 kg for drug vs 2.5 kg for placebo (LOCF). Response to therapy should be evaluated by week 12. If a patient has not lost at least 5 percent of baseline body weight, Belviq should be discontinued. The most common adverse reactions leading to discontinuation were headache, depression and dizziness. Belviq is classified as Schedule IV drug of the Controlled Substances Act, suggesting some abuse potential.

Case 2 Obesity and Bariatric Surgery

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Objectives

Describe the indications for bariatric surgery. Enumerate the commonly used bariatric operations, and provide an overview of the mechanisms by which these surgeries produce weight loss.

Describe the components of a successful surgical weight management program, and review the efficacy of surgical approach to the treatment of obesity and its co-morbidities.

Describe the nutritional and clinical management of bariatric patients after surgery.

CG is a 49-year-old Caucasian woman with a past medical history significant for class III obesity, diabetes mellitus, obstructive sleep apnea (OSA), hypertension, and dyslipidemia who presents to her primary care provider to ask if bariatric surgery could be an option for her. CG feels that her health is deteriorating, and she believes that the current medical treatments are not controlling her health problems. CG was told at a previous visit 3 months ago that insulin therapy needed to be initiated to better manage her diabetes, but she was very reluctant to start it. She also rejoined a low-calorie diet program at the University Weight Management Clinic. In spite of CG's motivation, she was only able to lose 4 pounds during these 3 months, and her blood glucose levels have not improved. She was also given an appetite suppressant, but was forced to stop after 2 weeks due to heart palpitations and an increase in her systolic blood pressure of 8 mmHg.

CG also complains of increased daytime sleepiness and fatigue, worsening shortness of breath, and edema of both lower extremities. She was diagnosed with OSA 8 years ago and was placed on a Continuous Positive Airway Pressure (CPAP) Device. The pressure of her CPAP machine has been gradually titrated up. Two weeks ago she saw her pulmonologist who increased the CPAP pressure to 20 cm H_2O.

Past Medical History and Medications

Obesity; CG has been "heavy" all her life and had enrolled in numerous weight-loss programs with only minor success.

Type 2 diabetes for 17 years. She is treated with sitagliptin and metformin HCl extended-release (Janumet[?]) 50/1000 mg twice a day, glipizide 40 mg/day, and pioglitazone 30 mg/day which was added 6 months ago. Her last A1C, 2 months ago, was 9.3%.

Sleep apnea for 5 years. She is treated with CPAP 20 cm H_2O.

Hypertension for 15 years. She is treated with lisinopril 80 mg/day, labetalol 900 mg twice/day, amlodipine 10 mg once a day, and hydrochlorothiazide 25 mg/day.

Hyperlipidemia for 17 years. She is treated with atorvastatin 80 mg/day.

Gastro-esophageal reflux disease (GERD) diagnosed 14 years ago, treated with omeprazole 40 mg/day.

Severe degenerative joint disease affecting both knees for the past 6 years. She is currently treated with acetaminophen/hydrocodone, with only minimal pain relief.

Laparoscopic cholecystectomy for symptomatic gallstones 10 years ago.

Hepatomegaly and non-alcoholic fatty liver disease (NAFLD) diagnosed 2 years ago.

Family History

CG's family history is positive for overweight and obesity, hypertension, diabetes mellitus, stroke, and coronary artery disease. CG's one brother and mother are both obese; her father and a sister are overweight. Her mother has diabetes and hypertension, and had a myocardial infarction at the age of 69. Her father is hypertensive and had a stroke at the age of 68. Her brother has diabetes type 2.

Social History

CG never smoked. She drinks two glasses of wine on the weekends. She does not use illegal drugs. It was recommended that she follow a diabetic diet, but she feels she is not adhering well. She states she has no time to exercise due to her work schedule and cannot do much

because of the pain in her knees. She works at a loan office; she is happily remarried and has two children from her first marriage.

Diet History

Breakfast: She eats breakfast only 3 to 4 times per week at work, which consists of a breakfast pastry or one large bagel with 2 Tbsp. regular cream cheese; coffee, (24 ounces), with flavored creamer.

Snack: medium apple or banana.

Lunch: On workdays, she eats fast food 2 to 3 times a week (¼ lb hamburger or crispy chicken sandwich, medium French fries, 24 ounces diet soda). She packs her lunch on other workdays and usually brings a frozen dinner.

Snack: Candy bar. At least 1 day a week she will drink a 16 ounces sweetened chai tea latte drink.

Dinner: Home-cooked meals 3 to 4 times/ week, consisting of a 4 to 6 ounces selection of meat, baked or broiled; 1 to 1½ cups of pasta or rice from a box mix; ½ cup vegetables with butter, usually corn or green beans; water for beverage.

Snack: 2 to 3 medium commercial cookies or 1 cup ice cream without toppings.

Bedtime snack: 1½ cup Honeynut Cheerios with 2 percent milk.

No nocturnal eating.

On non-working days CG typically eats two meals. She eats a later breakfast, grazes in the afternoon on cheese and crackers. She usually goes out to dinner one night on the weekend and has two glasses of wine with dinner.

Diet Quality

Estimated resting energy expenditure (REE) using Mifflin–St. Jeor equation for females is 1987 kcal/day. Estimated activity factor for sedentary level of activity is 1.2. Total energy needs for weight maintenance is 2384 kcal/day.

Review of Systems

General: Fatigue.

Skin: Venous stasis dermatitis involving both ankles.

HEENT: No visual complaints; last diabetic eye exam 10 months ago showed mild non-proliferative diabetic retinopathy.

Neurologic: Occasional headaches responding to Tylenol, no tremors, seizures, or depression.

Endocrine: Irregular menstrual cycles, last mensus was 10 months ago, denies abnormal heat or cold intolerances.

Gastrointestinal: Heartburns, normal bowel movements.

Cardiovascular: No palpitations, no orthopnea, no chest pain; the patient had a stress echocardiogram 6 months ago when she presented to ER with chest pain (CP); the test showed no ischemia and a normal left ventricular ejection fraction, and the CP was determined to be due to GERD.

Joints: Pain in both knees; patient had an intrarticular steroid injection in her right knee 2 months ago.

Physical Examination

Vital signs

Temperature: 98.4 °F (36.9 °C)

Heart rate: 80 BPM

Blood pressure: 145/98 mm Hg

Height: 5′8″ (173 cm)

Current weight: 294 lb (134 kg)

BMI: 44.7 kg/m^2

General: Obese woman in no acute distress; Pickwickian body habitus, no Cushingoid features

HEENT: No palpable thyroid; no acanthosis nigricans

Respiratory: Lungs clear to auscultation bilaterally

CV: Distant heart sounds, regular rhythm, no murmur heard

Abdominal: Abdomen soft, normal bowel sounds, difficult deep palpation due to subcutaneous adipose tissue

Extremities: 2+ pitting edema involving both ankles

Skin: Brownish pigmented skin of both ankles

Laboratory Data

Patient's Fasting Values	**Normal Values**
Glucose: 196 mg/dL	70–99 mg/dL
Potassium: 3.8 mEq/L	3.5–5.0 mEq/L
Cholesterol: 216 mg/dL	Desirable <200 mg/dL
Triglycerides: 308 mg/dL	Desirable <150 mg/dL
HDL-C: 42 mg/dL	Desirable ≥50 mg/dL
LDL-C: 112 mg/dL	Desirable <100 mg/dL
Hemoglobin A1C 9.4%	<7.0%
Thyroid-stimulating hormone (TSH): 3.4	0.5–5.0 µU/mL
Free thyroxin (T4): 1.8 ng/dL	0.9–2.4 ng/dL

Patient's Fasting Values	Normal Values
AST (SGOT): 48 IU/L	0–40 IU/L
ALT (SGPT): 69 IU/L	0–55 IU/L

A stress echocardiogram 2 weeks ago shows no left ventricular wall motion abnormalities; left ventricular ejection fraction of 60 percent; right atrial and ventricular enlargement, diagnosed as pulmonary hypertension.

Case Questions

Does CG meet the criteria for bariatric surgery?

What are the commonly performed types of bariatric surgery?

What are the expected benefits and risks of bariatric surgery?

There are several bariatric surgeons in the area where CG lives. She is asking her primary care physician to help her choose "the best." What is the most appropriate advice to give CG?

Describe the pre-surgical nutritional evaluation of CG for bariatric surgery.

Should CG lose weight before bariatric surgery?

What are the nutritional implications following bariatric surgery?

CG undergoes laparoscopic RYGB. No surgical and peri-operative complications occur. Outline the nutritional and medical management of this patient for the first 3 months following the surgery.

CG comes to the Bariatric Center for her 6-month follow-up visit complaining of nausea, shaking, diaphoresis, and diarrhea after eating. What is the most likely cause of these symptoms and how should she be treated?

Outline the long-term nutritional and medical management for patients who undergo bariatric surgery.

Answers to Questions: Case 2

Part 1: Screening and Procedure Options

1. Does CG meet the criteria for bariatric surgery?

The indications for the surgical management of obesity are outlined in the 2013 AHA/ACC/TOS *Guidelines for the Management of Overweight and Obesity in Adults*. Adults with a BMI 40 or 35 kg/m^2 with co-morbid conditions (diabetes, sleep apnea, obesity-related cardiomyopathy, or severe joint disease) may be candidates for

bariatric surgery. In addition, they must have acceptable risk for surgery and have failed previous non-surgical weight loss interventions. It is also very important that potential patients understand the role of bariatric surgery in treating obesity, and display commitment to enduring lifestyle changes and adherence to nutritional recommendations. Contraindications to bariatric surgery include patients with untreated major depression or psychosis, binge eating disorders, ongoing drug and alcohol abuse, severe cardiovascular diseases with prohibitive operative risks, severe coagulopathy, or inability to comply with nutritional requirements, specifically life-long vitamin supplementation. Age alone should not preclude surgical treatment for obesity in adult men and women. Review of the literature shows that bariatric surgery in adolescents (age 12–18) is safe and is associated with significant weight loss, correction of obesity co-morbidities, and improved self-image and socialization. There is emerging data that patients with BMI of 30–34.9 kg/m^2 with diabetes or metabolic syndrome may benefit from bariatric surgery although current evidence is limited by the number of subjects studied and lack of long-term data.

CG has a BMI of 44.7 kg/m^2, which indicates she is a candidate for bariatric surgery. In addition, she has significant co-morbidities:

diabetes mellitus (poorly controlled on oral medication), uncontrolled hypertension, sleep apnea, and debilitating degenerative joint disease. Possible secondary causes for obesity (hypothyroidism and Cushing syndrome) have been excluded by clinical evaluation and blood work. She has diligently undergone multiple lifestyle and pharmaceutical interventions, with modest and transitory success. She has no history or current use of illicit drugs or alcohol dependence, and she appears to have a good family support system. In addition, the psychological evaluation also showed that CG has no signs of depression or eating disorders, and that she is very motivated to proceed with the surgery. Her operative risk assessment indicates she is an acceptable candidate for bariatric surgery.

2. What are the commonly performed types of bariatric surgery?

The types of bariatric surgery are classified based on whether they encompass primarily restrictive or malabsorptive procedures (Table 1-9). The restrictive procedures limit caloric intake by decreasing the stomach's capacity. Currently, the two commonly used restrictive procedures in the United States are the laparoscopic adjustable gastric band (AGB) (as shown in Figure 1-5) and vertical sleeve gastrectomy (VSG) (Figure 1-6). The laparoscopic adjustable gastric band

compartmentalizes the upper stomach by placing a tight, adjustable prosthetic band around the entrance to the stomach. The band consists of a hollow silicone ring, and is placed just a few centimeters below the cardia of the stomach, creating a 15 mL gastric pouch. The band is connected to an infusion port placed in the subcutaneous tissue of the upper abdominal wall. The port may be accessed with relative ease by a syringe and needle, under topical anesthesia. Injection of saline into the port leads to reduction in the band diameter, which results in an increased degree of gastric restriction. VSG is a partial gastrectomy, in which the majority of the greater curvature of the stomach is removed and a tubular stomach is created (Figure 1-6). Although VSG is a restrictive procedure, changes in gastric motility and fewer ghrelin-producing cells (ghrelin is a a gut hormone involved in regulating food intake) left after partial gastrectomy may affect weight loss outcomes.

Table 1-9 Types of Bariatric Procedures

Source: Doina Kulick MD, FACP and Vicki Bovee, MD. 2014. Used with permission.

Restrictive
Laparoscopic adjustable gastric band
Vertical banded gastroplasty
Intragastric balloon

Primary Restrictive with a malabsorptive component Roux-en-Y gastric bypass
Malabsorptive Biliopancreatic diversion with duodenal switch Jejunoileal bypass Biliopancreatic diversion

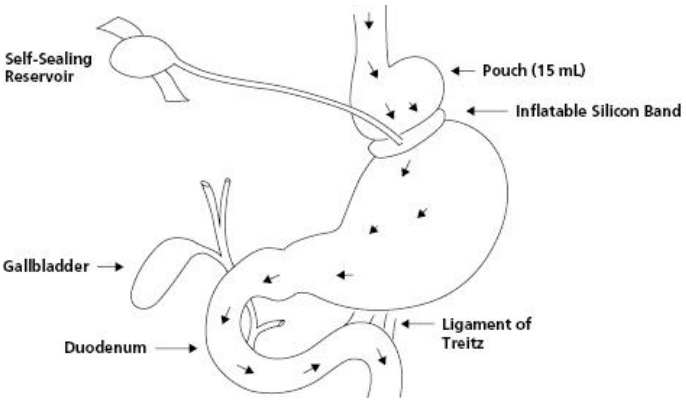

Figure 1-5 Laparoscopic Adjustable Gastric Banding (LAP-BAND). An Inflatable Silicone Band is Placed Around the Gastric Cardia to Achieve a 15-mL Gastric Pouch with an Adjustable Outlet that is Determined by the Volume of Fluid Inserted into the Band Reservoir. The Reservoir is Placed in the Subcutaneous Tissue of the Upper Abdomen, and can be Easily Accessed with a Syringe, Under Local Anesthesia (the Small Arrows Show the Path of the Ingested Food)

Source: Doina Kulick, MD, FACP. 2014. Used with permission.

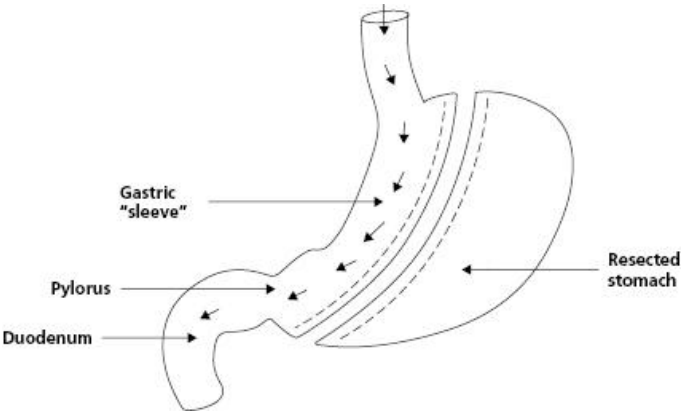

Figure 1-6 Vertical Sleeve Gastrectomy (VSG). The majority of the greater curvature of the stomach is removed and a tubular stomach is created. The tubular stomach has a small capacity, is resistant to stretching due to the absence of the fundus, and has few ghrelin producing cells (a gut hormone involved in regulating food intake).

Source: Doina Kulick, MD, FACP. 2014. Used with permission.

Other procedures have both restrictive and malabsorptive components. Roux-en-Y gastric bypass (RYGB) is a classic example (Figure 1-7): a small (<30 mL) proximal gastric pouch is created by separating it from the stomach remnant; the small intestine is then cut at a distance of 30–50 cm distal to the Ligament of Treitz and the distal limb of the intestine

(jejunum) is connected to the small pouch; the proximal limb (the duodenum and the first 15 to 20 cm of the jejunum) continues the gastric remnant and will be anatomized with the distal limb 50 to 100 cm from the proximal end of the distal limb. Even though RYGB is primarily a restrictive operation in which the small gastric pouch limits food intake, the small bowel reconfiguration produces mild malabsorption, by bypassing the rest of the stomach, the duodenum and first 15 to 20 cm. of the jejunum. There are also neuronal and gut hormonal changes, all of which provide additional mechanisms to facilitating weight loss. RYGB is still the most common bariatric surgery performed in the United States, and is considered the "gold standard".

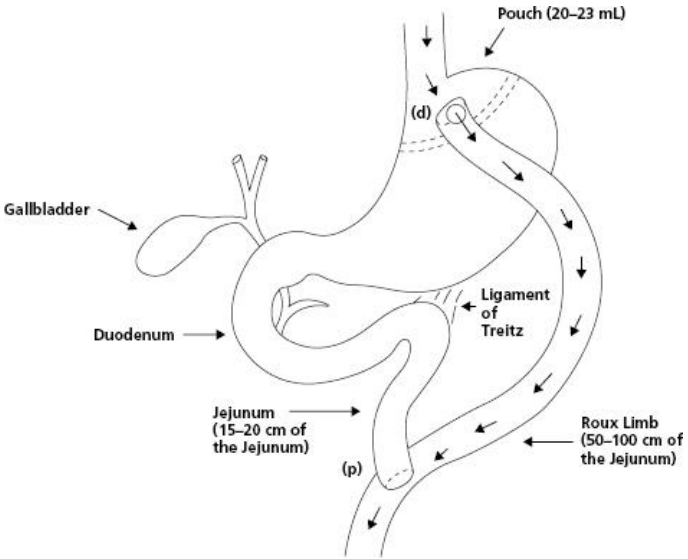

Figure 1-7 Roux-en-Y Gastric Bypass: The Stomach is Stapled Just Beneath the Gastroesophageal Junction. The Small Bowel (jejunum) is Divided Approximately 30 cm Distal to Ligament of Treitz. The Distal Cut End of the Small Bowel (d) is Anastomosed to the Proximal Gastric Pouch. The Proximal Cut End of the Small Bowel (p) is Anastomosed to the Limb 40 cm Distal to the Gastrojejunostomy (the Small Arrows Show the Path of the Ingested Food)

Source: Doina Kulick, MD, FACP. 2014. Used with permission.

The malabsorptive techniques produce primarily a decrease in the efficiency of nutrient absorption by shortening the length of the functional small intestine. Even though these procedures promote significant weight loss, the nutritional and metabolic complications – such as protein-caloric malnutrition and various micronutrient deficiencies – often offset the benefits of weight loss. All the procedures mentioned can be performed by minimally invasive techniques. The laparoscopic approach offers the advantages of decreased post-operative pain, shorter hospital stay, and decreased rates of wound infection and hernia formation. Currently there are no guidelines for choosing the most appropriate type of surgical procedure for the patient. The choice is based on clinical judgment, patient and surgeon preferences, patient's surgical risk, and

reimbursement issues. After discussing it with her physician, nutrition specialist, and the bariatric surgeon, CG chooses to undergo RYGB (Table 1-9).

3. What are the expected benefits and risks of bariatric surgery?

Bariatric surgery is not a cure for obesity, but it is the most effective modality currently available for weight management, and was proven in prospective studies to reduce morbidity and mortality in obese patients. Data reported from the Swedish Obese Subjects (SOS) study, a large prospective observational study of more than 2000 patients who underwent bariatric surgery, showed that mortality hazard ratio (HR) at 10 years was 0.71 following bariatric surgery compared with matched obese controls. After a 20-year follow-up, the same cohort demonstrated that HR for cardiovascular death (including stroke and myocardial infarction) among surgical subjects compared with obese controls was only 0.47. In another cohort of patients who underwent RYGP, all-cause mortality was reduced by 40 percent 7 years after surgery, compared with the control group, and cause-specific mortality in the surgery group decreased by 56 percent for coronary artery disease, by 92 percent for type 2 diabetes mellitus, and by 60 percent for cancer.

When comparing the three most common bariatric procedures for percentage of excess weight loss, RYBG performs the best, the ABG the least, and VSG has intermediate outcomes. For example, a study found that at 1-year follow-up, the percentage of excess weight loss was 70 percent for the RYGP, 49 percent for VSG, and, and 38 percent AGB groups.

In general, after RYGB, patients lose an average of ½ to 1 lb (0.22–0.45 kg) per day for the first 3 months, ¼ to ½ pound (0.11–0.22 kg) daily from 3 to 9 months, and ¼ pound (0.11 kg) daily thereafter for up to 12 to 18 months.

You could inform CG that she could expect to lose approximately 90 to 100 pounds (or one-third of her pre-operative weight) within 12 to 18 months after undergoing the RYGB procedure. This weight loss would bring her body weight to 196 pounds (BMI < 30 kg/m^2), which is a change in classification from class III obesity to overweight. Her diabetes mellitus, hyperlipidemia, hypertension, and OSA would likely also improve following bariatric surgery.

Bariatric surgery is the best long-term treatment for severe obesity; however, it carries risks of complication and potential mortality. Despite the known complications of bariatric surgery, overall mortality has improved significantly over the past two decades. The overall 30-day mortality for bariatric surgical procedures is <1 percent. The most common

causes of early mortality are pulmonary emboli and complications related to surgical leaks.

4. There are several bariatric surgeons in the area where CG lives. She is asking her primary care physician to help her choose "the best." What is the most appropriate advice to give CG?

A successful long-term outcome of bariatric surgery is dependent on the patient's understanding of the role of bariatric surgery in weight management and their commitment to a lifetime of dietary and lifestyle changes. Bariatric surgery is only a point in the continuum of care for obesity and the patient will need adequate support. Thus CG should be advised to seek a bariatric surgeon who operates as part of an experienced and knowledgeable multidisciplinary team of healthcare providers. This team will provide the pre-operative and post-operative education and health care. Usually the team consists of the following health professionals:

Obesity specialist An internist, endocrinologist, or a physician nutrition specialist who has a special interest and training in obesity. This physician, in close collaboration with the other health professional team members, coordinates the peri-operative care in order to optimize patient's co-morbidities and reduce the surgical risk. The physician adjusts medical treatments in

accordance with the rapidly changing metabolic status following surgery (especially for the procedures containing a malabsorptive component). This physician may also follow-up with patients annually, often in close collaboration with patients' primary care physicians.

Bariatric Surgeon A bariatric surgeon is a surgeon with special training in bariatric surgery, who has substantial experience with the procedure, but also with the pre- and post-operative management of severely obese patients. Bariatric surgery is considered one of the most challenging procedures performed by general surgeons. Recent studies evaluating outcomes after bariatric surgical procedures found that the surgeon's experience inversely correlated with the incidence of post-operative complications. The more experience they had, the lower the post-operative complications.

Registered Dietitian A required member of the bariatric team. As mentioned, bariatric surgery does not cure obesity, but significantly facilitates a patient's adherence to long-lasting dietary changes. Thus the decision to operate must include an assessment of patients' dietary habits, and their ability to comply with the post-operative dietary regimen. A dietitian performs a pre-op dietary assessment and provides instructions to help patients initiate dietary changes consistent with surgery. In

anticipation of surgery, the dietitian helps patients prepare their kitchens with the needed appliances (e.g., food processor, blender, and standardized measuring cups and spoons) and appropriate foods for a transition diet upon discharge from the hospital. The dietitian also provides counseling for patients as they advance their diet during the early (3 months) post-operative period, and periodically thereafter, especially when patients have difficulties in meeting nutritional goals.

Psychologist Psychological testing is a recommended part of the pre-operative assessment. Almost half of the patients referred for bariatric surgery may present with one of the following diagnoses: somatization, social phobia, obsessive–compulsive disorder, substance abuse/dependence, binge-eating disorder, night eating syndrome, post-traumatic stress disorder, generalized anxiety disorder, and depression. The psychologist may use various psychological tests and tools (the Beck Depression Inventory or the Minnesota Multiphasic Personality Inventory, the Boston Interview for gastric bypass, or the structured clinical interview with the Weight and Lifestyle Inventory from the University of Pennsylvania) to reveal potential problems, and help patients adopt the lifestyle behavior changes needed for a successful long-term surgical outcome.

Primary care physician (PCP) The PCP needs to become an active member of the team in the peri-operative stage, and most importantly facilitate long-term care of patients who undergo bariatric surgery. Often it is the PCP who will see patients annually for their post-op evaluation, review laboratory data, and will refer patients to the obesity specialist and dietitian whenever appropriate follow-up is indicated.

Part 2: Pre-Surgery Nutrition Assessment

5. Describe the pre-surgical nutritional evaluation of CG for bariatric surgery.

CG was evaluated and approved for surgery and her operative risk was assessed as being moderate. A comprehensive nutritional evaluation of CG shows the following: CG has been "heavy" all her life, and is now at the highest weight of her adult life. Her lowest adult body weight was 150 pounds at the age of 20, just before she got married (when she underwent a 16-week low-calorie diet program). She has gained weight progressively since that time during her pregnancies and family/social stressor events. CG has enrolled in numerous commercial and medically supervised weight loss programs (more than a dozen times over last 34 years) with only minor and transitory success.

CG's food history reveals that because of her work schedule, she frequently eats out, most often at fast food restaurants. To improve adherence to dietary recommendations after surgery, it is critical to have an understanding of meal patterns, eating habits, and typical foods consumed. With this information, plus an estimation of nutrient intake, the dietitian can work with the patient to develop pre-operative goals that will set a foundation for her post-operative eating plan.

CG's diet is deficient in dairy foods, vegetables, and fruits. She appears to consume adequate protein and grains; however, she eats sweets in excess. She has roughly two glasses of wine per week and her other drinks are usually calorie free. She has chai tea latte once a week. CG does not drink sufficient amounts of water. She takes a daily vitamin/mineral supplement. She is not participating in any intentional physical activity at this time due to knee pain. In addition to the lack of physical activity, she states that her biggest challenges in managing her weight are her sweet tooth, eating when bored, and not enough time for meal planning and preparation may negatively impact her long-term success.

However, CG's high intake of high-fat foods and sweets, grazing and meal skipping pattern, emotional eating, and time or schedule constraints for meal planning and preparation may negatively affect her long-term success.

The dietitian's recommendation is that CG is a candidate for gastric surgery but adherence to post-operative dietary changes may be difficult. Together, CG and the dietitian have developed a pre-operative nutrition plan until a surgery date has been scheduled when further guidelines will be provided. Immediate goals are:

Reduce intake of high-fat foods.

Use of meal replacement shake for breakfast.

Pack lunch or choose lower fat, fast food options at lunch.

Reduce intake of sweets.

Afternoon snack of fresh fruit or protein-based food.

Replace evening snack with a meal replacement shake.

Take prescribed dietary supplements as directed per dietary assessment and nutrient screening blood testing.

6. Should CG lose weight before the surgery?

Regarding the recommendation for pre-operative weight loss, the obesity specialist and the bariatric surgeon both agree that CG would benefit from preoperative weight loss. Preoperative weight loss can reduce liver volume and may help improve the technical aspects of bariatric surgery in patients with an enlarged liver or fatty liver disease, as is the

case with our patient. The patient had recently undergone a low-calorie diet program plus pharmacotherapy with unsatisfactory weight loss. It is possible that the recently added medication to her diabetic treatment, pioglitazone (which is known to produce water retention), could have tempered her weight loss. Two to four weeks of a very low calorie diet (VLCD; 800 calories) would be a reasonable pre-op weight loss treatment for CG.

The physician nutrition specialist prescribed a liquid meal replacement diet consisting of 800 calories per day. Attention was given to the macronutrient composition, and she was provided with an adequate amount of daily proteins and essential fatty acids. She was also recommended to take a daily multivitamin and two tablets of fiber supplements. The pioglitazone and glipizide were discontinued at the beginning of the VLCD. She remained on sitagliptin/ metformin, and supplemental short-acting insulin was added as need (prn). She was instructed to monitor her blood glucose three times a day. On this regimen, CG lost 23 pounds by the end of the fourth week.

Part 3: Post-Surgical Assessment and Medical Nutrition Therapy

7. What are the nutritional implications following bariatric surgery?

The nutritional goals following bariatric surgery are to produce a significant caloric deficit, while maintaining an adequate intake of essential macronutrients and micronutrients. Usually the more significant the component of malabsorption, the greater the success of weight loss; however, nutritional deficiencies follow the same trend.

Proteins are absorbed mainly in the jejunum and mid ileum, sites commonly bypassed by many bariatric procedures that have a malabsorptive component. Nonetheless, restrictive procedures could also lead to protein malnutrition due to significantly reduced food intake. The clinical signs of protein malnutrition are edema, alopecia, and low serum albumin level (<3.5 g/dL). Testing patient's serum albumin concentration is an effective and convenient method to monitor protein status. The incidence of protein malnutrition in purely restrictive procedures is very low (<2 percent), and has been found in 13 percent of patients after RYGB.

Iron deficiency is a common nutritional problem following RYGB surgery. Decreased ability to convert the dietary Fe^{3+} into the more absorbable Fe^{2+} form (due to low gastric acid production) and the bypassing of the duodenum and proximal jejunum (main sites of iron absorption) are the mechanisms leading to iron deficiency. Up to 50 percent of patients

who have undergone RYGB have iron deficiency 4 years post-op, and it is two times more common in females compared to males. The prevalence of iron deficiency is even higher in jejuno–ileal bypass and duodenal switch. Measurement of serum ferritin is the single best diagnostic test for iron deficiency and is the first test to show abnormal results. Occurrence of microcytic anemia is usually a late finding and denotes severe iron deficiency.

Calcium and Vitamin D deficiencies are also commonly encountered after bariatric surgery. Calcium absorbs primarily in the duodenum and proximal jejunum, and absorption is facilitated by the presence of gastric acid secretion and vitamin D. Calcium status can be monitored by total serum calcium concentration, but calcium levels may be artificially low in the setting of hypoalbuminemia. Vitamin D is primarily absorbed in the jejunum and ileum. Being liposoluble, the absorption of vitamin D requires adequate mixing and action of pancreatic and biliary secretions. Even before surgery, up to 25 percent of obese patients have subclinical calcium deficiency (elevated PTH, with normal calcium), and 50 percent are vitamin D deficient. After surgery, the procedures with a malabsorptive component result in significantly more calcium and vitamin D deficiency compared to the restrictive procedures. The best marker for vitamin D

deficiency is serum 25-hydroxy vitamin D. Low vitamin D and calcium levels trigger secondary hyperparathyroidism, which can be assessed by measuring PTH, which will be increased. All these nutritional and metabolic changes accelerate bone loss after bariatric surgery.

Vitamin B_{12} and Folic Acid Vitamin B_{12} is almost entirely absorbed in the terminal ileum in the presence of the intrinsic factor which is secreted from the antrum of the stomach. Adequate gastric and pancreatic enzyme secretion and mixing are also required to release vitamin B_{12} from food and then from binding protein, so that vitamin B_{12} is available to bind to intrinsic factor for absorption in the ileum. The human body stores substantial amounts of vitamin B_{12} (about 2000 μg), but at 3 years post-op, approximately one-third of patients who have had a gastric bypass present with vitamin B_{12} deficiency.

Folic acid deficiency is less common, because it is absorbed throughout the small intestine and deficiency is largely due to severely reduced dietary intake. Purely restrictive procedures are generally not associated with vitamin B_{12} or folic acid deficiencies. Serum levels of vitamin B_{12} and folic acid are used to monitor nutritional status of these vitamins. The use of methylmalonic acid to detect vitamin B_{12} deficiency is not routinely recommended.

Thiamin is absorbed primarily in the duodenum, mostly in the more acidic environment of its proximal portion. The pathogenesis of thiamin deficiency is believed to be due to decrease in acid production (resulting from a decreased gastric capacity) and restriction of food intake, in the context of profuse and protracted vomiting. Symptomatic thiamin deficiency in bariatric patients is rare, but can occur even in the case of a restrictive procedure. The clinical presentation of thiamin deficiency most often consists of Wernicke's encephalopathy: altered mental status, ataxic gait, double vision, nystagmus, and acute polyneuropathy with paralysis. Clinical recognition of this syndrome may be lifesaving, since the symptoms respond very well to prompt intravenous administration of thiamin. Deficiency of thiamin can be confirmed by measuring serum thiamin levels, or the erythrocyte thiamine transketolase (ETKA) (which is the most reliable method, but not often used in practice).

Other Vitamins and Minerals Low serum levels of vitamin A, K, and E have been documented after bariatric surgery, but clinical manifestation of such deficiencies has not yet been described. No clinical complications due to lack of vitamin C, magnesium, and selenium have been reported. Cases of zinc deficiency were found to occur following malabsorptive procedures, and usually manifest as alopecia. It

is important to emphasize to patients that nutritional deficiencies following bariatric surgery can be avoided or corrected by routine monitoring, adequate nutrition, and long-term supplementation.

8. CG undergoes laparoscopic RYGB. No surgical and peri-operative complications occur. Outline the nutritional and medical management of this patient for the first 3 months following the surgery.

After surgery, CG was advised to follow a full-liquid diet for the first week while at home. She was instructed to keep the volume small, no more than ¼ cup per meal, and to try to eat five to six times per day. Week two post-operatively, CG was instructed to begin adding pureed foods with an emphasis on including higher protein foods. Meal volume remained small and she was advised to slowly increase the volume of food. She was advised to begin adding semi-solid/soft foods into her diet as tolerated, usually about 14 to 21 days after surgery, and reminded to chew each small bite thoroughly. Foods not well tolerated during the first few months after surgery are red meat, chicken and turkey, white flour products, foods high in sugar and fat, and most raw fruits and vegetables.

The guidelines for continued weight loss were reviewed: keep portions small, no beverages

while eating and 30 minutes after eating, a minimum intake of 60 grams protein per day, eat at scheduled times and avoid grazing, and include physical activity most days of the week. At her 3-month post-operative visit, she was eating approximately ½ to 1 cup of food per meal, averaging 50 to 60 g of protein every day and 48 ounces of water. She had not yet tried to eat red meat or raw vegetables. She stated that even though she was not hungry, she still felt the desire to eat more food than she could tolerate.

9. CG comes to the Bariatric Center for her 6-month follow-up visit complaining of nausea, shaking, diaphoresis, and diarrhea after eating. What is the most likely cause of these symptoms and how should she be treated?

The symptoms described at this visit are suggestive of dumping syndrome. Dumping syndrome occurs initially in 70 to 76 percent of patients with RYGB. The clinical manifestations of dumping include GI and vasomotor symptoms. Dumping syndrome can be divided into early and late phases depending on the relation of symptoms to the time elapsed from meal intake. Symptoms of early dumping occur within 10 to 30 minutes after eating. They result from accelerated gastric emptying of hyperosmolar content into the small bowel, followed by fluid shifts from the intravascular

compartment into the intestinal lumen. These events are believed to be responsible for GI symptoms such as nausea, bloating, abdominal cramps, and explosive diarrhea. The majority of patients have early dumping. Late dumping occurs 1 to 3 hours after eating, and it is characterized predominantly by systemic vascular symptoms including flushing, dizziness, palpitations, and lightheadedness. Physical examination of these patients may reveal profound orthostatic changes. Late dumping occurs in approximately one-quarter of patients with dumping syndrome. Late dumping is considered to be the consequence of hypoglycemia from an exaggerated release of insulin.

An important element of the history that needs to be obtained from any patient presenting with these symptoms is a detailed food history, with particular attention to the intake of foods with a high content of sugar and/or fat. Our patient admitted that she had been snacking on her favorite cookies for the past month. Dumping syndrome usually responds to dietary interventions: reduction of carbohydrate intake, with preference for complex, rather than simple carbohydrates, avoidance of liquids for at least 30 minutes after a solid meal, and small portion size. In very rare cases, drug therapy may be required (octreotide). CG responded well to dietary interventions.

10. Outline the long-term nutritional and medical management of patients who have undergone bariatric surgery.

For her long-term diet, CG should continue to spend at least 20 to 30 minutes at each meal, taking her time to eat. She should slowly sip her fluids between meals (8 ounces of fluids over 30–40 minutes), but not during her meals or 30 minutes after eating. Food and liquids should continue to be low in fat and sugar. She was advised to eat at least 60 g of protein daily. Protein intake after bariatric surgery should be individualized, and guided by the dietician considering gender, age, and weight; a minimal protein intake of 60 g/d and up to 1.5 g/kg ideal body weight per day is considered adequate; higher amounts of protein intake up to 2.0 g/kg ideal body weight per day may be recommended on an individualized basis. Protein-rich foods include lean meat, low-fat milk and dairy products, beans, peas, lentils, eggs, and protein supplements if needed. Vitamins and minerals should be taken regularly.

During the first year following bariatric surgery CG was seen at 1, 3, 6, and 12-months. She should be monitored on an annual basis by an obesity specialist or her primary care physician. Visits with a dietitian or behavioral therapist should be recommended whenever patients have difficulty maintaining their dietary goals

or regain weight. One year after her surgery CG lost 101 lb, which was what was initially predicted. Her BMI is 27.8 kg/m^2. Her annual visits focus on building long-term healthy dietary behavior, continuing physical activity, and monitoring and correcting potential nutritional deficiencies.

Routine blood tests for her annual post-operative visits include a CBC, chemistry panel including liver enzymes, lipid panel, A1C, ferritin, iron, TIBC, TIBC saturation, vitamin B_{12}, 25(OH) vitamin D, and intact PTH. A DEXA scan and other lab tests may be indicated. Our patient, who was perimenopausal before surgery, has not had a period for the last 16 months, and is considered post-menopausal. This status, along with rapid weight loss, increases her risk of osteoporosis, and most clinicians would agree that she should have a DEXA scan.

Evaluation of her co-morbidities and adjustment of medical management should be done as part of the continuum of care. Her medications were drastically reduced: she is taking Metformin, 1000 mg once daily, and her A1C is 6.9 percent. She no longer requires hydrochlothiazide or labetalol to control her blood pressure, and her amlodipine was reduced to 5 mg once daily. She only needs half of the pre-operative dose of atorvastatin to keep her lipid panel at the ideal level. Her CPAP

machine was adjusted to 10 cm H_2O, which represents a significant improvement from the pre-operative status; she no longer has lower extremity edema or shortness of breath. She has been able to discontinue her GERD medication without return of symptoms, and her liver enzymes have normalized. She hopes that by losing more weight, she will be able to discontinue using her CPAP device. CG should remain for the rest of her life on the following daily nutritional supplements:

Two multivitamins/minerals tablets each containing iron, folic acid, and thiamin.

Vitamin B_{12} at a dosage of 500 μg to 1000 μg daily sublingual (or orally, if determined to be adequately absorbed to maintain B_{12} levels in the normal ranged). Sometime subcutaneous, or intramuscular route may be needed.

Calcium citrate 1200 to 1500 mg/day (depending on dietary calcium intake).

Vitamin D_3, 2000 to 3000 IU/day; (titrated to therapeutic 25- hydroxyvitamin D levels >30 ng/ml).

Iron 45 to 60 mg ferrous sulfate.

Thiamin supplementation should be included as part of routine multivitamin with mineral preparation. In bariatric patients at risk for thiamin deficiency (patients with rapid weight loss or protracted vomiting) supplementation with oral or intravenous thiamin, 100 mg/daily

should be given until risk factors subsided. Patients with thiamin deficiency (suspected or established) should be treated with intravenous thiamin, 500 mg/day, for 3 to 5 days, followed by 250 mg/day for 3 to 5 days or until resolution of symptoms; then to consider treatment with 100 mg/day, orally, usually indefinitely or until risk factors have resolved.

Folic acid supplementation (400 mg/day) should be part of a routine mineral-containing bariatric multivitamin preparation.

Routine supplementation with zinc, selenium, and copper in addition to the amount found in the bariatric multivitamins–minerals preparation is not recommended.

It is important to mention that many of these recommendations are based mainly on expert opinion, and more clinical studies in this area are needed.

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2
Vitamins, Minerals, and Dietary Supplements

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Objectives*

Know the major roles played by the various vitamins and the pathological consequences of deficiency or toxic excess.

Be aware of the physiological functions of the major minerals and their role in disease processes.

Understand how laboratory measurements can be used for the diagnosis of pathologies involving vitamins or minerals.

Appreciate the various circumstances that might warrant the use of vitamin or mineral supplements

*Source: Objectives for chapter and cases adapted from the *NIH Nutrition Curriculum Guide for Training Physicians*. (www.nhlbi.nih.gov/funding/training/naa)

The Need for Vitamins

Vitamins are organic chemical substances required for normal growth, development, and metabolism throughout all stages of life. Although humans mostly rely on exogenous sources of vitamins and minerals, certain intestinal microorganisms produce vitamin K and biotin, while vitamin D and niacin are synthesized from their chemical precursors, cholesterol and tryptophan, respectively.

As the importance of adequate vitamin balance for health and disease prevention has been increasingly discussed in the lay press, the annual expenditure for over-the-counter dietary supplements in the United States has grown to over $16 billion. Often these press articles highlight the findings of recently published research without contextualizing the information, misleading consumers into thinking that a new “magic bullet” for disease prevention has been discovered. Therefore, it is

essential for clinicians to assume a role in patient education regarding supplements while simultaneously emphasizing the importance of a varied diet as the best source of most vitamins and minerals.

It is also important to look for those individuals who may have increased vitamin and mineral requirements or inadequate intake. These include, but are not limited to, pregnant and lactating women; growing children; the elderly; those who have suffered severe trauma such as burns, fractures, or major surgery; those who have or are at high risk for infections, such as HIV and malabsorption syndromes; excess consumers of alcohol, cigarettes, or illicit substance abusers; and those taking medications that may interfere with the absorption and/or metabolism of nutrients.

While vitamins are discussed here individually, including their deficiency symptoms and clinical uses, it should be noted that isolated vitamin deficiencies are rare, as are scientifically proven benefits of supplementation. Symptoms described for primary vitamin deficiencies (e.g., pellagra or beriberi) are unlikely to be seen in clinical practice in developed countries (except in rare cases of extreme nutritional depletion), but mild relative deficiencies of individual or multiple vitamins may be more common than we suspect. This is because many of the

vitamins work synergistically together making clinical efficacy for individual supplements difficult to establish. For example, folic acid, B_6, and B_{12} have been used together to lower homocysteine levels (with unclear benefits to cardiovascular disease). Riboflavin is involved in pyridoxine, niacin, folate, and vitamin K metabolism. Vitamins C, E, and selenium have been tested as an antioxidant "cocktail" but have not reduced cancer incidence or recurrence. In spite of numerous negative clinical trials, patients continue to optimistically consume supplements in efforts to treat or prevent disease. Many patients feel better taking vitamins, and attempts to convince them of their lack of utility are unlikely to be worth the effort. Even lacking clinical trial data, it is impossible to prove that a specific supplement is not effective in a particular individual. Given our current inability to determine individual vitamin requirements, more specific advice regarding helpful vitamin or mineral supplementation for specific patients awaits the development of individualized medicine (which will continue during the practice lifetime of the student readers of this text).

Vitamin Intake Standards

Vitamin and mineral requirements change throughout the stages of life. The Food and

Nutrition Board of the National Research Council established a Recommended Daily Allowance (RDA) for most nutrients based on a review of published scientific data. A considerable body of knowledge exists for certain vitamins and minerals, and RDAs for various gender and age categories have been established. The RDA levels are set at two standard deviations above the mean requirement to cover the needs of practically all healthy persons.

It is important to note two caveats with regard to these recommendations. The first is that suggested levels were established for groups of healthy people. Thus, the requirements of any specific individual or for those with special nutritional needs due to medical conditions are not addressed. Second, the RDAs were developed with prevention of classic nutrient deficiencies in mind, rather than health enhancement or optimization of well-being. Active areas of research include developing vitamin requirements for patients with acute or chronic disease and determining the potential for supplements to improve health.

To address the changing needs for information, the Institute of Medicine of the National Academy of Sciences established the first Dietary Reference Intakes (DRIs) in 1997. The new DRIs move beyond the traditional RDAs to focus on the prevention of chronic disease. See

Tables 2-1, 2-2, and 2-3. Dietary Reference Intake is a collective term that refers to three nutrient-based dietary reference values for every stage of life and both genders in addition to the conventional RDA: Estimated Average Requirement (EAR), Adequate Intake (AI), and the Tolerable Upper Intake Level (TUL).

Table 2-1 Dietary Reference Intakes (DRIs): Recommended Intakes for Individuals, Vitamins (Food and Nutrition Board, Institute of Medicine, National Academies)

Life Stage Group	Vitamin A (μg/d)[a]	Vitamin C (mg/d)	Vitamin D (μg/d)[b,c]	Vitamin E (mg/d)[d]	Vitamin K (μg/d)	Thiamin (mg/d)	Riboflavin (mg/d)	Niacin (mg/d)[e]	Vitamin B_6 (mg/d)	Folate (μg/d)[f]	Vitamin B_{12} (μg/d)	Pantothenic Acid (mg/d)	Biotin (μg/d)	Choline[g] (mg/d)
Infants														
0–6 mo	400*	40*	5*	4*	2.0*	0.2*	0.3*	2*	0.1*	65*	0.4*	1.7*	5*	125*
7–12 mo	500*	50*	5*	5*	2.5*	0.3*	0.4*	4*	0.3*	80*	0.5*	1.8*	6*	150*
Children														
1–3 y	300	15	5*	6	30*	0.5	0.5	6	0.5	150	0.9	2*	8*	200*
4–8 y	400	25	5*	7	55*	0.6	0.6	8	0.6	200	1.2	3*	12*	250*
Males														
9–13 y	600	45	5*	11	60*	0.9	0.9	12	1.0	300	1.8	4*	20*	375*
14–18 y	900	75	5*	15	75*	1.2	1.3	16	1.3	400	2.4	5*	25*	550*
19–30 y	900	90	5*	15	120*	1.2	1.3	16	1.3	400	2.4	5*	30*	550*
31–50 y	900	90	5*	15	120*	1.2	1.3	16	1.3	400	2.4	5*	30*	550*
51–70 y	900	90	10*	15	120*	1.2	1.3	16	1.7	400	2.4[h]	5*	30*	550*
>70 y	900	90	15*	15	120*	1.2	1.3	16	1.7	400	2.4[h]	5*	30*	550*
Females														
9–13 y	600	45	5*	11	60*	0.9	0.9	12	1.0	300	1.8	4*	20*	375*
14–18 y	700	65	5*	15	75*	1.0	1.0	14	1.2	400[i]	2.4	5*	25*	400*
19–30 y	700	75	5*	15	90*	1.1	1.1	14	1.3	400[i]	2.4	5*	30*	425*
31–50 y	700	75	5*	15	90*	1.1	1.1	14	1.3	400[i]	2.4	5*	30*	425*
51–70 y	700	75	10*	15	90*	1.1	1.1	14	1.5	400	2.4[h]	5*	30*	425*
>70 y	700	75	15*	15	90*	1.1	1.1	14	1.5	400	2.4[h]	5*	30*	425*

Life Stage Group	Vitamin A (μg/d)[a]	Vitamin C (mg/d)	Vitamin D (μg/d)[b,c]	Vitamin E (mg/d)[d]	Vitamin K (μg/d)	Thiamin (mg/d)	Riboflavin (mg/d)	Niacin (mg/d)[e]	Vitamin B_6 (mg/d)	Folate (μg/d)[f]	Vitamin B_{12} (μg/d)	Pantothenic Acid (mg/d)	Biotin (μg/d)	Choline[g] (mg/d)
Pregnancy														
≤18 y	750	80	5*	15	75*	1.4	1.4	18	1.9	600[j]	2.6	6*	30*	450*
19–30 y	770	85	5*	15	90*	1.4	1.4	18	1.9	600[j]	2.6	6*	30*	450*
31–50 y	770	85	5*	15	90*	1.4	1.4	18	1.9	600[j]	2.6	6*	30*	450*
Lactation														
≤18 y	1200	115	5*	19	75*	1.4	1.6	17	2.0	500	2.8	7*	35*	550*
19–30 y	1300	120	5*	19	90*	1.4	1.6	17	2.0	500	2.8	7*	35*	550*
31–50 y	1300	120	5*	19	90*	1.4	1.6	17	2.0	500	2.8	7*	35*	550*

Note: This table (taken from the DRI reports, see www.nap.edu) presents Recommended Dietary Allowances (RDAs) in bold type and Adequate Intakes (AIs) in ordinary type followed by an asterisk (*). RDAs and AIs may both be used as goals for individual intake. RDAs are set to meet the needs of almost all (97 to 98 percent) individuals in a group. For healthy breastfed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover needs of all individuals in the group, but lack of data or uncertainty in the data prevent being able to specify with confidence the percentage of individuals covered by this intake.

[a] As retinol activity equivalents (RAEs). 1 RAE = 1 μg retinol, 12 μg β-carotene, 24 μg α-carotene, or 24 μg β-cryptoxanthin. The RAE for dietary provitamin A carotenoids is two-fold greater than retinol equivalents (RE), whereas the RAE for preformed vitamin A is the same as RE.

[b] As cholecalciferol. 1 μg cholecalciferol = 40 IU vitamin D.

[c] In the absence of adequate exposure to sunlight.

[d] As α-tocopherol. α-Tocopherol includes RRR-α-tocopherol, the only form of α-tocopherol that occurs naturally in foods, and the 2R-stereoisomeric forms of α-tocopherol (RRR-, RSR-, RRS-, and RSS-α-tocopherol) that occur in fortified foods and supplements. It does not include the 2S-stereoisomeric forms of α-tocopherol (SRR-, SSR-, SRS-, and SSS-α-tocopherol), also found in fortified foods and supplements.

[e] As niacin equivalents (NE). 1 mg of niacin = 60 mg of tryptophan; 0–6 months = preformed niacin (not NE).

[f] As dietary folate equivalents (DFE). 1 DFE = 1 μg food folate = 0.6 μg of folic acid from fortified food or as a supplement consumed with food = 0.5 μg of a supplement taken on an empty stomach.

[g] Although AIs have been set for choline, there are few data to assess whether a dietary supply of choline is needed at all stages of the life cycle, and it may be that the choline requirement can be met by endogenous synthesis at some of these stages.

[h] Because 10 to 30 percent of older people may malabsorb food-bound B_{12}, it is advisable for those older than 50 years to meet their RDA mainly by consuming foods fortified with B_{12} or a supplement containing B_{12}.

[i] In view of evidence linking folate intake with neural tube defects in the fetus, it is recommended that all women capable of becoming pregnant consume 400 μg from supplements or fortified foods in addition to intake of food folate from a varied diet.

[j] It is assumed that women will continue consuming 400 μg from supplements or fortified food until their pregnancy is confirmed and they enter prenatal care, which ordinarily occurs after the end of the periconceptional period—the critical time for formation of the neural tube.

Table 2-2 Dietary Reference Intakes (DRIs): Recommended Intakes for Individuals,

Elements (Food and Nutrition Board, Institute of Medicine, National Academies)

Life Stage Group	Calcium (mg/d)	Chromium (µg/d)	Copper (µg/d)	Fluoride (mg/d)	Iodine (µg/d)	Iron (mg/d)	Magnesium (mg/d)	Manganese (mg/d)	Molybdenum (µg/d)	Phosphorus (mg/d)	Selenium (µg/d)	Zinc (mg/d)
Infants												
0–6 mo	210*	0.2*	200*	0.01*	110*	0.27*	80*	0.003*	2*	100*	15*	2*
7–12 mo	270*	5.5*	220*	0.5*	130*	11*	75*	0.6*	3*	275*	20*	3
Children												
1–3 y	500*	11*	340	0.7*	90	7	80	1.2*	17	460	20	3
4–8 y	800*	15*	440	1*	90	10	130	1.5*	22	500	30	5
Males												
9–13 y	1300*	25*	700	2*	120	8	240	1.9*	34	1,250	40	8
14–18 y	1300*	35*	890	3*	150	11	410	2.2*	43	1,250	55	11
19–30 y	1000*	35*	900	4*	150	8	400	2.3*	45	700	55	11
31–50 y	1000*	35*	900	4*	150	8	420	2.3*	45	700	55	11
51–70 y	1200*	30*	900	4*	150	8	420	2.3*	45	700	55	11
>70 y	1200*	30*	900	4*	150	8	420	2.3*	45	700	55	11
Females												
9–13 y	1300*	21*	700	2*	120	8	240	1.6*	34	1,250	40	8
14–18 y	1300*	24*	890	3*	150	15	360	1.6*	43	1,250	55	9
19–30 y	1000*	25*	900	3*	150	18	310	1.8*	45	700	55	8
31–50 y	1000*	25*	900	3*	150	18	320	1.8*	45	700	55	8
51–70 y	1200*	20*	900	3*	150	8	320	1.8*	45	700	55	8
>70 y	1200*	20*	900	3*	150	8	320	1.8*	45	700	55	8
Pregnancy												
≤18 y	1300*	29*	1000	3*	220	27	400	2.0*	50	1,250	60	13
19–30 y	1000*	30*	1000	3*	220	27	350	2.0*	50	700	60	11
31–50 y	1,000*	30*	1000	3*	220	27	360	2.0*	50	700	60	11
Lactation												
≤18 y	1300*	44*	1300	3*	290	10	360	2.6*	50	1,250	70	14
19–30 y	1000*	45*	1300	3*	290	9	310	2.6*	50	700	70	12
31–50 y	1000*	45*	1300	3*	290	9	320	2.6*	50	700	70	12

Note: This table presents Recommended Dietary Allowances (RDAs) in **bold type** and Adequate Intakes (AIs) in ordinary type followed by an asterisk (*). RDAs and AIs may both be used as goals for individual intake. RDAs are set to meet the needs of almost all (97 to 98 percent) individuals in a group. For healthy breastfed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover needs of all individuals in the group, but lack of data or uncertainty in the data prevent being able to specify with confidence the percentage of individuals covered by this intake.
Source: *Dietary Reference Intakes for Calcium, Phosphorous, Magnesium, Vitamin D, and Fluoride* (1997); *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B_6, Folate, Vitamin B_{12}, Pantothenic Acid, Biotin, and Choline* (1998); *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids* (2000); and *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc* (2001). These reports may be accessed via www.nap.edu.

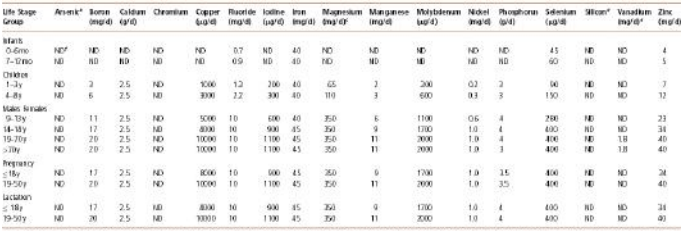
Table 2-3 Dietary Reference Intakes (DRIs): Tolerable Upper Intake Levels (TUL [a]), Vitamins (Food and Nutrition Board, Institute of Medicine, National Academies)

Life Stage Group	Vitamin A (µg/d) [b]	Vitamin C (mg/d)	Vitamin D (µg/d)	Vitamin E (mg/d)[c]	Vitamin K	Thiamin	Riboflavin	Niacin (mg/d)[d]	Vitamin B_6 (mg/d)	Folate (µg/d)[e]	Vitamin B_{12}	Pantothenic Acid	Biotin	Choline (g/d)	Carotenoids[f]
Infants															
0–6 mo	600	ND[g]	25	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
7–12 mo	600	ND	25	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Children															
1–3 y	600	400	50	200	ND	ND	ND	10	30	300	ND	ND	ND	1.0	ND
4–8 y	900	650	50	300	ND	ND	ND	15	40	400	ND	ND	ND	1.0	ND
Males/Females															
9–13 y	1700	1200	50	600	ND	ND	ND	20	60	600	ND	ND	ND	2.0	ND
14–18 y	2800	1800	50	800	ND	ND	ND	30	80	800	ND	ND	ND	3.0	ND
19–70 y	3000	2000	50	1000	ND	ND	ND	35	100	1000	ND	ND	ND	3.5	ND
>70 y	3000	2000	50	1000	ND	ND	ND	35	100	1000	ND	ND	ND	3.5	ND
Pregnancy															
≤18 y	2800	1800	50	800	ND	ND	ND	30	80	800	ND	ND	ND	3.0	ND
19–50 y	3000	2000	50	1000	ND	ND	ND	35	100	1000	ND	ND	ND	3.5	ND
Lactation															
≤18 y	2800	1800	50	800	ND	ND	ND	30	80	800	ND	ND	ND	3.0	ND
19–50 y	3000	2000	50	1000	ND	ND	ND	35	100	1000	ND	ND	ND	3.5	ND

[a]TUL = The maximum level of daily nutrient intake that is likely to pose no risk of adverse effects. Unless otherwise specified the TUL represents total intake from food, water and supplements. Due to lack of suitable data TULs could not be established for vitamin K, thiamin, riboflavin, vitamin B_{12}, pantothenic acid, biotin, or carotenoids. In the absence of ULs extra caution may be warranted. In consuming levels above recommended intakes.
[b]As preformed vitamin A only.
[c]As α-tocopherol; applies to any form of supplemental α-tocopherol.
[d]The ULs for vitamin E, niacin, and folate apply to synthetic forms obtained from supplements, fortified foods, or a combination of the two.
[e]β-Carotene supplements are advised only to serve as a provitamin A source for individuals at risk of vitamin A deficiency.
[f]ND = Not determinable due to lack of data of adverse effects in this age group and concern with regard to lack of ability to handle excess amounts. Source of intake should be from food only to prevent high levels of intake.

Table 2-3 (*continued*) Dietary Reference Intakes (DRIs): Tolerable Upper Intake Levels (TUL

a), Elements (Food and Nutrition Board, Institute of Medicine, National Academies)



Life Stage Group	Arsenic[a]	Boron (mg/d)	Calcium (g/d)	Chromium	Copper (µg/d)	Fluoride (mg/d)	Iodine (µg/d)	Iron (mg/d)	Magnesium (mg/d)[b]	Manganese (mg/d)	Molybdenum (µg/d)	Nickel (mg/d)	Phosphorus (g/d)	Selenium (µg/d)	Silicon[c]	Vanadium (mg/d)[d]	Zinc (mg/d)
Infants																	
0-6mo	ND[e]	ND	ND	ND	ND	0.7	ND	40	ND	ND	ND	ND	ND	45	ND	ND	4
7-12mo	ND	ND	ND	ND	ND	0.9	ND	40	ND	ND	ND	ND	ND	60	ND	ND	5
Children																	
1-3y	ND	3	2.5	ND	1000	1.2	200	40	65	2	300	0.2	3	90	ND	ND	7
4-8y	ND	6	2.5	ND	3000	2.2	300	40	110	3	600	0.3	3	150	ND	ND	12
Males, females																	
9-13y	ND	11	2.5	ND	5000	10	600	40	350	6	1100	0.6	4	280	ND	ND	23
14-18y	ND	17	2.5	ND	8000	10	900	45	350	9	1700	1.0	4	400	ND	ND	34
19-70y	ND	20	2.5	ND	10000	10	1100	45	350	11	2000	1.0	4	400	ND	1.8	40
>70y	ND	20	2.5	ND	10000	10	1100	45	350	11	2000	1.0	3	400	ND	1.8	40
Pregnancy																	
≤18y	ND	17	2.5	ND	8000	10	900	45	350	9	1700	1.0	3.5	400	ND	ND	34
19-50y	ND	20	2.5	ND	10000	10	1100	45	350	11	2000	1.0	3.5	400	ND	ND	40
Lactation																	
≤18y	ND	17	2.5	ND	8000	10	900	45	350	9	1700	1.0	4	400	ND	ND	34
19-50y	ND	20	2.5	ND	10000	10	1100	45	350	11	2000	1.0	4	400	ND	ND	40

[a]UL = The maximum level of daily nutrient intake that is likely to pose no risk of adverse effects. Unless otherwise specified the UL represents total intake from food water and supplements. Due to lack of suitable data ULs could not be established for arsenic chromium and silicon. In the absence of ULs extra caution may be warranted in consuming levels above recommended intakes.
[b]Although the UL was not determined for arsenic there is no justification for adding arsenic to food or supplements.
[c]The UL for magnesium represents intake from a pharmacological agent only and do not include intake from food and water.
[d]Although silicon has not been shown to cause adverse effects in humans there is no justification for adding silicon to supplements.
[e]Although vanadium in food has not been shown to cause adverse effects in humans there is no justification for adding vanadium to food and vanadium supplements should be used with caution. The UL is based on adverse effects in laboratory animals and this data could be used to set a UL for adults but not children and adolescents.
ND = Not determinable due to lack of data of adverse effects in the age group and concern with regard to lack of ability to handle excess amounts. Source of intake should be from food only to prevent high levels of intake.
Sources: *Dietary Reference Intakes for Calcium Phosphorous Magnesium Vitamin D and Fluoride* (1997); *Dietary Reference Intakes for Thiamin Riboflavin Niacin Vitamin B_6 Folate Vitamin B_{12} Pantothenic Acid Biotin and Choline* (1998); *Dietary Reference Intakes for Vitamin C Vitamin E Selenium and Carotenoids* (2000); and *Dietary Reference Intakes for Vitamin A Vitamin K Arsenic Boron Chromium Copper Iodine Iron Manganese Molybdenum Nickel Silicon Vanadium and Zinc* (2001). These reports may be accessed via www.nap.edu.

Estimated Average Requirement (EAR)

The EAR is the most useful DRI for assessing the nutrient intake of a population. This is the daily intake expected to meet the requirement of 50 percent of individuals in a particular life-stage and gender category. Individuals are advised to take in the EAR plus two standard deviations (the RDA) to ensure that their intake is adequate. An individual whose mean intake is below the EAR is, on average, getting insufficient amounts of that nutrient.

Adequate Intake (AI)

The AI is an approximation of the average nutrient intake by a population or subgroup that seems to be healthy and not at increased risk of a particular chronic disease. The AI is a rough equivalent of the RDA, but is based upon

estimation where adequate data for determining an EAR are unavailable.

Tolerable Upper Intake Level (TUL)

The TUL is the level of daily nutrient intake that is unlikely to pose risks of adverse health effects to almost all (97 to 98 percent) individuals in a specified life-stage and gender group. These levels, taken together, allow one to estimate a range of safe levels for supplementation.

The Vitamins

Vitamin A

Vitamin A is a group of fat-soluble compounds that includes retinoic acid, retinol, and carotenoids. Retinol, also known as pre-formed vitamin A, is the most active form and is found mostly in foods of animal origin. Beta-carotene, also known as provitamin A, is the most common of the plant carotenoids, and is converted in the body to retinol.

Forms and Absorption Following ingestion of beta-carotene (or other carotenoids), the body enzymatically cleaves some of these compounds to retinol, which is esterified in the intestinal cell to retinyl esters that, along with the remaining carotenoids, are incorporated into chylomicrons in the enterocytes for transport into the lymphatics and eventually the blood. Dietary retinyl esters follow a similar

path and are likewise incorporated into chylomicrons, eventually delivering the retinyl esters and carotenoid pigments to the liver for storage. When a particular part of the body, such as the eyes, requires vitamin A, the liver releases the retinol, bound to retinol binding protein (RBP).

Function Vitamin A plays an essential regulatory role:

in the development or maintenance of the mucus membranes, cornea, and conjunctiva in the eye,

in a process known as phototransduction; all-*trans* retinal is linked to a protein to form rhodopsin in the rod cells and iodopsin in the cone cells of the retina; these cells are required for night vision and the perception of color in bright light,

in the normal integrity and growth of skin and tissue cells, including the mucus membranes of the mouth, intestinal, respiratory, genitals, and urinary tracts,

in the production of keratin, a component of skin and epithelia,

in the form of all-*trans* retinoic acid, which assists in the functioning of testicles and ovaries and aids in the development of the embryo,

as an antioxidant (many carotenoids function as antioxidants).

Retinol Equivalents Vitamin A is ingested either as pre-formed vitamin A (retinol or retinyl ester), or a beta-carotene that can be split into retinol in the intestine. Beta-carotene is the most abundant carotenoid present in green, yellow, and orange fruits and vegetables. Due to inefficient conversion, 12 μg of beta-carotene in food yields only about 1 μg retinol, and therefore a serving of food that contains 12 μg of beta-carotene is said to contain 1 μg RAE (retinol activity equivalent; older literature uses a similar concept with the abbreviation RE, for retinol equivalent). Because other carotenoids are even less efficiently converted to retinol, 1 μg RAE equates to 24 μg of these other carotenoid species.

International units (IU) are also used to express the amount of vitamin A in supplements and occasionally in foods; 100 IU of retinol in supplements translates to 30 μg RAE, while 100 IU of beta-carotene equates to 5 μg RAE.

Deficiency Vitamin A deficiency is one of the most common forms of malnutrition worldwide, with infants and young children most affected. Primary deficiency is due to inadequate intake of vitamin A and its precursors, whereas secondary deficiency occurs from poor absorption of fat-soluble vitamins, which may occur in patients with cystic fibrosis, Crohn's disease, tropical sprue,

or liver disease, or in those with excessive alcohol intake.

Clinical problems associated with vitamin A deficiency include perifollicular hyperkeratosis, night blindness, xerophthalmia (which can progress from conjunctival thickening to corneal ulceration and eventual irreversible blindness), and impairment of both humoral and cell-mediated immunity; this latter effect is known to increase mortality from certain infectious diseases, such as measles, in developing countries.

Toxicity Chronic excesses in vitamin A intake of 30 mg/day (100,000 IU/day) or acute doses of 150 mg (500,000 IU) can cause a variety of symptoms ranging from bone and skin changes and liver abnormalities (hepatomegaly) to headache, nausea, vertigo, blurred vision, and lack of muscle coordination. Recently, attention has been directed at elucidating whether chronic vitamin A intake only modestly higher than recommended levels might have adverse effects on bone health and the risk of osteoporosis. Research results have been mixed and complicated by inadequate measures of vitamin A status. However, vitamin A intake tends to be adequate or more than adequate in the United States, and supplementation with preformed vitamin A resulting in total intake which exceeds the RDA should be discouraged. A recent case of hypervitaminosis A which

resulted in liver damage, was caused by ingesting a combination of a nutrition shake as a meal replacement and multivitamins over an extended period of time.

Consuming too much vitamin A, especially retinoic acid, during the first trimester of pregnancy can cause birth defects to the developing embryo. Therefore, women who are using vitamin A for the treatment of acne, or for other purposes, require reliable forms of birth control.

Because only limited amounts of carotenoids are converted to vitamin A, excessive intake of beta-carotene has not been shown to produce toxic effects. People who consume large doses of beta-carotene, either through dietary sources or supplements, may develop a yellow tinge to the skin. This carotenosis, commonly seen in babies whose caretakers give them squash and sweet potatoes as their predominant early solid food, has no harmful effects. While many in vivo and in vitro studies have supported a link between vitamin A and the treatment of epithelial cancers, intervention trials have been disappointing.

Supplement Issues Certain forms of vitamin A, specifically the all-*trans* form of retinoic acid, have proven useful for the treatment of dermatological disease such as acne and psoriasis, presumably because of their effects on gene expression and cell differentiation.

Retinoic acid has also been found to be effective in the treatment of acute promyelocytic leukemia; however, studies attempting to establish a role for retinoic acid in the treatment of other cancers have generally been disappointing. Retinol supplementation has been shown to decrease the risk of melanoma in women but there was no reduction in those with a higher dietary intake of retinol or those taking carotenoid supplements. High serum levels of vitamin A have been linked to a lower incidence of non-Hodgkins lymphoma and vitamin A supplements have been shown to decrease the risk of cervical cancer in women. While higher serum levels of carotenoids have been associated with a lower risk of coronary heart disease (CHD), randomized trials of beta-carotene have shown no benefit for the prevention of acute myocardial infarction (AMI). Long-term use of a multivitamin supplement, however, has been linked to a decrease in the rate of heart attacks in women with no history of previous cardiovascular disease.

Vitamin A plays an important role in the health of children. Children with sickle cell disease (SC) have been shown to have lower serum vitamin A levels but supplementation with the recommended daily amount did not improve the vitamin A status. This suggests supplementation at larger than recommended amount may be needed to correct blood levels

for those with SC. Vitamin A is commonly prescribed to nursing mothers who might be deficient to improve the health of the baby and reduce morbidity and sickness in parts of the developing world. Vitamin A supplementation has been shown to result in a decrease in hearing loss in children at risk for poor nutrition. Pre-term birth caused by bacterial vaginosis was reduced with vitamin A supplementation. Lung function was improved for children from an undernourished population when the mother had taken a vitamin A supplement during pregnancy.

Vitamin A Food Sources See Appendix A.

Vitamin D

Vitamin D is a fat-soluble vitamin, naturally occurring in two forms: vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol). Vitamin D_2 is a plant or yeast steroid commonly used to fortify milk, while vitamin D_3 is from animal sources or produced in the skin upon exposure to adequate amounts of sunlight. Recent literature reviews indicate that these two forms may not be equivalent; one study concluded that vitamin D_2 potency is less than one-third that of vitamin D_3. Over the past few years there has been an explosion of research on the importance of vitamin D and the health effects of marginal levels. This has led to a marked increase in healthcare providers

measuring and correcting serum vitamin D levels in their patients.

Forms and Absorption Since vitamin D is fat-soluble, some fat is required in the diet for its absorption, and fat malabsorption conditions adversely affect vitamin D absorption. Once absorbed it is transported to the liver as a component of chylomicrons or bound to vitamin D binding protein (DBP), where it undergoes hydroxylation to 25-hydroxy vitamin D [25(OH)D or calcidiol]. Further conversion to its physiologically active form, 1,25-dihydroxy-vitamin D [$1,25(OH)_2D$ or calcitriol], takes place in the kidneys or in target tissues. The synthesis and metabolism of vitamin D are closely coupled to calcium homeostasis; therefore, when calcium levels in the blood are low, the body releases parathyroid hormone (PTH), which stimulates the kidney to convert 25(OH)D to $1,25(OH)_2D$. Elevations in $1,25(OH)_2D$ stimulate the gastrointestinal tract to increase calcium absorption from about 10 to 30 percent and phosphorous absorption from about 60 to 80 percent. Serum 25(OH)D is the best indicator of vitamin D status. It reflects vitamin D produced cutaneously and that obtained from food and supplements, and has a half-life of 15 days.

Units The most common unit reported for vitamin D is International Units (IU). Vitamin

D may also be listed in micrograms (μg). Use the following conversion: 1 μg = 40 IU.

Functions Vitamin D plays an essential regulatory role in:

intestinal absorption of calcium and phosphorus,

regulation of calcium and phosphorous deposition in the bones, teeth, and cartilage in children and adults,

maintenance of blood calcium and phosphorus levels,

a variety of physiological functions, including immunity, neuromuscular functions, blood pressure regulation, insulin production, reduction of inflammation, and apoptosis.

Deficiency Vitamin D deficiency can be due to impaired availability of vitamin D (inadequate dietary intake or fat malabsorptive disorders, coupled with a lack of sun exposure) or impaired metabolism (in the liver, kidney, or end organs). Serum levels less than 20 ng/mL are indicative of low serum vitamin D. Groups with increased risk for low vitamin D levels are breastfed infants, older adults, obese individuals (BMI > 30 kg/m^2), people with dark skin, and those with limited sun exposure. Five to 30 minutes of sun exposure between 10 a.m. and 3 p.m. at least twice a week without sunscreen has been suggested to provide sufficient vitamin D synthesis in temperate

zones. Studies in healthy college and medical students in Boston have documented deficient serum levels at the end of winter. Strict vegetarians and those who have a milk allergy or lactose intolerance, are also at risk. Older adults and seniors are at increased risk for vitamin D deficiency, especially those who are bed-ridden or who live in nursing homes and so may not have adequate exposure to sunlight coupled with inadequate dietary intake. Reduced levels of vitamin D in the second trimester have been shown to increase the risk of pre-clampsia in pregnant women and have been found in women with breast cancer.

Vitamin D deficiency results in rickets in infants and children and osteomalacia (softening of the bones) in adults. Rickets causes retarded growth, swelling and tenderness at the ends of the bones, and malformation of the joints. Rickets in infants also leads to a delay in the closure of the skull bones, possibly leading to a larger skull ("frontal bossing"), as well as bowed legs, pigeon breast, and beaded ribs ("rachitic rosary") seen in older children. Osteomalacia may lead to pain in the legs, ribs, hips, and muscles, and easily breakable bones. Osteomalacia may occur when long-term anticonvulsant medications such as phenobarbital or phenytoin are taken because they increase the liver's breakdown of vitamin D. Individuals with chronic kidney disease often

develop osteodystrophy, secondary to the kidney's inability to convert vitamin D to its active form and hyperparathyroidism aggravated by the lack of activated vitamin D.

Toxicity Chronically elevated doses of vitamin D may lead to kidney stones, nausea, headaches, weakness, anorexia, frequent urination, weight loss, irregular heartbeat, and weak bones and muscles. Excess levels may also lead to an elevation in serum calcium, which can cause calcification of soft tissues such as organs and blood vessels, possibly resulting in irreversible damage. In infants and children, too much vitamin D can lead to retarded growth, rounding of the skull, mental retardation, and death. However, excessive levels of vitamin D are believed to occur only through the use of supplements rather than from food or too much sun exposure. The tolerable upper limit for vitamin D has been established at 50 µg/day (2000 IU/day) but recently, vitamin D researchers have questioned whether this level is set too low.

Supplement Issues Vitamin D supplements are available in two forms: D_2 and D_3. Vitamin D_3 has been shown to be more effective at raising and maintaining serum 25(OH)D levels. A meta-analysis of randomized controlled trials indicated that vitamin D_3 supplementation led to a decreased risk of all-cause mortality with a relative risk of 0.93. The mean daily dose was

528 IU (with a range of 300 to 2000 IU). Although the mechanism for this is unclear, studies have suggested that the risk for certain cancers (notably colorectal and breast) may be significantly reduced in individuals with higher than normal serum levels of vitamin D, corresponding to intakes of 1000 to 4000 IU/day. Studies with supplement dosages at the current RDA levels (400 IU/day) showed no benefit, but arguments have been made that the RDA is too low and that the upper limit of 2000 IU/day is too restrictive and could be raised by a factor of five. Compounding the problem is that the vitamin D content of most foods is quite low, and even 8 ounces of milk provides only 100 IU. Five to 30 minutes of sun exposure several times a week yields blood levels of vitamin D much higher than is achievable orally, and is argued to represent the "natural" level for this vitamin. The level of 25(OH)D has been shown to be affected by the types of fat in the diet when vitamin D is taken as a supplement: those high in monounsaturated fats resulted in higher levels than those high in polyunsaturated fats. In 2011, the Food and Drug Administration (FDA) warned consumers to stop taking a vitamin D supplement called Soladek, due to several reported cases of vitamin D toxicity.

Studies of the effect of vitamin D on fractures showed no benefit at the standard dosage of 400 IU/day, but recent meta-analyses of

studies using higher vitamin D dosages (800 IU/day or greater), when accompanied by significant calcium supplementation, show significant reductions in hip fractures (18 percent to 24 percent). (See Chapter 4 for current vitamin D recommendations for infants and children.)

Inadequate levels of vitamin D have been associated with a number of prevalent health conditions. Vitamin D has been shown to accelerate the resolution of the inflammatory response in those receiving treatment for tuberculosis. Vitamin D supplements were also shown to decrease the incidence of metabolic syndrome in young adults. Lower levels of vitamin D have been observed in older women with heart disease, hypertension, and those who develop Alzheimer's disease compared to women of the same age without the disease. Reduced levels of vitamin D also were observed in menopausal women with depression. A recent study that requires confirmation has demonstrated reductions in blood pressure and measures of depression among women with type 2 diabetes.

Vitamin D Food Sources See Appendix B.

Vitamin E

Vitamin E is another fat-soluble vitamin group consisting of alcohol compounds called tocopherols and tocotrienols. Each of these

exist in alpha, beta, gamma, and delta forms for a total of eight compounds with vitamin E activity. Each of the eight compounds have two racemic forms "*d*" and "*l*," so supplements are labeled "*d*-alpha" or "*l*-alpha." Of the various tocopherols, alpha-tocopherol has the highest biological activity and only the *d*-isomer is physiologically effective.

Forms and Absorption Vitamin E is absorbed passively in the ileum, requiring the presence of bile salts and dietary fat, as with all of the fat-soluble vitamins. Once absorbed, vitamin E is incorporated into chylomicrons for delivery to the liver and other tissues.

Functions Vitamin E plays an essential regulatory role in:

antioxidant activity; protection of polyunsaturated fatty acids within cell membranes from peroxidation,

inhibition of cell proliferation, platelet aggregation, and monocyte adhesion,

assisting in the maintenance of fertility.

Alpha-tocopherol has also been shown to inhibit protein kinase C, thereby promoting differentiation of smooth muscle cells and potentially reducing the damage to endothelial cells caused by blood-cell components adhering to them.

Deficiency Vitamin E deficiency is rare, except in people who cannot absorb fat, for example patients with cystic fibrosis or pancreatic insufficiency. Clinical signs include neurologic dysfunction, loss of deep tendon reflexes, and diminished vibratory or position sense. A conditional deficiency may be created in premature infants treated with oxygen who may develop retrolental fibroplasias, leading to visual impairment and possibly blindness. This may be prevented by vitamin E supplements. The National Health and Nutrition Examination Survey (NHANES) studies have documented that most Americans seem to take in less than the RDA of vitamin E but this may be inaccurate because of failure to adequately account for added fats and oils.

Toxicity Vitamin E is considered non-toxic except at very high doses. Reports indicate that very large doses of vitamin E can interfere with the vitamin K formation of functional clotting factors, resulting in hemorrhage. For this reason, large doses of vitamin E should be avoided 2 weeks before and after surgery as well as when taking anticoagulation medications, such as Coumadin. It has also been reported that premature infants may be especially sensitive to excess vitamin E, with overdose resulting in hemorrhage and sepsis. The TUL for vitamin E has been established at 1000 mg/ day. Excess levels of vitamin E taken by

pregnant women has been linked to an increase in children with congenital heart defects.

Relationship to Disease Prevention Vitamin E is considered to be nature's most effective lipid-soluble antioxidant, protecting cell membranes from oxidative damage. Promising in vitro and case-control studies led to vitamin E supplements becoming very popular to prevent heart disease, but more recent large clinical trials have failed to demonstrate any benefit from vitamin E in reducing the risk of heart attacks or deaths from heart disease. Despite previous reports, recent studies have shown that vitamin E supplementation has no effect on macrovascular outcomes or mortality in diabetic patients who smoke. Daily supplementation with vitamin E has been reported to increase the risk of prostate cancer in men. With disappointing results from alpha-tocopherol studies, research interest (and speculative supplementation), has shifted to gamma-tocopherol, but no large-scale studies on its efficacy are available. The theory is that alpha-tocopherol supplements may be counter-productive because they cause lower serum levels of gamma-tocopherol.

Vitamin E Food Sources See Appendix C.

Vitamin K

Vitamin K is a fat-soluble vitamin that is obtained from dietary sources and is produced by intestinal bacteria. Phylloquinone is the predominant form of vitamin K from dietary sources while menaquinone is produced by gut micro-flora. The difference between the two forms has to do with the side chain off of the napthoquinone rings.

Forms and Absorption Absorption of vitamin K occurs primarily in the proximal small bowel and requires bile salts. Following intestinal absorption, vitamin K is transported by chylomicrons for storage mostly in the liver.

Function Vitamin K is a required cofactor for enzymes involved in the post-translational carboxylation of glutamate moieties in proteins involved in clotting and bone mineralization. Vitamin K allows the formation of calcium-binding gamma-carboxyglutamate (gla) that binds calcium and is required for the activity of factors VII, IX, X, and prothrombin as well as osteocalcin and gla matrix protein. Additionally, anticoagulant proteins S and C require vitamin K for their activity.

Deficiency Deficiency of vitamin K in otherwise healthy individuals is rare, but may occur in people with fat malabsorption or those on prolonged antibiotic therapy, due to the disruption of the intestinal microbiota that

produce vitamin K. Symptoms of vitamin K deficiency include signs of impaired coagulation such as easy bruisability, mucosal bleeding, melena, and hematuria.

A recent observational study suggested that a low plasma level of vitamin K might be associated with a higher prevalence of osteoarthritis of the hands and knees. Also, a meta-analysis of randomized controlled trials suggested that vitamin K supplementation reduced bone loss, with a positive effect on fractures.

Infants are given a vitamin K injection at birth to prevent hemorrhagic disease. Infants' intestinal tracts lack the necessary bacteria to synthesize vitamin K adequately until approximately 1 week after birth and the newborn liver is therefore unable to produce adequate levels of coagulation factors.

Toxicity Toxicity to phylloquinone or menaquinone is virtually unknown, although allergic reactions to mega doses of vitamin K have been reported. Severe jaundice may occur in infants treated with doses of menadione. There is no tolerable upper level for vitamin K. Patients taking warfarin (Coumadin) as an anticoagulant are cautioned to avoid marked changes in their intake of vitamin K-rich foods or supplements since the dose of Coumadin is titrated to maintain a narrow range of

anticoagulation, which may be reversed by increased intake of vitamin K.

Vitamin K and Disease Prevention Studies of elderly patients with osteoporosis have demonstrated greater rates of vitamin K insufficiency, but long-term clinical trials with vitamin K supplements have produced mixed results regarding potential benefits in preventing osteoporosis. There may be differences in obtained results based on the source of vitamin K (dietary vs endogenous). Recent work indicates that very little of the vitamin K produced by intestinal bacteria is absorbed and that fermented foods may be a better source of menaquinone.

Vitamin K Food Sources See Appendix D.

Ascorbic Acid (Vitamin C)

Ascorbic acid is a water-soluble vitamin commonly known as vitamin C. It is the least stable of all the vitamins, and is easily destroyed during cooking and processing.

Form and Absorption The jejunum and ileum efficiently absorb vitamin C. The amount of vitamin C in the blood is modulated by renal excretion, with levels exceeding the reabsorption threshold being excreted in the urine.

Functions Vitamin C plays an essential role in:

the formation of collagen, which is responsible for strengthening bones and blood vessels, anchoring teeth into the gums, as well as forming the substances necessary for body growth, tissue repair, and wound healing,

the synthesis of neurotransmitters such as norepinephrine,

antioxidant activity.

Deficiency Individuals who do not have access to fresh citrus fruits and juices, such as urban or poor older adults, may have insufficient vitamin C intake. Individuals with severe burns, fractures, pneumonia, rheumatic fever, and tuberculosis, as well as those who have recently undergone surgery, have increased requirements for vitamin C. Alcohol decreases absorption and cigarette smoking depletes tissue levels. Thus, alcoholics and smokers should increase their dietary intake or take supplemental vitamin C.

Vitamin C deficiency is characterized by the development of scurvy, in which impaired collagen synthesis results in muscle weakness, joint pain, impaired wound healing, loose teeth, bleeding and swollen gums, bruised skin, fatigue, and depression.

Toxicity Since vitamin C is water-soluble, the body excretes the excess when intake exceeds the body's requirements. However, because vitamin C is metabolized to oxalic acid,

consuming too much may cause increased excretion of oxalate, which suggests that patients with a history of forming oxalate kidney stones should avoid high doses of this vitamin. Doses in excess of the UL (2000 mg/day) can have other side effects including nausea, diarrhea, and abdominal cramps.

Relationship to Disease Prevention Vitamin C is a powerful antioxidant that provides the first line of defense against free radicals in the aqueous compartments of the body. However, to date, studies have been unable to demonstrate a clear protective role for vitamin C. Numerous studies of even mega doses have not proven effective in cancer prevention or treatment or in atherosclerosis prevention. One study of women undergoing breast cancer therapy demonstrated an 18 percent reduction in mortality and a 22 percent reduction in recurrence in women using antioxidants (vitamins E and C), and a multivitamin. The role of vitamin C in the prevention and treatment of the common cold remains controversial with high doses having a mild antihistamine effect, but many patients are convinced of the benefits of daily supplementation. Increased levels of vitamin C from either the diet or from supplements have been associated with lower blood pressure.

Vitamin C Food Sources See Appendix E.

Thiamin (Vitamin B_1)

Form and Absorption Thiamin is a water-soluble vitamin. It is primarily absorbed in the jejunum via active transport when intake levels are low and passive transport when intake levels are high. Absorption is significantly reduced in the presence of alcohol and in individuals with folate deficiency. Once absorbed, thiamin is primarily found in skeletal muscles, liver, heart, kidneys, and brain; however, it is not stored in the body to any great extent, so daily intake is required.

Functions Thiamin is an essential prosthetic group in a number of enzymes that play key roles in the production of energy from carbohydrate and protein and is an essential component in the pentose phosphate pathway that generates NADPH and ribose for nucleic acids.

Deficiency Primary thiamin deficiency due to poor intake of thiamin-containing foods, which can lead to beriberi, is rare in the United States because the majority of grain products are fortified with thiamin. However, thiamin deficiency may occur in individuals who abuse alcohol because excessive alcohol intake significantly decreases thiamin absorption and interferes with its metabolism. Early thiamin deficiency is characterized by poor appetite, irritability, apathy, confusion, and weight loss. Clinicians should be aware of low micronutrient

intake among patients on weight-loss regimens as the recent A-to-Z study comparing the Atkins, Ornish, LEARN and Zone diets demonstrated decreased intake and blood levels of thiamin in patients following either the Atkins, LEARN or Ornish plans. For this reason, a multivitamin should be advised for patients restricting their diet for weight loss or other reasons. Advanced stages of beriberi are characterized by the system affected: neurologic or cardiovascular systems. Wet beriberi refers to a form characterized primarily by abnormal heart rhythms, cardiomyopathy, heart failure, and edema. The neurological manifestations vary from pain, numbness or tingling of the lower extremities to difficulty walking and loss of deep tendon reflexes, to Wernicke's encephalopathy or Korsakoff's psychosis.

Causes and Effects of Toxicity Thiamin toxicity has not been described.

Relationship to Disease Prevention Although thiamin is not generally associated with disease prevention, prompt administration of thiamin is indicated for the alcoholic patient who shows signs of Wernicke's disease, and is often used presumptively in patients who have acute mental status changes.

Riboflavin (Vitamin B_2)

Riboflavin is water soluble. It functions as a precursor to the flavin category of enzyme

prosthetic groups – flavin-adenine dinucleotide (FAD) and flavin mononucleotide (FMN) – that participate in oxidation/reduction reactions, many of which are involved with energy production.

Form and Absorption Free riboflavin is released from foods by digestive enzymes and is actively absorbed by an ATP-requiring process in the jejunum. Some of the riboflavin circulating in the blood is loosely bound to albumin, although significant amounts also combine with other serum proteins. Once riboflavin is delivered to a variety of cells, it is converted into FMN or FAD.

Functions Riboflavin plays an essential role in:

normal growth and development,

breakdown of glucose to yield energy for all cells,

facilitation of glycogen production and digestion of fats,

synthesis of niacin from tryptophan,

maintenance of normal mucous membranes and protection of the nervous system, skin, and eyes,

metabolism of vitamin K, folate, and pyridoxine.

Deficiency Riboflavin deficiency can result from inadequate intake, lack of absorption, poor utilization, or increased excretion. Riboflavin deficiency symptoms include inflammation of the oral mucosa or tongue, cheilitis, stomatitis, glossitis, seborrheic dermatitis, and normochromic-normocytic anemia. The eyes may become bloodshot, itchy, watery, and sensitive to bright light. Riboflavin deficiency typically develops in conjunction with deficiencies of other water-soluble (B) vitamins, which are commonly found in the same foods. In those with reduced riboflavin levels, supplementation has been shown to lower total plasma homocysteine. High homocysteine levels are associated with an increased risk of cardiovascular disease (CVD), but B vitamin supplements have not proven successful at lowering CVD in experimental trials.

Toxicity No adverse effects from a high intake of riboflavin have been reported and hence there is no TUL established for this vitamin. Riboflavin in brightly pigmented and causes a very yellow urine in patients taking it.

Relationship to Disease Prevention There are no specific indications for riboflavin supplementation for disease prevention, but at-risk groups include those with high alcohol intake and the elderly, particularly those with

limited income who may have poor dietary intake.

Niacin (Vitamin B_3)

Niacin is a water-soluble vitamin, found in two common forms: nicotinic acid and nicotinamide. Niacin is the precursor to the coenzymes nicotinamide adenine dinucleotide (NAD) and NAD phosphate (NADP), electron carriers used in synthetic reactions and for ATP production.

Form and Absorption Niacin and nicotinamide are absorbed through the intestine by passive diffusion. Niacin and nicotinamide are metabolized via different pathways.

Functions Niacin plays an essential role in:

normal enzyme production in at least 200 reactions in the body involved in energy production; most enzymes require niacin to accept electrons (redox) or donate hydrogen molecules (hydrogenase),

normal production and breakdown of glucose, fats, and amino acids, thereby helping the body to metabolize these substances,

normal development, maintenance, and function of the skin, gastrointestinal tract, and nervous system,

synthesizing DNA.

Deficiency Niacin is found primarily in protein-rich foods, and a deficiency is rare in the United States. Because some, but not all, of our niacin requirement can be met by conversion from the amino acid tryptophan, niacin deficiency historically developed in those whose diet mainly consisted of corn, which is both low in niacin and lacks tryptophan. The synthesis of niacin from tryptophan requires riboflavin, pyridoxine, and heme-iron-containing enzymes, therefore vitamin B_6 deficiency can also contribute to a niacin deficiency. Individuals who abuse alcohol are also at increased risk of niacin deficiency because alcohol significantly reduces niacin absorption.

The initial signs of niacin deficiency include fatigue, loss of appetite, weakness, mild gastrointestinal disturbance, anxiety, irritability, and depression. A severe deficiency causes pellagra ("rough skin") showing symptoms of diarrhea, dermatitis (pigmented skin rash, especially to sun-exposed skin), dementia, and if left untreated, death ("4 Ds"). Additional symptoms include inflammation of the mucous membranes of the mouth (magenta tongue), apathy, fatigue, and loss of memory.

Toxicity Niacin toxicity from food sources has not been documented. Pharmacologic doses of niacin used to treat hypercholesterolemia (lowers LDL and raises HDL) commonly cause

minor adverse effects, including flushing, nausea, salivation, and dizziness. Based on estimated minimum levels that produce these symptoms, a TUL for niacin has been established at 35 mg/day. Niacin at pharmacological doses (>2000 mg/day) over a long period has been associated with elevated liver enzymes and elevated blood sugar levels in some individuals.

Recently, it has been reported that individuals seeking to "beat" urine drug screening have presented at Emergency Departments with symptoms of niacin toxicity, sometimes life-threatening. This misguided use of niacin at levels exceeding even usual pharmacologic doses have resulted in symptoms ranging from nausea and vomiting to metabolic acidosis and electrocardiogram abnormalities.

Relationship to Disease Prevention In addition to hypercholesterolemia, niacin has been used to treat dizziness and tinnitus, and to prevent premenstrual headaches. Pharmacological doses of nicotinic acid (between 1 and 3 g/day) have demonstrated utility in clinical trials at reducing CVD. Nicotinamide does not have this effect. When applied to the skin, niacin has recently been shown to improve the appearance of wrinkles around the eyes and in combination with *N*-acetyl glucosamine, has been used to decrease irregular pigmentation of the skin and

to decrease the immunosuppression observed with exposure to ultraviolet light. Side effects of mega doses of niacin include flushing, which may be minimized by administering an aspirin prior to ingesting each dose of niacin or by using a sustained release preparation. Both niacin and niacinamide have been used topically but itching and burning of the skin may occur.

Pantothenic Acid

Pantothenic acid is another B-complex vitamin. It is a precursor of coenzyme A (CoA) and the acyl-carrier protein (ACP) moiety of the enzyme fatty acid synthase, both necessary for the metabolism of fats, carbohydrates, and proteins. CoA derived from food is hydrolyzed in the small intestine to form pantothenic acid, which is then absorbed in the jejunum.

Functions Pantothenic acid, as a component of CoA, is essential for:

synthesis of fatty acids, triglycerides, cholesterol, and acetylcholine,

metabolism of protein and amino acids, fat, and carbohydrates,

synthesis of cell membranes.

Deficiency Lack of pantothenic acid in the body is very unlikely and there is no evidence that a deficiency of this vitamin can occur naturally. However, a deficiency created

experimentally in test subjects has produced the following symptoms: indigestion, abdominal pain, burning sensation in the feet, arm and leg cramps, insomnia, and nerve inflammation (neuritis). Damage to the adrenal cortex, nervous system, skin, and hair has also been observed. It is thought that alcoholics may exhibit neuritis due to a lack of pantothenic acid; however, further evidence is needed for confirmation.

Toxicity Unknown.

Relationship to Disease Prevention While many people take pantothenic acid supplements as part of "stress" formulas, to treat rheumatoid or osteoarthritis, acne, or as a immune booster due to its role in the synthesis of adrenal hormones, the National Institutes of Health (NIH) has concluded that there is insufficient scientific evidence to determine its effective for these uses.

Biotin

Biotin is also a member of the water-soluble B-complex of vitamins.

Forms and Absorption Biotin is absorbed in the proximal small intestine. Intestinal bacteria also synthesize biotin, which can contribute to body stores.

Functions Biotin is an important prosthetic group in the carboxylase class of enzymes,

which use bicarbonate to attach a CO_2 group onto various metabolic substrates; as such, biotin plays a key role in glucose synthesis.

Deficiency Biotin deficiency in humans is rare. Experimentally, biotin deficiency has developed in humans who consume large quantities of raw egg whites. The protein avidin in eggs binds to biotin in the intestine preventing absorption. Symptoms of biotin deficiency include inflammation of the skin, hair loss, muscle pain, increased skin sensitivity, loss of appetite, nausea, mental problems, high cholesterol, and decreased hemoglobin levels. Low levels of biotin have been found in some pregnant women, dialysis patients, and people who lack sufficient biotinidase, an enzyme needed for biotin absorption (although the symptoms of biotin deficiency and biotinidase deficiency are not identical).

Toxicity There is no evidence of biotin toxicity.

Relationship to Disease Prevention Because biotin deficiency leads to thinning hair and skin sensitivity, it is included in many "hair support" vitamin products. It has been used successfully in seborrheic dermatitis in infants, but scientific evidence for a role in hair growth is lacking.

Pyridoxine (Vitamin B_6)

Vitamin B_6 is a water-soluble vitamin that is one of a group of compounds that includes pyridoxine and pyridoxamine, mainly found in plants, and pyridoxal, derived from animal products. All of these compounds are easily converted to pyridoxal phosphate, a coenzyme involved in the metabolism of amino acids.

Forms and Absorption Vitamin B_6 and its related compounds are absorbed in the jejunum and widely distributed in the body, primarily in muscle tissue.

Functions Vitamin B_6-dependent enzymes perform a number of biochemical functions, such as:

varied reactions involving amino acids, including transamination,

synthesis of a variety of biogenic amines, including serotonin, dopamine, norepinephrine, and histamine,

heme synthesis,

conversion of the amino acid tryptophan to niacin; breakdown of glycogen to glucose phosphate; and the conversion of homocysteine to cysteine.

Deficiency Vitamin B_6 deficiency, while relatively rare, can occur as a consequence of an adverse interaction with the antitubercular

drug, isoniazid, or penicillamine. This deficiency is characterized by cheilosis, glossitis, a pellagra-like dermatitis, depression, confusion, and EEG abnormalities.

Asthma, renal disease, Hodgkin's disease, sickle cell anemia, and diabetes have all been associated with a decrease in the blood levels of pyridoxal phosphate. Low serum vitamin B_6 levels have been observed in pregnant women experiencing nausea and supplements have been shown to be safe and effective.

Toxicity The tolerable upper intake level for vitamin B_6 has been established at 100 mg/day. Reports of toxicity have been noted in individuals taking 100 to 300 mg/day. Megadoses of 500 mg/day or higher of vitamin B_6 for 2 months or more can cause photosensitivity and a polyneuropathy characterized by failure of muscular coordination and sensory nerve damage.

Relationship to Disease Prevention The NIH lists vitamin B_6 as “possibly effective” for upset stomach and vomiting in pregnancy, premenstrual syndrome (PMS) symptoms such as breast pain and depression, oxalate kidney stones, movement disorders (tardive dyskinesia) in people taking medicines for mental disorders, behavior disorders in children with low levels of serotonin, reducing lung cancer risk in men who smoke, and macular degeneration (see Chapter 5: Case 2).

In addition, B_6 in the form of pyridoxine hydrochloride, has been utilized to treat diabetes during pregnancy, carpal tunnel syndrome, asthma, depression, and diabetic neuropathy. Studies have failed to document any decreased risk of myocardial infarction in patients post-coronary artery bypass graft surgery or any decreased risk of cancer incidence in those with prior cardiovascular disease.

Vitamin B_{12}

Vitamin B_{12} is a water-soluble vitamin that exists in many forms referred to as cobalamins. Cyanocobalamin is the synthetic form used in supplements. Cobalamins are produced by bacterial fermentation (e.g., in the rumen of cattle); therefore animal products and fermented foods (e.g., nutritional yeast) provide the only dietary sources.

Form and Absorption Adequate absorption of Vitamin B_{12} depends on the presence of stomach acid and pepsin, pancreatic proteases, intrinsic factor (IF), and IF receptors on the terminal ileum. Because there is a low (~1 percent) rate of absorption even in the total absence of IF, individuals with B_{12} malabsorption (pernicious anemia) may be maintained with large oral doses of vitamin B_{12} (250 to 1000 μg/day) after initial parenteral loading.

Functions Vitamin B_{12} is a prosthetic group required for two important enzymes – methionine synthase and methylmalonyl-CoA mutase – which are essential for cell replication and neurological function. Methionine synthase is present in the cell's cytoplasm and catalyzes the transfer of a methyl group from *N*-methyl-tetrahydrofolate to homocysteine to yield methionine and to liberate tetrahydrofolate. Thus it is required for folic acid metabolism and methyl group transfer reactions. Methylmalonyl-CoA mutase resides in the mitochondria and transforms methylmalonyl-CoA (from uneven numbered fatty acids) into succinyl-CoA, for further metabolic use.

Deficiency Vitamin B_{12} deficiency is a specific concern of those following a vegetarian dietary pattern (particularly vegans). While tempeh, miso, and sea vegetables have been shown to contain B_{12}, absorption from these sources may not be sufficient to prevent deficiency. Individuals lacking IF fail to absorb sufficient B_{12} and develop pernicious anemia. Some people develop pernicious anemia as a consequence of autoimmune inactivation of IF. Others at risk include patients who have had their terminal ileum surgically removed as therapy for inflammatory bowel disease, cancer, or trauma. Patients taking proton pump inhibitors on a long-term basis may develop B_{12} deficiency secondary to inadequate stomach

acid to release B_{12} from food resulting in malabsorption. Many older people develop achlorhydria and lose their ability to release B_{12} from protein, so they absorb less vitamin B_{12}. Alcohol abuse also reduces absorption and is a risk factor for dietary B_{12} deficiency. According to the Merck Manual, less common causes of inadequate vitamin B_{12} absorption include chronic pancreatitis, gastric surgery, malabsorption syndromes, AIDS, and the use of certain drugs (e.g., antacids, metformin, or repeated exposure to nitrous oxide).

Symptoms of vitamin B_{12} deficiency include megaloblastic anemia, nerve damage (tingling in the hands and feet), and a swollen, painful red tongue. Long-term vitamin B_{12} deficiency, if not treated, can cause severe, irreversible damage to both peripheral nerves, such as paresthesias and numbness in the limbs, and to spinal cord tracts, causing ataxia and loss of vibration sense, and dementia. Lowered levels of vitamin B_{12} have been observed in those with Parkinson's disease and recent research has demonstrated the effectiveness of B_{12} in reversing the sensory neuropathy associated with chronic cough.

Toxicity No toxic or adverse effects have been associated with large intake or parenteral administration of vitamin B_{12}. When high doses of vitamin B_{12} are given orally, only a small

percentage is absorbed, which may explain its low toxicity. There is no TUL.

Vitamin B_{12} is a product of bacterial fermentation. The only dietary sources of vitamin B_{12} are foods of animal origin such as meat, chicken, fish, eggs, and dairy products. Fortified foods, such as brewers yeast and soy milk, contain added vitamin B_{12}. Seaweed, algae, spirulina, and fermented plant foods, such as tempeh and miso, are touted as vegetarian sources of vitamin B_{12} but contain only trace amounts.

Relationship to Disease Prevention When taken as a supplement along with folate, vitamin B_{12} resulted in improved cognitive function and memory as well as a decrease in depressive symptoms in older adults with psychological distress. Given the widespread use of medications that interfere with B_{12} absorption (metformin and gastric acid inhibitors), clinicians should be alert to potential symptoms of B_{12} deficiency in their older patients.

Folate (Folic Acid)

Folate is a water-soluble B vitamin also known as folacin or folic acid. Folate is found in both plant and animal food sources. Dietary folate in the form of the polyglutamates is digested to the monoglutamate form and actively absorbed in the jejunum.

Functions Folate plays an essential role in transferring single carbon units to acceptor molecules and thus is important for:

synthesis of DNA and RNA, cell division, and growth and development,

synthesis of heme for the formation of blood cells,

serving as a methyl donor for the enzyme involved in the conversion of homocysteine to methionine.

Deficiency Folate deficiency in humans is attributed to sub-optimal dietary intake of folate, inadequate absorption (e.g., as a consequence of gluten enteropathy), inadequate utilization (e.g., from drug antagonists such as methotrexate or enzyme deficiencies), increased demands (e.g., pregnancy), or increased losses (e.g., liver disease or dialysis). Although folate deficiency is rare in the United States, it may occur in alcoholics, or individuals who are unable to absorb folate, such as those with Crohn's disease, ulcerative colitis, or short bowel syndrome. Unlike other vitamins, the recommended amounts of folate are the same for men and women but recent evidence suggests that larger amounts might be needed in men.

Folate deficiency in the elderly may be the result of a poor diet or the use of drugs that impede the absorption of folate. Antacids

hinder the absorption of folate by raising the pH levels of the upper intestine. Cimetidine, sulfasalazine, and phenytoin also impede the absorption of folate. Folate supplementation can reverse the macrocytic anemia seen in pernicious anemia; however, it will not reverse the neurologic damage caused (see vitamin B_{12}).

A lack of folate affects cell division, resulting in abnormalities in red blood cell formation in the bone marrow. Symptoms of folate deficiency commence with macrocytosis and progress to macrocytic anemia. As the oxygen-carrying capacity of the blood gradually diminishes, symptoms such as weakness, fatigue, irritability, headache, palpitations, and shortness of breath may occur. Folate deficiency also results in elevated blood homocysteine levels. It is estimated that two-thirds of individuals with high homocysteine levels have poor folate intake.

Toxicity The TUL for folate has been set at 1 mg/day. Although folate seems to have little or no toxicity *per se*, the TUL was established because excessive consumption of folic acid may mask vitamin B_{12} deficiency, allowing neurologic sequelae to progress even though the anemia associated with this deficiency resolves.

Relationship to Disease Prevention Since folate is involved in the synthesis of DNA and proteins, adequate levels are particularly

important at times of rapid cell growth, such as during fetal development. It has been demonstrated that neural tube defects occur from a dietary deficiency of folate combined with a genetic defect in enzymes involved in folate metabolism. Folate administration during the very early stages of pregnancy has been convincingly demonstrated as important in preventing many neural tube defects. Fortification of certain foods with folate has been credited with substantially reducing the incidence of neural tube defects and perhaps some other birth defects (Chapter 4: Case 2).

People with high blood levels of the amino acid homocysteine (HCys) have been shown to have an increased risk of developing heart disease. The "salvage" of HCys (a product of methylation reactions) by conversion to methionine requires methyl tetrahydrofolate; thus, a block in this reaction from inadequate folate or B_{12}, results in elevations of HCys in the body. As vitamin B_6 is required for the lone alternative pathway for HCys utilization, a lack of any of these B vitamins causes especially high levels of HCys. Therefore, researchers have suggested that increasing folate, either through the diet or supplements, will reduce HCys levels in the blood and lower the risk of heart disease as well. This beneficial effect of folate is decreased by antiplatelet medications. However, recent findings report no beneficial vascular effects in high-risk populations, suggesting that elevated

HCys may be a marker of increased risk of CVD rather than a causative agent.

Folic acid has recently been shown to decrease the risk of some types of strokes in smokers. Folate has been used effectively as an adjunct in depressed patients who fail to respond to selective serotonin reuptake inhibitor (SSRI) treatment. Lower folate levels have been associated with an increased risk of depression and dementia in the elderly, and folate supplementation increased cognitive functioning in older adults. Lower folate levels have also been correlated with an increased risk of prostate cancer in men and pancreatic cancer in women.

Folate Food Sources See Appendix F.

Minerals

Mineral elements are inorganic substances that occur as salts, such as sodium chloride (NaCl), or as a component of organic compounds, such as the iron in the tetrapyrrole ring of heme (e.g., hemoglobin) or the sulfur found in certain amino acids. Minerals are classified as macrominerals or microminerals, based on their percentages of total body weight. Macrominerals constitute more than 0.005 percent of the body's weight, or 50 parts per million (ppm). Examples include calcium, chloride, phosphorus, potassium, magnesium,

sodium, and sulfur. Microminerals fall into two categories:

Minerals with identified roles in health maintenance, including chromium, cobalt, copper, fluoride, iodide, iron, manganese, molybdenum, selenium, and zinc.

Minerals found in body tissues with no currently established roles in health maintenance, such as arsenic, boron, cadmium, nickel, silicon, tin, and vanadium.

In foods, minerals commonly occur as salts, such as sodium chloride or as enzyme cofactors. Because salts are usually water soluble, some loss occurs during cooking, such as when vegetables are boiled. The body is capable of storing some minerals (e.g., iron in ferritin, calcium in bone) so that deficiencies may require a prolonged period of poor intake before symptoms develop.

Calcium

Calcium is an abundant mineral in the body, with 99 percent of body calcium stored in the bones and teeth. The remaining 1 percent is active in enzyme activation, blood clotting, and muscle contraction. Most calcium absorption occurs in the duodenum, but the jejunum and ileum contribute substantially to overall calcium absorption.

Vitamin D levels in the body regulate calcium absorption. The parathyroid gland responds to low serum calcium levels by releasing PTH, which stimulates many tissues to convert vitamin D to its active form (calcitriol). Activated vitamin D, in turn, increases the absorption of calcium from the intestine and regulates calcium excretion via the kidneys.

When calcium levels in the blood are elevated, the hormone calcitonin, released from the parafollicular cells (or "C cells") in the thyroid gland, prevents bone from releasing calcium and promotes calcium excretion. Individuals who have poor vitamin D intake and low sun exposure have poor calcium absorption. Lactose, the sugar in dairy products, improves calcium absorption in infants, whereas oxalate (which is present in spinach and rhubarb) and, to a lesser extent phytate, can inhibit calcium absorption. Calcium excretion is related to dietary protein intake – high protein diets increase urinary excretion of calcium; however, protein intake accompanied by adequate calcium intake increases bone mass.

Functions Calcium plays an essential role in:

bone mineralization; calcium levels are maintained in equilibrium by the movement of 250 to 1000 mg of calcium in and out of bone tissue every day,

maintenance of cell membrane permeability,

muscle contraction,

blood clotting,

nerve impulse conduction.

Calcium Deficiency Calcium deficiency usually remains undiagnosed for years because the bones serve as an effective reservoir and continue to release calcium into the blood. Symptoms of calcium deficiency (hypocalcemia) include irritability, “pins and needles” sensation in hands and feet (paresthesia), muscle cramps and twitching (tetany), and possible seizures (convulsions). Over time, persistent low calcium intake can manifest as osteoporosis, with accompanying bone fractures and loss of height. Calcium deficiency in children is characterized by paresthesia of the mouth or extremities, stunted growth, tetany, and seizures.

Problems related to poor calcium intake include:

Rickets is caused most commonly by vitamin D deficiency, but lack of calcium and phosphorus can also be a basis for this disease. Rickets is characterized by abnormal bone formation, bending and distortion of the bones, nodular enlargements of the boney epiphyses, delayed closure of the fontanels, and bone pain.

Osteoporosis is defined as a reduction in bone density, rendering bones brittle and susceptible to fractures. Symptoms of osteoporosis may

include altered posture caused by deformity of the spine, postural slumping due to acute pain, waddling gait, loss of height, muscle weakness, and kyphosis. The bones most commonly affected include the hip, spine, wrist, and upper arm. A low calcium diet and lack of adequate physical activity are primary factors believed to contribute to the development of osteoporosis. Excessive alcohol intake, family history of osteoporosis, race, early menopause, short stature, and cigarette smoking are major contributors as well.

Calcium Toxicity Hypercalcemia may be seen in people with a hyperactive parathyroid gland, excessive intake of vitamin D, or certain cancers, including breast and lung cancer. Hypercalcemia may result in dehydration, lethargy, nausea, vomiting, anorexia, and possibly death. The tolerable upper limit for calcium intake has been established at 2500 mg/day. Adults with a history of calcium oxalate kidney stones should be advised to limit their protein intake to the RDA level of 0.8 g/kg bodyweight per day, avoid oxalate-rich foods, and limit salt intake.

Supplement Issues The lifetime risk for osteoporotic fractures in women is estimated to be as high as 50 percent, and costs associated with hip fracture alone are estimated at $13 to $18 billion/year in the United States. These facts combined with the exponential increases

expected as the population ages, make prevention key. While osteoporosis is a multifactorial disorder, calcium intake during adolescence and throughout life and adequate vitamin D is critical to achieving optimal peak bone mass and may play a significant role in preventing degenerative bone diseases in later years. Adolescents need to be educated about the importance of calcium for health, recommended intake, and good food sources of calcium, particularly lower-fat dairy products. Calcium supplements may be helpful for populations of:

post-menopausal women,

amenorrheic women,

patients who avoid dairy foods, including strict vegetarians, vegans, and lactose-intolerant persons.

Relationship to Disease Prevention
Calcium supplementation to pregnant women with low calcium intakes reduces the severity of preeclampsia, maternal morbidity, and neonatal mortality. After birth, however, calcium supplementation may result in lower bone densities in the mother. In a recent research study, calcium and vitamin D supplementation did not lower blood pressure or decrease the risk of breast cancer in older women. A meta-analysis of cohort studies and clinical trials failed to show any reduction in fractures with increased calcium intake,

therefore more focus on the contribution of vitamin D and phosphate in combination with calcium supplementation is required. The role of milk has also been called into question as the results of the Nurse's Health Study failed to show that women who drank more than one serving of dairy daily (three are currently recommended to meet calcium intake requirements), had lower risk of osteoporosis. Supplementation with calcium and vitamin D has also not been shown to produce a change in lipids in the body or cause weight loss but long-term use has been associated with an increase in urinary track stones and may decrease iron absorption.

Calcium Food Sources (including fortified sources) See Appendices G, H.

Magnesium

Forms and Absorption Magnesium is absorbed primarily in the distal jejunum and ileum and is more efficiently absorbed when intake is low. Magnesium competes with calcium for absorption, and its absorption is also slightly enhanced by vitamin D. Magnesium is found in bone, muscle, and intracellular and extracellular fluid. The kidney is the principal modulator of magnesium homeostasis through filtration and reabsorption.

Only 1 percent of the body's magnesium pool is found in the blood and magnesium is a co-factor in more than 300 enzymatic reactions.

Functions Magnesium plays a role:

in hundreds of ATP-requiring reactions in metabolism and active transport by acting as a necessary chelator for the highly negatively charged ATP and ADP molecules,

in transmitting neural impulses and thereby eliciting muscle contractions in conjunction with calcium, sodium, and potassium,

as a component of bones and teeth,

in protein synthesis and cell replication,

in suppressing PTH secretion, although it is only about one-half as effective as calcium.

Magnesium Deficiency Although overt magnesium deficiency is rare due to its presence in a wide variety of foods, the average intake of magnesium is below what it should be for disease prevention. A study evaluating data from the NHANES study 1999–2000 found that the median daily intake of magnesium in Caucasian males was about 100 mg less than the RDA. For women the deficit was 80 mg and among ethnic minority respondents, the deficits were even greater. Deficiency can occur in individuals who have absorption or excretion problems. These conditions include intestinal malabsorption, surgical removal of the lower

part of the intestine, diuretic medications, severe vomiting, and kidney disease. Individuals with protein-calorie malnutrition, chronic alcohol abuse, hyperparathyroidism, and liver cirrhosis may have low serum magnesium levels. Recent studies have documented the relationship of low serum magnesium with insulin resistance and increased risk of metabolic syndrome. Since magnesium is required for normal PTH functioning, low magnesium levels may alter calcium and phosphorous homeostasis. Magnesium is also diminished by food processing (e.g., refining grains or boiling greens).

Indications of magnesium deficiency include low levels of calcium and potassium in the blood, as well as changes in the gastrointestinal, neuromuscular, and cardiovascular systems. In patients with low serum potassium levels that seem not to rise with supplementation, a magnesium infusion allows potassium levels to be restored to normal. Magnesium deficient individuals may have fatigue, lethargy, weakness, poor appetite, impaired speech, anemia, irregular heartbeat, tremors, and failure to thrive. Clinical signs of advanced magnesium deficiency include rapid heart rate, cardiac fibrillation, and convulsions.

Hypomagnesemia was found to be common in children during to cardiac bypass surgery and

was ameliorated with magnesium supplements, thus lowering post-op arrhythmias. Following either the Atkins or LEARN diet was associated with inadequate dietary intake of magnesium, so supplementation during dietary restriction for weight loss may be indicated.

Magnesium Toxicity Elevated blood magnesium levels may be seen in people with renal failure or those receiving high doses of magnesium supplements. High blood levels typically cause diarrhea and may result in changes in mental status, muscle weakness, nausea, extremely low blood pressure, difficulty breathing, and an irregular heartbeat. The tolerable upper limit for magnesium has been established at 350 mg/day for adults and adolescents.

Supplement Issues Low magnesium intake has been correlated with hypertension, cardiovascular disease, and osteoporosis in several studies of older Americans. Recent research has demonstrated that low magnesium intake is associated with an increased risk of developing metabolic syndrome and type 2 diabetes. Low magnesium levels have been observed in obese children with insulin resistance, although a cause-and-effect relationship has not yet been established. In overweight, non-diabetic adults, magnesium supplements increased insulin sensitivity.

Magnesium supplementation may benefit patients:

with asthma,

taking diuretics or certain chemotherapy medications for the treatment of cancer,

with malabsorptive diseases, such as gluten enteropathy,

with chronically low levels of potassium or calcium,

with diabetes or prediabetes,

who are elderly.

For patients with renal disease, serious accumulation of magnesium can occur. High doses (1000 to 5000 mg) may cause toxicity symptoms.

Relationship to Disease Prevention In addition to the potential impact of magnesium supplementation on hypertension (small but significant decreases in blood pressure for those with mild hypertension) and diabetes (improved insulin sensitivity), supplements have been shown to decrease bone turnover in post-menopausal women with osteoporosis; and reduce the frequency of migraine headaches. Intravenous infusions of magnesium lower the risk of arrhythmias post-myocardial infarction leading to fewer deaths and may help in severe asthma attacks. Magnesium supplementation has also been

shown to increase testosterone levels in males who exercise (magnesium losses in sweat may be significant), and to decrease fat absorption which can help prevent atherosclerosis. When taken with zinc and melatonin, it improved insomnia in older individuals.

Magnesium Food Sources (including enriched sources) See Appendix K.

Phosphorus

Phosphorus is second in abundance to calcium and is an essential mineral present in bones and teeth, as well as phospholipids, proteins, carbohydrates, enzymes, DNA, and ATP.

Form and Absorption Phosphorous is absorbed in the form of phosphate primarily in the small intestine. Absorption rates are generally high (about two-thirds is absorbed), and fairly consistant; however, while vitamin D may promote uptake by active transport, the observed constancy of phosphate fractional absorption suggests that most uptake occurs by a passive, concentration-dependent process. Aluminum-containing antacids can reduce phosphate absorption.

Function Phosphorous plays an essential role in:

the normal construction of bones and teeth,

DNA and RNA synthesis,

energy synthesis (ATP, ADP),

metabolism of protein, fat, and carbohydrate,

maintenance of the body's normal pH levels,

normal cell membrane structure.

Phosphorus Deficiency Phosphorous deficiency is generally regarded as rare, but occurs most commonly in chronic alcoholics during withdrawal or in persons experiencing diabetic ketoacidosis. It may be observed in individuals who consume excessive and prolonged amounts of aluminum hydroxide-containing antacids as the aluminum binds dietary phosphorous, preventing its absorption. Symptoms of phosphorous deficiency include weakness as a consequence of decreased levels of ATP and anorexia, bone pain, and proximal muscle myopathy in some instances. Prolonged deficiency can result in rickets or osteomalacia, due to the need for phosphate for hydroxyapatite formation in bone.

Phosphate Toxicity Abnormal elevated blood phosphorus levels appear in individuals with renal failure and can give rise to the precipitation of calcium phosphate in various tissues (metastatic calcification) which may further compromise kidney function. High dietary intake of phosphate in persons with normal kidney function does not seem to cause toxicity. Recent data have suggested that

elevated phosphorus levels are a risk factor for CVD and mortality. Elevated levels of phosphorous are associated with an increase in carotid intima media thickness, which is related to atherosclerosis and arterial stiffness. Fibroblast growth factors (FGF), a recently characterized family of polypeptides, have diverse roles in angiogenesis, wound healing, and embryonic development. During embryonic development, FGFs regulate cell proliferation, migration, and differentiation. In adults, FGFs are homeostatic factors and function in tissue repair and response to injury. One of the FGFs (FGF23) plays a role in controlling both phosphorous reabsorption and excretion in the renal tubule. The TUL for phosphorus has been established at 4000 mg/day.

Supplement Issues None.

Iron

Iron is an essential element in all cells of the body. As a component of hemoglobin, myoglobin, and cytochrome enzymes, iron plays a key role in oxygen transport and normal cellular respiration.

Forms and Absorption Iron is absorbed in the duodenum via iron-binding proteins that transfer it across the intestinal mucosa. Non-heme iron absorption requires an acidic gastric pH to convert it from ferric (Fe^{3+}) to

ferrous (Fe^{2+}) forms. Once absorbed, ferrous iron is converted back to ferric iron in intestinal mucosal cells and then combined with apoferritin to form ferritin. Some ferritin is transported out of the mucosal cell into plasma bound to transferrin and transported to bone marrow or other iron storage sites where it is stored as either ferritin or hemosiderin. The absorption of iron from plants (non-heme iron) is enhanced by the concurrent ingestion of vitamin C (which aids in reducing the valence of ferric iron) and is increased in iron-deficient individuals through upregulation of the divalent metal transporter. Heme iron is absorbed considerably more efficiently than non-heme iron.

Function Iron plays an essential role in the following physiological functions:

Synthesis of hemoglobin and myoglobin. About 70 to 75 percent of the body's iron is bound to hemoglobin and myoglobin while the other 25 to 30 percent is stored as ferritin and hemosiderin in the liver, bone marrow, and spleen. Iron is transported in the serum bound to transferrin, which represents about 1 percent of the body's iron stores.

Synthesis of cytochrome protein. Many cytochrome proteins contain heme-bound iron; these enzymes function in a variety of roles, including metabolic reactions, electron transport, and drug detoxification.

Iron Deficiency Iron deficiency is one of the most prevalent nutritional problems in the world. Populations at risk include menstruating or pregnant females, infants and children, and those with celiac disease. Iron deficiency not associated with chronic blood loss is most frequently caused by inadequate dietary intake, or with a diet with low bioavailable iron, as seen with vegetarians or infants not given iron-fortified formula or cereal after the age of 6 months. In the United States, the iron intake of most boys and men exceeds the RDA, while the intake of most girls and women (up to the age of 50) is less than the RDA. Iron deficiency is characterized by weakness, fatigue, poor work performance, adverse pregnancy outcomes, developmental delays, and cognitive impairment. Symptoms of iron deficiency include fatigue, feelings of faintness, cold or abnormal sensations of the extremities, shortness of breath, and greater susceptibility to infections. Signs of iron deficiency include poor capillary bed refilling, pale mucosa, and soft, concave, or brittle nails. Infants and young children with iron deficiency may have low IQ levels and learning and/or behavioral problems.

Iron Toxicity Excessive iron ingestion may cause deposition of iron in the tissues. Prolonged iron overload (e.g., hemochromatosis) may cause bronzed pigmentation to the skin and damaged liver and pancreas tissue and may possibly cause

diabetes. The hemochromatosis gene is present in 1 in 200 non-Hispanic white Americans, although even among homozygous individuals, only 1 percent develop signs of iron overload. The TUL for iron has been established at 45 mg/day for normal adults based upon gastrointestinal side effects.

Supplementation Issues Iron deficiency anemia is a prominent cause of morbidity in several populations (i.e., infants, pregnant women, women with heavy menstrual losses). Iron supplementation for infants is indicated for pre-term or low birth weight infants, children whose diet does not include foods fortified with iron, or those with anemia. Iron supplementation for even marginally low birth weight infants reduces iron deficiency and anemia. However, iron can be toxic at doses not much higher than the therapeutic range and a meta-analysis of data currently available indicates that giving iron supplementation to children who are already iron replete can cause adverse effects on weight gain and possibly increased susceptibility to infection. Similarly, while iron deficiency is a common cause of anemia in pregnancy and can be prevented with supplementation, recent data suggest that iron supplementation in non-anemic pregnant women can cause increases in hypertension and small-for-gestational-age births.

Although it is commonly believed that older adults are at high risk for iron deficiency, results are mixed. Data from the Framingham Heart Study showed that elevated iron stores (evidenced by high serum ferritin) are four to five times more common than iron deficiency among white Americans aged 67 to 96 years. Similar results have been obtained in other countries. Because of known risks for heart disease and cancer attributable to excessive iron, older patients should be advised against taking iron supplements unless iron deficiency is documented by laboratory results.

Iron Food Sources (including fortified sources) See Appendix L.

Zinc

Forms and Absorption Zinc status is determined through a balance of absorption in the intestine (principally the jejunum) and secretion of endogenous reserves; zinc depletion increases the efficiency of its absorption. Zinc absorption is reduced in the presence of copper, iron, oxalate, calcium, phytate, and fiber. Once absorbed, zinc is widely distributed throughout the body, with the highest levels found in the prostate, skin, brain, liver, pancreas, bone, and blood.

Function Zinc plays an essential role:

as a cofactor for over 100 enzymes in carbohydrate, fat, and protein metabolism,

in normal cell division, growth, and repair at all stages of life, especially during fetal growth,

in the synthesis of DNA and RNA and in gene regulation,

in normal immune function including wound healing and skin integrity,

in sexual maturation, fertility, and reproduction,

in the maintenance of a normal sense of taste and smell.

Zinc Deficiency Zinc deficiency, which can occur due to poor intake or with malabsorption syndromes, can be manifested as symptoms of poor appetite, changes in taste perception, anosmia (loss of sense of smell), hair loss, skin problems, poor wound healing, impaired cell-mediated immunity, and growth retardation in infants, children, and adolescents. If affected, the cornea, which has a very high zinc concentration, may develop edema and opacification.

Zinc Toxicity Zinc toxicity is rare, but high intakes can cause diarrhea, nausea, and vomiting. Chronic toxicity can impair copper status, and may depress immune function. High doses of zinc have also been associated with urinary tract infections and other negative effects on the urinary tract. The importance of the relationship between zinc and copper is illustrated by the fact that patients with copper

overload from Wilson's disease benefit from treatment with 50 mg zinc acetate three times daily or more.

Zinc Requirements Individuals with intestinal resection or surgical removal of all or part of their intestines may require zinc supplementation, as both transit time and surface area influence zinc absorption. The TUL for zinc has been established at 40 mg/day.

Supplementation Issues Individuals who may benefit from zinc supplementation include:

those with malabsorption or chronic diarrhea,

vegetarians, due to lower efficiency of zinc absorption from plant material,

alcoholics, as alcohol inhibits zinc absorption and promotes excretion,

children who exhibit growth failure accompanied by zinc deficiency,

lactating women, as there is a greater need for zinc during this period,

those with chronic skin ulcers or bed sores,

those who smoke cigarettes heavily.

Zinc supplements should not be taken simultaneously with either calcium or iron supplements in the absence of food as these interfere with zinc absorption. Long-term high doses can cause copper deficiency, which produces white patches on brittle nails, anemia,

and weaken immune function. Doses exceeding 40 mg per day may interfere with white blood cell function. Zinc supplementation has been shown to significantly reduce the frequency and severity of childhood diarrhea and respiratory illnesses. A zinc supplement in conjunction with antioxidant vitamins has been shown to significantly reduce the risk of vision loss from age-related macular degeneration. A combination of trace mineral supplements (zinc, copper, and manganese) have been shown to be important in the maintenance of bone mass in post-menopausal women.

Copper

Form and Absorption Copper absorption occurs in the small intestine. Absorption is enhanced in an acidic medium and decreased by the presence of calcium, phytates, fiber, or zinc. About 30 to 50 percent of the copper in the diet is absorbed.

Functions Copper plays an essential role in:

production of skin, hair, and eye pigment (melanin),

synthesis of connective tissue (copper functions in the development of healthy bones, teeth, and vascular structures),

protection of cells from oxygen damage (as a component of antioxidant enzymes),

maintenance of the myelin sheath surrounding nerve fibers,

metabolism of catecholamines required in the functioning of the nervous system,

promotion of iron metabolization (anemia is a consequence of copper deficiency).

Copper Deficiency Copper deficiency is rare though it can occur in malnourished infants, and as a result of poor copper absorption that can occur in certain disease states (e.g., Menkes' syndrome). Copper deficiency results in anemia and connective tissue damage, which can cause lung damage or excessive bleeding. Low levels of copper in the blood are seen in nutritional disorders such as kwashiorkor, anemia, tropical sprue, and celiac disease.

Copper Toxicity Excessive copper intake or poisoning may occur with consumption of acidic beverages stored in containers made with copper. Symptoms of copper toxicity include nausea, diarrhea, vomiting, anemia, anuria, and, in extreme cases, death.

The genetic syndrome Wilson's disease results in increased copper deposits in the brain, kidney, cornea, and liver but with decreased blood copper levels. Untreated, it can result in nervous system and liver damage. The TUL for copper has been established at 10,000 μg/day.

Supplement Issues When taken as a supplement in older Americans, copper was

shown to increase the activity of copper metabolism enzymes and there was some evidence of a decrease in markers associated with CVD. Copper supplements may improve the effectiveness of vitamin D and calcium in improving bone density in post-menopausal women.

Sodium

Functions Sodium functions together with chloride to regulate hydration and cell membrane potentials. Sodium is the predominant extracellular cation.

Sodium Deficiency Sodium deficiency is uncommon. Most Americans consume 3000 to 4000 mg of sodium daily (about 9 g of table salt), while the recommended upper limit for daily intake is 2300 mg. Fluid retention or sodium loss can cause low serum sodium levels (hyponatremia) which may represent a relative deficiency of sodium. Prolonged vomiting, diarrhea, excessive or persistent sweating (such as in triathlon participants or marathon runners), and certain forms of kidney disease also cause sodium deficiency. A “salt-wasting” crisis can also occur as a consequence of insufficient aldosterone production, as seen in congenital adrenal hyperplasia. Symptoms of hyponatremia include headache, nausea, vomiting, muscle cramps, fainting, fatigue, and death.

Sodium Toxicity Excess serum sodium (hypernatremia) is generally caused by inadequate hydration rather than excess sodium intake. Symptoms of hypernatremia include vomiting, diarrhea, excess sweating, mental status changes due to cerebral edema, seizures, and death.

Relationship to Disease Prevention

Hypertension Hypertension affects about one in four adults or about 50 million Americans. It is a leading cause of stroke and can contribute to a heart attack, heart failure, and kidney failure. It is well-known that diets high in sodium are associated with a higher risk of developing hypertension in salt-sensitive populations. Studies, including the DASH trials, have shown that restricting sodium intake to below 1.2 g/day (<3 g of salt, sodium chloride) is effective in lowering systolic blood pressure by 6 to 9 mm Hg and can improve the action of certain medications, such as diuretics, in lowering blood pressure. However, other studies have reported that for the United States population mean intake, increases in sodium actually correlated with a decrease the risk of CVD and all-cause mortality, although a few studies of populations with high sodium intakes (4.4 to 5.4 g/day) showed reductions in CVD with salt restriction. Thus, health benefits from salt restriction may be limited to persons with

excessive intake or other conditions that alter risk.

Osteoporosis Because high salt intake has been shown to increase the amount of calcium excreted in the urine, lowering an individual's sodium intake may decrease the risk of osteoporosis. By decreasing salt intake, more calcium remains in the body thereby decreasing the risk for bone loss.

Sodium Food Sources See Appendix I.

Potassium

The predominant intracellular cation; even small changes in the concentration of extracellular potassium greatly affect the extracellular to intracellular potassium ratio and thereby affect neural transmission, muscle contraction, and vascular tone.

Function Potassium is an extremely important electrolyte that functions in the maintenance of:

water balance and distribution,

acid–base balance,

muscle and nerve cell function,

heart function,

kidney and adrenal function,

glycogen storage; low potassium suppresses insulin secretion.

Potassium Deficiency Hypokalemia (low levels of potassium in the blood), is most commonly a result of excess potassium losses. These losses can occur from vomiting, diarrhea, kidney disease, or metabolic disturbances, as well as sweat-producing exercise where potassium and electrolytes are not replenished. Thiazide diuretics (used in hypertension or congestive heart failure) or excessive use of laxatives can also cause hypokalemia (defined as a serum potassium level below 3.5 mmol/L). Because potassium is found mainly in fruits and non-grain vegetables, a diet lacking in these foods can lead to potassium deficiency. In potassium deficiency there may not be sufficient glycogen reserves, and muscle weakness progressing to respiratory failure can occur. Other symptoms include fatigue, constipation, impaired renal function resulting in excessive urination (polyuria), and adverse cardiac effects on persons taking digitalis. Severely low levels of potassium can lead to cardiac arrhythmias.

Potassium Toxicity Potassium toxicity is unlikely, except in patients with poor renal function or excessive supplementation. Hyperkalemia can be seen in trauma or severe burns that lead to significant tissue damage resulting in release of potassium into the blood. Symptoms of hyperkalemia include tingling in the hands and feet, muscle weakness, and temporary paralysis. Hyperkalemia causes

characteristic EKG changes and when severe, can lead to ventricular asystole or fibrillation. Left untreated, hyperkalemia can result in cardiac arrest. Near fatal hyperkalemia has been seen in people using a nutritional supplement or a salt substitute in combination with certain medications such as potassium-sparing diuretics.

Supplementation Issues Potassium helps to maintain proper function of both the heart and nervous system. Regular consumption of high-potassium foods or potassium supplements may help to lower and control blood pressure in people with a high salt intake. People with heart failure or high blood pressure benefit from adequate amounts of this mineral. An elevated potassium intake has also been linked to decreasing the risk of stroke, osteoporosis, and calcium-containing kidney stones.

Potassium Food Sources See Appendix J.

Selenium

Selenium is an essential trace mineral in the body that contributes to antioxidant defense mechanisms.

Form and Absorption Selenium absorption is efficient and is not regulated. Selenium in the form of selenocysteine and selenomethionine in the diet is absorbed in the gastrointestinal tract

in the range of 50 to 100 percent. Selenium leaves the body via urine, feces, skin, or pulmonary metabolites that are exhaled.

Functions

Selenium is an essential component of the enzyme glutathione peroxidase, which protects cells from the damaging effects of free radicals. For example, LDL oxidation is reduced by selenium.

Selenium is essential for normal functioning of the immune system and thyroid gland.

Epidemiological and animal studies have shown that selenium may have anti-cancer properties, possibly related to its antioxidant function.

While scientists have identified 25 selenium-containing proteins, the physiologic role is known for only half of them.

Selenium Deficiency Selenium deficiency is not common in the United States and seldom causes illness when it occurs in isolation. However, selenium deficiency has been seen in people maintained on total parenteral nutrition (TPN) as their only source of nutrition. People with gastrointestinal problems can have impairment of selenium absorption. Low selenium intake has been seen in children with kwashiorkor because selenium is absorbed only in amino acid form.

Signs of selenium deficiency are seen in countries where the selenium content in the soil is very low and therefore the selenium intake of domestic animals is poor. Selenium deficiency causes white muscle disease in livestock. These areas include China, New Zealand, and Venezuela. Furthermore, people living in areas of China, New Zealand, and Venezuela may develop an enlarged heart with poor cardiac function as a result of selenium deficiency. Lower selenium levels have been observed in both men and women with goiters but selenium supplementation did not improve thyroid hormone levels.

Selenium Toxicity Selenium toxicity is rare in the United States and the few reported cases have been associated with industrial accidents or from a manufacturing error that led to an excessively high dose of selenium in a supplement. High blood levels of selenium (selenosis) lead to symptoms including gastrointestinal upset, joint pain, hair loss, nail discoloration, and fatigue. Acute toxicity can lead to respiratory distress syndrome, myocardial infarction, and renal failure. The TUL established for selenium is 400 µg/day.

Supplement Issues Most cases of selenium deficiency occur as a consequence of a gastroenterological disturbance, such as Crohn's disease. Preliminary studies have shown a correlation between low plasma

selenium levels and cancer risk. Selenium is being studied for its possible role in prostate cancer prevention. The Selenium and Vitamin E Cancer Prevention Trial (SELECT) is a phase III randomized, placebo-controlled trial of selenium (200 μg/day) and/or vitamin E (400 IU/day) supplementation for a minimum of 7 years (maximum of 12 years) in American men 50 years of age and older. Selenium supplementation did not decrease the incidence of prostate cancer in men with an increased risk of the disease. The Nutritional Prevention of Cancer study has reported that selenium supplementation is associated with reduced risk of colorectal cancer and adenomas in subjects with a low baseline selenium level. Despite concerns raised by earlier reports, supplementation with selenium has not been shown to increase the risk of type 2 diabetes. Selenium supplementation has been shown to decrease the risk of premature rupture of membranes in pregnant women.

Fluoride

Fluoride is found at varying concentrations in drinking water and soil. It is not an essential nutrient in the customary sense, but helps protect the teeth against dental caries. Although found in bone, fluoride has not convincingly been shown to prevent fractures or osteoporosis. About 99 percent of the fluoride in the body is in the bone and teeth. When

fluoride is consumed in optimal amounts from water and food, or used topically in toothpastes, mouth rinses, and professionally applied office treatments it functions to:

increase tooth mineralization and bone density,

reduce the risk and prevalence of dental caries,

promote enamel re-mineralization throughout life for individuals of all ages.

Fluoride Deficiency As there is no known metabolic function for fluoride, a deficiency state cannot be defined.

Water Fluoridation Fluoridation of public water supplies has been endorsed by over 90 health professional organizations as the most effective dental public health measure in existence. Still, about half of the United States population fails to receive the maximum benefits possible from community water fluoridation and the use of fluoride products. Although fluoride treatment has long been recognized as being of benefit to children, a recent meta-analysis indicated that fluoride also causes significant reduction in dental caries in adults of all ages.

Fluoride Toxicity Fluoride can be toxic when consumed in excessive amounts, so concentrated fluoride products should be used with caution. To prevent the possibility of acute fluoride poisoning, fluoride products should be kept out of reach of small children. Fluorosis

results from excessive fluoride ingestion prior to tooth eruption and results in a disruption of tooth enamel formation. Fluorosis can range from mild to severe. In cases of mild fluorosis, teeth are highly resistant to dental caries but may have chalky white spots or patches. Severe fluorosis can result in teeth with brown discoloration and is most often seen in areas of the country that have excessive concentrations of natural fluoride in water supplies, such as wells.

Swallowing of fluoride toothpaste in early years, misuse of dietary fluoride supplements, or long-term use of infant formula (when concentrates are reconstituted with fluoridated water) can lead to fluorosis. To minimize the risk of excessive exposure, the American Dental Association requires toothpaste manufacturers to include the phrase “use only a pea-sized amount (of toothpaste) for children under six” on labels.

Supplement Issues Fluoride supplementation may benefit children and adults who do not have fluoride added to their public drinking water. The addition of both fluoride and probiotic bacteria to milk significantly reduced dental caries and ear infections in young children.

Fluoride Sources The primary dietary source of fluoride is fluoridated water. The average child under age 6 consumes less than half a liter

of water a day and would consume less than 0.5 mg/day of fluoride from drinking optimally fluoridated water. The TUL for infants 0 to 6 months is 0.7 mg/day and 1.3 mg/day for children aged 1–3 years.

Iodine

Iodine is essential for humans as a component of thyroid hormones (thyroxine). Approximately 40 percent of the body's iodine is stored in the thyroid gland.

Forms and Absorption Iodine in nature is found mostly as a salt in the iodide form. It is absorbed in the gastrointestinal tract in the ionized form (I^-). Extra iodine in the body is excreted via the urine.

Iodine Deficiency If there is not enough iodine in the body, there is a decrease in the production of the thyroid hormones (T_3 and T_4). To compensate for this lack of production the thyroid gland hypertrophies causing a goiter. Symptoms of iodine deficiency include lethargy, dry skin, thick lips, enlarged tongue, reduced muscle and skeletal growth, and mental retardation (cretinism). Currently 40% of the world's population is felt to be at risk of iodine deficiency. Risk factors other than deficient intake include pregnancy, excessive tobacco or alcohol consumption, oral contraceptive use, excessive calcium intake or

selenium deficiency, or exposure to radiation, perchlorates, or thiocyanates.

Iodine Toxicity Excessive dietary intake of iodine results in inhibition of thyroid hormone synthesis. Generally, the body will adapt to the higher intake, but a few individuals will develop goiters due to reduced iodine absorption when iodine blood levels are too high. The TUL for iodine has been established at 1100 μg/day.

Supplement Issues Iodine deficiency affects 1.9 billion people worldwide, and is a common worldwide cause of endemic goiter and cretinism in children who do not have access to iodized salt or live in mountainous places where iodine is not found. Newborns can experience maternal, fetal, or combined hypothyroidism. Congenital hypothyroidism has been reported to occur at a rate of about one out of every 4000 children and early treatment with iodine is necessary to avoid mental retardation. Iodide supplements have been shown to prevent goiter and to produce an increase in height and weight and to advance pubertal development. Many people are interested in potassium iodide supplements to prevent radioactive iodine uptake in the event of a nuclear accident or after exposure to medical radiation. Supplementation with iodine has been shown to be effective in reducing the risk of an iodine-deficient child developing thyroid cancer

after exposure to radiation from an accidental contamination or from medical procedures.

Chromium

Chromium is proposed to potentiate the action of insulin and has been identified as a "glucose tolerance factor."

Form and Absorption Chromium exists in various inorganic forms; most chromium found in food is in the trivalent chromium(III) form. Chromium absorption depends on the form and physiochemical reactions in the intestinal lumen, but generally the efficiency of absorption is low (<3 percent). Fiber and phytates reduce absorption and a deficient diet results in higher fractional absorption rates.

Functions Chromium is hypothesized to potentiate the action of insulin via an oligopeptide that has been named "chromodulin," which binds to the insulin receptor stimulating its tyrosine kinase activity.

Chromium Deficiency A diet high in refined grains and simple sugars promotes chromium excretion and may lead to long-term chromium deficits. Since it is not possible to determine chromium status, it is difficult to determine the impact of low chromium intake.

Chromium Toxicity As no adverse effects have been observed from excess chromium intake from food, no TUL has been established.

The predominant form of chromium in food and supplements is the trivalent form (Cr^{3+}), which is not believed to have toxic effects. However, hexavalent chromium at high levels in drinking water in a Chinese province is believed to be responsible for increased mortality from stomach cancer, creating concerns about the overuse of chromium supplements. A meta-analysis reported that hexavalent chromium was only weakly linked to lung cancer and not to any other cancers.

Supplement Issues In diabetic subjects, chromium supplementation, usually with chromium picolinate or chloride, has been shown to improve insulin sensitivity and to reduce serum lipids in some, but not all, studies. When diabetic subjects were divided into groups based on sensitivity to insulin, it was observed that chromium supplements increased the response to insulin in the group that was previously shown to be insulin resistant. In the group of diabetics that responded to chromium, there was a decrease in fasting blood glucose, cholesterol, and low density lipoprotein (LDL). These responses varied with the form of chromium supplement: chromium dinicocysteinate and a yeast supplement enriched with chromium were shown to be more effective than chromium picolinate. A recent review of 41 separate studies concluded that while chromium supplementation in patients with type 2

diabetes had a modest beneficial effect on glycemia and dyslipidemia, the overall poor quality of the studies limited the strength of the conclusion. Unfortunately, much of the older literature used supplements of CrCl which is not very biologically active and those using yeast sources were dosed at only 200 μg of chromium daily. More recent studies using more bioavailable chromium (chromium bound to niacin or biotin) and in doses closer to 1000 mg daily have been shown to have improved efficacy. These higher levels may be appropriate given recent research documenting a relationship between urinary chromium losses and degree of insulin resistance. Different chromium preparations may also have different effects, for example, when chromium picolinate was given to obese adults considered to be at risk for diabetes, there was no change in insulin sensitivity. A similar study in overweight children did demonstrate improved insulin sensitivity. HIV infection produces numerous metabolic changes and in HIV infected patients, chromium supplementation decreased insulin resistance and produced improvements in triglycerides and body fat. The Office of Dietary Supplements of the NIH has concluded that "the value of chromium supplements for diabetics is inconclusive and controversial."

Case 1 Iron Deficiency Anemia in Women

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Objectives

Describe the prevalence of and risk factors for iron deficiency in United States women.

Recognize signs and symptoms of iron deficiency.

Evaluate and interpret laboratory values used to diagnose iron deficiency.

Become familiar with methods for prevention and treatment of iron deficiency.

AP, a 36-year-old Chinese American woman, presents to her family physician complaining of fatigue lasting over the past year and of "always being cold." One year ago, she gave birth to a full-term healthy baby. She initially assumed her symptoms were due to the demands of caring for her infant, but reports that her fatigue is much greater in severity than that

experienced after delivering her first child 7 years ago. She was an avid runner throughout her adult years, but has been unable to run even a mile over the past few months due to the overwhelming fatigue. She feels a lack of energy throughout the day, and has difficulty focusing while at work.

AP has a history of heavy menses; she typically uses more than five sanitary pads on each of the first 2 days of her period, which lasts 7 days. She resumed menstruating 4 months after giving birth. She occasionally has small amounts of blood in her stool from hemorrhoids, but has not had any frank gastrointestinal bleeding and denies other sources of blood loss.

Past Medical History

AP has a recent history of iron deficiency anemia. At 6 months' gestation, routine hemoglobin screening revealed a normal value of 12.5 g/dL. One month after giving birth, AP's hemoglobin was tested by her gynecologist, revealing a significantly reduced level of 7.4 g/dL. Iron deficiency anemia was suspected. Her laboratory results confirmed the diagnosis and AP's gynecologist prescribed ferrous sulfate (325 mg, three times per day) for 6 months. Unfortunately, AP found that the iron supplements caused constipation and abdominal pain. She discontinued them and began taking a multivitamin containing iron.

Diet History

AP avoids red meat due to its saturated fat content, and eats chicken and fish at least once a week. In an effort to increase the calcium in her diet, she generally tries to eat a dairy food at each meal: milk with cereal for breakfast, yogurt and fruit at lunch, and cheese with pasta or in a casserole for dinner. She obtains most of her vegetable intake from salads containing lettuce, cucumbers, and tomatoes. She does not each much fruit.

Physical Examination

Vital Signs

Temperature: 98.6 °F (37 °C)

Heart rate: 80 BPM

Respiration: 26 BPM

Blood pressure: 110/60 mm Hg

Height: 5′8″ (173 cm)

Current weight: 145 lb (65.8 kg)

BMI: 24 kg/m^2

Exam

General: Well-developed, well-nourished female in no acute distress

Skin: Pallor

Eyes: Conjunctiva pale

Nails: No spoon nails

Laboratory Data

Current Labs	Normal Values
Hemoglobin: 9.5 mg/dL	12–16 g/dL
Hematocrit: 35%	37–48%
MCV: 82 fL	86–98 fL
Ferritin (serum): 7 ng/mL	Females: 12–150 ng/mL
Iron (serum): 40 µg/dL	50–150 µg/dL
TIBC: 425 µg/dL	250–370 µg/dL

Case Questions

What are the prevalence of, and risk factors for, iron deficiency anemia in pre-menopausal women in the United States?

What are the clinical signs and symptoms of iron deficiency?

How was the diagnosis of iron deficiency anemia confirmed in this patient?

What diet history questions should be asked of patients suspected of iron deficiency? How would you counsel this patient to improve her dietary iron intake and absorption?

Who should be screened for iron deficiency and when?

How should iron deficiency be treated?

What aspects of iron metabolism are important to remember for patient care?

Answers to Questions: Case 1

Part 1: Prevalence and Diagnosis

1. What are the prevalence of, and risk factors for, iron deficiency anemia in pre-menopausal women in the United States?

Iron deficiency is a fairly prevalent problem in pre-menopausal women. According to the NHANES III data (1994–1998), 5 percent of women aged 20 to 49 have iron deficiency anemia, and 11 percent have iron deficiency without anemia. The prevalence of iron deficiency was similar in NHANES III and NHANES 1999–2000 in most age and sex groups, but newer data from NHANES 2003–2006 found that the prevalence of iron deficiency without anemia had increased to 12 percent among females age 20 to 49.

Risk for iron deficiency is a function of levels of iron loss, iron intake, iron absorption, and physiologic demands. Populations most at risk include pregnant women, women of child-bearing age, and women with heavy

menses. Other populations at risk include strict vegetarians and vegans, infants, toddlers, and adolescents. Low iron intake and decreased iron absorption are the most common etiologies.

Women in their child-bearing years have greater iron needs than men due to menstrual blood losses, iron demands of the developing fetus during pregnancy, and blood loss during childbirth. Uterine fibroids (common, benign tumors often found in women of child-bearing age) may cause heavy and prolonged menses, resulting in increased blood loss. In order to avoid the development of iron deficiency during this time, dietary iron intake must keep pace with increased demands. Those not consuming adequate quantities of iron-rich foods may develop iron deficiency.

Iron deficiency in women (and in men) may also be caused by other sources of blood loss including frequent blood donation, gastrointestinal bleeding, neoplasms, inflammatory bowel disease, parasitic infections (more common in third world populations than developed countries), and hemorrhoids. Chronic blood loss may occur from the urinary tract as well. In this case, AP's heavy menstrual periods and aspects of her dietary intake increase her risk for iron deficiency. Occasional bleeding from hemorrhoids is most likely not a contributing factor.

2. What are the clinical signs and symptoms of iron deficiency?

Clinical signs of anemia include pallor, mouth changes such as glossitis (atrophy of the lingual papillae), and angular stomatitis, as well as tachycardia. Symptoms are generally non-specific and may include fatigue, palpitations, or dyspnea. When prolonged, iron deficiency can lead to softening of the nail matrix causing koilonychia or spoon nail deformity. Fatigue is a common presentation of iron deficiency with or without anemia. Iron is necessary for hemoglobin synthesis in red blood cells, which functions in oxygen transport and delivery from the lungs to the tissues. Iron deficiency can lead to fatigue as oxygen is needed for energy (ATP) production. In addition, iron serves as a cofactor for many physiologically important enzymes, including those involved in oxidative metabolism, dopamine, DNA synthesis, and free radical formation in neutrophils.

Iron deficiency may cause a sensation of feeling cold, affect work capacity and exercise tolerance, reduce neurotransmitter function, and diminish immunologic and inflammatory defenses presumably due to a lack of oxygen needed for energy and heat production. Other symptoms of iron deficiency include cold intolerance, and pica (compulsive eating of non-food items typically clay or laundry starch)

or pagophagia (compulsive eating of ice). Patients having any of these signs and symptoms should receive a laboratory evaluation for iron deficiency.

3. How was the diagnosis of iron deficiency anemia confirmed in this patient?

Laboratory evaluation along with physical signs and symptoms can confirm a diagnosis of iron deficiency. Serum ferritin, iron, and total iron binding capacity (TIBC) were outside the normal reference range. A complete blood count revealed a microcytic anemia with a low mean corpuscular volume (MCV) of 82 fL. In this patient, serum ferritin was low at 7 ng/mL. Serum iron was low at 40 µg/dL, and TIBC was high at 425 µg/dL (the TIBC, or transferrin, concentration increases to compensate for low iron availability), confirming the diagnosis of iron deficiency. The patient's hemoglobin, hematocrit, and MCV were low, indicating a microcytic anemia, and reticulocyte count was low, indicating decreased red blood cell production.

Serum ferritin is the single best non-invasive, sensitive marker of iron status. Serum ferritin concentrations reflect body iron stores (1 µg/L of serum ferritin concentration is equivalent to approximately 10 mg of stored iron). Compared to the gold standard of a bone marrow biopsy, serum ferritin is a sensitive and

specific indicator of iron depletion. Levels below 15 mg/mL are 75 percent sensitive and 98 percent specific for iron deficiency. However, because serum ferritin is an acute phase reactant, chronic infection, inflammation, or diseases causing tissue and organ damage can raise its concentration independent of iron status, masking depleted tissue stores of iron.

Transferrin saturation (which is equivalent to serum iron concentration divided by TIBC × 100) reflects the extent to which iron binding sites are vacant on transferrin. It is another commonly used measure to assess iron deficiency. Normal saturation falls between 30 and 35 percent, whereas levels less than 15 percent indicate decreased iron availability for erythropoiesis in the bone marrow.

Overall, this measure does not perform as well as ferritin among non-pregnant women of childbearing age. As with ferritin measurements, factors other than iron status can affect results of this test. Serum iron varies diurnally (higher in the a.m., lower in the p.m.), increases after meals, and is decreased by infection and inflammation. Inflammation, chronic infection, malignancies, liver disease, nephrotic syndrome, and malnutrition can reduce TIBC, and oral contraceptive use and pregnancy can increase it.

Erythrocyte protoporphyrin concentration can also be used to assess whether adequate iron is available for red blood cell synthesis. Protoporphyrin levels remain elevated when there is inadequate iron available to be integrated into hemoglobin. Normal protoporphyrin levels vary from 16 to 65 μg/dL in adults but with iron deficiency, anemia levels may exceed 100 μg/dL.

Iron deficiency often exists without anemia, but deficiency without anemia will progress to anemia if the causes of deficiency are not corrected. Red blood cells are typically microcytic (small), due to insufficient hemoglobin production, and hypochromic (pale). In addition, reticulocyte counts (the number of new red blood cells), are low indicating decreased bone marrow production of red blood cells.

In the presence of an inflammatory or infectious state, when iron deficiency risk factors or symptoms of iron deficiency are present but ferritin is in the normal range, a complete blood count (CBC) and a reticulocyte count may be quite helpful. If iron deficiency is indeed present, erythrocyte indices (e.g., MCV) should improve with iron administration, and a therapeutic trial of supplementation will help to confirm or rule out iron deficiency.

Part 2: Medical Nutrition Therapy and Treatment

4. What diet history questions should be asked of patients suspected of iron deficiency? How would you counsel this patient to improve her dietary iron intake and absorption?

Sources of dietary iron include red meat, poultry, fish and shellfish, nuts and seeds, legumes and bean products, green leafy vegetables, raisins, whole grains, and fortified cereals. In evaluating a patient for iron deficiency, the clinician should inquire about dietary intake of iron-rich foods, as well as dietary factors that may influence the absorption of iron (e.g., low vitamin C intake). Ascorbic acid (vitamin C) can reduce ferric iron to its more soluble ferrous form, which decreases the formation of insoluble complexes. Thus, ascorbic acid can enhance iron absorption by forming soluble complexes with iron at low pH that remains soluble in the more alkaline environment of the duodenum.

Iron absorption is not directly correlated to iron intake. As physiologic iron levels decrease, the efficiency of gastrointestinal absorption of iron increases. The bioavailability of iron, or the percentage of dietary iron absorbed and ultimately physiologically available, varies depending on the dietary source of the iron and other foods consumed at the same time as the

iron-containing foods. Heme (dietary iron attached to heme-containing proteins, such as myoglobin or hemoglobin) and non-heme iron are absorbed by different receptors on the intestinal mucosa. Iron bound to heme is highly absorbable and represents 40 percent of iron from animal sources. The absorption of non-heme iron can be increased or decreased by various factors. Phytates, or inositol phosphate salts that store minerals in plant matter, bind to iron in the lumen of the intestine and decrease its absorption. Polyphenols in tea, coffee, cocoa, spinach, and oregano inhibit iron absorption as well.

Iron is best absorbed in its ferrous form, and thus ascorbic acid in fruits, vegetables, and fortified cereals increases iron absorption. Calcium inhibits the absorption of both heme and non-heme iron by an unknown mechanism, and epidemiologic studies show a correlation between intake of milk and the prevalence of iron deficiency. Thus, it is important for patients to also be asked about their intake of dairy foods. Those eating dairy foods or taking a calcium supplement or calcium-containing antacids at each meal may have lower iron absorption.

One of the easiest ways for AP to increase her dietary iron would be to add red meat to her diet at least on a weekly basis, and to increase her consumption of chicken. She could also be

counseled to eat iron-rich grains and vegetables at two meals a day with fruits, and she may be advised to eat iron fortified foods such as oatmeal or breakfast cereal.

5. Who should be screened for iron deficiency and when?

Current screening recommendations are being reviewed by the United States Preventive Services Task Force (USPSTF), but currently the recommendations are to screen routinely for iron deficiency anemia in asymptomatic pregnant women. Insufficient evidence exists for or against routine screening in asymptomatic children aged 6 to 12 months. Routine screening is not recommended for any other groups (e.g., menstruating women).

6. How should iron deficiency be treated?

A ferritin level of less than 12 ng/mL in women is indicative of sub-optimal iron stores, and patients with levels in this range should receive a course of replacement therapy. Iron is best absorbed in its ferrous form, and ferrous salts of iron are generally used for oral supplementation. Ferrous sulfate, succinate, lactate, fumarate, glycine sulfate, glutamate, and gluconate are all about equally well-absorbed and tolerated. Standard doses are 60 mg of oral elemental iron twice daily. Vitamin C taken concurrently with the iron will

increase absorption. Constipation and gastrointestinal distress are common side effects of oral iron supplementation. When these symptoms occur, the dose should be reduced by one-half but continued. Enteric-coated or delayed-release preparations should not be used; with these preparations iron is released distally in the small intestine or in the colon where it is not well absorbed. Stool softeners may also be prescribed.

Parenteral iron therapy, which is administered via intramuscular or intravenous routes, may be required in patients with severe malabsorption, ongoing blood loss, those requiring chronic hemodialysis, and those who are unable to tolerate oral iron. Iron dextran is the most widely available parenteral form and contains 50 mg/mL of elemental iron. However, there are multiple serious side effects associated with parenteral iron including muscle necrosis, phlebitis, and in rare cases, anaphylaxis. The most serious side effect of parenteral iron is anaphylaxis, which occurs in less than 1 percent of treated patients. Because of this risk, small test doses (25 mg of iron dextran) should be administered and the patient should be observed in a controlled setting for 1 hour before full doses are administered for the first time.

With iron dextran, a delayed reaction can be seen 24 to 48 hours after administration and

can include symptoms such as wheezing, dyspnea, arthralgias, myalgias, hypotension, chills, dizziness, fevers, headache, malaise, or nausea and vomiting. Symptoms generally subside within a week. This syndrome is most common in settings where a total replacement dose is administered during a single infusion and is less likely if smaller doses are administered on separate occasions. Intramuscular administration of iron dextran may cause local skin site reactions and potentially carry a risk of carcinogenesis at the injection site and are not recommended. Other intravenous preparations such as iron sucrose, iron saccharate, and sodium ferric gluconate are commonly used in Europe and may be better tolerated than iron dextran.

A 3- month course of oral therapy is recommended for the treatment of iron deficiency. In the presence of anemia, reticulocyte counts will begin to rise after a few days of supplementation and will peak in approximately 7 days. Hemoglobin will begin to rise after 10 to 14 days, and will generally normalize in 2 months. Some hematologists recommend continuing supplementation for 6 to 12 months. However, as iron status improves, a lower proportion of the supplement dose is absorbed and the benefits of supplementation are thus reduced as the course of therapy is lengthened. During therapy,

patients should be monitored carefully for adherence because side effects are common.

During the course of supplementation, patients should be advised about diets that are higher in iron-containing foods and given advice on optimizing their iron absorption. Patients with sources of ongoing physiologic blood loss, such as heavy menses, may require continuous low-dose supplementation, such as an iron-containing multivitamin, after a full course of supplementation is complete. Any correctable causes of blood loss should be addressed while replacement therapy is administered. In situations such as this case, when heavy menses are the most likely cause of iron deficiency, low-dose oral contraceptives may be helpful to reduce menstrual flow.

If the anemia does not correct with iron supplementation, several causes must be considered, including:

Impaired absorption (may be seen with celiac disease, malabsorptive disease, or concomitant use of binders).

Poor adherence due to side effects.

Excess iron loss or increased need.

Thalassemia.

7. What aspects of iron metabolism are important to remember for patient care?

The normal total circulating iron pool is 3 to 4 mg. Iron is transported in plasma bound to transferrin. Normally, plasma transferrin is 30 to 40 percent saturated by iron. The iron pool remains stable despite variation in iron stores, suggesting that iron release from macrophages is determined by tissue uptake. Kupffer cells in the liver recycle heme iron from senescent red blood cells back to transferrin. The mechanisms controlling macrophage iron output are unclear, but likely involve plasma erythropoietin-mediated increased generation of unsaturated transferrin that causes greater iron extraction from macrophages. In iron deficiency, elevated transferrin levels maintain the circulating iron pool despite the marked decrease in transferrin saturation. In iron-overload, serum iron levels are high, circulating transferrin levels are low, and increased transferrin saturation is found. During inflammatory states (including end-stage renal disease), circulating transferrin levels decrease, but transferrin saturation is normal because of iron release from the reticuloendothelial system.

Because of the importance of iron to various infectious agents, iron is closely controlled in the human body. Most iron binding proteins are acute phase reactants, meaning that during infection, their production is increased. This helps the body to reduce the availability of iron to the infectious agent. A recently discovered

hormone, hepcidin, plays a central role in controlling iron absorption and hepcidin levels are influenced by inflammatory markers such as interleukin (IL)-6 and 22 and type 1 interferon.

Case 2 Drug–Herb Interaction with St. John's Wort

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Objectives

Describe the hypothesized mechanism of action and metabolism of St. John's Wort.

Evaluate the safety and efficacy of St. John's Wort for the treatment of depression.

Provide effective dietary counseling for patients on warfarin therapy.

Recognize the importance of quality control when recommending over-the-counter dietary and herbal supplements.

Recognize the potential for toxicity and drug–herb interaction with St. John's Wort and other commonly used botanicals.

LB is a 54-year-old Caucasian woman who was in good health until 2 weeks ago when she developed acute shortness of breath and palpitations while driving to work. On arrival in the emergency room she was found to have atrial fibrillation with a rapid ventricular response. She was admitted to the cardiac intensive care unit and treated with beta-blockers to slow down her heart rate. She was also started on intramuscular and then anticoagulants to reduce her risk of stroke. She was discharged on the fourth hospital day and came to see her primary care provider for management of her warfarin anticoagulation 1 week post-hospital discharge. LB had been on a warfarin dose of 3 mg/day, and at discharge, had an International Normalized Ratio (INR) of 2.6. At the 1 week post-hospital discharge visit, her INR was sub-therapeutic at 1.2. She denied any changes in medication or diet, and has not "any recent antibiotic exposure."

Upon further questioning, LB admitted taking some over-the-counter dietary supplements. She currently takes vitamin E (400 IU) once daily as a "cardioprotective antioxidant," calcium carbonate (500 mg) twice per day for bone health, and St. John's Wort (300 mg) twice per day. She stated that she started St. John's Wort 3 weeks ago because a friend told her it might help "lift her spirits". She has no known food or drug allergies.

Past Medical History

LB has a history of mild hypertension which she controls primarily with hydrochlorothiazide (HCTZ) and a sodium-restricted diet. She also has a history of mild depression, which she attributes to being perimenopausal. She has never had an episode of major depression or psychiatric hospitalization and has never been treated with prescription anti-depressants. She denies any thoughts of suicide.

Medications

Warfarin (oumadin): 3 mg at bedtime

HCTZ: 25 mg once daily in the morning

Atenolol: 50 mg daily – started in the hospital

Social History

LB lives with her husband and their two cats. Her children are grown and in college. She explains that she has not been feeling like herself since the hospitalization. She often awakens during the night and has a difficult time going back to sleep. She still enjoys playing bridge and gardening but describes herself as frequently distracted and occasionally “blue”. She avoids alcohol and tobacco and drinks one cup of coffee daily.

Review of Systems

General: She reports losing 5 pounds since her hospital admission

GI: Poor appetite

Pulmonary: no shortness of breath or cough

Cardiovascular: no dyspnea on exertion, no palpitations

Physical Examination

Vital Signs

Temperature: 98.6 °F (37 °C)

Heart rate: 64 BPM

Respiration: 16 BPM

Blood pressure: 118/84 mmHg

Height: 5′4″ (152.4 cm)

Current weight: 150 lb (68.04 kg)

Usual weight: 155 lb (70.31 kg)

BMI: 25.7 kg/m^2

Exam

General: Well-developed, well-nourished woman in no apparent distress

Skin: Warm and dry

HEENT: Within normal limits

Cardiac: Irregular radial pulse. Normal S1 & S2 without S3 or S4

Abdomen: Soft, non-tender, non-distended

Extremities: No clubbing, cyanosis, or edema

Neurologic mental status exam: Alert and oriented to person, place, and time with slightly depressed affect. Sensory and motor exams are grossly intact

Laboratory Data

Patient's Lab Values	**Normal Values**
Prothrombin time: 13.4 seconds	<13 seconds
International normalized ratio (INR): 1.2	*
Thyroid stimulating hormone (TSH): 3.1 μU/mL	0.5–5.0 μU/mL

*Target therapeutic range for patients being anti-coagulated with warfarin is 2–3 for stroke prevention in atrial fibrillation.

Case Questions

What is known about the mechanism of action and metabolism of St. John's Wort?

What safety issues are of concern for patients taking St. John's Wort alone or in combination with other drugs?

Is St. John's Wort effective in the treatment of depression?

What issues related to product quality are important to consider when assessing over-the-counter dietary supplements?

Based on LB's depression, what treatment recommendations would be appropriate for LB at this time?

What dietary advice should be provided to all patients on warfarin (anticoagulant) therapy?

Answers to Questions: Case 2

Part 1: Mechanisms of Action and Safety

1. What is known about the mechanism of action and metabolism of St. John's Wort?

St. John's Wort (SJW), also known as *Hypericum perforatum*, is one of the most commonly used herbal remedies in the Western world. Extracts of this popular botanical have been used since the early nineteenth century to treat mood disorders. The exact mechanism of action of SJW remains largely unknown, but

like many herbs it is involved in multiple metabolic pathways due to its several constituents. A number of early studies suggested that *Hypericum* inhibits monoamineoxidase (MAO), an enzyme involved with the breakdown of some neurotransmitters that influence mood. Other postulated mechanisms from animal studies suggest the inhibition of serotonin reuptake, the downregulation of serotonin receptors, and inhibition of gama-aminobutyric acid (GABA) pathways.

St. John's Wort's major active constituents are thought to be hypericin and hyperforin. Hypericin has anti-viral properties, while hyperforin seems to be an active anti-depressant. Hyperforin has been shown to inhibit the uptake of serotonin, dopamine, noradrenaline, GABA, and glutamate. However, even hyperforin-free extracts of SJW have anti-depressant effects, hence other ingredients are likely involved.

Metabolism of SJW constituents is especially relevant because of potential toxicity and drug–herb interaction. In a study of the action of *Hypericum* on human cytochrome P450 activity, it was found that long-term administration in humans resulted in a significant and selective induction of CYP3A4 and CYP2C9 activity in the intestinal wall. CYP3A4 is one subtype of the many cytochrome

P450 enzymes that help to detoxify and metabolize drugs. If an herbal supplement induces one of these enzymes, then other drugs may be metabolized faster. If an herbal supplement inhibits this enzyme, then the functional level of other drugs may rise and cause toxicity. In this case, blood levels of drugs metabolized by this enzyme, such as cyclosporine, digoxin, warfarin, theophylline, and protease inhibitors (antiretrovirals) can be expected to fall during short- and long-term intake of SJW.

2. What safety issues are of concern for patients taking St. John's Wort alone or in combination with other drugs?

When used in monotherapy at doses up to 900 mg/day, SJW has been shown to be safe with a better side-effect profile compared to prescription anti-depressant agents. One study found that 3 percent of SJW-treated patients experienced significant side effects (gastrointestinal irritation, dizziness, confusion, tiredness, and restlessness) compared to 16 percent in the imipramine group. In a multicenter trial involving 340 subjects, 900 mg of SJW caused more anorgasmia and frequent urination compared to placebo, but SJW caused fewer side effects compared to 50 to 100 mg of sertraline. Importantly, a systematic review of clinical trials involving SJW concluded that this herb can decrease the

bioavailability of several conventional drugs if taken at the same time.

Relevant to this patient, SJW can reduce the efficacy of warfarin and thus lead to inadequate anticoagulation. This might increase the risk of thromboembolic complications in patients with atrial fibrillation. Thus, while LB was previously therapeutically anticoagulated on a 3 mg dose of warfarin, her recent daily use of SJW has likely caused her INR to be sub-therapeutic, thereby possibly increasing her risk of stroke.

When used in combination with other drugs, SJW can cause clinically significant toxicities related to the upregulation of CYP3A4. As a result, there are several reports of transplanted organ rejection related to concomitant use of SJW and cyclosporine. Additionally, SJW can reduce the levels of digoxin, often used to treat patients with heart failure or for rate control in atrial fibrillation. These are just some of the examples of possible drug–herb interactions. Table 2-4 lists other drug–herb interactions for commonly used botanicals.

Table 2-4 Selected Drug–Herb Interactions

Botanical	Common Usage	Drug/Drug Class	Potential Interaction
Green tea extract	Antioxidant	Warfarin	Decreased drug activity
Kava	Anxiety	Benzodiazepines	Additive sedative effect. Kava has recently (2004) been related to possible hepatotoxicity
Valerian	Insomnia	Barbituates	Additive sedative effect
St. John's Wort	Depression	Cyclosporine digoxin, warfarin, indanavir, oral contraceptives, amitryptiline, theophylline	Decreased drug activity
St. John's Wort	Depression	SSRIs	Increased drug activity
St. John's Wort	Depression	Oral contraceptives	Intermenstrual bleeding
Echinacea	Immune stimulant	Immunomodulatory drugs (prednisone, Methotrexate, Cyclosporine)	Decreased drug activity
Garlic	Hypercholesterolemia	Warfarin	Decreased drug activity
Gingko	Memory enhancement	Warfarin, aspirin	Increased risk of bleeding
Panax Ginseng	Increase well-being	Warfarin	Decreased drug activity
Panax Ginseng	Increase well-being	Hypoglycemic drugs	Enhanced drug activity
Yohimbine	Increase libido	TCA	Hypertension
Ephedra	Weight loss/energy	Antihypertensives	Decreased drug activity
Cranberry Juice	Reduce urinary tract infection	Warfarin	Possibly potentates anticoagulant action of Warfarin

Source: Adapted from *Guide to Natural Products*. 2nd edition (DerMarderosian A, editor) Facts & Comparisons, St. Louis MO. 2001 (Reprinted with permission).

Part 2: Treatment and Recommendations

3. Is St. John's Wort effective in the treatment of depression?

There are numerous randomized, placebo-controlled trials evaluating the safety and efficacy of SJW in treating mild to moderate depression and more recently, major depressive disorders. SJW has been compared with tricyclic anti-depressants (amitryptilline, imipramine) and with two SSRIs, fluoxetine and sertraline. The majority of placebo-controlled studies have shown that standardized extracts of SJW ranging from 300 to 900 mg daily are moderately effective in the treatment of mild-to-moderate depressive

symptoms. Some studies have shown equivalence of 900 mg of SJW to low-dose imipramine and low-dose fluoxetine. A study of patients with major depression failed to show significant improvement over both placebo and standard doses of sertraline over a short period of time. Differences in study design (lack of active control and placebo), study populations (major vs mild/moderate depression), length of time, and dosing of SJW or comparator agents are likely responsible for some of the variance in results. However, the authors state that over long periods of time, both SJW and sertraline were equally effective. The data supports SJW as a potential alternative treatment for depression when taken at low doses and when drug interactions are not of concern.

4. What issues related to the product quality are important to consider when assessing over-the-counter dietary supplements?

The Dietary Supplement and Health Education Act (DSHEA) of 1994 created a new class of compounds called “dietary supplements” that are not required to meet the same regulatory scrutiny as prescription pharmacologic agents. As a result of DSHEA, herbal remedies marketed as dietary supplements cannot make claims that their products can be used to “diagnose, prevent, mitigate, treat, or cure a specific disease”. DSHEA thus led to a marked

increase in the availability and popularity of dietary supplements in the United States. While DSHEA required that botanicals be labeled with the parts of the plant used and the strength of its ingredients, many herbal products have been found to contain less or none of the proposed active compounds. This stems in part from the complexity of herbal preparations, which can contain several potentially bioactive constituents. The strength and potency of an herbal extract can depend, among other things, on the time of year the plant was cultivated, the quality of the soil, the parts of the plant that are used, and methods of processing the herb.

The problems of quality control can be illustrated with SJW. The most common analytical "marker" compound used in standardizing SJW extracts is hypericin, even though it is not the only active principle. SJW also contains among other substances pseudohypericin, protohypericin as well as flavonoids and volatile oils. The majority of the American products are standardized to contain at least 0.3 percent hypericin. Some recent products are standardized to what is believed to be the major anti-depressive agent, hyperforin, at a level between 3 and 5 percent. Some products are sold as capsules while others are liquid extracts. Finally, many products contain SJW as one of several possibly active compounds. Of note, the majority of clinical studies conducted in Europe use a specific

extract called LI-160 delivering 900 mg/day of the aerial parts (leaves and flowers) of the dried herb. Even when products are standardized, batch to batch variability can lead to inconsistent therapeutic effects. Thus, the quality of a dietary supplement is difficult to ascertain for consumers who must rely on independent testing of products (www.consumerlabs.com) or use products specifically tested in clinical trials. A recent study of 16 SJW products found that most did not pass quality tests. Some had lower amounts of hypericin and hyperforin, and some had not labeled the plant part used, as the aerial parts are required for proper isolation and extraction. It is important that high quality extracts of SJW from reliable sources be used and that quality standardization is monitored to ensure the proper concentration and safety of the supplement.

5. Based on LB's depression history, what treatment recommendations would be appropriate for LB at this time?

By acquiring a thorough medication and supplement history, the primary care provider will recognize that the recent addition of SJW may have reduced the effectiveness of warfarin. LB was counseled to stop taking SJW and increase the dose of warfarin for 3 days before returning to her stable dose of 3 mg. A more in-depth psychosocial history did not reveal

evidence for major depression. LB was diagnosed with adjustment disorder and was recommended to follow-up in 1 week for a re-evaluation of her INR. An alternative approach might have been to continue her SJW as long as it is from a trusted manufacturer and to increase her warfarin to a level that will produce the desired INR. The patient would need to be instructed that if she decides to stop taking SJW she would also need to reduce her warfarin dose.

6. What dietary advice should be provided to all patients on warfarin (anticoagulation) therapy?

Vitamin K intake will adversely influence the efficacy of warfarin-based anticoagulant therapy, therefore the most important dietary advice to give patients is to keep their intake of vitamin K-containing foods and dietary supplements fairly constant from day to day. An understanding of the dietary vitamin K–warfarin interaction and knowledge of high, medium, and low dietary sources of vitamin K is necessary for successful anticoagulation.

Higher concentrations of vitamin K are found in dark green leafy vegetables such as spinach, kale, and collard greens, and in the outer peels of certain fruits, such as apples and grapes. Other significant dietary sources of vitamin K are certain oils including soybean, canola, cottonseed, and olive, although values may

fluctuate due to the susceptibility of the vitamin K in these oils to both daylight and fluorescent light (see Appendix D for foods high in vitamin K).

Case 3 Nutrient Deficiencies and Lead Poisoning in Children

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Objectives

Describe the most common sources of pediatric lead exposure in the United States.

Describe the current guidelines for the screening and diagnosis of pediatric lead exposure.

Describe the physiologic effects and nutritional consequences of pediatric lead exposure and toxicity.

Understand the pathophysiologic processes caused by lead toxicity that lead to vitamin D deficiency.

Summarize the current recommendations and guidelines for treatment of pediatric lead exposure.

JC is a 4-year-old boy of Hispanic descent who lives in an apartment in an older building in a city in the northeastern region of the United States with his parents and older siblings. In August, JC presented for a routine pre-school physical. His mother stated that he is a happy but quiet child who prefers to sit and read or watch TV. Sometimes when he is playing he will suddenly stop running and sit down and cry for several minutes and not want to play anymore. Since he was born, JC and his parents have traveled to Mexico three times to visit relatives.

Past Medical History

JC was born in the United States and has one recorded non-scheduled medical clinic visit to follow-up for an accidental buckle fracture of his distal right radius bone that occurred when he fell off a swing set when he was 40 months old. He has no other medical or surgical history, takes no medications, has no allergies, and is up to date on all his childhood immunizations.

Social/Diet History

JC's mother reports that he is a fussy eater and normally just picks at the food she gives him, which consists primarily of fruits and breads.

With the help of a nutritionist, JC's mother estimates that he eats approximately 1000–1200 kcal/day with less than 30 to 50 grams of protein per week.

Physical Examination

Vital Signs

Temperature: 98.4 °F (36.6 °C)

Heart rate: 110 BPM

Respiratory rate: 28 BPM

Blood pressure: 92/64 mmHg

Anthropometric Data

Height: 40.16 inches (102 cm) (15th percentile)

Weight: 35.64 lb (16.2 kg) (25th percentile)

BMI: 15.6 kg/m^2 (50th percentile)

Exam

General: 4-year-old-boy who is quiet and preoccupied with a small toy

Skin: Pale, warm and dry

HEENT: Normocephalic

Lungs: Clear to auscultation

Heart: Regular rate and rhythm

Abdomen: Soft and non-tender

Extremities: Fully developed and full range of motion

Neuro: No deficits

Laboratory Data

Current Labs	Normal Values
WBC: 4800/mm^3	5.5–15.5/mm^3
Hemoglobin: 8.5 g/dL	11.5–15.5 g/dL
Hematocrit: 29.3%	34–40%
Platelets: 165,000/mmol	150–440,000/mmol
MCV: 73.25 fL	75–87 fL
MCHC: 29.0 g/dL	32–36 g/dL
Serum lead: 35 mcg/dL	<3 mcg/dL
Serum 25-hydroxyvitamin D: 10 mcg/dL	(25 nmol/L)
X-rays: Increased calcification at the growth plates of the long bones (lead lines)	

Case Questions

What is the most common etiology for pediatric lead exposure in the United States?

What are the current guidelines for the definition and description of lead exposure in children?

How does lead toxicity result in vitamin D deficiency?

What are the signs and symptoms associated with vitamin D deficiency?

What are the current recommendations for treatment of lead exposure and toxicity and vitamin D deficiency?

Answers to Questions: Case 3

1. What is the most common etiology for pediatric lead exposure in the United States?

No safe or acceptable blood lead level (BLL) in children has been identified. Despite significant progress over the past four decades in reducing the prevalence of lead exposure, according to the Centers for Disease and Prevention (CDC) more than half a million American children between 1 and 5 years old are estimated to have BLLs more than 5 μg/dL. The CDC states that poisoning, which causes learning and behavioral problems and organ damage, affects one in 38 young children. The source of lead exposure varies depending on the region and historic and cultural background. There are three main lead source classifications: environmental, occupational, and miscellaneous.

Environmental Exposure of the Child In the environment, lead can be found in leaded

paint, dust, soil, water, air, and food. The largest contribution in lead contamination in the environment worldwide is from leaded fuel. Tetraethyl lead (TEL) has been used to reduce engine knock since the 1920s. Despite recognition of the health hazards from lead-containing gasoline, it was not until 1970 that the Clean Air Act required the American petroleum industry to lower the lead content in gasoline. The Clean Air Act Amendments of 1990 further mandated the elimination of lead from all motor fuel by 1996. In 1996, about 80 percent of gasoline sold in the world was unleaded and in many countries lead content in leaded fuel has been lowered. TEL gasoline was the primary source of atmospheric lead air pollution in the twentieth century but it has been replaced by airborne industrial emissions in the United States. Current major sources of lead emission are ore and metal processing and aircraft engines operating on leaded aviation fuel.

Chipped lead paint and contaminated soil and dust from chipped paint are the primary sources of pediatric lead poisoning in the United States. In 1972 the Lead-based Paint Poisoning Prevention Act recognized that chipped lead paint is a hazard and banned the use of lead paint (defined as lead content of 1 percent by weight or higher) in residential housing. In 1997, the maximum allowed lead content in paint was lowered to 0.06 percent by

the Consumer Product Safety Commission. Because of these regulations, the age of housing is closely related to the presence of lead-containing paint in the house. It is estimated about two-thirds of houses built in the 1960s and 1970s used lead-containing paint. Children are often exposed to lead through peeled or chipped paint, indoor dust, outdoor soil, and dust by their hand–mouth behavior. Renovation of old houses can become a source of lead exposure.

Soil and dust become contaminated with lead paint, TEL gasoline, and lead-containing industrial emissions. Because of congested traffic patterns and crowded housing, soil in urban areas has a higher lead concentration than rural soil. In some geographic regions, lead-contaminated dust has been identified as the most common source of pediatric lead exposure.

In the past, lead was used for plumbing and soldering and so lead may come into contact with drinking water when older plumbing systems corrode. In 1991, the Environmental Protective Service published the Lead and Copper Rule (LCR), a regulation that limits the concentration of lead and copper in public drinking water. Although most drinking water systems in the United States are compliant, the LCR does not apply to private wells or to water systems that serve less than 25 people, so these

may serve as significant sources of lead in selected patients.

Occupational Exposure Lead was the first industrial metal used by humans and still is one of the most widely used metals in many industries. It is estimated that 0.5 to 1.5 million workers are exposed to lead in the workplace in the United States. People who have contact with lead or lead-containing materials at their work – such as lead miners, refiners, smelters, and construction workers – are at risk of lead exposure. Some artists may use lead paint or lead-containing materials for their work. Shooting range instructors and gunsmiths can be exposed to lead since some ammunitions contain lead. This also may put police officers at higher risk of lead exposure. “Take-home exposure” can occur through exposed workers bringing contaminated work clothes home to their family members who may actually be more vulnerable than the workers themselves because of age, pre-existing medical conditions, and lack of preparedness or personal protective equipment.

Other Sources Food and beverages can be contaminated with lead. Lead in soil, air, and water can contaminate vegetables, rice, milk, and fish in some areas. Intake of illicitly produced spirits (moonshine) leads to elevated blood lead levels because of contamination

from lead-containing automobile radiators used in the distillation process.

Food and beverages packed or stored in lead-lined containers may become contaminated. When dinnerware decorated with or containing lead is used for serving, lead from the glaze and paints can leach into the food. Lead contamination of imported medications, herbs, cosmetics, and home remedies has been extensively reported. Mexican home remedies for 'empacho' (a stomach condition) such as azarcon and greta have been known to contain lead and may become a source of lead poisoning in Hispanic patients. Ayurvedic medications have been described as another source of lead and other heavy metal poisoning.

Although the use of lead paint on products marketed for children has been banned in the United States since 1978, other countries still may use lead paint for toys that may be imported into the United States. Lead used in the creation of plastic toys is regulated but not banned. Inexpensive plastic jewelry for children might become another source of lead exposure to children. Although simply wearing lead-containing plastic jewelry is not thought to increase blood lead levels, this jewelry is not recommended for use by children due to the risk of ingestion.

2. What are the current guidelines for the definition and description of lead exposure in children?

In 1991, the CDC described blood lead levels of ≥10 μg/dL as a "level of concern;" however, in May 2012, the CDC revised this term and replaced it with an upper reference interval value for children aged 1 to 5 years of ≥5 μg/dL. The CDC based this revision on a recommendation from its Advisory Committee on Childhood Lead Prevention. The National Health and Nutritional Examination Survey cycle from 2007 to 2010 estimates that approximately 2.6 percent (535,000) United States children aged 1 to 5 years have blood lead levels ≥5 μg/d.

The American Academy of Pediatrics Committee on Environmental Health recommends that practitioners be aware of their local state and community guidelines regarding lead screening for children and if there are none, screen every child. All children should be tested at least once when they are 2 years of age or, ideally twice at 1 and 2 years of age. Blood lead levels usually peak at 2 years of age, but that may be too late to prevent peak exposure. A low blood lead level at 1 year of age does not mean that the level will be similarly low at 2 years of age, so regardless of what the level is in a 1-year-old child, the level should be repeated at 2 years of age with special

consideration given to at-risk populations such as immigrants, foreign-born adoptees, refugees, or children whose parents work with lead or lead dust or who live in old houses.

3. How does lead toxicity result in vitamin D deficiency?

Lead poisoning typically is the result of oral ingestion or inhalation of lead, with 40 to 45 percent of ingested particles absorbed by the goastrointestinal (GI) tract and 30 to 40 percent of inhaled particles absorbed by the lungs. Additionally, those individuals with diets deficient in iron, calcium, and zinc are at a higher risk for lead poisoning due to the enhanced GI absorption of lead resulting from these mineral deficiencies. This relationship is fairly well established and numerous studies show a significant negative correlation between blood lead levels and calcium intake in children. Once absorbed, children store 70 percent of the body's total lead burden in bone, whereas adults store 90 percent of their lead burden in bone. This deposition in bone is one of the mechanisms by which lead is thought to impair new bone formation, explaining the skeletal signs and symptoms associated with lead poisoning, such as lead lines. Lead also impacts the kidney, impairing the renal biogenesis of $1,25[OH]_2D_3$ by inhibiting the mitochondrial P450 1-hydroxylase enzyme. This interaction results in an inverse relationship between lead

and $1,25[OH]_2D_3$. As the blood lead level increases, the serum $1,25[OH]_2D_3$ concentration is decreased. Due to this decrease in $1,25[OH]_2D_3$ concentration, as a result of the renal enzymatic inhibition by lead, vitamin D is no longer able to fulfill its role in the maintenance of calcium homeostasis, resulting in an overall negative impact on bone formation.

4. What are the signs and symptoms associated with vitamin D deficiency?

Vitamin D is a steroid pro-hormone found in certain foods, and produced in the skin from the reaction between 7-dehydrocholesterol and ultraviolet radiation. After conversion in the skin to pre-vitamin D_3, it undergoes additional reactions in the liver and kidneys, eventually becoming $1,25[OH]_2D_3$ or calcitriol, the biologically active form of vitamin D. Calcitriol has several vital physiologic roles, the most important of which is to promote cell differentiation and intestinal absorption of calcium and phosphorous. Calcitriol is also a potent stimulator of osteoclast-mediated bone resorption. These actions work to increase the serum concentration of calcium, making calcitriol one of three vital factors in the regulation of both calcium and phosphorous homeostasis along with parathyroid hormone (PTH) and fibroblast growth factor 23 (FGF23).

Because of the vital role it plays in calcium homeostasis, vitamin D deficiency manifests as the failure of mineralization of growing bone and cartilage. In children, this failure is designated as rickets and in adults it is categorized as osteomalacia. Depending on the severity, children may present with an array of symptoms, ranging from none to pain, irritability, motor delays, poor growth, and increased susceptibility to infections. Some associated signs of vitamin D deficiency include widening at the wrists and ankles, genu varum (bowed legs) or valgum (knocked-knees), prominence of the costochondral junction, delayed closure of fontanelles, craniotabes, and frontal bossing. Radiographic imaging may show low bone density, loss of the demarcation between the metaphyses and growth plate, loss of the provisional zone of calcification, and widening of the growth plate. Vitamin D deficiency in adolescents and adults resulting in osteomalacia may be asymptomatic or may manifest as isolated or generalized muscle and bone pain. Adults and children with severe vitamin D deficiency, occurring most often during periods of increased growth velocity, may present with hypocalcemia, leading to apneic spells, stridor or wheezing, hypotonia, muscular weakness, and brisk reflexes, eventually resulting in tetany or seizures.

5. What are the current recommendations for treatment of lead

exposure and toxicity and vitamin D deficiency?

The treatment of lead-exposed children is a specialized area of toxicology and consultation with a healthcare provider familiar with the management of lead toxicity and chelation therapy is recommended. Recommendations for chelation are controversial. Any child with evidence of CNS involvement should be hospitalized and chelation initiated with BAL and $CaNa^2EDTA$. Parents of all children should be informed of the dangers of lead and recommendations of how to remediate environmental sources of lead. Succesive elevations of blood lead should incorporate the strategies outlined in Table 2-5 for lower levels.

Table 2-5 Strategies for Treating Lower Levels of Lead in the Blood

Blood Lead Level (µg/dL)	**Recommendations**
10–19	Dietary and environmental Intervention and 3-month follow-up
20–44	Lab and X-ray evaluation including Hgb, Hct, iron, abdominal radiography and neurodevelopmental monitoring and lead hazard reduction

Blood Lead Level (µg/dL)	Recommendations
	Decontamination for radiographic evidence of lead contamination
45–69	Chelation therapy with dimercaptosuccinic acid (DMSA or succimer)
≥70	Hospitalization and chelation therapy with either succimer for asymptomatic patients or BAL/ $CaNa^2EDTA$ for symptomatic patients

Treatment of vitamin D deficiency due to lead exposure should begin with amelioration of the lead toxicity and include high strength calciferol (ergocalciferol or colecalciferol) for 8 to 12 weeks, followed by daily or weekly vitamin D supplements.

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Part II
Nutrition Throughout the Life Cycle

3
Nutrition in Pregnancy and Lactation

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Objectives*

Understand the metabolic and physiologic consequences of pregnancy and lactation.

Recognize the importance of incorporating nutrition into the history, review of systems, and physical examinations of pre-pregnant and pregnant women.

Recognize the additional nutritional requirements for women during pregnancy and lactation and provide appropriate counseling.

Understand the appropriate weight gain during pregnancy for normal-weight,

underweight, and overweight pregnant women.

Recommend dietary modifications to help alleviate common nutrition-related problems experienced during pregnancy.

*Source: Objectives for chapter and cases adapted from the *NIH Nutrition Curriculum Guide for Training Physicians*. (www.nhlbi.nih.gov/funding/training/naa)

Introduction

While adequate nutrition is important throughout the lifespan, it is especially crucial for pregnant and lactating women, whose nutrient and energy demands substantially increase in order to provide for the needs of their fetus and infant. By understanding the changes in nutritional requirements throughout pregnancy and during lactation, healthcare providers can make informed recommendations regarding diet alterations and supplementation.

Numerous studies have demonstrated that maternal nutrition not only affects the health and development of the newborn, but also the subsequent health of the growing child, even into adulthood. Avoiding nutritional deficiencies during pregnancy promotes

optimal outcomes for both mother and baby; avoiding nutritional deficiencies during lactation promotes prolonged breastfeeding, maternal health and satisfaction, and optimal infant development.

Metabolic and Physiologic Consequences of Pregnancy

The physiological and biochemical changes that occur during pregnancy have evolved to accommodate and promote the growth and development of the fetus. These changes include the development and growth of the feto-placental unit, increased maternal blood volume, increased maternal adipose tissue, decreased gastrointestinal (GI) motility, and breast enlargement to prepare for lactation. Throughout pregnancy, hormonal alterations create maternal insulin resistance and increase the uptake of fatty acids in extra-uterine tissues, both of which promote the transport of glucose to the developing fetus. In order to support the additional energy requirements of her developing fetus, a woman must adjust her daily caloric intake throughout pregnancy. The increased requirements depend upon pre-conception body mass index (BMI), maternal developmental stage (adolescence versus adulthood), and the gestational age of the pregnancy. Additionally, because the developing fetus depends entirely on maternal

dietary consumption to support nutritional and metabolic needs, it is crucial that a pregnant woman increases her intake of various nutrients to ensure that her own resources are not depleted and that fetal requirements are adequately met.

Integrating Nutrition into the Obstetric History

Ideally, every woman should meet with a healthcare provider for a pre-pregnancy physical examination and nutritional assessment; however, according to the March of Dimes, half of pregnancies are unplanned. A major objective of the healthcare team is to collect sufficient information to evaluate the pregnant woman's nutritional status and identify risk factors for the pregnancy. For each pregnant patient, a detailed obstetric history should be reviewed, because the outcomes of previous pregnancies have implications for the current pregnancy. This history should include the total number and dates of prior pregnancies, maternal and fetal outcomes, and any previous complications, including: low birth-weight infant (<2500 g; <5 pounds 8 ounces), macrosomia or high birth-weight infant (>4000 g; >8 pounds 13 ounces), or small or large for gestational age infant (<10th or >90th percentile for gestational age).

Weight-gain patterns during previous pregnancies, prior history of nausea, vomiting, or hyperemesis during pregnancy, gestational diabetes, eclampsia, anemia, pica, current and previous weight (BMI), and patterns of contraception use should also be determined. Previous breastfeeding experience should be assessed, as well as the woman's planned breastfeeding preference.

The medical history should also identify maternal risk factors for nutritional deficiencies and chronic diseases with nutritional implications (e.g., absorption disorders, eating disorders, metabolic disorders, infections, diabetes mellitus, phenylketonuria (PKU), sickle cell trait, or renal disease). Woman who have had a short pregnancy interval (i.e., less than a year between pregnancies) are at increased risk of having depleted nutrient reserves. Maternal nutrient depletion may be associated with an increased incidence of pre-term birth, intrauterine growth restriction (IUGR), and maternal morbidity/mortality. Caffeine, tobacco, alcohol, and recreational drug consumption should be quantified in the medical history, as should any vitamin or herbal supplementation or alternative pharmacological therapies. A history of medication use should also be obtained to evaluate the extent to which past or present medications may affect nutrient absorption.

In addition to the medical history, questions regarding professional, social, economic, and emotional stresses and specific religious practices (including dietary restrictions and fasting) should be included to account for any possible effects on the patient's nutritional status. Some work environments adversely impact dietary intake, as they may not provide adequate time to eat or allow access to only nutritionally marginal food. For this reason, pregnant patients should be asked about the conditions of their employment, and limitations and potential solutions should be discussed. For women of lower socioeconomic status, it is important to inquire about access to nutritious food and the ability to store and prepare food, and referral to food assistance programs may be appropriate (e.g., Women, Infants and Children – WIC).

Nutrition Assessment in Pregnancy

The purpose of a nutrition assessment is to identify women with nutritional risk factors that could jeopardize their health or the health of their fetus. A thorough evaluation of a woman's nutritional status prior to or during pregnancy includes clinical, dietary, and laboratory components. Both patient interviews and written questionnaires are appropriate for gathering information about current and past

dietary practices. Pertinent dietary information includes appetite, meal patterns, dieting regimens, cultural or religious dietary practices, vegetarianism, food allergies, and cravings and/or aversions. Information about abnormal eating practices, such as following food fads, bingeing, purging, laxative or diuretic use, or pica (eating non-food items such as ice, detergent, starch, chalk, clay, or rocks) is essential. Other relevant information includes the habitual use of caffeine-containing beverages (more than 200 mg/day), sugar substitutes and other special "diet" foods, vitamins, minerals, and herbal supplements. Use of dietary supplements may not be volunteered and their use should be elicited as they may be inappropriate or dangerous during pregnancy. A woman's current dietary practice can be assessed using the 24-hour recall, usual intake, or food frequency questionnaire discussed in Chapter 1.

Some women are receptive to nutrition counseling just prior to or during pregnancy, making this an opportune time to encourage the development of good nutritional and physical activity practices aimed at preventing future medical problems such as obesity, diabetes, hypertension, and osteoporosis. Pregnant and lactating women found to have nutritional risk factors may benefit from a referral to a registered dietitian (See Table 3-1).

Table 3-1 Medical Conditions Where Consultation with a Registered Dietitian is Advisable

Source: Lisa Hark, PhD, RD. 2014. Used with permission.

Pregnancy involving multiple gestations (twins, triplets)
Frequent gestations (less than a three month inter-pregnancy interval)
Use of tobacco, alcohol, or chronic medicinal or illicit drug use
Severe nausea and vomiting (hyperemesis gravidarum)
Eating disorders, including anorexia, bulimia, and compulsive eating
Inadequate weight gain during pregnancy
Adolescence
Restricted eating (vegetarianism, macrobiotic, raw food, vegan)
Food allergies or food intolerances
Gestational diabetes mellitus (GDM) or history of GDM
Prior history of low-birth-weight babies or other obstetric complications
Social factors that may limit appropriate intake (e.g., religion, poverty)

Physical Examination

An essential part of the clinical evaluation is assessing pre-pregnancy weight for height by calculating the BMI or using BMI tables (Figure 1-1). The BMI is used to evaluate weight status and should be explained to the patient to help her set appropriate weight-gain goals. Whenever possible, pre-pregnancy weight should be ascertained from clinical records obtained just prior to pregnancy. Current weight should be measured and rate of weight gain assessed at each visit.

Maternal Weight-Gain Recommendations

Maternal weight gain is attributable both to increases in the mother's tissue (increased circulating blood volume, breast mass, uterine size) and feto-placental growth within the uterus (increased size of the fetus, placenta, and amniotic fluid volume). During the first half of gestation, weight gain primarily reflects changes in maternal stores and fluid status. In the second half of gestation, weight gain is the result of continued maternal accumulation, as well as fetal growth. Rapid weight gain near the end of gestation, after approximately 32 weeks, usually represents the increase in tissue edema.

The rate of weight gain during pregnancy is important because maternal weight gain and

infant birth weight are correlated. Most weight gain should occur in the second and early third trimesters (18 to 30 weeks). Adequate weight gain in the second trimester of pregnancy seems to be predictive of fetal and neonatal weight, even if weight gain is inadequate during the remainder of the pregnancy.

The Institute of Medicine recommendations (Table 3-2) state that women with low pre-pregnancy BMI (<18.5 kg/m^2) should increase their caloric intake substantially to attain a weight gain between 28 and 40 pounds during the course of pregnancy. Women with normal pre-pregnancy BMI (18.5–24.9 kg/m^2) should increase their caloric intake moderately to gain between 25 and 35 pounds during the course of pregnancy, and overweight women with high BMI (25.0 to 29.9 kg/m^2) should increase their caloric intake in a more limited fashion, with a goal of a 15- to 25-pound weight gain during the course of pregnancy. An area of controversy is the weight gain needs of obese women. Women with a BMI greater than 30 kg/m^2 are considered obese and should gain as little as 11 to 20 pounds during the pregnancy. For twin pregnancies, the Institute of Medicine recommends a gestational weight gain of 37 to 54 pounds for women of normal weight, 31 to 50 pounds for overweight women, and 25 to 42 pounds for obese women. Data are insufficient

to determine the optimal weight gain for women with triplet and higher order gestations.

Table 3-2 Recommended Weight Gain During Pregnancy

Source: Recommended Weight Gain During Pregnancy. Institute of Medicine.

BMI	Weight Gain (kg)	Weight Gain (lb)
Underweight BMI < 18.5	12.7–18.2	28–40
Normal weight BMI 18.5–24.9	11.4–15.9	25–35
Overweight BMI 25–29.9	6.8–11.4	15–25
Obese		
BMI > 30.0	6.8	15
Twin gestation	15.9–20.4	35–45

Low Pre-conception BMI (underweight)

Women with low pre-conception BMI (<18.5 kg/m^2) are at risk for delivering low-birth-weight infants. If a woman who was underweight before conception does not gain adequate weight during her pregnancy, these risks are increased. As with general nutritional assessment and treatment, the optimal time for

evaluating and treating underweight women is prior to conception; however, this is often an unrealistic option. A woman with a BMI of less than 18.5 kg/m^2 who is considering pregnancy should be encouraged to gain weight before conceiving. If an underweight woman has conceived without gaining adequate weight, she should be encouraged to gain between 28 and 40 pounds over the course of her pregnancy. Protein–calorie supplementation may assist in correcting preconception nutritional deficits and provide adequate nutrients for fetal development.

Inadequate weight gain (<2 lb/month during the second and third trimesters) is associated with low-birth-weight infants, IUGR, and fetal complications. Inhibited fetal growth usually correlates with inadequate weight gain. Signs of IUGR include a discrepancy between gestational age and uterine size or fetal biparietal diameter measured by ultrasonography. Women with inadequate weight gain or weight loss should have repeated and thorough nutritional evaluations. Careful diet histories should be taken to determine the adequacy of dietary intake, supplementation should be provided as necessary, and referral to a registered dietitian is recommended.

Overweight and Obesity

Women with a high preconception BMI (>26 kg/m^2) are at risk for developing gestational diabetes mellitus, gestational hypertension, thromboembolic events, preeclampsia, and for delivering macrosomic infants (>4000 g or 8 pounds 13 ounces). Additionally, the rate of cesarean delivery increases with an increasing BMI.

To avoid inadequate intake of crucial nutritional components, which can adversely affect both mother and fetus, pregnant women with a high pre-conception BMI should limit their weight gain during the course of their pregnancies. However, they should not severely restrict their caloric intake such that the nutrients required to sustain a healthy pregnancy are insufficient. Although there is considerable controversy regarding the management of pregnancy in obese women, the current guidelines call for limited maternal weight gain. Despite the presence of pre-conception obesity, severe caloric restriction during pregnancy should not be considered, as caloric restriction is linked to inadequate intake of important macro- and micronutrients. Even in severe obesity, carbohydrate recommendations are 175 g/day. Adequate consumption of calcium, iron, folate, B vitamins, and protein are particularly crucial during pregnancy, regardless of maternal

weight. If caloric intake is inadequate, ingested proteins are catabolized for energy needs and are thus unavailable for maternal/fetal protein synthesis. An estimated 32 kcal/kg per day is necessary for optimal use of ingested protein. Severe restriction of caloric intake, paired with severe restriction of carbohydrate intake, can result in ketosis, which in studies of diabetic women has been shown to be detrimental for the developing fetus. Ketone bodies are concentrated in amniotic fluid and absorbed by the developing fetus. Studies have also suggested an association between ketosis and reduced uterine blood flow. The mental development of children whose mothers have had ketonuria during pregnancy has been shown to be stunted, although the direct causal link between fetal ketosis and inhibited mental development has yet to be definitively established.

Rapid, excessive weight accumulation is usually the result of fluid retention, which may indicate development of preeclampsia. Fluid retention in the absence of hypertension or proteinuria is not an indication for salt restriction or diuretic therapy, but women who retain fluid should be monitored for other signs of preeclampsia. Edema in the lower extremities is caused by the accumulation of interstitial fluid secondary to the obstruction of the pelvic veins that commonly occurs during the later stages of

pregnancy. Edema can be treated by elevating the legs and wearing support hose.

Slow excessive weight accumulation during pregnancy may be caused by fat deposition. As excessive weight gain is associated with both maternal and fetal morbidities; weight gain that exceeds the recommendations appropriate for pre-conception BMI should be monitored. A careful dietary history should be taken to determine the source of excess weight gain and recommendations for dietary changes should be offered accordingly.

Adolescence

It is helpful for the healthcare team to stress the importance of good, life-long nutritional habits, as well as the nutritional changes necessary for optimal pregnancy outcomes. Young adolescents, in particular, may still be growing and may need to gain additional weight to accommodate normal growth during the 40 weeks of the average gestation.

The pattern of weight gain, as well as the total weight gain during pregnancy, has been shown to be particularly important in adolescent women. Inadequate weight gain prior to 24 weeks, even if total pregnancy weight gain is adequate, is associated with low-birth-weight deliveries in the adolescent population. Pregnant adolescents should strive for weight gain patterns similar to those recommended for

women with low pre-pregnancy BMI. Adolescents need to fulfill the nutritional requirements of their own continued growth and development as well as the energy requirements of their developing fetuses. However, adolescents are more likely to consume diets that are low in micronutrients, such as iron, zinc, folate, calcium, and vitamins A, B_6, and C, and higher in energy from macronutrients including total fat, saturated fat, and sugar.

Recent research on adolescents suggests that the macronutrient components of the diet are also important determinants of birth weight. Adolescents whose diets are higher in total carbohydrates seem to have lower overall risk of delivering a low-birth-weight baby or having a pre-term delivery compared to adolescents with diets lower in carbohydrates.

Laboratory Evaluation

Routine tests related to the nutritional status of pregnant women should be performed at the beginning of pregnancy and again during the second trimester. Screening for anemia by checking hemoglobin and hematocrit is recommended in the first trimester and again at 24 to 28 weeks. When these measures are low, iron stores should be assessed with serum ferritin and mean corpuscular volume (MCV) levels. The clinician must be aware of ethnic or

racial differences when interpreting these laboratory studies. For example, African–American women tend to have higher levels of ferritin than Caucasian women. Patients of African–American, Southeast Asian, and Mediterranean descent are also at increased risk for having sickle cell disease, sickle cell trait, and/or thalassemia. They should be evaluated for these inherited disorders if their initial screen shows anemia in the presence of normal iron stores. Screening for gestational diabetes using a 1-hour glucose tolerance test should be done in all patients at 24 to 28 weeks gestation. Urinary screening for the presence of glucose and protein, as a screen for diabetes and renal disease, respectively, should be conducted at every visit.

Maternal Nutrient Needs: Current Recommendations

Energy and Protein

The total maternal energy requirement for a full-term pregnancy is estimated at 80,000 calories. Basal requirements can be determined based on maternal age, stature, activity level, pre-conception, BMI, and weight gain goals. During the first trimester, total energy expenditure does not change greatly and weight gain is minimal; therefore, additional energy intake is recommended only in the second and

third trimesters. An additional 340 kcal/day is recommended during the second trimester and 452 kcal/day during the third trimester. Additional protein is needed during pregnancy for fetal, placental, and maternal tissue development. Protein recommendations are therefore increased from 46 g/day for an adult, non-pregnant woman to 71 g/day during all trimesters.

Vitamin and Mineral Supplementation Guidelines

Routine vitamin/mineral supplementation for women reporting appropriate dietary intake and demonstrating adequate weight gain (without edema) is not mandatory. However, most healthcare providers prescribe a prenatal vitamin and mineral supplement because many women do not consume an adequate diet to meet their increased nutritional needs during the first trimester of pregnancy, especially with regard to folic acid.

Folic Acid

Folic acid deficiency is the most common vitamin deficiency during pregnancy, and insufficient levels of folic acid are known to cause neural tube defects (NTDs) in the fetus. NTDs include defects in the formation of the fetal skull, scalp, brain tissue, spinal cord, and vertebrae. For decades, the association between

low levels of folic acid and fetal NTDs has been understood. In addition, medications known to interfere with folate metabolism such as diphenylhydantoin, aminopterin, or carbamazepine cause fetal NTDs. In 1991, the Medical Research Council Vitamin Study Research Group published a study that demonstrated women with a history of a NTD in a prior pregnancy who took 4 mg of folic acid per day before pregnancy and through the 12th week of gestation experienced a 72 percent reduction in their recurrence risk of NTD. In 1992, the Centers for Disease Control and Prevention (CDC) recommended that all women of childbearing age take 400 μg/day of supplemental folic acid, in order to ensure adequate levels of folate are present when pregnancy occurs, whether intended or not. Because neural tube development and closure is complete by 18 to 26 days after conception, the neural tube is nearly formed by the time a woman misses her period and becomes aware she is pregnant. Thus, it is especially crucial that women planning to become pregnant consume adequate folic acid before pregnancy, and continue their supplementation during the first four weeks of pregnancy. The RDA for folate in women of childbearing age is currently 400 μg/day, and for pregnant women is 600 μg/day. Women with a history of NTD should be advised to consume 4 mg (400 μg) per day of folic acid.

Typically, the diet in the United States has lacked folate-rich food sources and patients might have been deficient in folate. For this reason, the government began a folic acid fortification program in 1997. Grain products, such as cereals, pastas, rice, and breads, are now fortified with folic acid. Good dietary sources of natural folate include dark green leafy vegetables, green beans and lima beans, orange juice, fortified cereals, yeast, mushrooms, pork, liver, and kidneys. (See Appendix F: Food Sources of Folate.)

Dietary folate is dramatically influenced by food storage and preparation; for instance, it is destroyed by boiling or canning. Folate stores are likely to be easily depleted among women who are of lower socioeconomic status, have folate-deficient diets, or are alcoholics. Additionally, evidence exists to suggest that the long-term use of oral contraceptives inhibits folate absorption and enhances folate degradation in the liver. Therefore, folate stores may be more rapidly depleted in women who have used oral contraceptives, which may lead to a higher incidence of folate deficiency in such women if they become pregnant.

Choline

While not essential because it is present in many foods and can be synthesized by the liver, choline is a popular supplement for pregnant women. Research studies in animals and a

limited number of human trials have demonstrated reduced risk of NTDs with choline supplementation but an active area of interest is the possibility of reduced risk factors for schizophrenia and increased IQ.

Calcium

Calcium is needed for fetal skeletal development. Additionally, evidence has shown that calcium supplementation reduces the risk of developing gestational hypertension. Over the course of pregnancy, a single fetus requires between 25 and 30 g of calcium, which represents only 2.5 percent of total maternal stores. In the first half of pregnancy, calcium requirement is just an additional 50 mg/day above the 1000 mg/day required for non-pregnant women. Most of the additional calcium requirement during pregnancy occurs during the third trimester, during which the fetus absorbs an average of 300 mg/day. In contrast to maternal iron and folate stores, which are relatively small and therefore easily depleted, maternal calcium stores are large and are mostly stored skeletally, allowing for easy mobilization as needed.

The RDA for calcium in women aged 9 to 19 is 1300 mg/day, and in women aged 19 to 50, the RDA is 1000 mg/day. Obtaining adequate intake of dietary calcium presents no problem for women who consume at least three servings of dairy foods every day. Women who limit

their intake of dairy foods because of lactose intolerance can often satisfy their daily calcium requirement by eating yogurt, cheese, calcium-rich vegetables, and products fortified with calcium, such as soymilk, orange juice, cereal, and bread. (See Appendices G and H: Food Sources of Calcium.)

If increased intake is not possible or effective, supplementation may be needed. Calcium carbonate, gluconate, lactate, or citrate may provide 500 to 600 mg/day of calcium to account for the difference between the amount of calcium required and that consumed. The tolerable upper intake for calcium during pregnancy is 2500 mg/day. The standard prenatal vitamin contains 250 mg. Multivitamins marketed to the non-pregnant population generally have less than 200 mg/serving. Calcium is thought to be absorbed in doses up to 600 mg at one time, making it unlikely that pregnant women would reach the upper tolerable limit.

Iron

Iron deficiency anemia during pregnancy has been associated with an increased risk of maternal and infant death, pre-term delivery, and low-birth-weight babies; and has negative consequences for normal infant brain development and function. The prevalence of prenatal iron deficiency is higher in African–American women, low-income women,

teenagers, women with less than a high-school education, and women who have had more than two prior pregnancies. *Healthy People 2020* goals include reducing anemia among pregnant females in their third trimester from 29 to 20 percent and reducing ethnic and income disparities. WIC Programs have been successful in reducing the prevalence of iron deficiency anemia during pregnancy and postpartum.

According to the CDC, screening for anemia should take place prior to pregnancy, as well as during the first, second, and third trimesters in high-risk individuals. The diagnosis of anemia by trimester is shown in Table 3-3. Since hemoglobin levels normally decline during pregnancy due to the significant increase in maternal blood volume, ferritin and MCV should be measured as diagnostic criteria, since these values remain constant. A serum ferritin level of less than 15 ng/mL warrants aggressive treatment and may require parental iron rather than oral supplementation.

Table 3-3 Diagnosis of Anemia in Pregnancy

Lab Test	1st Trimester	2nd Trimester	3rd Trimester
Hemoglobin (g/dL)	<10	10.5	<10
Hematocrit (%)	<37	35	<33

Source: Centers for Disease Control and Prevention.

A total iron increase of over 1000 mg is required during pregnancy. Maternal blood volume increases throughout pregnancy by 30 percent, and this increased erythropoeisis

requires an additional 450 mg of iron to be delivered to the maternal marrow. The fetus and the placenta require 350 mg of iron, and approximately 250 mg of iron is lost in blood during delivery. It is difficult for many women to meet the iron requirements of pregnancy by diet alone. Healthcare providers generally recommend iron supplementation as a daily supplement of 30 mg of elemental iron in the form of simple salts, beginning around the twelfth week of pregnancy for women who have normal pre-conception hemoglobin measurements.

The RDA for iron is 27 mg/day in pregnancy and 9 mg/day for lactating women. For women who are pregnant with multiple fetuses or those with low pre-conception hemoglobin measurements, a supplement between 60 and 100 mg/day of elemental iron is recommended until hemoglobin concentrations are normal. After normalization, iron supplementation of 27 mg/day should be continued. There are various forms of ferrous salts on the market, each containing a different amount of elemental iron:

ferrous fumarate: 106 mg elemental iron/tablet,

ferrous sulfate: 65 mg elemental iron/tablet,

ferrous gluconate: 28 to 36 mg iron/tablet.

Iron supplementation can have gastrointestinal side effects such as constipation, therefore a

stool softener or natural laxative should be prescribed with the iron supplement. Because the degree of gastrointestinal side effects directly correlates with the amount of elemental iron ingested, changing to a lower-dose of elemental iron is very effective. For example, if a patient cannot tolerate a tablet of ferrous sulfate (containing 65 mg elemental iron), changing to ferrous gluconate (containing 28 mg elemental iron) or iron bis-glycinate (Ferrochel, Gentle Iron) (containing 27 mg elemental iron) can be effective. Because iron is best absorbed in an acidic medium, iron can be taken with a 250 mg ascorbic acid tablet or a half-glass of orange juice for optimal absorption. If a patient is also taking antacids for gastro-esophageal reflux disease, advise the patient that iron and antacids should not be taken concurrently. (See Appendix L: Food Sources of Iron.)

Vitamin D

Vitamin D is a fat-soluble vitamin obtained largely from consuming fortified milk or juice, fish oils, and dietary supplements. It also is produced in the skin with exposure to sunlight. Vitamin D that is ingested or produced in the skin must undergo hydroxylation in the liver to 25-hydroxyvitamin D [25(OH)D], then further hydroxylation primarily in the kidney to the physiologically active 1,25-dihydroxyvitamin D. This active form supports absorption of calcium

from the gut and enables normal bone mineralization and growth. During pregnancy, severe maternal vitamin D deficiency has been associated with skeletal anomalies, fractures, and congenital rickets. Vitamin D deficiency in pregnancy occurs commonly in certain high-risk groups, including vegetarians, women with limited sun exposure (e.g., those who reside in northern latitudes) and in women with darker skin. Although there is insufficient evidence to recommend screening all pregnant women for vitamin D deficiency, maternal serum 25(OH)D levels can be measured in women at high risk for deficiency. Although there is no consensus on an optimal serum 25(OH)D level in pregnancy, most agree that a serum level of at least 20 ng/mL (50 nmol/L) is needed to avoid bone loss. When vitamin D deficiency is identified during pregnancy, 1000 to 2000 international units (IU) per day of vitamin D_3 is recommended. (See Appendix B: Food Sources of Vitamin D.)

Vitamin A

The RDA for vitamin A is 770 µg/day in pregnancy and 1300 µg/day during lactation. Severe vitamin A deficiency is rare in the United States and an adequate intake of vitamin A is readily available in a healthy diet. Women with lower socioeconomic status, however, may consume diets with inadequate amounts of vitamin A. Increasing dietary intake

of vitamin A is possible and should be encouraged in lieu of supplementation to avoid excessive intake, which has been reported to be teratogenic, leading to spontaneous abortions and fetal malformations including microcephaly and cardiac anomalies. A safe upper limit for vitamin A intake during pregnancy has been recognized at 3000 μg/day. Over-the-counter multivitamin supplements may contain excessive doses of vitamin A and thus should be discontinued during pregnancy. Additionally, topical creams that contain retinol derivatives commonly used to treat acne should be discontinued during pregnancy and in women trying to become pregnant.

Omega 3 Fatty Acids

N-3 Fatty acids are another popular supplement used by many pregnant women, specifically docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). Some research studies have demonstrated higher IQ in babies born to supplemented mothers. Practitioners might encourage fish oil supplements in their patients who don't consume fish.

Dietary Fiber

There are no specific recommendations for dietary fiber intake during pregnancy; however, increased intake of high-fiber foods, such as vegetables, whole grains, and fruit, is recommended for the prevention and treatment

of constipation. Constipation is a common complication of pregnancy due to hormonal changes because progesterone produced in pregnancy relaxes smooth muscle in the colon and decreases peristalsis. Emphasizing adequate fluid intake is important when increasing dietary fiber. (See Appendix O: Food Sources of Dietary Fiber.)

Fluids

Pregnancy represents a unique state where circulating blood volume increases by 50 percent. Tissue fluid also increases, while blood pressure decreases in the second trimester and then returns to pre-pregnant levels near term. The dynamic changes of blood volume and blood pressure during pregnancy require substantial fluid intake in order to maintain blood flow to vital organs. Inadequate fluid intake is associated with premature uterine contractions, pre-term delivery, intrauterine growth restriction, and hypertensive disorders of pregnancy. General recommendations are to drink at least 64 ounces (1920 mL) of water per day. In areas where the water supply is suspected to contain lead, women should be encouraged to drink bottled water. Excessive lead intake may result in spontaneous abortion, decreased stature, and impaired neuro-cognitive development of the baby.

Food Contamination

Food contaminated by contact with heavy metals or pathogenic bacteria can produce devastating effects on the developing fetus, as most heavy metals are considered teratogenic. In particular, case reports of teratogenicity or embryotoxicity have been reported involving methyl mercury, lead, cadmium, nickel, and selenium. In addition, heavy metals can have neurotoxic effects on the fetus. Mercury can be removed from vegetables by peeling or washing well with soap and water. Consumption of raw fish products and highly carnivorous fish (including tuna, shark, tilefish, swordfish, and mackerel) should be limited or avoided during pregnancy. All foods should be handled in an appropriately sanitary manner to prevent bacterial contamination. All dairy foods and juices consumed during pregnancy should be pasteurized.

Listeria monocytogenes contamination results in food poisoning during and outside of pregnancy. In pregnancy, however, listeriosis can develop into a blood-borne, transplacental infection that can cause chorioamnionitis, premature labor, spontaneous abortion, or fetal demise. To avoid listeriosis, pregnant women should wash vegetables and fruits, cook meats, and avoid processed, pre-cooked meats (cold cuts) and raw cheeses (brie, blue cheese, Camembert, and Mexican caso-blanco).

Alcohol

Alcohol is a known teratogen. Excessive consumption of alcohol by pregnant women can result in fetal alcohol syndrome (FAS) which manifests in such fetal deformities as microcephaly, cleft palate, and micrognathia. Heavy alcohol consumption during pregnancy is also associated with low neonatal weight, and deficiencies in B vitamins and protein. Maternal alcoholism contributes to fetal nutritional deficiencies because it inhibits maternal absorption of nutrients, and increases nutrient losses (e.g., zinc).

While it is certain that heavy maternal drinking is harmful to developing fetuses, the issue of whether a modest amount of alcohol consumption is acceptable during pregnancy remains controversial. There is no known safe level of alcohol consumption during pregnancy; therefore, it is currently recommended that alcohol intake be avoided by pregnant women and women attempting to become pregnant. According to the American College of Obstetrics and Gynecology, no amount of alcohol consumption can be considered safe during pregnancy. Alcohol should be avoided entirely throughout the first trimester. Although the debate remains as to whether mild-to-moderate drinking affects fetal development in the latter trimesters of pregnancy, the Council on Scientific Affairs of the American Medical

Association also recommends abstinence from alcohol throughout pregnancy. The CDC recommends that clinicians identify women at risk in the preconception period and provide education and support for cessation of alcohol use.

Cigarette Smoking

Nicotine consumption during pregnancy has been consistently associated with low neonatal weight. If women who smoke become pregnant, they should be advised to discontinue cigarette use for the sake of their fetuses.

Caffeine

According to the March of Dimes, women who are pregnant or trying to become pregnant should limit their caffeine intake to no more than 200 mg/day, which is equivalent to about two 8-ounce cups of brewed coffee. During the first trimester, excessive caffeine intake is shown to increase the risk of spontaneous abortion (miscarriage). The United States Food and Drug Administration recommend that pregnant women reduce their intake of caffeine from all sources. Since caffeine is present in teas, hot cocoa, chocolate, energy drinks, coffee ice-cream, and soda, it is best to advise decaffeinated beverages for women who are pregnant or trying to become pregnant.

Exercise during Pregnancy

Many studies support the benefits of moderate exercise in women whose pregnancies are considered low risk. According to the American College of Obstetricians and Gynecologists, most pregnant women should participate in 30 minutes or more of moderate exercise on most, if not all, days. Safe activities include walking, swimming, dancing, and yoga. Regular physical activity improves posture, promotes muscle tone, strength, endurance, energy level, and mood, while reducing constipation, backache, fatigue, sleep disturbances, and varicose veins. It may help reduce the risk of diabetes and high blood pressure during pregnancy and help women recover faster after delivery.

Pregnant women should be advised to avoid contact sports and any activities that can cause even mild trauma to the abdomen, such as ice hockey, kickboxing, soccer, and basketball, as well as activities with a high risk for falling, such as gymnastics, horseback riding, downhill skiing, vigorous racquet sports, and scuba diving. They should be advised to drink plenty of fluids before, during, and after exercise and avoid hot tubs, saunas, and jacuzzis. Warning signs to stop exercising include vaginal bleeding, uterine contractions, decreased fetal movement, fluid leaking from the vagina, dizziness or feeling faint, increased shortness of

breath, chest pain, headache, muscle weakness, and calf pain or swelling.

Common Nutrition-related Problems during Pregnancy

Discomforts of pregnancy such as nausea and vomiting, constipation, and heartburn may generally be improved by implementation of the guidelines summarized here.

Nausea and Vomiting

Nausea and vomiting seem to be associated with increased levels of the pregnancy hormone human chorionic gonadotropin (HCG), which doubles every 48 hours in early pregnancy and peaks at about 12 weeks gestation. Nausea is experienced by 60 percent of pregnant women and, of these, only a small percent require hospitalization for severe hyperemesis gravidarum.

Heartburn and Indigestion

Heartburn and indigestion are usually caused by gastric content reflux that results from both lower esophageal pressure and decreased motility. Limited gastric capacity, secondary to a shift of organs to accommodate the growing fetus, contributes to these symptoms in the third trimester of pregnancy. Strategies for managing heartburn or indigestion are the

same as those suggested for managing nausea and shown in Table 3-4.

Table 3-4 Strategies for Managing Nausea, Vomiting, Heartburn, and Indigestion in Pregnancy

Source: Lisa Hark, PhD, RD. 2014. Used with permission.

Eat small, low-fat meals and snacks (fruits, pretzels, crackers, non-fat yogurt) slowly and frequently
Avoid strong food odors by eating room temperature or cold foods and using good ventilation while cooking
Drink fluids between meals, rather than with meals
Avoid foods that may cause stomach irritation such as spearmint, peppermint, caffeine, citrus fruits, spicy foods, high-fat foods, or tomato products
Wait 1 to 2 hours after eating a meal before lying down
Take a walk after meals
Wear loose-fitting clothes

Constipation

Constipation during pregnancy is associated with an increase in water reabsorption from the

large intestine. In addition, smooth muscle relaxation with resultant slower gastrointestinal tract motility occurs during pregnancy. The pregnant woman often notes overall gastrointestinal discomfort, a bloated sensation, an increase in hemorrhoids and heartburn, and decreased appetite. Strategies for managing constipation during pregnancy are shown in Table 3-5.

Table 3-5 Strategies for Managing Constipation in Pregnancy

Source: Lisa Hark, PhD, RD. 2014. Used with permission.

Increase fluid intake to 2 or 3 quarts per day (water, herbal teas, non-caffeinated beverages)
Increase daily fiber intake (high-fiber cereals, whole grains, legumes, bran)
Use psyllium fiber supplement (Metamucil)
Increase consumptions of fruits and vegetables (fresh, frozen, and dried)
Participate in moderate physical activity (walking, swimming, yoga)

Gestational Diabetes Mellitus

Gestational diabetes mellitus (GDM) is defined as glucose intolerance with onset or first recognition during pregnancy. It occurs in approximately 4 percent of all pregnancies,

resulting in more than 135,000 cases annually. GDM is caused by the insulin-antagonizing effects of pregnancy hormones, including human placental lactogen, growth hormone, corticotropin releasing hormone, and progesterone. Prevalence rates are higher in African–American, Hispanic, Native American, and Asian women than in white women. Current recommendations are that all pregnant women be screened for GDM at 24 to 28 weeks of gestational age, as the use of risk factors alone may fail to identify up to 50 percent of patients with GDM. For high-risk patients, screening at the first prenatal visit, or by 16 weeks, is recommended. High-risk patients are those with a personal history of abnormal glucose tolerance, obesity, a first-degree relative with type 2 diabetes, ethnic groups with a high prevalence of gestational diabetes (African–American, Native American, Southeast Asian, Pacific Islander, Hispanic), glucosuria, or prior obstetric history consistent with diabetes (e.g., macrosomia, fetal anomalies, neonatal hypoglycemia).

The main screening tool for GDM is a 150 mL, 50-g glucose load with a 1-hour serum glucose blood test. A result greater than or equal to 130 to 140 mg/dL for the 1-hour screen is abnormal. For the roughly 20 percent of patients who test positive, a 3-hour 100-g glucose load test is performed. The diagnosis of GDM is made

when two or more serum glucose values are met or exceeded on the 3-hour test.

After delivery, approximately 90 percent of all women with GDM become normoglycemic but they are at increased risk of developing type 2 diabetes later in life. According to the Diabetes Prevention Program (DPP), this risk is at least 40 percent over the 3 years following the pregnancy. Additionally, women with a history of GDM have a 33 to 50 percent risk of recurrence in a subsequent pregnancy, and some of these recurrences may represent unrecognized type 2 diabetes. Thus, it is recommended that a patient with GDM be re-screened for type 2 diabetes after pregnancy.

The goal of treatment is to prevent the maternal and fetal complications associated with GDM. These complications include fetal macrosomia and its attendant fetal and maternal injury associated with delivery (increased risk of cesarean section, operative vaginal delivery, and shoulder dystocia). Additional fetal complications include a possible increased incidence of fetal death and ketonemia, which has been associated with lower intelligence scores at 2 to 5 years of age.

Medical Nutrition Therapy for Gestational Diabetes

The goals of medical nutrition therapy for GDM are to provide appropriate calories for

gestational weight gain, achieve and maintain normoglycemia, and avoid ketonemia and ketonuria. Individualization of the meal plan is recommended as the ideal percentage and type of carbohydrate are uncertain. Monitoring blood glucose, urine or blood ketones, appetite, and weight gain is essential for individualizing the meal plan and for adjusting the meal plan throughout pregnancy.

Generally, 40 to 45 percent of total energy intake should be from carbohydrate, which is distributed throughout the day into three small-to-moderate size meals and two to four snacks. An evening snack is usually needed to prevent accelerated ketosis overnight. Carbohydrate is not as well tolerated at breakfast as it is at other meals, possibly due to the associated increased levels of cortisol and growth hormones. Therefore, the initial meal plan may limit carbohydrate to 30 g at breakfast with adjustments made later based on blood glucose monitoring results. To satisfy hunger, protein-rich foods can be added.

Patients with serum glucose values persistently above the thresholds require the addition of insulin therapy in order to achieve adequate glycemic control. Recent data evaluating the use of second-generation sufonylureas, like glyburide, are encouraging but require more study.

Pregnancy following Bariatric Surgery

As the rate of obesity increases worldwide among reproductive-age women, so too does the rate of women seeking weight-loss surgery – known as bariatric surgery. Therefore, it is important for healthcare providers to know how to care for this specific population. Bariatric surgery may be considered in patients with class III obesity (BMI >40 kg/m^2) or class II (BMI >35 kg/m^2) with co-morbid conditions and failure of nonsurgical treatment. There are two major types of bariatric surgical procedures as reviewed in Chapter 1, Case 2: (1) malabsorptive procedures including the Roux-en-Y gastric bypass (RYGB) and biliopancreatic diversion (BPD) and (2) restrictive procedures including adjustable gastric banding.

Patients who have undergone malabsorptive procedures are at high risk for nutritional deficiency after surgery. After bariatric surgery, manipulation of the gastrointestinal tract prevents adequate absorption of iron, folate, vitamin B_{12}, calcium, and vitamin D from the small intestine. Reduction in stomach size also alters production of intrinsic factor, which is needed for absorption of vitamin B_{12} in the terminal ileum.

If micronutrient supplementation is inadequate after bariatric surgery, poor pregnancy outcomes can be expected. Iron and vitamin B_{12} deficiencies will lead to maternal anemia. Case reports have described neural tube defects from folate deficiency, microphthalmia from vitamin A deficiency, fetal cerebral hemorrhage from vitamin K deficiency, and Wernicke's encephalopathy from thiamin deficiency.

Vitamin and mineral supplementation should be tailored to meet each patient's particular surgical history. Often, it is possible to replace the patient's multivitamin with a prenatal vitamin, and add additional calcium, vitamin B_{12}, iron, and folate as necessary. Patients may find chewable and liquid prenatal vitamins most palatable and best tolerated. Vitamin A causes birth defects and thus the total amount of vitamin A should still be limited to 5000 IU/ day during pregnancy.

Screening for micronutrient deficiency is of utmost importance in pregnant patients who have undergone bariatric surgery. Studies have shown that fewer than half of post-operative bariatric surgery patients continue to take the prescribed multivitamin supplement long-term; and thus, patients without pre-conception counseling may have micronutrient deficiencies at the start of pregnancy. Pre-conception evaluation should include the following:

complete blood count, ferritin, iron, vitamin B_{12}, thiamin, folate, calcium, and vitamin D,

If it is not possible to undergo pre-conception counseling, checking levels at the first prenatal visit is recommended. Any deficiencies should be corrected and monitored monthly. Each trimester, complete blood count, iron, ferritin, vitamin B_{12}, calcium and vitamin D_3 should be evaluated. Monitoring and supplementation should be continued while the patient is breastfeeding. Supplementation should first begin with an oral preparation; however, a parental form may be required if levels continue to be inadequate.

The American College of Obstetricians and Gynecologists recommends that obese women who have undergone bariatric surgery receive the following counseling before and during pregnancy:

All patients are advised to delay pregnancy for 12 to 18 months after surgery so that pregnancy is avoided during the rapid weight loss phase.

Women with gastric banding should be monitored by their general surgeons during pregnancy because adjustments of the band may be necessary.

Patients should be evaluated for nutritional deficiencies, including iron, vitamin B_{12}, folate, vitamin D, and calcium, and supplemented with vitamins as necessary.

Fetal Growth after Bariatric Surgery The data on fetal growth after bariatric surgery is inconclusive. However, studies have shown that caloric and protein restriction during pregnancy can impair fetal growth and does not improve pregnancy outcome. Thus, even patients who continue to be obese after bariatric surgery should not restrict calories during pregnancy.

To monitor for intrauterine growth restriction and small-for-gestational-age fetuses, maternal weight gain should be carefully monitored, and an early third trimester ultrasound to evaluate fetal growth should be performed.

Gestational Diabetes Screening after Bariatric Surgery Patients are typically screened for gestational diabetes using a 50-g glucose load at 24 to 28 weeks of gestation. However, patients who have undergone RYGB may experience dumping syndrome after consuming this glucose load, and thus the 1-hour glucose tolerance test is not recommended in these patients. Dumping syndrome may occur after consumption of a high sugar load, which causes a hyper-osmolar environment in the small bowel. This causes fluid to shift rapidly from the blood into the small bowel, which causes distension, cramping, nausea, vomiting, and diarrhea. The decrease in intravascular blood volume can cause tachycardia, palpitations, and diaphoresis, while a hyperinsulinemic response

can cause reactive hypoglycemia. To screen for GDM in patients who have undergone RYGB, patients can be instructed to check their fasting and 2-hour post-breakfast blood sugars for 1 week during the period of 24 to 28 weeks gestation. Of note, patients who regularly drink and tolerate sugared soft drinks are unlikely to experience dumping syndrome after the 1-hour glucose tolerance test and can be screened using the traditional method.

Lactation

Metabolic and Physiologic Changes during Lactation

Breast enlargement begins early in pregnancy due to the hormones generated by the pituitary gland and the corpus luteum. The lacteal cells also differentiate in preparation for milk production that begins when the infant is born. As the breast undergoes these preparatory changes, the areola (the pigmented area surrounding the nipple) becomes darker and more prominent, and the skin over the nipple becomes more elastic and more erect in order to facilitate suckling.

Lactogenesis is believed to be initiated by the abrupt decrease in progesterone and estrogen following parturition (giving birth). As the infant begins to suckle, stimulating the receptors in the nipple and areola, nerve

impulses are sent to the hypothalamus. The hypothalamus, in turn, stimulates the release of the hormones oxytocin and prolactin from the posterior pituitary gland. Prolactin stimulates milk production in the breast, and oxytocin stimulates myoepithilial cells around ducts to contract and ejects milk from the alveolus. Milk accumulates in the lactiferous sinuses under the areola and is released when the areola is compressed between the baby's tongue and palate.

Benefits of Breastfeeding

Breast milk contains the following components and many of these work alone or in combination to minimize the risk of infection in the nursing infant:

Leukocytes (specifically, macrophages)

Immunoglobins (secretory IgA, IgG, IgM, and antiviral antibodies)

Bifidus factor (to support *Lactobacillus bifidus*)

Lysozymes (to promote bacterial lysis)

Interferon

Lactoferrin (to bind whey protein and inhibit *Escherichia coli* colonization)

Lactadherin (to protect against symptomatic rotavirus infections)

Growth factors and cytokines (bFGF, EGF, NGF, TGF, G-CSF, interleukins, TNF-alpha and others)

Prostaglandins

Hormones (pituitary, hypothalamic, and steroid)

Gastrointestinal peptides (VIP, gastrin, GIP)

Other unique components (e.g., complement factors, glutamine, oligosaccharides, nucleotides, and long-chain polyunsaturated fatty acids).

Breastfed infants are hospitalized less frequently during the first 6 months of life. Significant healthcare cost savings from the decreased incidence of lower respiratory infections, otitis media, and gasteroenteritis are associated with breastfeeding. Strong evidence suggests that human milk also decreases the incidence and severity of diarrhea, bacteremia, bacterial meningitis, urinary tract infections, and necrotizing enterocolitis. Many studies have demonstrated the protective effect of breast milk against immune- or autoimmune-related diseases (e.g., chronic and inflammatory bowel diseases, type 1 diabetes, allergic diseases). Breast feeding infants may also prevent sudden infant death syndrome (SIDS) and cancers such as leukemia and lymphoma. Breastfeeding promotes jaw and

tooth development in the infant, and enhances maternal–fetal bonding.

Breastfeeding mothers experience an earlier return to pre-gravid weight, decreased accumulation of adipose tissue, delayed return of ovulation with increased pregnancy spacing, improved bone remineralization upon resumption of menses, and reduced risk of ovarian and premenopausal breast cancer. Breast milk also offers the added benefit of convenience; it is at the proper temperature, and requires neither preparation nor storage.

Types of Breast Milk

As time passes, the composition of breast milk changes from colostrum, to transitional, to mature milk. Colostrum is produced during the later stages of pregnancy and is present in highest concentration during the first few days of lactation. It is high in protein, immunoglobins, beta-carotene, sodium, potassium, chloride, fat-soluble vitamins, minerals, and hormones. Colostrum promotes growth of bifidus flora and maturation of the gastrointestinal tract and meconium passage. Transitional milk is produced 1 to 2 weeks post-partum. It is higher in fat and lactose and lower in protein and minerals than colostrum. Mature milk is usually produced by the fifteenth day of lactation through the termination of lactation. It is composed of

emulsified fat and lactose, it provides 20 to 22 calories/ounce and is nutritionally optimal.

Breast milk is rich in nutrients and other substances essential to growth and development during the first 6 months of life. When breastfeeding, women should encourage their infants to suckle on each breast for as long as the infant shows signs of hunger; approximately 10 to 15 minutes per breast. It is important to teach nursing mothers early signs of hunger. Crying is a very late sign. Signs of hunger include sucking movements, bringing the hands to the mouth, rapid eye movements, soft cooing or sighing sounds, and restlessness. Mothers should be encouraged to feed at least eight times in each 24-hour period, as breast milk is easily digested and clears the gut faster than formula. The emptying time of breast milk from the infant's stomach is, on average, 1.5 hours, compared with 3 hours for formula-fed infants.

Breast Milk Composition

Fat Breast milk is rich in most nutrients required to sustain the newborn's appropriate growth during the first 6 months of life. The total amount of fat in breast milk is constant, but its composition varies with the duration of the feeding. Initially, breast milk has a relatively low fat content. Following the first let-down reflex, breast milk becomes higher in fat and calories. The fat content of breast milk provides

50 percent of the infant's total energy requirements in readily absorbable form. Therefore, it is essential that the infant be allowed to nurse on each breast until he or she is satisfied to derive the fat calories from the feeding. Encouraging the infant to suckle on each breast for 10 minutes or more ensures adequate calorie consumption.

Protein Breast milk contains whey and casein proteins. Whey accounts for roughly 70 percent of the total protein in breast milk, mainly in the form of alpha-lactalbumin, lactoferrin, and secretory IgA. Casein accounts for the remaining 30 percent of breast milk's total protein composition and forms micelles that enhance the absorption of calcium, phosphorous, iron, zinc, and copper. The total protein concentration is relatively low, but it is the optimal concentration for infant nutrition.

Carbohydrate The primary carbohydrate source in breast milk is the disaccharide lactose. Small amounts of glucose and immunologically active oligosaccharides and glycoproteins are also present.

Vitamin D Some breastfed infants are at risk for rickets caused by vitamin D deficiency because breast milk contains only small quantities of this nutrient. The risk is enhanced for dark-skinned infants of mothers with decreased vitamin D_3 levels resulting from dietary deficiencies and/or minimal sun

exposure. Currently, the American Academy of Pediatrics recommends that all exclusively breastfed infants receive 400 IU of vitamin D daily by 2 months of age regardless of skin color.

Vitamin K Breast milk contains only small traces of vitamin K. However, supplementation is generally unnecessary, as most infants receive vitamin K injections immediately following delivery to prevent hemorrhagic disease of the newborn. All breastfed infants should receive 1 mg of vitamin K oxide intramuscularly after the first feeding is completed. This should be within the first 6 hours of life.

Nutritional Recommendations for Lactating Women

Energy and Protein

Approximately 85 kcal are required to produce 100 mL of breast milk. Stored energy from maternal fat reserves provides 100 to 150 kcal/day, but this may not be sufficient. Therefore, daily caloric intake of lactating women is recommended at 500 kcal/day for the first 6 months and 400 kcal/day for 7 to 9 months. This may not be necessary for all women. Postpartum women should avoid diets and medications that promise rapid weight loss. Weight loss should always be gradual,

particularly for lactating women, who require more calories than non-lactating women to support breast milk production. Protein requirements for lactating women are recommended at 71 g/day.

Calcium

Normally 2 to 8 percent of total body calcium is mobilized for breast milk production during lactation and this will be restored following the onset of menses. Diets of adults of low socioeconomic status are often low in calcium.

Iron

Iron requirements are lower during lactation (9 mg/day) than during pregnancy (27 mg/day) until menstruation resumes (18 mg/day). In the United States, studies of lactating women consuming 2700 kcal/day suggest that they are not likely to meet the RDAs for calcium and zinc. Diets that contain less than 2700 kcal/day may also be low in magnesium, vitamin B_6, and folate. Adolescent mothers' diets may be particularly low in iron.

Vitamin Supplements

Prenatal vitamin supplements are routinely prescribed to lactating women to ensure adequate intake. However, lactating women should be encouraged to obtain their nutrients from a well-balanced, varied diet. Also, they

should continue to drink to thirst or about 2 to 3 quarts of fluids per day to prevent dehydration. Guidelines from the American Academy of Pediatrics advise supplementation with 400 IU of vitamin D_3 should be initiated within days of birth for all breastfed infants.

Common Problems Experienced while Breastfeeding

Healthcare providers can readily manage most of the common problems associated with breastfeeding; however, referral to a mother-to-mother support group can be very helpful for many common problems and referral to a Certified Lactation Consultant can ensure continued lactation when problems are more complex.

Mastitis Mastitis is an infection of the breast tissue that up to 30 percent of lactating women may experience. Symptoms include breast pain, swelling, flu-like symptoms, headache, and fever. Mastitis is caused by bacteria that enter the breast through a break or crack in the skin of the areola or through the opening to the milk ducts. Bacteria from the skin or the infant's mouth enter the milk duct and can multiply, leading to pain, redness, and swelling of the breast as the infection progresses. Clogged milk ducts, cracked nipples, feeding on one breast only, wearing a tight bra, wet breast pads, infrequent feeding, anemia, fatigue, and stress

can also increase the risk of developing mastitis. It is important to advise women to nurse frequently, feeding on the unaffected breast first. Antibiotics are typically prescribed and should be taken for 10 to 14 days. Getting plenty of rest, wearing a comfortable bra, and changing breast pads often can help prevent the development of mastitis.

Contraindications to Breastfeeding

Infectious Disease Women with active, untreated tuberculosis, typhoid, active herpes in the area of the breast, rubella, mumps, or human immunodeficiency virus (HIV) should not breastfeed their infants. In some developing countries, the infant mortality risks of not breastfeeding may override the morbidity and mortality risks associated with the possible acquisition of such maternal infections. The main route of transmission of HIV from mother to child is breastfeeding; transmission of the virus can be prevented by encouraging use of commercial infant formulas and discouraging breastfeeding for infants of HIV-positive mothers. Other common infections, such as influenza, should not interfere with breastfeeding.

Other contraindications for breastfeeding in the United States are infants with classic galactosemia, mothers who are positive for human T-cell lymphotropic virus type I or II, mothers receiving exposure to radioactive

isotopes, mothers on specific antimetabolite or chemotherapeutic agents, and mothers using drugs of abuse. It is important to note that there are many conditions for which mothers have been told to avoid breastfeeding that are indeed compatible with breastfeeding. Cytomegalovirus (CMV) is not a contraindication for breastfeeding in the term baby. The clinician must weigh the risk benefit of breastfeeding in the premature infant born to a mother with CMV. Women who have hepatitis B or C can be encouraged to breastfeed.

Medications As in pregnancy, some medications, herbal remedies, nutritional supplements, and alternative therapies should be avoided during lactation. Several drugs, including nicotine and estrogen-containing oral contraceptives, can decrease milk supply and interfere with milk production. Medications can pass through human milk to the infant. It is best to evaluate each medication individually before making a decision about use. Considerations include the molecular weight of the drug, peak concentration, protein binding, half-life, relative infant dose (RID), infant age, maternal dose, risk/benefit to mother and baby, and alternative medication options. Drugs pass into human milk if they are highly lipid soluble, have a low molecular weight (<500), low protein binding, or are in high concentration in maternal plasma.

There are several resources available to help make decisions about medication use. The American Academy of Pediatrics' position statement, entitled “The Transfer of Drugs and Other Chemicals Into Human Milk,” is included in the *Breastfeeding Handbook for Physicians*. Discussion about contraception should include the risk of milk supply depletion with all hormone-related forms of birth control. Medications that are contraindicated for breastfeeding women include bromocriptine, tetracycline, cyclophosphamide, cyclosporine, doxorubicin, ergotamine, lithium, methotrexate, phencyclidine (PCP), and phenindione.

Substance Abuse Substance abuse and the use of recreational drugs should be actively discouraged during lactation. Illegal substances, such as amphetamines, cocaine, heroin, or marijuana, as well as nicotine pass into breast milk when ingested by the mother and should be discouraged. Addicted women should be encouraged to enter appropriate treatment programs and should be drug free before lactation is initiated. Lactating women should be advised to quit smoking because in addition to the long-term health risks, smoking decreases breast milk volume and is associated with shortened exclusive and total breastfeeding duration. Modest consumption of coffee and alcohol (i.e., less than one to two cups/drinks daily) is not known to adversely

affect lactation or the infant's health. Alcohol does pass readily into breast milk so its intake should be limited.

Promotion and Support of Breastfeeding

As healthcare professionals, it is our ethical and professional responsibility to promote, protect, and support breastfeeding. Women should be informed of not only the benefits of breastfeeding but the inherent risks of not breastfeeding. Position papers published by the American Academy of Pediatrics, American Dietetic Association, and the International Lactation Consultants Association provide guidance for clinicians in supporting breastfeeding efforts. The American Academy of Family Physicians also has excellent guidelines on the clinical management of breastfeeding. Breastfeeding infants should be monitored closely for their growth and observation of the mother–infant dyad should be a routine part of postpartum care. Breast milk is the optimal food source for infants.

Case 1 Prevention of Neural Tube Defects

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Objectives

Define the prevalence, etiology, and pathogenesis of neural tube defects (NTDs).

Describe the association between folate levels and prevention of NTDs in the developing fetus.

Evaluate the risk of having a child with a NTD given a pre-pregnant woman's detailed medical, obstetric, dietary, and social history,

Evaluate the nutritional adequacy of a pre-pregnant woman's diet.

PL is a 32-year-old married Puerto-Rican–American woman who has missed her period and discovers that she is pregnant. This was an unplanned pregnancy and PL presents for her first prenatal visit at 5 weeks of gestation (normal gestation period is 40 weeks). She is a gravida 3 para 1011; G3P1011.

Obstetrical History Notation

The mother's obstetrical history is described in an acronym in terms of gravity (G): the number of times the mother has been pregnant; and parity (P) the number of times the mother has had a birth. Parity includes four components – TPAL: T = full-term births >38 weeks gestation; P = pre-term births <37 weeks gestation; A = spontaneous, therapeutic abortions, ectopic pregnancies; L = live children.

When accessing PL's gravity and parity status her obstetrical history includes: one full-term birth, no pre-term births, one miscarriage and one living child at home and she is currently pregnant, thus her G and P would be documented as: G2 P1011.

Past Medical/Surgical and Obstetric History

PL's previous birth was delivered by cesarean section for arrest of the normal progress of labor at 39 weeks gestation. Her infant weighed 7.5 pounds (3.4 kg) at birth. She was not hypertensive and had no history of gestational hypertension during her previous gestation. Her 1-hour glucose tolerance test at 28 weeks was normal in her first pregnancy. She denies

any history of chronic medical problems or any surgeries other than the cesarean section and a dilation and evacuation at the time of her miscarriage. PL currently takes no medications, vitamins, minerals, or herbal supplements. She denies any allergies or food sensitivities to medications or foods.

Social History

PL stays at home to care for her 2-year-old daughter. She reports having little free time to exercise. She does not smoke or drink alcohol. She denies any history of sexual abuse or domestic violence. She lives at home with her husband and daughter.

Family History

PL has a sister-in-law (her husband's sister) who had a 24-week loss of a baby found to have anencephaly. Her parents, siblings, and other nieces and nephews are all in good health and free from chronic diseases. Both of her paternal grandparents had coronary artery disease prior to their deaths in their mid-sixties. Her maternal grandmother has type 2 diabetes mellitus which is controlled on oral hypoglycemic agents and her maternal grandfather died at 54 years of age from a myocardial infarction.

Physical Examination

Vital Signs

Temperature: 98.4 °F (37 °C)

Heart rate: 80 BPM

Respiration: 18 BPM

Blood pressure: 120/70 mm Hg

Height: 5′6″ (168 cm)

Current/usual weight: 145 lb (66 kg)

BMI: 23.5 kg/m^2

Exam

General: Tired-looking, pale, in no acute distress

Heart: Regular rate and rhythm with no murmurs, rubs, or gallops

Resp: Lungs clear to auscultation and percussion

Abdomen: Soft and non-tender without any masses

Pelvic: External genitalia normal, cervix clear on speculum exam, uterus soft and top-normal size (consistent with 5 week pregnancy) with no adenexal masses on bimanual exam, no tenderness

Extremities: Varicose veins with no clubbing, cyanosis or edema, veins non-tender and not inflamed

PL's 24-Hour Dietary Recall

Breakfast (home)	
Bagel	1 large
Cream cheese	1 Tbsp.
Coffee	1 cup
2 percent low-fat milk	1 ounce (30 mL)
Lunch (home)	
Turkey breast lunchmeat	3 ounces (85 g)
Potato bread	2 slices
Mayonnaise	1 Tbsp.
Diet Coke	12 ounces (360 mL)
Snack (home)	
Pretzels	1 ounce (28 g)
Dinner (home)	
Fried flounder	5 ounces (142 g)
Corn on the cob	1 ear
Margarine	1 Tbsp.
Diet Coke	12 ounces (360 mL)
Low-fat frozen yogurt	1 cup

Total calories: 1521 kcal

Protein: 80 g (21 percent of total calories)

Fat: 54 g (32 percent of total calories)

Carbohydrate: 179 g (47 percent of total calories)

Calcium: 608 mg

Iron: 10 mg

Folate: 238 μg

Case Questions

What is the physiologic basis for the increased folate requirements for normal neural tube development during pregnancy?

What is the prevalence of neural tube defects (NTDs) in the United States and who is at higher risk of having a child with an NTD?

What is the evidence that folic acid supplementation reduces the risk of neural tube defects?

How can an individual develop a folate deficiency? Which populations are at risk for low-folate intake?

Describe the rationale for the food fortification program and its potential benefits.

List food sources high in folate. Based on the nutrition assessment of PL's diet history, what dietary modifications would you suggest?

Should a vitamin and mineral supplement be considered for this patient? Why or why not?

Answers to Questions: Case 1

Part 1: Physiology and Prevalence

1. What is the physiologic basis for the increased folate requirements for normal neural tube development during pregnancy?

The correlation between folate and the incidence of NTDs has been linked since the late 1970s. Folate is a water-soluble B-complex vitamin that plays an important role in nucleic acid biosynthesis. Folic acid is the most active form and its bioavailability is twice that of folate. It is the form used in vitamin supplements and fortification of food. Folate, in its metabolically active form 5-methyl tetrahydrofolate (5-THF), is a cofactor for the enzymes involved in one-carbon transfer reactions that include the synthesis of nucleic acids and several amino acids. Once converted to 5-THF, folate can be transported into the cell via folate receptors. Studies have demonstrated that adequate folate levels are particularly important at times of rapid cell growth, such as in fetal and placental development. Women are thought to have pregnancies affected by NTDs for two reasons, and frequently for a

combination of these two reasons. The first is an increased folate demand in pregnancy and decreased dietary intake, and the second is a genetic defect in the production of enzymes involved in folate metabolism.

The neural tube is formed very early in pregnancy, between 18 and 30 days post-conception. This means that formation is initiated even before the woman may know she is pregnant, since the missed period would generally occur at 14 days post-conception. Since the neural tube goes on to form the spine and brain, defects in the formation of the neural tube can include the absence of formation of most of the brain (anencephaly) as well as defects in the closure of the lower tube (spina bifida) to open NTDs (meningoceles, and myoceles). This early formation combined with the detrimental effects of folate deficiency on neural tube formation, is the basis for the public health initiative that mandates all women of childbearing age begin folic acid supplementation at a dose of 0.4 mg (400 ug) per day prior to conception and at least through the first trimester of pregnancy for the prevention of NTDs.

2. What is the prevalence of neural tube defects (NTDs) in the United States and who is at higher risk of having a child with an NTD?

Neural tube defects are one of the most common malformations of the central nervous system. NTDs occur when the brain and spinal cord fail to close properly during the first 4 weeks of gestation resulting in damage to the exposed underlying neural tissue. Spina bifida and anencephaly, the two most common types of NTDs, occur in approximately 1 per 2000 births each year in the United States. Prevalence varies according to race and ethnicity, with Hispanic women demonstrating the highest rates, while the lowest rates are found among black (0.35 per 1000 births) and Asian women. In Mexico, the prevalence of NTDs is higher (3.2 per 2000 births). Ninety percent of NTDs occur in women without a family history; however, women who have had a previous NTD-affected pregnancy or who are personally affected by an NTD are at a 2 to 3 percent higher risk in a current pregnancy. A family history of a close family member (sibling, niece, or nephew) with an NTD raises a woman's risk of having an affected pregnancy to approximately 1 percent, as does the consumption of certain anti-seizure medications such as valproic acid or carbamazepine. Maternal pre-gestational insulin-dependent diabetes and maternal pre-pregnant obesity are among the most consistently observed environmental risk factors associated with NTDs. It has been suggested that the increased risk in diabetic women may be due to consumption of a high

glycemic diet and poor pre-conceptual glycemic control. Since PL's sister-in-law lost a baby at 24 weeks gestation with anencephaly, her risk increases.

In women with a history of a previously affected pregnancy, supplementation with 4 mg (4000 μg) of folic acid per day, initiated 1 month prior to attempting to conceive and continued throughout the first trimester of pregnancy is recommended. This recommendation is based upon results of the United Kingdom's Medical Research Council Vitamin Study Research Group study, which demonstrated a 72 percent reduction in risk of a repeat NTD. When recommending higher levels of supplementation to patients, it is important to emphasize that a separate folic acid supplement and *not* multiple doses of multivitamins (MVI) be utilized. Additional daily MVI consumption could lead to toxicity of other vitamins, particularly vitamin A, which is teratogenic to the developing fetus. Possible risk factors associated with NTDs requiring a higher dose of folic acid are listed in Table 3-6.

Table 3-6 Risk Factors Associated with Neural Tube Defects

Source: Office of Dietary Supplements, National Institutes of Health, Dietary Supplement Fact Sheet: Folate.

Personal or family history of NTD-affected pregnancy
Maternal diabetes mellitus
Maternal obesity
Epilepsy/antiepileptic medications such as valproate, phenytonin, carbamazepine, primidone
Genetic variants
Conditions associated with decreased serum folate levels including alcohol abuse, hemolytic anemias, liver disease, malabsorption syndromes, gastric bypass
Other medications such as methotrexate (folate antagonist) and sulfasalazine (used to treat ulcerative colitis)

Part 2: Folate and Neural Tube Defects

3. What is the evidence that folic acid supplementation reduces the risk of NTD?

Several controlled and observational trials have shown that periconceptional and early pregnancy consumption of folic acid supplements can reduce a woman's risk for having an infant with an NTD by as much as 50 to 70 percent. The exact mechanism by which folic acid reduces the risk of NTDs is unclear and remains an area of intense research. To

increase folic acid consumption by women of childbearing age, the United States Food and Drug Administration (FDA) mandated folic acid fortification of grain products beginning January 1998. Since that time the Centers for Disease Control and Prevention (CDC) has evaluated the impact of folic acid fortification on the prevalence of NTDs.

Using data from eight population-based birth defect surveillance systems with prenatal diagnosis of NTDs, the CDC reported that the prevalence of NTDs in the United States declined by an estimated 1000 cases from 4000 (1995–1996) to 3000 (1999–2000). This decrease in NTD-affected pregnancies since mandatory folic acid fortification began highlights the effectiveness and success of this public health policy. Besides the United States, mandatory fortification programs in Canada, Chile, Costa Rica, and South Africa have shown reductions in the occurrence of NTDs from a 28 percent decrease in the United States to a 46 percent decrease in Canada. Not all countries, however, have instituted mandatory food fortification, citing concerns about the potential for adverse effects.

Given the mandatory folic acid fortification public health initiative in the United States and the reduction in NTDs, the American College of Medical Genetics along with the American College of Obstetricians and Gynecologists has

updated its guidelines on folic acid for the prevention of NTDs as follows:

All women planning a pregnancy should consume 400 μg (0.4 mg) of folic acid daily which can be taken as a supplement, multivitamin, in fortified foods, or combination of each. Supplementation should begin at least 1 month prior to conception and throughout the first trimester of pregnancy.

Women who have had a previous NTD-affected pregnancy, have a NTD themselves, have a first or second degree relative with a NTD, or who have type 1 diabetes should take 4 mg of folic acid 3 months prior to attempting conception and continue throughout the first trimester and seek genetic counseling.

There should be increased public health efforts to raise awareness of the role of folic acid in reducing the incidence of NTDs.

Additional research is warranted to better determine the potential risks and benefits of increasing fortification of foods with folic acid.

4. How can an individual develop a folate deficiency? Which populations are at risk for low-folate intake?

The term folate includes all compounds that have the vitamin properties of folic acid – including folic acid and naturally occurring compounds in food. Folate deficiency in humans is attributed to sub-optimal dietary

intake of folate, behavioral and environmental factors, and genetic defects. Humans cannot synthesize folate from other sources and are therefore entirely dependent on dietary sources or supplements to meet their folate requirements.

Folate deficiency is common today since most adults frequently consume diets high in fat and processed foods, with less than the daily recommended servings of fresh fruit and vegetables. Minority women from low socioeconomic and educational backgrounds have been found to have poor folate intakes due to limited use of folate rich foods. In pregnancy, the increased demand for folate is not met by self-selected diets because only 50 percent of the folate occurring naturally in foods is bioavailable.

Folate functions as a methyl donor for the enzyme methylenetetrahydrofolate reductase (MTHFR), which is involved in the conversion of homocysteine to methionine (see Figure 3-1). Folate deficiency results in an elevated serum homocysteine level. It is estimated that two-thirds of hyperhomocysteinemia is due to a folate deficiency. Mutations in the MTHFR gene that have been linked to an increased risk of NTD increase the metabolic requirement for folate and also result in elevated serum homocyteine levels. These levels can be normalized by additional folate intake.

However, genetic defects appear to account for only a small percentage of cases of folate deficiency. Clinical folate deficiency is defined as a serum folate concentration less than 3 ng/mL or a red blood cell folate concentration of less than 140 ng/mL.

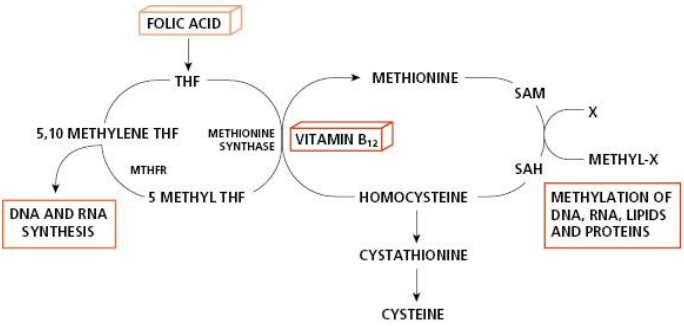

Figure 3-1 Folate and Vitamin B_{12} Pathway

Source: American Academy of Pediatrics, American College of Obstetricians and Gynecologists. *Breastfeeding Handbook for Physicians*. 2011.

5. Describe the rationale for the food fortification program and its potential benefits.

In September 1992, the United States Public Health Service (PHS) recommended that all women of childbearing age consume 400 μg of folate daily (600 μg during pregnancy) to lower their risk of having a child with a NTD. The PHS indicated that this could be achieved by (1) improving dietary habits, (2) fortification of the food supply, and (3) daily consumption of a folic acid supplement. However, most women

were not getting this amount from their diets and were not taking folic acid supplements. Data from the third National Health and Nutrition Examination Survey (1989–1991) showed that mean folate intake was 230 ± 7.8 μg/day for non-pregnant woman age 20 to 29 and 237 ± 9.0 μg/day for ages 30 to 39, levels below the Dietary Reference Intakes (DRI).

Bentley et al. analyzed food and supplement data since the mandatory folate fortification and found that the median daily total folate intake (from food and supplements) for all women of childbearing age increased by at least 100 μg. Although this is significant, only 39 percent of non-Hispanic whites, 28 percent of Hispanics, and 26 percent of non-Hispanic black women are reported to consume the recommended 400 μg per day, which falls far short of the FDA's target goal of 50 percent.

The March of Dimes has conducted public education campaigns encouraging women of childbearing age to consume an adequate daily intake of folate. Since 1995, The Gallup Organization has been commissioned by the March of Dimes to conduct surveys on national samples of women aged 18 to 45 to measure changes in behavior, knowledge, and awareness relative to folate consumption. In 2007, 40 percent of women reported taking a daily folic acid supplement, which is an increase from 28 percent in 1995. Only 12 percent of women,

however, were aware that folic acid should be taken before pregnancy and only one in five women knew that folic acid prevented birth defects. Efforts to educate young women (18 to 24 years) on the importance of folic acid supplementation should be increased since this group demonstrated the least awareness, knowledge, and practice of all age groups surveyed.

Folic acid, also known as pteroylmonoglutamic acid, is the synthetic compound used in dietary supplements and fortified foods. Since January 1, 1998, the FDA has required fortification of all enriched grain products (flour, breads, rolls and buns, corn, grits, cornmeal, farina, rice, and noodle products) with 140 μg of folic acid per 100 g (3.5 ounces) of grain product to prevent NTDs. Adding folic acid to enriched foods has ensured that most women of childbearing age consume additional folic acid without requiring the behavior changes that are necessary to increase intake of folate rich foods or folic acid supplements. To not exceed the DRI's “tolerable upper level” of 1000 μg/day for adults, higher levels were not recommended. Although folic acid is a water-soluble vitamin with no known toxicity, higher doses of folic acid might mask a vitamin B_{12} deficiency. Folic acid would correct anemia (pernicious, megaloblastic, or macrocytic anemia) but does not prevent the neurological consequences associated with a vitamin B_{12} deficiency.

Folate fortification of foods has been associated with decreased prevalence of NTDs and possible improvement in first-year survival rates among infants with spina bifida. Folate status, as measured by mean serum and red blood cell folate concentrations has more than doubled in non-pregnant women across all population groups in the United States since mandatory fortification. A recent report by Pfeiffer et al., however, looking at NHANES survey data from 1999 to 2000 through 2003 to 2004 suggests a decline in blood folate concentrations particularly among non-Hispanic whites. This underscores the need to continue monitoring the changes in folic acid intake and folate status in American women of childbearing age to evaluate, revise, and implement new and existing policies and programs aimed at reducing cases of NTDs.

Fortification of flour with folic acid has shown benefit in reducing NTDs in developing countries as well. In 2009, fifty-one countries required mandatory flour fortification programs that included folic acid. Most developing countries have few other sources of folic acid compared to developed countries, which have ready-to eat cereals and other voluntarily fortified foods and supplements. By increasing the number of countries with mandatory folic acid flour fortification this global public health burden can be reduced.

Part 3: Medical Nutrition Therapy

6. List food sources high in folate. Based on the nutrition assessment of PL's diet history, what dietary modifications would you suggest?

Major sources of dietary folate include dark green leafy vegetables, dried beans, citrus fruits, wheat germ, and fortified cereals. Orange juice is the largest single source of folate consumed by Americans, and it is estimated that it contributes approximately 10 percent of the daily intake of dietary folate. (See Appendix F: Dietary Sources of Folate.)

Most dietary folate occurs naturally as polyglutamate, which is converted to monoglutamate and absorbed in the proximal small intestine. Foods containing 55 µg folate per serving are considered to be excellent sources of folate. When assessing dietary folate intake, it is important to ask very specific questions since there are wide variations in folate content within each food group. For example, 8 ounces of orange juice contains approximately 100 µg of folate as compared to negligible amounts in apple juice.

An analysis of PL's intake shows that she consumed only 238 µg of folate, well below her recommended intake. An individual can easily consume 400 to 500 µg of folate daily by eating 3 to 5 servings of vegetables (2.5 cups), 2 to 4

servings of fruits (2 cups), and 6 servings of grain daily (with at least one-half coming from whole grain sources). PL's diet is deficient in fruits and vegetables. Recommended dietary modifications could include either adding orange juice or a fresh orange or grapefruit to breakfast, carrots sticks to lunch, and a green vegetable, such as broccoli or asparagus, to dinner. In addition to these naturally occurring sources of folate, a ready-to-eat fortified breakfast cereal could contribute significantly to PL's folate intake. Folate is also contained in whole grains and whole grain products such as oatmeal or oat bran cereals, wheat germ, whole grain breads and brown rice, which could easily be incorporated into PL's diet.

7. Should a vitamin and mineral supplement be considered for this patient? Why or why not?

In the United States at least 50 percent of all pregnancies are unplanned. Therefore, the American Academy of Pediatrics, along with the United States PHS, recommends that women of childbearing age consume 400 μg folic acid per day. This is the amount contained in an over-the-counter multivitamin supplement. Since PL is at a slightly higher risk for a NTD affected birth she should consult with her doctor at her 5-week pre-natal visit to discuss the amount of supplemental folic acid she

should take. Pre-natal supplements generally contain 1000 μg of folic acid.

There is currently insufficient evidence to provide a recommendation to use dietary folate as the sole method to reduce the risk of NTDs; however, women still should be advised to consume a high folate diet. Folic acid is the most active form of this vitamin and the form used in vitamin preparations and food fortification. When synthetic folic acid is consumed as a supplement in the fasting state, it is nearly 100 percent bioavailable. In contrast, when folic acid is consumed with food, as in fortified cereal grain products, its absorption is reduced to approximately 85 percent. Naturally occurring food folate is only 50 percent absorbed, because the polyglutamate side chain must be cleaved before absorption can occur. Thus, supplemental folic acid taken on an empty stomach is approximately two times more bioavailable than dietary folate, and folic acid taken with food (including folic acid in fortified foods) is approximately 1.7 times more bioavailable than dietary folate. These are only estimates and may be revised over time as more data are gathered and analyzed. Future research should also be aimed at the dose–response relationship of folate and NTD prevention and quantifying, more precisely, the dose needed to prevent recurrences.

Case 2 Encouraging Breastfeeding

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Objectives

Identify the documented advantages of breastfeeding for both mothers and infants.

Effectively encourage pregnant women to initiate and continue breastfeeding their infants for at least the first year of life.

Effectively counsel women regarding techniques and positioning in order to successfully breastfeed their infants.

Provide appropriate nutritional recommendations for breastfeeding women.

Compare and contrast the growth patterns of breastfed and formula-fed infants.

LW is a 26-year-old Korean woman who is gravida 1, para 0, in her thirty-seventh week of gestation. She is 5′6″ (168 cm) tall and weighed 160 pounds (72.7 kg) prior to becoming

pregnant (pre-pregnancy BMI: 25.8 kg/m^2). She now weighs 190 pounds (86 kg), and her pregnancy has been uncomplicated. LW is considering breastfeeding and questions her childbirth provider about it and whether she can continue after she returns to work 8 weeks postpartum. LW had been trying to lose weight before she got pregnant. LW plans to lose her pregnancy weight quickly and fears dieting will keep her from producing enough breast milk to feed the baby adequately.

Follow-up

LW, who has been breastfeeding her infant, returns at 6 weeks postpartum for her checkup. She has lost 20 pounds (9 kg) and currently weighs 170 pounds (77 kg) (BMI = 27.4 kg/m^2). She reports that she is even hungrier than she was during her pregnancy, but cannot find time to eat. She is afraid that she is not producing enough milk because the baby always seems hungry and is not as chubby as her friend's formula-fed baby. She reports that her mother told her she should avoid eating vegetables and chocolate because they will upset the baby's stomach and produce gas. A friend told her that it was not safe for her to try to lose weight while breastfeeding, saying she might get “too skinny.” LW is also concerned about how to feed the baby when she returns to work in 2 weeks. A 24-hour recall is as follows.

LW's 24-Hour Dietary Recall

Breakfast (home)	
She reports that she often skips breakfast.	
Corn flakes	1 cup
Skim milk	1/2 cup
Lunch (home)	
Whole-wheat bread	2 slices
Peanut butter	2 Tbsp
Jelly	1 Tbsp
Orange juice	8 ounces (240 mL)
Snack (home)	
Snickers candy bar	1–2 ounces (57 g)
Water	1 cup
Dinner (home)	
Baked chicken	2 thighs (6 ounces) (170 g)
Baked potato	1 medium
Margarine	2 Tbsp
Apple sauce	1/2 cup
Diet cola	12 ounces (360 mL)
Snack (home)	
Ice cream	1 cup

Total calories: 2035 kcal

Protein: 78 g (15% of calories)

Fat: 95 g (41% of calories)

Carbohydrate: 228 g (44% of calories)

Calcium: 505 mg

Iron: 8.4 mg

Case Questions

What advice can be given to LW to help her decide whether to breastfeed her infant?

How quickly can a postpartum woman expect to lose weight?

What dietary recommendations should be given to LW to ensure that her baby will receive adequate nutrition?

What are the guidelines regarding frequency and length of time to breastfeed an infant?

How will LW know if her breastfed baby is getting enough to eat? Compare the growth patterns of breastfed and formula-fed infants.

How should LW's weight loss and dietary intake be assessed?

How can breastfeeding women prepare to return to work?

Part 1: Encouraging Breastfeeding

1. What advice can be given to LW to help her decide whether to breastfeed her infant?

According to the Institute of Medicine, American Academy of Pediatrics (AAP), American Academy of Family Physicians (AAFP), American College of Obstetrics and Gynecology (ACOG), and the American Dietetic Association (ADA), breastfeeding is the recommended way to feed infants in the United States. Exclusive breastfeeding is the preferred method for normal full-term infants from birth to 6 months because of the documented advantages for both the baby and the mother. Breastfeeding, complemented by appropriate introduction of solid foods after 6 months of age, is recommended for the remainder of the first year, and longer if desired (AAP, AAFP, ACOG, ADA). To achieve this goal, it is important to learn how to breastfeed during the early months and after returning to work. For that reason, LW should be encouraged to contact a licensed International Board Certified Lactation Consultant (IBCLC) and only if no IBCLC is available, a leader from a mother-to-mother support group such as La Leche League or a peer counselor program.

It is important that a mother receive social and emotional support for her decision to breastfeed. Women are most likely to succeed at

breastfeeding when encouraged by their healthcare provider(s) during pregnancy, and outside sources for support and assistance (husband or significant other, patient's mother or mother-in-law, mother-to-mother support groups).

2. How quickly can a postpartum woman expect to lose weight?

A woman should not expect to return to her pre-pregnancy weight immediately after delivery. On average, a new mother loses 15 pounds (6.8 kg) within the first week after delivery. Many mothers are concerned about their weight gain during pregnancy and worry that they may not return to their pre-pregnancy weight since many women retain 5 to 10 pounds (2.3 to 4.5 kg) per pregnancy. Lactating women eating nutritionally balanced diets typically lose 1 to 2 pounds (0.45 to 0.9 kg) per month during the first 4 to 6 months of lactation, a rate more rapid than if they were bottle-feeding their infants. A weight loss of more than 1.5 pounds (0.68 kg) per week, even in women with excess fat stores, can decrease breast milk production and jeopardize the nutritional status of both the mother and the baby. However, not all women lose weight during lactation. Some studies suggest that approximately 20 percent of women maintain or gain weight during this time and may lose the additional weight after they wean their infants.

3. What dietary recommendations should be given to LW to ensure that her baby will receive adequate nutrition?

The Institute of Medicine makes the point that breast milk will be ideal even if the diet is not ideal. Lactating women should be encouraged to obtain their nutrients from a well-balanced, varied diet to meet their nutritional needs while lactating, as they have an increased need for essentially all nutrients, especially protein, calcium, and vitamins A, C, and D, compared with non-lactating women. Pregnant and lactating women have been noted to have sub-normal vitamin D levels contributing to an increased incidence of sub-clinical rickets in breastfeeding infants. The specific needs of individual women vary depending on the volume of milk produced daily, the age and size of their infants, their individual metabolism, and their postpartum nutritional status. Supplementing vitamin D (1000 IU per day) is an acceptable recommendation.

During pregnancy, most women store approximately 2 to 4 kg of body fat, which can be mobilized to supply a portion of the additional calories used for lactation. Body fat supplies an estimated 200 to 300 kcal per day during the first 3 months of lactation. An additional 500 kcal per day, which is needed for lactation, must come from the diet.

4. What are the guidelines regarding frequency and length of time to breastfeed an infant?

Breastfeeding should ideally be initiated within the first hour after birth. Skin-to-skin contact is essential for getting breastfeeding off to a good start. Feeding the baby on demand, frequent suckling, and completely emptying milk from the breasts helps to increase the mother's milk supply. The duration of a feeding should not be limited during the first few days. In the beginning, it may take 2 to 3 minutes of suckling to stimulate the release of oxytocin (a hypothalamic hormone produced in the posterior pituitary gland). Oxytocin initiates “let-down,” the term for the process by which the milk begins to empty from the breast due to the contraction of myoepithelial cells. Prolactin, a hormone produced in the anterior pituitary gland, stimulates milk production. Early and frequent feeding reduces the risk of engorgement. Removing the infant from the breast prior to let-down does not stimulate milk supply and may frustrate both the mother and infant.

The infant should be encouraged to suckle the first breast until the milk flows. When the infant stops suckling and pulls away from the breast the baby should be placed on the other breast after burping for as long as the infant suckles. Although the duration of feeding may

vary among infants, feeding should be infant-led and not clock-led.

The composition and volume of breast milk change during each feeding. The milk provided after about 5 to 10 minutes is the richest in fat and therefore caloric content. It is called the "hind milk." Infants need to nurse long enough to become satiated and to obtain sufficient calories from the breast milk for appropriate growth and development. Mothers should be instructed that the infant will get 75 percent of the milk volume in the first 5 to 10 minutes after the "let-down," but only 50 percent of the calories because breast milk becomes higher in fat and calories after the first five minutes.

Once lactation is established, an infant who suckles vigorously usually empties the breast 10 to 20 minutes after let-down has occurred. It may take up to an hour to "empty" both breasts. Infants will suckle until satisfied and should alternate starting breasts with each feeding in order to ensure even milk production. A full-term newborn infant should feed 8 to 12 times during 24 hours. Human milk is easily digested and empties from the infant's stomach in 90 minutes, while formula empties in 3 to 4 hours.

5. How will LW know if her breastfed baby is getting enough to eat? Compare the growth patterns of breastfed and formula fed infants.

The best way to be sure that babies are receiving adequate amounts of breast milk is to monitor their growth and development. Milk production generally works on the principle of supply and demand. That is, the more a baby feeds, the more milk is produced. In the first few days of life, it is not uncommon for a full-term newborn to feed every 1 to 3 hours during each 24-hour period; this helps to stimulate initial milk production. About 6 weeks postpartum, feeding frequency will diminish to about 8 times in 24 hours once the milk supply has been established.

Full-term newborns experience an initial weight loss. It is very important to monitor weight gain in the first few days of life. Women who have received intravenous fluids during labor may pass extra fluid via the placenta to the baby whose birth weight increases. These babies void larger amounts in the first few days. They may lose 10 percent of their birth weight. This does not reflect poor feeding. A return to birth weight should occur by day 10. If weight gain is not achieved then the patient should be referred to the physician and a lactation professional. A baby who has at least six wet diapers and a minimum of three stools per day and is gaining weight appropriately (at least 7 ounces per week) is usually consuming enough milk.

Breastfed and formula-fed infants have slightly different growth patterns. In the first 2 to 3

months human milk-fed infants gain weight more rapidly. After the first few months of life, the weight gain is similar to formula-fed infants and then begins to slow down. The current Centers for Disease Control and Prevention growth charts are based on NHANES data of only a few healthy breastfed and formula-fed children. It is an average of fat and thin, not a standard. The WHO also has developed growth charts based on breastfeeding infants in good health and represent how infants should grow. They are the new international standard.

Although breastfed infants consume less milk over a 24-hour period and therefore have a lower energy intake, they are more energy efficient than formula-fed infants. By their third birthday, breastfed infants have a lower percentage of body fat and are rarely obese. Data from the Darling Study have shown that breastfed infants are less likely to be overfed and have a decreased risk of becoming overweight or obese later in life compared to formula-fed children, which may be because they learn to stop eating when they are satisfied. Breast feeding is one suggestion experts are advocating as a way to prevent obesity in children (see Chapter 4).

Part 2: Follow-up

6. How should LW's weight loss and dietary intake be assessed?

Although LW desires to lose weight, the goal should be for her to achieve slow and steady weight loss so that she does not compromise her own health or milk supply. Currently, her dietary intake is slightly below what is recommended to support lactation. Her calorie requirements for lactation are estimated to be 2225 to 2325 kcal/kg/day, calculated on the basis of 25 kcal/kg per day (based on BMI > 25 kg/m^2) plus an additional 300 to 400 kcal/day for lactation. Extra calories for lactation should be adjusted based on the BMI, activity level, and age of the woman. Her diet does not provide adequate amounts of iron, calcium, vitamin A, vitamin D, vitamin B_{12}, vitamin D, folate, and zinc. To enhance her nutrient intake she should be encouraged to increase her intake of lean proteins, fruit and vegetables, low-fat vitamin D-enriched milk or yogurt, and include an iron-rich snack, such as raisins or dried fruit in the morning. She should limit her intake of concentrated sweets. She should also be advised to continue to take her prenatal vitamin. She may also need to consider taking a vitamin D supplement. The AAP recommends that exclusively breastfed infants receive oral vitamin D drops of 400 IU shortly after birth. This would be the ideal time to encouraged LW to start her baby on vitamin D. In addition, her fluid intake is low and she should be encouraged to drink more nutritious fluids (up

to 2 liters per day), such as skim milk fortified with vitamin D, 100 percent juices, and water.

7. How can breastfeeding women prepare to return to work?

A mother returning to work can continue to breastfeed by renting or purchasing a breast pump to remove milk during the day for use at home while she is working. The advantages of pumping the breast at least every 4 hours are to ensure that the baby will receive breast milk when the mother is at work and to promote the continued supply of breast milk even though the baby is not feeding during the day. It is important for the mother to pump to avoid engorgement and mastitis. Breastfeeding exclusively whenever the woman is not working will help milk production to continue. According to the Human Milk Banking Guidelines, breast milk can be stored in the refrigerator for less than 4 days, in the freezer for less than 3 months, and in a deep freezer (−18 to −20 °C) for less than 12 months for term infants.

The father or a caretaker should offer the bottle because the baby may expect to breastfeed when the mother is present. Offering one bottle of expressed breast milk about once a day, starting about 2 weeks before the mother returns to work, may help the infant learn how to suck from a bottle, which is different from breastfeeding. Once the mother returns to

work, the baby should be given expressed breast milk during the day. When the mother returns from work, she should breastfeed as soon as possible.

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4
Infants, Children, and Adolescents

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Objectives*

Take an appropriate pediatric history relating to the nutritional assessment and management of children and adolescents.

Evaluate growth parameters of an infant, child, or adolescent using the appropriate growth charts.

Select laboratory tests and diagnostic procedures appropriate to assess, support, and manage the nutrition of infants, children, and adolescents.

Summarize the current recommendations (proposed by relevant health-professional organizations and government agencies) for

healthy nutrition of infants, children, and adolescents by age and sex.

*Source: Objectives for chapter and cases adapted from the *NIH Nutrition Curriculum Guide for Training Physicians*. (www.nhlbi.nih.gov/funding/training/naa)

Assessment of Nutritional Status and Dietary Intake in Children

The assessment of nutritional status is critical in the care of sick and well children since nutritional status affects the child's response to and recovery from illness, and supports healthy growth and development. Dietary intake during infancy, childhood, and adolescence influences normal growth and development and provides a foundation for adult health. Many changes in growth and body composition happen during infancy, childhood, and adolescence. Therefore, healthcare professionals need to understand normal growth to recognize abnormal patterns of growth and development. Historically, childhood malnutrition was equated with low weight for height (length), weight loss, stunted growth, and impaired development. Currently, childhood malnutrition also encompasses "over-nutrition" and obesity. All forms of malnutrition have been associated with micronutrient deficiencies or excesses,

co-morbidities, and mortality. Children, who suffer acutely from malnutrition from either inadequate intake or an underlying condition that changes nutrient needs or absorption/ utilization, may develop nutritional deficiencies that require attention and proactive management. There are currently new efforts aimed at better defining pediatric nutritional status to improve its recognition and thus treatment outcomes. More recently, authors proposed that the definition of malnutrition be not only based on anthropometric factors, but also chronicity, etiology, mechanisms of nutrient imbalance, severity of malnutrition, and its impact on outcomes. Healthcare professionals care of infants, children, and adolescents can profoundly influence their immediate and long-term health and longevity by helping support good nutrition. Therefore, clinicians must become adept at assessing the nutritional status of children, developing an appropriate nutritional management plan, and counseling caregivers and children to foster healthy eating habits and to support optimal nutrition and health.

Assessing Growth and Development

Evaluation of growth and development is the cornerstone of pediatric nutrition assessment. Updated growth charts were released in 2006

by the World Health Organization (WHO) and in 2000 by the Centers for Disease Control and Prevention (CDC), based on National Health and Nutrition Examination Survey (NHANES) data collected from 1971 to 1994. Weight, height, head circumference are available in both surveys. The CDC charts represent the combined growth patterns of breastfed and formula-fed infants in diverse United States racial and ethnic groups. The WHO growth charts were created with longitudinal length and weight data measured at frequent intervals among breastfed children up to 2 years of age and cross-sectional data up to 5 years of age (60 months old), using data from six countries (Brazil, Ghana, India, Norway, Oman, and the United States). A variety of growth charts for infants born from pre-term deliveries are also available. The most commonly used neonatal charts in the United States are from Fenton and Olsen. The Olsen neonatal growth charts (23 to 42 weeks gestation) are gender specific and based on infants from a racial and ethnic mix born in the United States (1998–2006). The Olsen growth charts are available on the American Academy of Pediatrics website (www2.aap.org/sections/perinatal/PDF/GrowthCurves.pdf). The Fenton neonatal growth curves (22 to 43 weeks gestation) are not gender specific and based mainly on Caucasian infants born in Canada, Australia, and Sweden (1977–1995) and were smoothed at 40 weeks of gestation to the recent WHO

growth charts at birth. The Fenton charts are available on the website (http://members.shaw.ca/growthchart/Fenton%20WHO%20growth%20chart%2008.pdf)

Children's and adolescents' height should be measured without shoes using a wall-mounted stadiometer and weight taken wearing light clothing. A length board should be used for infants. Body mass index (BMI) for children aged 2 to 18 years old is calculated based on weight divided by height squared (kg/m^2). Standard BMI definitions for overweight and obesity are available for adults. However, as BMI for children varies by age, BMI percentiles (Figure 4-1; www.cdc.gov/growthcharts) should be utilized to define relative weight for children. For infants and children less than 2 years of age, weight-for-length (WL) rather than BMI should be assessed because of the persistent correlation between BMI and length in this age group. Once the child can stand, weight-for-height can be substituted (typically between 2 and 3 years old). Although WL, weight-for-height (WH), and BMI provide data on relative weight, WL and WH are typically used to classify and monitor malnutrition in hospital settings while BMI is more commonly used in outpatient settings. For children and adolescents 2 to 18 years, BMI (kg/m^2) can be

calculated as a measure of relative weight (Table 4.1 and Figure 4-1).

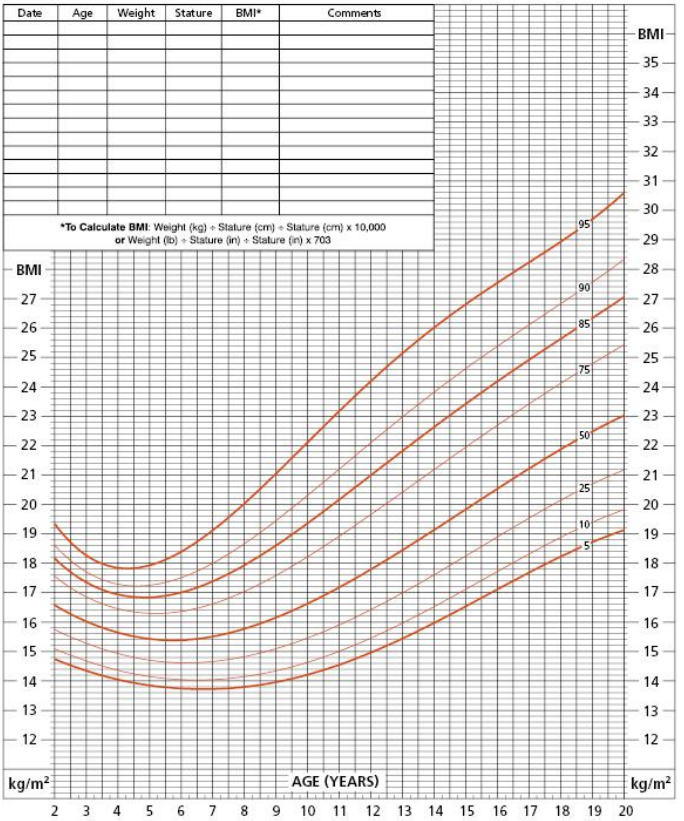
2 to 20 years: Boys
Body mass index-for-age percentiles

NAME _____

RECORD # _____

Date	Age	Weight	Stature	BMI*	Comments

*To Calculate BMI: Weight (kg) ÷ Stature (cm) ÷ Stature (cm) x 10,000
or Weight (lb) ÷ Stature (in) ÷ Stature (in) x 703



Published May 30, 2000 (modified 10/16/00).
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000). http://www.cdc.gov/growthcharts

CDC
SAFER · HEALTHIER · PEOPLE™

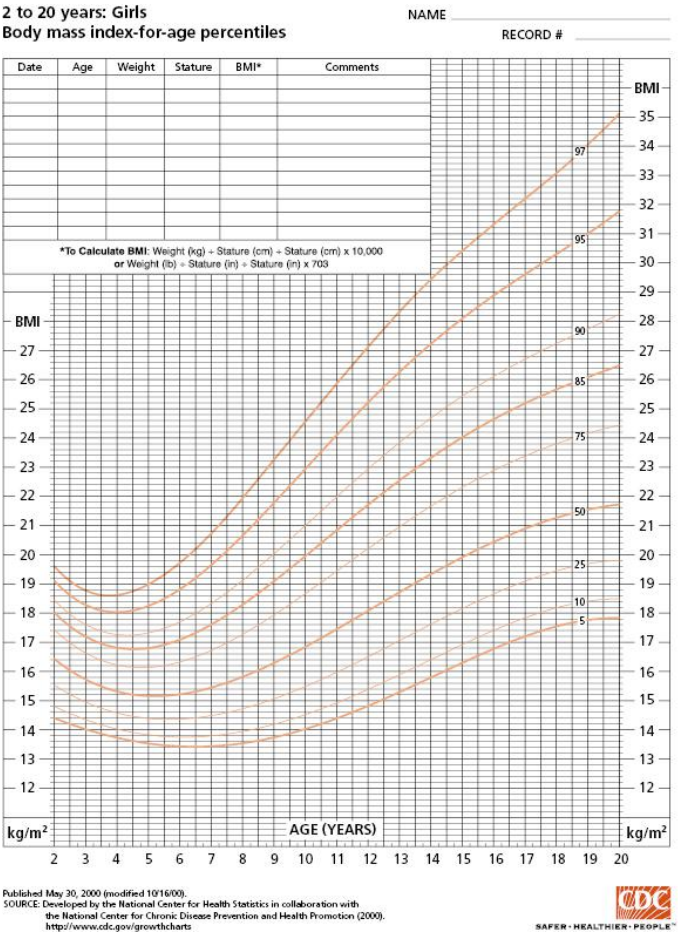


Figure 4-1 BMI Percentiles

Source: Data from Centers for Disease Control and Prevention. http://www.cdc.gov/nchs/data/nhanes/growthcharts/set1clinical/cj41l023.pdf http://www.cdc.gov/nchs/data/nhanes/growthcharts/set1clinical/cj41l024.pdf

Table 4-1 BMI Classification for Children and Adolescents (CDC)

Source: Centers for Disease Control and Prevention. 2014. Used with permission.

BMI Category	Recommended Terminology
<5th percentile	Underweight
5th–84th percentile	Healthy weight
85th –94th percentile	Overweight
95th –97th percentile	Obesity
98th –99th percentile	Moderately obese
>99th percentile	Severely obese

Height (stature) or length (recumbent), weight, and WL or BMI should be plotted on a sex-specific growth chart kept with the child's medical records (paper or electronic) so that the individual values and a longitudinal record of the child's growth can be examined and evaluated. Plotted values of all three of these growth parameters should be assessed to determine:

whether they are following consistently along a particular percentile or z-score line,

the degree to which particular plotted values deviate from the child's prior pattern of growth,

whether these values are outliers relative to the growth charts norms,

whether the growth pattern for height/length, weight, and head circumference are similar.

For children under 2 years of age, the CDC and American Academy of Pediatrics (AAP) recommend using the WHO growth charts. For these young children, growth assessment should also include measuring head circumference. Note also that measurements of length and height differ so standard growth curves for evaluating length and height should not be used interchangeably. WHO recommends the use of a formula to transform length to height or height to length to plot children on the appropriate growth chart, when necessary. Infants corrected age (chronological age in weeks – [40 weeks – gestational age in weeks]) may be calculated between birth and 24 months of age for infants born from pre-term deliveries. Premature infants can be plotted on the neonatal charts until the infant reaches 40 weeks expected gestational age. After 40 weeks expected gestational age, infant growth charts can be used. Children who are underweight (BMI <5th percentile), losing weight, or whose linear growth has slowed or ceased, should be assessed for medical conditions that could impair growth or nutritional status and cause

nutritional deficiencies. Similarly, children observed to be gaining weight rapidly or to have an increasing BMI percentile (typically crossing two major percentile curves, WL greater than the 95th percentile [children younger than 2 years old]), or BMI more than the 95th percentile (children at or greater than 2 years old) warrant further evaluation. Classification of BMI for children and adolescents according to the CDC is shown in Table 4-1 while classification of malnutrition according to the WHO is shown in Table 4-2. Although the CDC growth charts are recommended for the growth and nutritional assessment of all children, a number of condition/syndrome-specific growth charts have been published (e.g., achondroplasia, Brachmann-de Lange syndrome, cerebral palsy, Down syndrome, Marfan syndrome, myelomeningocele, Noonan's syndrome, Prader-Willi syndrome, sickle cell disease, Silver-Russell syndrome, Turner's syndrome, Williams syndrome). Of note, classification of malnutrition has changed over time but some of the older classifications are still in use at this time, especially in hospital settings (Table 4-3).

Table 4-2 Nutrition Status: WHO Classification

Z-Score (0–5 y old)	Length/Height-for-Age	Weight-for-Age	Weight-for-Length/Height	BMI-for-Age
Above 3			Obese	Obese
Above 2			Overweight	Overweight
Above 1				
0 (median)				
Below −1				
Below −2	Moderately stunted	Moderately underweight	Moderately wasted	Moderately wasted
Below −3	Severely stunted	Severely underweight	Severely wasted	Severely wasted
Z-Score (5–19 y old)	**Height-for-Age**	**Weight-for-Age (to 10 y old)**	**Weight-for-Height**	**BMI-for-Age**
Above 3				Severe obesity
Above 2				Obesity
Above 1				Overweight
0 (median)				
Below −1				
Below −2	Moderately stunted	Moderately underweight		Moderate thinness
Below −3	Severely Stunted	Severely underweight		Severe thinness

Source: The WHO Child Growth Standards. www.who.int/childgrowth/standards/en/

Table 4-3 Common Classification of Malnutrition in the Hospital and Outpatient Settings

Classification	Indicator	Severity	Percent of Median[a]
Gomez (1955)	WA	Mild	75–90
		Moderate	60–74
		Severe*	<60
Waterlow (1972)	WH (wasting)	Mild	80–89
		Moderate	70–79
		Severe	<70
Waterlow (1972)	HA (stunting)	Mild	90–94
		Moderate	85–90
		Severe	<85
McLean (1975)	WL	Mild	85–90
		Moderate	75–84
		Severe	<75

[a]Percentage of the median is calculated by the following formula: e.g., WA

% weight = (actual weight/median weight) × 100 for age and sex

*WA < 60% has been associated with increased mortality risk.

Evaluating Dietary Adequacy in Children

Dietary intake is difficult to assess accurately in an outpatient setting, as it is based on recall and requires that both the healthcare provider and the patient or caregiver understand portion

sizes and content of a variety of foods. Infants, children, and adolescents being evaluated for abnormal growth or development should generally be assessed by a pediatric nutrition professional such as a registered dietitian. Nevertheless, with the high prevalence of overweight and obesity in the pediatric population, primary care providers must be able to make a general assessment of eating behavior and estimate calorie and nutrient intake in order to provide basic counseling, or appropriate referral to a pediatric nutrition professional, for all patients and caregivers.

The most common method for making such assessments in the clinical setting is the 24-hour recall. The 24-hour recall includes asking the child and caregiver about all foods consumed by the child in the last day. Once a list of foods has been compiled, the provider can probe for more details about each, including portion size, preparation, and brand names. The provider should also probe for foods and drinks that may have been missed with questions like “Did you eat anything between lunch and dinner?” or “Did you have anything to drink with your breakfast?” Although asking about only 1 day has its limitations, the 24 hour recall provides a basic overview of the child's eating habits, can highlight problem areas, and stimulate further discussion about the child's diet. It should be noted that studies show that children and

adults commonly underreport their dietary intake.

Pediatric Calorie and Nutrient Requirements

Nutrient requirements are largely determined by lean body mass, activity level, and basal metabolic rate. Therefore, body composition, which changes during the course of growth and development, must be considered when estimating nutrient needs of children and adolescents. Percent body fat, or fat mass, is high in infants and toddlers and decreases as children enter their elementary school years. During puberty, percent body fat increases in both boys and girls. Lean body mass (LBM) also increases, approximately tripling in boys and doubling in girls. As adolescents reach adulthood, females retain a higher percentage body fat and lower lean body mass than males. Pubertal changes in body composition drive changes in nutrient requirements and the difference in lean body mass between men and women accounts for differences in calorie and nutrient requirements.

Various recommended energy and nutrient allowances have been formulated for growing children based on the changing nutritional needs associated with growth and development. For the general population, the USDA has developed My Plate based on the *Dietary*

Guidelines for Americans (www.choosemyplate.gov). Nutritional guidelines were originally aimed at preventing undernutrition; recent guidelines have evolved to support overall good nutrition, and to prevent over- and under-nutrition. The MyPlate guidance system is intended to provide a framework for adults and children for determining what and how much to eat each day using the familiar image of a place setting for a meal. The MyPlate image replaced the MyPyramid system in 2011. The ChooseMyPlate.gov website provides of well-organized information to help Americans make the best food choices. It also allows for the development of individualized dietary and physical activity plans. Dietary Reference Intake (DRI) values developed by the Food and Nutrition Board, Institute of Medicine, National Academy of Sciences provide another useful tool for determining specific energy and protein requirements as shown in Table 4-4. DRIs can be used by dietitians and health professionals to help patients with specific dietary planning needs, but MyPlate is more practical and easy-to-understand tool for initial dietary changed.

Table 4-4 Energy and Protein Requirements in Children and Adolescents

	Energy (kcal/day)		Protein (g/day)	
Age	Males	Females	Males	Females
0–6 months	570	520	9.1	9.1
7–12 months	743	676	11	11
1–2 years	1046	992	13	13
3–8 years	1742	1642	19	19
9–13 years	2279	2071	34	34
14–18 years	3152	2368	52	46

Source: Institute of Medicine, *Dietary Reference Intakes for Energy and Protein*. National Academy of Science, National Academy Press, Washington, DC: 2008.

Adjustments for Activity and Illness

In pediatric acute care settings, specific adjustments are made for special circumstances such as differing activity levels and illness. Nutrient requirements are estimated based on specific equations using resting energy expenditure and a stress factor to account for the underlying condition. For example, fever increases energy needs by 7 percent for each degree above 98.6 °F of body temperature (or 12 percent for each degree above 37 °C). Illness, trauma, major surgery, extensive burns, recovery from undernutrition, and intensive exercise or manual labor cans double energy requirements. Chronic under-nutrition with loss of lean body mass can decrease energy needs by 20 to 30 percent. However, energy needs may increase rapidly in the malnourished child who is being nutritionally repleted. For example, with significant malnutrition, a child may be dehydrated and in a state of slowed metabolism, an adaptation that decreases calorie and nutrient requirements. Nutrionally

related laboratory assessments may seem relatively normal. However, refeeding causes anabolism and a rapid increase in metabolic processes, greatly increasing caloric and nutrient needs. These changes, along with rehydration, can unveil significant electrolyte and micronutrient deficiencies (e.g., phosphorus, potassium, magnesium). Overly aggressive refeeding without adequate nutrient supplementation can be associated with serious morbidity, including cardiac dysfunction, arrhythmias, congestive heart failure, and even death. Therefore, a significantly malnourished child must be repleted slowly, under close monitoring and supervision (see Chapter 4: Case 2).

For healthy children, level of physical activity should be considered when determining their dietary needs. Table 4-5 illustrates estimated energy requirements for children based on age, gender, and activity level.

Table 4-5 Estimated Energy Requirements (EER) (in kcals) for Gender and Age Groups Based on Activity Level

		Activity Level		
Gender	Age (years)	Sedentary	Moderate	Active
Child	2–3	1000	1000–1400	1000–1400
Female	4–8	1200	1400–1600	1400–1800
	9–13	1600	1600–200	1800–2200
	14–18	1800	2000	2400
Male	4–8	1400	1400–1600	1600–2000
	9–13	1800	1800–2200	2000–2600
	14–18	2200	2400–2800	2800–3000

Source: NHLBI expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: Summary report. National Heart, Lung, and Blood Institute; National Institutes of Health; US Department of Health and Human Services. http://www.nhlbi.nih.gov/guidelines/cvd_ped/summary.htm.

Laboratory Assessment

As part of a regular nutritional evaluation, broad screening using laboratory tests is generally not recommended. General assessments can include a complete blood count (CBC), serum electrolytes, creatinine, and albumin. Serum albumin is commonly used as an assessment of general long-term nutritional and protein status; however, it is an insensitive marker of nutrition status but a good predictor for mortality. Pre-albumin has a half-life a few days (as opposed to a few weeks for albumin) and may have utility as a short-term marker of protein-related nutritional status in the absence of inflammation (C-reactive protein (CRP) values are within normal range). Evaluation of the CBC, including white blood cell morphology and red blood cell size, can provide evidence of deficiencies in iron, folate, and vitamin B_{12}. Blood chemistries can indicate electrolyte and mineral imbalances, though blood levels are not always good indicators of whole body nutritional balance.

Fasting Glucose

It is estimated that about 150,000 to 200,000 individuals under the age of 20 have diabetes. As opposed to the epidemiology in adults, most children with diabetes have type 1 diabetes. However, over the past 20 years, the rate of type 2 diabetes in children and adolescents has

increased significantly, especially in some at-risk groups. Children with type 2 diabetes are frequently more than 10 years old, obese, and have a family history of type 2 diabetes. Rates are higher in some racial/ethnic groups, such as Asian/Pacific Islander, Native American, Black, and Hispanic descent children. Rates of undiagnosed type 2 diabetes and "prediabetes" (impaired fasting glucose (≥100 mg/dL; 5.6 mmol/L) in young persons are not well defined, though it is assumed the official statistics only identify a portion of the affected persons. Using fasting glucose levels and primary care provider diagnosis of diabetes from NHANES 1999–2000 to 2007–2008, May and colleagues (2012) reported that the prevalence of prediabetes/diabetes among adolescents aged 12 to 19 years old has increased from 9 percent to 23 percent. A study using NHANES 1999–2000 to 2007–2008 data predicted that the number of youth with type 1 diabetes and type 2 diabetes may increase by 23 percent and 49 percent, respectively. Overweight and obese children less than 18 years with two or more other risk factors (Table 4-6) should be screened for type 2 diabetes every 2 to 3 years. A fasting plasma glucose assessment (>125 mg/dL is consistent with diabetes; 101 to 125 mg/dL defines impaired fasting glucose or prediabetes) is most commonly used as a screening test for children, adolescents, and adults. In the evolution of type 2 diabetes, post-prandial glucose increases

earlier than fasting glucose; some experts therefore recommend determining plasma glucose two hours after a standard glucose load or two hours after a meal. Thus, significant elevations in non-fasting glucose tests, especially those >200 mg/dL should be further evaluated. Diabetes screening recommendations for children and adolescents are shown in Table 4-6. Though in adults, screening tests for diabetes and prediabetes include hemoglobin A1C, or a 2-hour plasma glucose level as part of an oral glucose tolerance test, such recommendations have not been broadly applied to children. Similarly, though HbA1C is now considered as a good tool for screening and monitoring for T2DM in adults, there are concerns about the use of A1C to evaluate children and adolescents for T2DM. Given that cardiovascular disease risk factors tend to cluster together, screening for other such risk factors (e.g. hypertension, dyslipidemia) should be considered for children and adolescents at risk for developing type 2 diabetes.

Table 4-6 Guidelines for Diabetes Screening for Children

Overweight plus two other risk factors:
1st or 2nd degree relative with type 2 diabetes mellitus

Higher risk race/ethnic group (African–American, Native American, Asian American, Pacific Islander, Latino)
Other conditions associated with insulin resistance (hypertension, dyslipidemia, acanthosis nigricans, polycystic ovary syndrome)

Elevated glucose levels, especially in the hospital setting, may occur at times of significant stress and acute illness, such as infection or sepsis, or as a side effect of some medications, such as steroids. Such secondary causes should be considered when assessing a child with hyperglycemia. Low glucose levels related to malnutrition are relatively rare, and usually occur in late stage, severe malnutrition. Neonates and premature infants are among higher risk groups for low and high glucose levels at times of stress.

Lipids

Encouraging a healthy lifestyle and consideration of cardiovascular disease risk factors should start relatively early in life. Screening for hypercholesterolemia should start around 3 years of age, and target children with a positive family history of early atherosclerotic vascular disease (AVD) or parental dyslipidemia. (Table 4-7 and Figures 4-2 and 4-3). A positive family history of early AVD is

defined as a parent, grandparent, aunt/uncle, or sibling with a heart attack, sudden death thought to be related to AVD, angina, angioplasty, peripheral vascular disease, or cerebrovascular disease before age 55 in males or before 65 in females. Screening should also be considered in children at higher risk for developing adult heart disease, such as those with diabetes, hypertension, and obesity. Children with high cholesterol levels tend to become adults with high cholesterol levels. However, as tracking of lipid levels over time is not perfect, not all the hypercholesterolemic children will become hypercholesterolemic adults. Screening in high-risk children should consist of the average of two fasting lipid profiles obtained on two separate occasions. Low-density lipoprotein cholesterol (LDL-C) ≥ 130 mg/dL or triglycerides >110 mg/dL are generally considered elevated and should be evaluated further for secondary causes and potential intervention (see Table 4-7 and Figures 4-2 and 4-3). The initial intervention in children with primary hypercholesterolemia is dietary and lifestyle assessment and intervention.

Table 4-7 Acceptable, Borderline-High and High Plasma Lipid, Lipoprotein and Apolipoprotein Concentrations (mg/dL) for Children And Adolescents
*

Category	Acceptable	Borderline	High†
TC	<170	170–199	≥200
LDL-C	<110	110–129	≥130
Non-HDL-C	<120	120–144	≥145
ApoB	<90	90–109	≥110
TG			
0–9 years	<75	75–99	≥100
10–19 years	<90	90–129	≥130

Category	Acceptable	Borderline	Low†
HDL-C	>45	40–45	<40
ApoA-1	>120	115–120	<115

Note: Values given are in mg/dL. To convert to SI units, divide the results for total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and non-HDL-C by 38.6; for triglycerides (TG), divide by 88.6.
* Values for plasma lipid and lipoprotein levels are from the National Cholesterol Education Program (NCEP) Expert Panel on Cholesterol Levels in Children. Non-HDL-C values from the Bogalusa Heart Study are equivalent to the NCEP Pediatric Panel cutpoints for LDL-C. Values for plasma ApoB and ApoA-1 are from the National Health and Nutrition Examination Survey III.
† The cutpoints for high and borderline-high represent approximately the 95th and 75th percentiles, respectively. Low cutpoints for HDL-C and ApoA-1 represent approximately the 10th percentile.
Source: NHLBI expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: Summary report. National Heart, Lung, and Blood Institute; National Institutes of Health; US Department of Health and Human Services. http://www.nhlbi.nih.gov/guidelines/cvd_ped/summary.htm

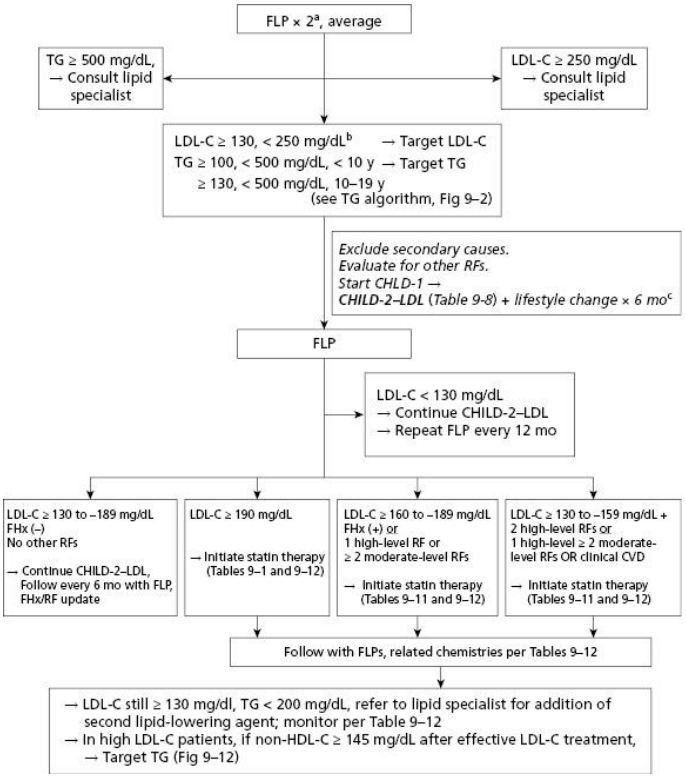


Figure 4-2 Dyslipidemia Algorithm

Source: NHLBI expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: Summary report. National Heart, Lung, and Blood Institute; National Institutes of Health; US Department of Health and Human Services. http://www.nhlbi.nih.gov/guidelines/cvd_ped/summary.htm

FLP = fasting lipid profile

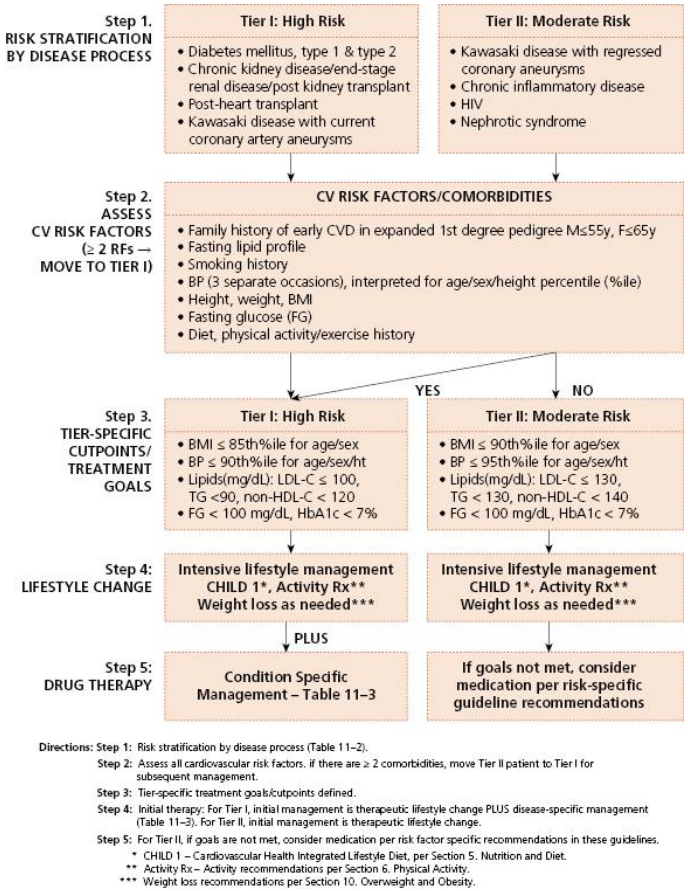


Figure 4-3 Risk Stratification and Managementfor Children with Conditions Predisposing to Accelerated Atherosclerosis and Early CVD

Source: NHLBI expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: Summary report. National Heart, Lung, and Blood Institute; National Institutes of Health; US Department of

Health and Human Services.
http://www.nhlbi.nih.gov/guidelines/cvd_ped/summary.htm

Universal screening is recommended for children 9 to 11 years old, and can consist of a non-fasting non-high-density lipoprotein cholesterol (non-HDL-C) assessment. Children with non-HDL-C greater than 145 mg/dL and/or HDL-C less than 40 mg/dL should be considered for further assessment, including fasting lipid profiles. A general summary of the National Heart, Lung, and Blood Institute expert panel's recommendations regarding lipid screening is shown in Table 4-7 and Figures 4-2 and 4-3, and further details are available at http://www.nhlbi.nih.gov/guidelines/cvd_ped/summary.htm. Guidelines are also available for the management of patients with obesity and dyslipidemia.

Iron Status

Though significant progress has been made in decreasing rates of iron deficiency in children in the United States over the past several decades, iron deficiency is likely the most common micronutrient deficiency in the United States. Iron deficiency is usually due to inadequate dietary intake of iron, especially during times of rapid growth or increased blood loss, such as infancy and early childhood, and during adolescence (especially for girls). Pre-term infants and infants with intrauterine growth

retardation are also born with decreased iron stores and thus should receive iron supplements. Adolescent athletes, for reasons that are not totally clear, are another at-risk group. A higher prevalence of iron deficiency has also been observed in obese children across a broad age range. Even in the absence of anemia, iron deficiency is associated with poor growth and neuro-cognitive development in infants and behavioral and learning problems in older children and adolescents. Iron deficiency and iron-deficiency anemia are also associated with decreased exercise capacity and physical endurance. Thus it is very important to identify and treat iron deficient children.

As specific measures of iron stores (e.g., serum ferritin, transferrin, iron binding capacity, free erythrocyte protoporphyrin) are costly and not widely available, hemoglobin and red blood cell indices (derived from a simple CBC) are the laboratory parameters most commonly used to evaluate children for iron deficiency. However, these are relatively insensitive measures of true iron status. It should be noted that transient decreases in hemoglobin levels are relatively common with infections, thus a single low hemoglobin level should be confirmed or assessed further before initiating therapy. An alternative to more specialized testing is providing a therapeutic iron supplement challenge. An iron deficient child should respond to such a challenge with a

reticulocytosis and increase in hemoglobin within a few weeks. Screening for iron deficiency should thus focus on at-risk children, as noted above, and especially those at-risk children who have not been receiving iron-sufficient diets, or iron supplements, as appropriate.

Vitamin D

Vitamin D deficiency, defined based on the serum or plasma measurement of 25-hydroxyvitamin D [25(OH)D], is a common and poorly recognized condition that occurs in infants, children, adolescents, and adults. Many affected children are dark skinned and have limited exposure to UV light, are fed unfortified "health food" milk alternatives, or are breastfed without vitamin D supplementation by mothers with vitamin D insufficiency or deficiency.

As reviewed by the Institute of Medicine (IOM) taskforce in 2011, vitamin D is essential for skeletal health but there is currently a lack of convincing evidence to link vitamin D supplements with benefits for other nonskeletal outcomes such as cardiovascular disease, death, cancer, and quality of life. There is no additional benefit currently identified for levels of 25(OH)D above 20 ng/mL (50 nmol/L), therefore the IOM considered the 20-ng/ml level as the upper range of human requirements, meeting the needs of most individuals in the general populations

(regardless of other factors such as skin color). However, these guidelines are not specific for individuals with underlying conditions or diseases. The United States Institute of Medicine Recommended Dietary Allowance of vitamin D is 400 IU per day for children younger than 1 year of age, 600 IU per day for children at least 1 year of age and adults up to 70 years, and 800 IU per day for older adults. The AAP recommendations for children is similar to the IOM but that of the pediatric endocrine society is not. Premature infants, dark-skinned infants and children, and children who reside at higher latitudes (particularly above 40°) may require larger amounts of vitamin D supplementation, especially in the winter months. The principal source of vitamin D is solar UV-B (wavelengths of 290–315 nm) irradiation. Dietary sources of vitamin D other than vitamin supplements are limited and include oily fish, some fish oils, and egg yolks. Although some foods in the United States are vitamin D fortified, including milk, some cereals, orange juice, some yogurts, and margarine, most United States children do not eat sufficient quantities of vitamin D-containing foods to provide adequate vitamin D intake.

Although 25(OH)D serum/plasma levels are considered the gold standard to identify vitamin D deficiency, this may be a poor marker in chronic conditions such as obesity and conditions with inflammation. Youth who are

obese tend to have 25(OH)D levels in the deficient range but studies of bone density in this population are similar to reference populations, thus there is currently no evidence that these lower vitamin D levels in obese children have a demonstrable effect on bone health . New screening and treatment guidelines for obese children with low vitamin D levels have not been developed.

Infant Feeding

Many nutritional recommendations for children and infants are based upon expert consensus and opinion, and thus should be considered in this context. This is not to say these recommendations should be discounted – but concrete data to support these recommendations may not be available.

Breast or Bottle

Lactation is discussed in Chapter 3.

The AAP states that breastfeeding and human milk are the normative standard and recommends exclusive breastfeeding up to approximately 6 months for almost all infants (see iron and vitamin D section above for recommendations regarding supplements for breastfed infants). Breastfeeding is associated with numerous medical and neurocognitive advantages. Though true contraindications to breastfeeding are rare, there are significant

obstacles to breastfeeding in the United States, including lack of knowledge, limited experience with breastfeeding, lack of support for breastfeeding mothers at home or in the workplace, and misguided social “norms”. All healthcare providers, including hospitals, obstetricians, and pediatricians, and all pediatric care providers should encourage breastfeeding whenever possible, and work to encourage community-based supports for breastfeeding mothers. Certified breastfeeding counselors and breastfeeding support groups should be used when appropriate to help establish and support effective breastfeeding. Interventions to overcome problems with breastfeeding must be considered as relatively urgent, to avoid interruptions in the mother's milk supply or other problems which may interfere with longer term success with breastfeeding. The WHO/Unicef Baby Friendly Initiative launched in 1991 and revised in 2006 has contributed to increased rates of exclusive breastfeeding and improved infant health and survival.

Except for special formulas, manufacturers of infant formulas try to approximate the composition of human breast milk. For example, formula manufacturers add omega-3 and omega-6 fatty acids, docosahexaenoic acid (DHA), and arachidonic acid (ARA) to infant formulas, as these fatty acids are found in

breast milk and support normal brain and eye development.

Iron and Vitamin D Supplementation

Even though breast milk is lower in iron than cow's milk, the iron in breast milk is more readily absorbed. Pre-term infants and infants with intrauterine growth retardation are born with decreased iron stores and thus should receive iron supplements (for breastfed infants 2 mg/kg per day elemental iron is recommended as a supplement; formula-fed infants should receive iron fortified formula and 1 mg/kg per day elemental iron as a supplement is appropriate). Recommendations for breastfed infants, beginning around 4 to 6 months, include 1 mg/kg per day of iron. For older infants, iron supplements may be required if adequate intake from complementary foods is not assured.

Supplementation with 400 IU of vitamin D should be initiated within days of birth for all breastfed infants, and for non-breastfed infants and children who do not ingest at least 1 litre of vitamin D-fortified formula or milk daily, and consideration should be given to supplementing with up to 800 IU of vitamin D per day.

Weaning Babies from Breast Milk or Formulas

Infants should remain on breast milk or formula until the age of 1 year, as the AAP recommends that cow's milk not be given to children under 1 year of age. Most healthcare providers feel that cow's milk is an important source of calories, protein, and calcium for children over 1 year of age. Earlier introduction of cow's milk is associated with gastrointestinal blood loss due to a milk protein-induced inflammatory reaction in the small bowel. This blood loss may be sufficient to deplete iron stores and to produce anemia. In addition, cow's milk has a higher protein and phosphorus content than breast milk or infant formula. These components present a solute load that exceeds the capacity of the immature kidney and may precipitate dehydration and electrolyte imbalance in infants.

Introducing Solid Food

Recommendations concerning the introduction of solid food have changed considerably over the years. In the past, many children ate a wide variety of foods as early as the first month of life. The consensus among healthcare providers is to delay the introduction of solid foods until the child is at least 4 months old. The AAP and WHO both recommend breast milk as the sole nutrient source until 6 months of age.

Infants are not physiologically ready to accept solid foods from a spoon until they are at least 4 months of age. It is around this time that the oral extrusion reflex becomes extinguished and infants develop sufficient head and neck control and coordination of the oral musculature to begin taking solid foods. Recent data also suggests that early introduction of solid foods (defined as before 4 months of age in this study) may predispose the child to excess weight gain and obesity.

The introduction of solid foods marks the beginning of a critical period during which the infant learns to master eating from a spoon and to accept different tastes and textures. Not coincidentally, an infant's readiness for these experiences generally corresponds to a physiologic need to supplement the amounts of calories and nutrients available from breast milk or formula. However, breast milk, formula, or a combination should still continue to be the major source of calories and nutrients during the remainder of the infant's first year.

Preventing and Managing Food Allergies

Introducing solid foods earlier in an infant's life may stimulate the development of food allergies. Infants from families with known food allergies are most at risk. Food allergies – actually, food hypersensitivity reactions – occur

in 2 to 8 percent of children less than 3 years of age. Approximately 90 percent of food allergies are associated with the following group of eight foods: peanuts, tree nuts (such as walnuts or cashews), eggs, milk, fish, shellfish, soy, and wheat. Approximately 2.5 percent of infants will experience allergic reactions to cow's milk in the first 3 years of life, 1.5 percent to egg, and 0.6 percent to peanuts. Many children outgrow food allergies during the first few years of life. Approximately 85 percent of children with reactions to milk and eggs become tolerant to them by 5 years of age. Even a peanut allergy may remit in up to 20 percent of children. It should be noted that celiac disease is related to a reaction to gluten, may cause symptoms similar to food allergies (diarrhea, abdominal pain), but is not an allergy, and does not remit with time.

General Guidelines for Introducing New Foods

Most experts agree that new foods should be introduced gradually, with an interval of at least 3 days between successive new food introductions. Following this procedure makes it easier to detect a child's inability to tolerate a newly introduced food. Table 4-8 summarizes how to feed an infant during the first year of life and is often very helpful to hand out to parents of infants.

Table 4-8 How to Feed Your Infant During the First Year of Life

Age (months)	Breast Milk or Iron Fortified Infant Formula*	Cereals & Breads	Fruits & Fruit Juices†	Vegetables	Protein Foods	Dairy Foods
0–4	5–10 feedings/day 17–24 fluid ounces a day (510–720 mL)	None	None	None	None	None
4–6	4–7 feedings/day 24–32 fluid ounces/day (720–960 mL/day)	First food for formula-fed infants: rice or barley infant cereals (iron fortified). Mix cereal with Formula until thin. Start with 1 Tbsp. at each feeding for a few days, and increase to 3–4 Tbsp. per day. Feed with small baby spoon (don't expect baby to eat much at first).	None	None	First food for breastfed or partially breastfed infants: smooth preparations of single meats (beef, veal, lamb, turkey, chicken) in small quantities of up to 2 Tbsp/day.	None
7–8	4–6 feedings/day 24–32 fluid ounces/day (720–960 mL/day)	Single grain infant cereals: rice, oatmeal, barley (iron fortified) in the morning. 3–9 Tbsp/day, mixed with breast milk or infant formula. Two feedings/day. Oven-dried toast or teething biscuits, crackers, or toast strips.	Strained or mashed fruits (fresh or cooked), mashed bananas, applesauce. 4-ounce jar or ½ cup/day. Infant 100% fruit juices: <4 ounces/day mixed with water and served in a cup.	Strained or mashed, well-cooked dark yellow or orange (not corn), dark green vegetables. Start with mild vegetables such as green beans, peas, or squash. 1/2–1 jar or 1/4–1/2 cup/day.	Smooth preparations of single meats: beef, veal, lamb, turkey, chicken in small quantities (up to 2 Tbsp/day).	Cottage cheese, yogurt
Age (months)	**Breast Milk or Iron Fortified Infant Formula***	**Cereals & Breads**	**Fruits & Fruit Juices†**	**Vegetables**	**Protein Foods**	**Dairy Foods**
8–9	3–4 feedings/day 24–32 fluid ounces/day (720–960 mL)	Infant cereals or plain hot cereals mixed with breast milk or formula. 8–12 Tbsp/ day. Toast, bagels, crackers, teething biscuits. Small pieces of cooked noodles, potatoes.	Peeled soft fruit wedges: bananas, peaches, pears, oranges, apples (skin removed). ½–½ cup/day. 100% fruit juices† including orange and tomato juices. 4–6 ounces/day (120–180 mL).	Cooked, mashed vegetables. 1/3–½ cup per day	Well cooked, strained, ground, or finely chopped chicken, fish, and lean meats: 2–3 Tbsp/day (remove all bones, fat, skin). No peanut butter until 1 year. Cooked dried beans. Egg yolks and whites.	Cottage cheese, yogurt, bite-size cheese strips.
10–12	3–4 feedings a day 24–32 fluid ounces/day (720–960 mL) by cup or bottle	Infant or cooked cereals mixed with breast milk or formula. ¼ cup/day. Unsweetened cereals, whole wheat breads. Mashed potatoes, rice, noodles, spaghetti. ¼ cup up to 4 times/day.	All fresh fruits peeled and seeded or canned fruits packed in water. ½– ¾ cup/day. 100% fruit juices 4–6 ounces/day (120–180 mL).†	Cooked vegetable pieces. Some raw vegetables: tomatoes, cucumbers. ½–¾ cup/day.	Small tender pieces of chicken, fish or lean meat. Cooked beans, pasta.	Cottage cheese, yogurt, bite-size cheese strips.

Source: adapted from Lisa Hark, PhD, RD and Diane Bansky, MD, 2014. Used with permission.
*These are general guidelines. Feeding schedules vary somewhat between children.
†There is no specific need for juice in an infant's diet.

Cereals For formula-fed infants, iron-fortified cereals are the first recommended solid food. Generally offered first at 6 months of age, rice cereal is fortified with iron, is generally non-allergenic, and is usually well tolerated. Begin with 1 to 2 tablespoons in the morning, mixed with formula or breast milk. The cereal should be mixed to a consistency similar to that of applesauce. Cereal can be thickened as the child grows older. Feeding cereal from a spoon helps the baby learn this new skill, which takes a few weeks. Parents should be advised to avoid putting cereal in a bottle, as it does not, as commonly believed, help children to sleep

through the night. Furthermore, the need to make a larger hole in the nipple to prevent clogging may cause a rapid intake of this viscous mixture and lead to choking.

Vegetables Cooked, strained vegetables, without added salt, either homemade or as commercially prepared baby food, are appropriate to start at 6 to 8 months of age. The importance of avoiding salt should be stressed. Infants do not require extra sodium, and adding salt may encourage a greater salt intake later in life. Raw vegetables that are soft or cooked (steamed) may be introduced at 1 year of age. Hard vegetables such as raw carrots should not be introduced until the child's top and bottom molars have erupted and she can adequately chew and swallow these items without choking. It is advised that vegetables be introduced prior to fruits, because infants are likely to prefer the sweet taste of fruits to vegetables. Introducing vegetables first gives them a better chance of being accepted by the child.

Fruits and Fruit Juice Cooked and strained or pureed fruits, either homemade or purchased baby food without added sugar, may be started after rice cereal and vegetables. Fresh, mashed bananas also may be introduced at this time. Peeled, soft fruits such as peaches and pears may be cut into small pieces and started at 8 to 10 months of age. It is recommended that foods that are harder to chew, such as apples, should

be deferred until the child has a greater capacity to chew. Juices made from 100 percent fruit, such as apple juice, may also be offered at this time. According to the AAP, no juice should be given to babies younger than 6 months of age. Juice intake should be limited to less than 4 ounces per day for children over 6 months to ensure adequate intake of other foods. Encourage parents to dilute juice with water and to only offer 100 percent juice without added sugars.

Parents who do not themselves eat a wide range of fruits and vegetables may hesitate to offer such foods to their infants. Research suggests that taste preferences are inherited, so if a parent does not like broccoli, there is an increased chance that the child will also not like it. However, as noted below, repeated offering of a new food may overcome a child's initial resistance or rejection of an unfamiliar taste or texture.

Eggs In the past, experts recommended that cooked egg yolks be introduced to infants over the age of 6 months, but that the introduction of egg whites should be delayed until the child reaches 1 year of age because of the potential risk of inducing an allergy to eggs in younger infants. However, recent recommendations from the AAP state that there is no convincing evidence that delaying the introduction of highly allergenic foods, such as eggs, has a

significant protective effect on the development of atopic disease.

Meat Red meat can be an important source of iron. For breastfed and partially breastfed infants, smooth preparations of single meat (beef, veal, lamb, turkey, chicken) are suggested as the first solid food. Recent research indicates that the early consumption of meats improves the iron and zinc status of the older infant. Meats should be well puréed to avoid the risk of choking. Iron supplementation of vegetarian breastfed babies who will not be given meat should be considered (elemental iron 1 mg/kg per day) if dietary sources of iron are not adequate.

Starch/Carbohydrates Children tend to like pasta, spaghetti, noodles, and dry cereal. However, other essential foods with higher nutrient density should be introduced first during the meal to ensure that the child's diet is complete and balanced. Whole grains are recommended over their white counterparts for added nutrients and fiber and introducing whole grains early may help children to acquire a life-long taste for them.

Fats High saturated fat intake is associated with a greater risk of AVD and other conditions in adults. However, the high caloric density of fat makes it an important source of calories for the rapidly growing infant. Unfortunately, cases have been reported of failure to thrive, in which

young children were fed an inappropriate, very low-fat, calorically inadequate diet, so it is important to provide guidance to ensure that children are receiving a nutritionally adequate diet if modification of fat intake is implemented. A longitudinal study has reported normal growth and development over more than 10 years in a group of children whose parents were counseled to follow a lower fat, nutritionally adequate diet starting in infancy.

To be prudent, the AAP recommends that dietary fat should not be limited before age 2. However, in order to support the development of healthy eating habits, children should not have the opportunity to eat popular high-fat foods such as french fries, chicken nuggets, pizza, macaroni, and cheese, every day.

Beverages Soft drinks such as soda (regular and diet) are acidic and contribute to dental caries in children by demineralizing and eroding tooth enamel. In addition, the sugar content of these beverages sustains bacterial growth around the teeth, which also produces acidic by-products that demineralize teeth and cause cavities. Soda and other sweetened beverages, such as juice drinks, iced teas, and sports drinks, can contribute to excess calorie intake. It is recommended that children and adults alike avoid consumption of such beverages. These beverages as well as 100 percent fruit juices may contribute to obesity.

They should not be given to young children and only provided in limited amounts to older children. Juices provide nutrients, but commonly contain as many calories as soda.

Choking Hazards Parents and caregivers should be warned not to feed infants foods that pose a hazard for choking or aspiration. These include nuts, popcorn, grapes, raisins, raw carrots or celery, and hot dogs.

Psychosocial and Behavioral Implications and Recommendations

Eating habits formed in the first 2 years of life are thought to persist for several years, if not for a lifetime. Therefore, healthy eating patterns should be established as early as possible. New foods may need to be introduced 5 to 10 times before a child will accept them. Children imitate the eating behaviors that they observe, so parental role-modeling exerts a strong influence on a child's development of healthy eating patterns. Children's appetites vary with their growth rate and may fluctuate from day to day. Studies have shown that when children are allowed to determine on their own how much they eat, their intake may vary considerably from meal to meal, but over a period of several days, it will, in almost all cases, be appropriate to their needs.

Potential Feeding Problems

Children begin expressing personal preferences at an early age and simultaneously develop mechanisms for self-control. Parents must therefore take care to strike a balance between helping guide a child's food choices to develop healthy eating habits and providing sufficient opportunities for experimentation and control. Over-controlling parental behaviors have been associated with a child's decreased ability to appropriately control his/her own caloric intake. Children of authoritarian parents (those who set limits, but respect their child's likes and dislikes) do best with regulating their own intake. Parents should provide children with a healthy selection of food and children should be allowed to determine how much food they need to eat. Children who consume a variety of foods over time and demonstrate appropriate growth are likely to be consuming an adequately balanced diet. Allowing children to dictate what and when they will eat likely promotes poor eating habits. Parents who worry that their child is not eating enough and allow the child to eat anything and at any time of the day simply to ensure that he or she eats something may be promoting poor eating habits.

Problems also surface when parents engage in power struggles with their children over eating issues. Toddlers and young children may experience “food jags” where they want to eat

the same food for days at a time. Meeting the child's request, while offering other healthy foods alongside the desired food, may be a better response than turning mealtime into a battle. Left on their own, children eventually will tire of the same food, but if winning each mealtime struggle is in the balance, these episodes may worsen.

Confusion and rushing at mealtimes, as well as distractions such as television, may also disrupt the formation of appropriate eating habits. The following are recommended best practices for caregivers feeding young children:

Offer meals and snacks around the same time each day. Eating opportunities should be 2 to 4 hours apart. This allows the child to regulate his/her own hunger.

Allow children to have only water between scheduled meals and snacks. Do not allow “grazing”.

Sit with children at the table and eat together as often as possible. Engage in pleasant mealtime conversation as a family. Be a role model by eating healthful foods in front of young children

Do not allow the child to dictate what will be served at meals and snacks. Caregivers are responsible for making this decision and should not short-order cook to cater to the likes of each child. However, ensuring that at least one food

item offered is accepted by the child can make mealtimes easier.

Do not force children to eat. Similarly, do not restrict them to only set portions. Healthy children are able to regulate their own hunger.

Do not use food for bribing, rewarding, or punishing children.

Nutrition During Adolescence

Adolescents undergo major physical and psychological changes that affect their behavior and nutritional status. Issues of autonomy and rebellion, testing and searching behaviors, and the development of formal operational thought (logical reasoning) are all normal characteristics of adolescents that must be considered when addressing their nutritional needs and behavior.

Requirements for Growth

Adolescents' energy and nutrient needs increase as they enter their pubertal growth spurt, but on a per kilogram basis, are generally lower than those of infants and children. Infants typically double their body weight over a few months, whereas older children and adolescents may double their weight over a period of 6 to 9 years. However, the energy needs of adolescents may vary considerably – between those whose activity level decreases

considerably as they transition from a younger child who plays a lot to inactive "couch potatoes" and internet surfers, or those who are active multiple sport participants. The iron requirements of adolescent girls also increase as they begin to menstruate.

Lifestyle Issues

Adolescence marks a time of psychological, physical, and social changes that may influence eating habits. In particular, adolescents commonly have (1) a tendency to skip meals (especially breakfast and lunch); (2) sufficient money and opportunities to purchase foods (including fast foods) on their own outside the home or school environment; (3) increased consumption of "junk food" and sweetened beverages (adolescent males in particular); (4) a tendency to diet, particularly adolescent girls; (5) changes in physical activity including increased activity among adolescents participating in competitive sports or, conversely, decreased physical activity such as with non-athletic adolescents.

Some adolescents also explore restrictive dietary practices, fad diets, or vegetarianism that may put them at risk for vitamin, mineral, and trace element deficiencies. Eating disorders such as anorexia nervosa and bulimia nervosa also become a concern in adolescence. They occur across all major ethnic groups and all socioeconomic levels, and teen athletes may be

at higher risk of developing an eating disorder, especially those participating in sports where low weight, a weight target or limiting weight gain is encouraged. Common features of eating disorders include dysfunctional eating habits, body image misperception, and rapid weight loss. Eating disorders are generally classified as mental health problems, therefore a team approach to treatment that includes medical management, psychological interventions, and nutritional counseling is recommended (see Chapter 4: Case 3).

Malnutrition in Childhood and Adolescence

For millennia, custom, ancestral teaching, seasonal availability and climate, and the luck of the hunter governed what was put on the table to nurture and sustain families, tribes, and societies. Travel, trade, agriculture industrialization, and now a global marketplace have altered the forces that govern available foods and diet. Choices of when, where, and how much to eat may still follow culture and custom, but they are also influenced by education, marketing, and socioeconomic status. Biological mechanisms that control eating and metabolism evolved in this historic context but now interact with a modern environment in which Western-style, calorie-dense foods are widely available and

intensely promoted. High-energy-density foods such as fats and sweets are generally less expensive than low-energy-density foods such as fruits and vegetables. Furthermore, the cost of foods high in fat and simple carbohydrates rises little even during economic inflation while the cost of fruits, vegetables, dairy products, meat, and fish increases substantially. Despite our relative affluence, many United States children and adolescents are poorly nourished.

Undernutrition in Children

Undernutrition may be the result of a poor or suboptimal diet; total calorie intake may be inadequate or excessive, and specific nutrient intake may be inadequate or unbalanced. Adequate and appropriate nutrition during childhood and adolescence promotes normal growth and development. Furthermore, nutrition and physical activity during childhood and adolescence may influence disease risk, productivity, and quality of life during childhood and during adulthood. Inadequate calorie and nutrient intake may impair linear growth, neuro-cognitive development, and specific organ system development, and may increase mortality.

Malnutrition in pediatrics is poorly defined. The prevalence of underweight (defined as <5th percentile for age and sex-specific norms) in United States children and adolescents is below

the expected rate of 5 percent. Among low-income children from birth to age 5 years, the overall prevalence of underweight decreased from 6 percent in 1995 to 4.7 percent in 2004. Although it is important to identify, evaluate, and treat underweight children, acute undernutrition is not currently considered a major public health concern in the United States. Much of the underweight and undernutrition observed in children occurs in those with medical conditions associated with altered metabolism, intestinal malabsorption, or decreased caloric intake (e.g., congenital heart disease, cystic fibrosis, inflammatory bowel disease, poorly controlled type 1 diabetes, and significant food allergy and intolerance). Athletes in certain sports (e.g., gymnastics, wrestling, distance running) who sometimes use extreme methods to lose or maintain weight should also be considered an at-risk group.

For the past two centuries, pediatricians in western societies have described malnourished children using the term “failure to thrive” (FTT). FTT is considered to be due to physical or psychological problems in early childhood that result in growth delay and cognitive deficiencies. However, there is no consensus on a FTT definition. Unlike undernutrition, the diagnosis of FTT is solely based on anthropometric parameters. Currently used anthropometric criterion for FTT include any of the following: (1) weight, 75 percent of median

weight-for-age (Gomez criterion); (2) weight, 80 percent of median weight-for-length (Waterlow criterion); (3) BMI, <5th percentile; (4) weight-for-age, <5th percentile; (5) length-for-age, <5th percentile; (6) weight deceleration crossing more than two major percentile lines; percentile lines used: 5, 10, 25, 50, 75, 90, 95, from birth until weight within the given age group; and (7) conditional weight gain = lowest 5 percent, adjusted for regression towards the mean from birth until weight within the given age group. Unfortunately, the sensitivity and positive predictive value of single criteria are poor at detecting children with growth patterns likely to reflect significant undernutrition. It is therefore recommended to use several criteria to diagnose FTT.

Gross micronutrient deficiencies are rare in the United States, but the risk of deficiencies may be increased in certain situations. For example, laboratory anomalies may be observed during the refeeding syndrome (typically phosphorus, but also potassium, calcium, magnesium and thiamine) when rapidly feeding patients who are chronically or severely undernourished. Another example – deficiencies of fat-soluble vitamins – may occur with intestinal malabsorption and result in xerophthalmia (vitamin A) and peripheral neuropathy (vitamin E). Deficiencies following gastric bypass surgery (completed most commonly as a treatment for obesity) may be associated with vitamin B and

D deficiencies. Signs and symptoms associated with vitamin deficiencies are described in Chapters 1 and 2.

Treatment of Deficiencies

As part of the evaluation for a suspected nutritional deficiency, it is important to also assess the cause for the deficiency, as the therapy for the deficiency will be related to the etiology. For example, milder deficiencies related to inadequate dietary intake of a nutrient may be managed with dietary modification, or a relatively short term of therapeutic supplementation followed by long-term dietary modification. In patients with significant malabsorption, such as that due to cystic fibrosis or short bowel syndrome, long-term high-dose supplementation may be necessary. Non-enteral avenues of delivery of the supplement may also be considered. In cases of deficiency that require active therapeutic supplementation, it is also important to judge the appropriate rate of rehabilitation. For example, xerophthalmia due to vitamin A deficiency is a medical emergency requiring immediate and aggressive vitamin A supplementation to prevent blindness. On the other hand, overly aggressive and rapid supplementation of vitamin D without adequate calcium supplementation may precipitate severe hypocalcemia in patients with significant vitamin D deficiency.

Overweight and Obesity in Children

Overweight and obesity affect one-third of United States children and represent major threats to their current and future health (Figure 4-4). The prevalence of obesity is higher among African–Americans and Hispanics than among Caucasians in the United States as shown in Figure 4-5.

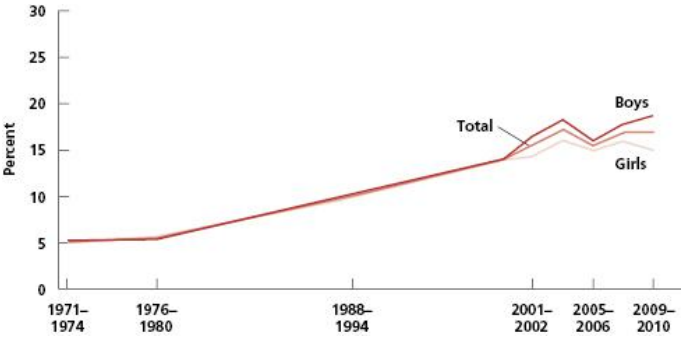


Figure 4-4 Trends in Obesity Among Children and Adolescents Aged 2–19 years, by Sex: United States, 1971–74 through 2009–2010. Obesity is Body Mass Index Greater Than or Equal To the 95th Percentile of the Sex- And Age-Specific 2000 CDC growth charts

Source: CDC/NCHS, National Health and Nutrition Examination Surveys (NHANES) I–III; and NHANES, 1999–2000, 2001–2002, 2003–2004, 2005–2006, 2007–2008, and 2009–2010; http://www.cdc.gov/nchs/data/hestat/obesity_child_09_10/obesity_child_09_10.htm

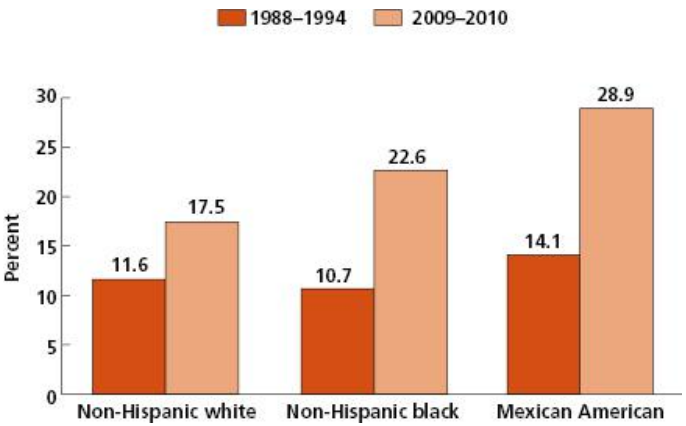


Figure 4-5 Prevalence of Obesity Among Boys Aged 12–19 Years, by Race and Ethnicity: United States, 1988–1994 and 2009–2010. Obesity is Body Mass Index Greater Than or Equal To the 95th Percentile of the Sex- And Age-Specific 2000 CDC growth charts

Source: CDC/NCHS, National Health and Nutrition Examination Survey (NHANES) III, 1988–1994, and NHANES, 2009–2010; http://www.cdc.gov/nchs/data/hestat/obesity_child_09_10/obesity_child_09_10.htm

Co-morbidities associated with obesity in youth can influence most of the body's systems including: cardiovascular (dyslipidemia, hypertension), endocrine (impaired oral glucose tolerance test, type 2 diabetes mellitus, polycystic ovary syndrome), gastrointestinal (anemia, constipation, fecal soiling, gastroesophogeal reflux disease, non-alcoholic fatty liver disease), orthopedic (Blount's

disease, slipped capital femoral epiphysis (SCFE), flat feet), neuropsychiatric (binge eating, compulsive eating, night eating, depression, anxiety, weight teasing), and pulmonary (asthma, sleep apnea).

Children who are overweight or obese are at substantially increased risk for type 2 diabetes, hypertension, and other cardiovascular disease risk factors. The prevalence of hypertension has been increasing in children and adolescents, likely linked to the increasing rate of obesity. Guidelines to screen at-risk children, as well as guidelines for the measurement, evaluation, and treatment of high blood pressure, hypercholesterolemia, and dyslipidemia in children and adolescents have been issued (Table 4-7 and Figures 4-2 and 4-3),(www.nhlbi.nih.gov; http://www.nhlbi.nih.gov/health/prof/heart/hbp/hbp_ped.pdf). Children should have their blood pressure checked annually, starting at the age of three. Using the correct cuff size is important, especially for obese children. Children's blood pressure percentile ranges vary by age, gender, and height, and are generally lower than adult blood pressure levels. It is important to use specific pediatric blood pressure standards when assessing blood pressure in children and adolescents.

Obesity related co-morbidities can have a substantial impact on the lives of children and

adolescents, on their utilization of healthcare services, and on their ability to attend school and engage in activities that support healthy growth and development. Children and adolescents exhibiting co-morbidities including dyslipidemia, insulin resistance, and glucose intolerance, and show evidence of endothelial dysfunction and increased carotid intima-media have an increased risk of cardiovascular disease in adulthood.

In contrast to their non-obese peers, individuals who were obese during adolescence and young adulthood have diminished academic achievement, lower household incomes, and higher rates of household poverty. In adults, obesity increases the risk of injury, illness, and absence from work. Compared to their normal weight peers, overweight children and adults utilize more healthcare resources and the cost of their care is greater. The costs of overweight and obesity to individuals, to families, and to society at large are staggering and are predicted to increase over the coming decades. Obesity seems to be both a cause and a consequence of increasing social inequalities in the United States.

Though it is clear that a predisposition to excess weight gain and obesity is inheritable, genetic studies of specific genetic variants explain only a small proportion of the variability in weight (except in some very rare, extreme

circumstances). It has been postulated that humans evolved in an environment which offered a survival advantage for individuals able to store energy efficiently during times of plenty and mobilize these stored calories during times of scarcity. Exposed to an environment with abundant food, these individuals would continue to store excess calories as fat and to become obese, and be somewhat resistant to attempts to lose weight.

The current “westernized” environment commonly provides easy access to excess calories, in calorically dense foods, and also provides many energy saving devices (e.g., driving cars instead of walking), and situations which limit energy expenditure (e.g., TV watching, playing video games, computer use or playing on smart phones or tablet devices). Thus, it is proposed that the interaction between humans' genetic predisposition to weight gain in times of plenty, and protective mechanisms preventing or limiting weight loss interact with the environment which encourages excess caloric intake and discourages caloric expenditure to support the rising prevalence of obesity. Several observational studies in developing countries support this hypothesis.

Epigenetic modifications of the genome have been postulated as a mechanism whereby the metabolic environment may affect or alter gene

expression. This could potentially occur in utero or during postnatal life. Although the molecular mechanism is not clear, the intrauterine environment affects the risk of obesity, insulin resistance, and cardiovascular disease. Children born to mothers who were obese prior to and during pregnancy or those who had hyperglycemia, glucose intolerance, or diabetes during pregnancy are at increased risk of obesity, insulin resistance, and cardiovascular disease later in life.

Prevention and Management Issues

Decreasing risks of long-term health complications is the ultimate goal of treating the obese child. After completing a medical, lifestyle (food, physical activity, and sleep habits), and psychosocial assessment, the clinician can offer individualized treatment. The family background, culture, and readiness to change are important considerations in the treatment plan. In some cases, the family may need to be connected to other resources like behavioral health or social services before weight management counseling can begin.

There are no evidence-based standardized practices for individualized treatment of pediatric obesity. Therefore; healthcare professionals rely on expert recommendations which are supported by the AAP.

The AAP recommends a multi-stage approach which trends toward more intensive care if each successive intervention is unsuccessful. The first step, "Prevention Plus" involves the primary care provider working with the family on targeted lifestyle behaviors (Table 4-9). If progress has not been made toward an improved BMI after 3 to 6 months, step 2 is "Structured Weight Management". This happens in an ambulatory care setting and involves support from other healthcare professionals, mainly registered dietitians. The next step, "Comprehensive Multidisciplinary Intervention" takes place in a specialty clinic and uses a team approach that includes a physician, a registered dietitian, a mental health provider, and/or an exercise specialist. "Tertiary Care Intervention" is the final step and can involve pharmacological or surgical treatment. This step occurs in a tertiary care setting.

Table 4-9 Healthy Lifestyle Recommendations to Maintain or Achieve Healthy Weight

Source: Adapted from Andrew Tershakovec, MD. 2014. Used with permission.

Limit consumption of sugar-sweetened and fruit juice beverages to 0–1 serving (6 ounces)/day
Increase fruit and vegetable consumption to ≥5 servings/day (see USDA guidelines-

www.choosemyplate.gov) (needs hanging indent)

Limit TV and other screen time to <2 hours/ day (none before 2 years of age)

Greater than 1 hour/day physical activity

Incorporate physical activity (e.g., walking, bike riding) into normal routine

Remove TVs and other screens from child's primary sleeping area

Eat a healthy breakfast daily

Limit eating out at restaurants and eat home cooked meals as often as possible

Encourage family meals together at the table

Offer structured meals and planned snacks in the home

Involve the whole family in lifestyle changes

Provide age-appropriate portion sizes

Avoid the imposition of overly restrictive control on eating

When a family is ready to change, the child's primary care provider focuses on lifestyle changes using motivational interviewing (a non-judgmental counseling approach used to elicit behavior change in individuals). To pinpoint barriers and facilitate change, referrals

to specialty providers or multidisciplinary teams may also be helpful.

Specific behavioral goals for families hinge on several factors, but a main variable is determining the agent of change (the person responsible for behavior change in an individual). In children 5 years and under this is the parent, but for older children and teenagers, the agent of change can vary. As the child works toward improved weight status, defining roles of the parents and the child is essential. For example, the parents will ensure that healthy after school snacks are available in the home daily after school, while the child is responsible for eating these healthy snacks rather than stopping at a corner store for unhealthy snacks instead. In this case, both the parents and the child have defined responsibilities to fulfill. Involvement of the entire family is vital to achieving and maintaining lifestyle changes.

When families are ready to change, the clinician can focus on target areas based on the child's current lifestyle and behaviors. If the child is not showing improvement in behaviors or BMI status, barriers may need to be further explored and motivation to change may need to be re-addressed. At this point the patient may need to move to the next stage of treatment as outlined above.

Medications

Options for the pharmacologic treatment of pediatric obesity are limited and provide only moderate results (BMI loss of 1 to 3 kg/m^2) and are commonly associated with side effects. Weight regain with the discontinuation of the agent is also common. Currently, there is not enough evidence for the long-term safety and efficacy of pharmacological agents to treat pediatric obesity. Orlistat is available for individuals aged 12 years and older as an adjunct therapy to behavior modification. It is most beneficial to those with poor adherence to dietary changes, and are at higher risk of cardiovascular disease. Orlistat affects fat digestion resulting in a reduction in calories digested, and improved BMI and cardiovascular blood markers. The unpleasant gastrointestinal side effects of orlistat may limit long-term compliance.

Although metformin is frequently prescribed by physicians to treat outpatient pediatric obesity, its use is not approved by the Food and Dug Administration (FDA) except for adolescents age 10 years and older who have type 2 diabetes. In fact, long-term findings from a recent randomized clinical trial of metformin to treat adolescent obesity were rather disappointing, and could even exacerbate weight gain at discontinuation.

Bariatric Surgery

There is increasing evidence that pediatric obesity surgery is relatively safe and effective particulary when the risks of surgery must be weighed against the progressive nature of conditions associated with obesity. For example, for a morbidly obese adolescent with poorly controlled diabetes, timing of surgery may be critical to the prevention of significant organ damage.

Obesity surgery is a treatment option for pediatric individuals who are emotionally and physically mature, and meet criteria for weight and medical severity. The Roux-en-Y gastric bypass, a restrictive and malabsorptive procedure, is the preferred surgical procedure because it has the most long-term data in both adults and adolescents. However, vitamin deficiencies, anemia, and ulcers are of particular concern in non-compliant adolescents. Therefore the laparoscopic sleeve gastrectomy, a restrictive procedure, is becoming a more attractive alternative in non-compliant individuals, especially adolescents. As opposed to the Roux-en-Y procedure, the band, which is purely restrictive, requires research consent as it is not FDA approved. A multidisciplinary team and a strong pre- and post-operative program are imperative (see Chapter 1, Case 2).

Childhood Nutritional Factors in Preventing Adult Cardiovascular Disease

The association between elevated cholesterol levels and heart disease has been well documented in adults. Several studies suggest that adult atherosclerosis has its roots in childhood, and link early atherosclerosis and vascular dysfunction in children with childhood dyslipidemia. Furthermore, lifestyle factors, such as diet and physical activity, have been linked to lipoprotein levels and other cardiovascular disease risk factors in children and adults. This is especially important to consider given the association between obesity and dyslipidemia (including increased triglycerides and decreased HDL-C).

Vascular Disease and Dysfunction in Children and Adolescents

The atherosclerotic process has been noted to begin in childhood and adolescence. The earliest atherosclerotic lesion is the fatty streak, a collection of lipid-laden macrophages in the intima of an artery. Autopsy studies of children and young adults from the Bogalusa Heart Study who died of various causes, principally trauma, have shown a correlation between pre-morbid cholesterol levels and early

atherosclerotic changes, and the prevalence of changes was positively associated with age, blood pressure, and BMI. Other studies have demonstrated an association between atherosclerotic disease and other factors, such as age, smoking, BMI, and elevated blood pressure, and the extent of vascular lesions rises exponentially with an increasing number of risk factors in young adults.

Imaging and functional studies have also identified the onset of vascular disease and dysfunction in childhood. Carotid intima-media thickness, assessed by ultrasound as a surrogate marker for atherosclerosis, has been observed to be increased in adolescents and young adults with hypercholesterolemia, and in those with a positive family history of premature heart disease. Arterial stiffness and distensibility, also assessed by ultrasound, are associated with familial and non-familial hypercholesterolemia, elevated blood pressure, decreased cardiovascular fitness, and obesity.

Dietary and Lifestyle Recommendations for Hyperlipidemia

In addition to the focus on children at risk, a healthy lifestyle and diet are recommended for all children as part of population-based prevention. Though a low-fat diet is not

recommended for children less than 2 years of age, a healthy well-balanced diet is appropriate at all ages. The recommended diet should provide adequate calories and nutrients to support normal growth and development, and no more than 30 percent of calories from fat, less than 7 to 10 percent of calories as saturated fat, and less than 300 mg cholesterol per day. The intake of trans fatty acids should be limited as much as possible. The Dietary Approaches to Stop Hypertension (DASH)-style diet is a diet relatively high in fruits, vegetables, low-fat or non-fat dairy products, whole grains, fish, poultry, beans, seeds, and nuts, and relatively low in sweets, added sugars, fats, and red meat (compared to the typical American diet). It has been shown to help decrease blood pressure in adults and when modified for children, it is recommended as a healthy diet construct for children and adolescents. This diet is also recommended as initial therapy for children over the age of 2 years with hypercholesterolemia. Further restricting saturated fat intake to less than 7 percent calories, and cholesterol intake to 200 mg/day may be considered as appropriate for hypercholesterolemic children. Children under the age of 2 years require a higher fat diet to maintain normal growth and central nervous system development and thus the AAP does not recommend a lower fat diet for children less than 2 years old.

Though the initial National Cholesterol Education Program (NCEP) dietary recommendations did not focus on caloric intake, given the rising prevalence of obesity, and the interaction between obesity and lipid levels (especially triglycerides and HDL-C), these dietary recommendations for the general population and for hypercholesterolemic children have evolved to aim for caloric intake that maintains or achieves a healthy weight as a priority. Consistent with this, dietary intervention must be viewed as one component of a comprehensive program to reduce cardiovascular disease risk. Exercise, blood pressure, sedentary/physical activities, smoking (active and passive), relative weight and excessive weight gain, and risk factors for the development of diabetes are all factors that should be assessed in the general population and especially in children and adolescents with hyperlipidemia.

For children and adolescents with mixed dyslipidemia, dietary management should focus on limiting the intake of simple carbohydrates, and include a special focus on weight management, in addition to the general healthy diet recommendations.

Lipid lowering drug therapy in children and adolescents should be considered only after implementing healthy diet and lifestyle recommendations, and in limited high-risk

circumstances. In general, children and adolescents should be referred to a pediatric lipid specialist before instituting lipid lowering drug therapy. Guidelines for lipid lowering therapy are available at http://www.nhlbi.nih.gov/guidelines/cvd_ped/summary.htm.

Conclusion

In conclusion, nutrition during childhood and adolescence has both immediate and long-term effects on growth, development, health, and quality of life. An evaluation of physical growth, nutrient intake, and energy balance, and recommendations to follow a healthy diet and lifestyle should be part of routine pediatric care. Children and families should be supported to make healthy eating and living a regular habit. Physical examination and selected laboratory tests may be needed to identify specific nutrient deficiencies, biochemical abnormalities, or modifiable risk factors for disease (e.g., dyslipidemia, iron-deficiency anemia, vitamin D deficiency) that could be managed with nutritional counseling, dietary modification, and supplementation, as appropriate. Pediatric healthcare providers need to be aware of the medical conditions and activities of children and adolescents which may be associated with malnutrition or deficiencies and be extra vigilant in the care of these children. Healthcare providers must identify nutritional

inadequacies and counsel parents and children regarding appropriate food intake and levels of physical activity to support optimal growth and development and to prevent disease and disability. Promoting good nutrition is important for all patients, but is a required, extremely important aspect of good pediatric care.

Case 1 Overweight Child with Insulin Resistance

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Objectives

Take an appropriate dietary and medical history including family history of overweight or obesity, and social history regarding physical activity, sedentary activity, and other lifestyle issues.

Perform an appropriate physical examination for an overweight or obese child or adolescent; evaluate the patient for other signs and symptoms of chronic diseases associated with obesity (e.g., hypertension,

insulin resistance, dyslipidemia, sleep apnea, orthopedic problems, etc.).

Identify factors responsible for increasing weight in order to recommend suitable dietary or lifestyle changes.

Recognize the importance of the patient and patient's family involvement in making changes as well as the social, emotional, and psychological factors that may support the development of obesity and may influence the response to intervention.

AN is a 14-year-old boy who comes to see his physician for a health maintenance visit. His parents report that he has gained a lot of weight over the past two summers while attending an overnight teen travel camp that involved sitting on a bus for many hours and eating all meals at food courts, hotels, or fast food restaurants. They are asking for help because AN has become less interested in sports and prefers to play video games rather than play outside with his friends as he used to.

Past Medical History

AN was a full-term infant (birth weight 3950 g). His mother notes he was always thin as a child and is now shorter than most of the boys his age. Growing up he always had a good appetite but rarely ate vegetables. AN's mother notes his

weight gain had been relatively stable until he reached the age of 12, when his rate of weight gain increased over the subsequent 2 years.

Family History

AN's family history is positive for type 2 diabetes, obesity, and heart disease. His mother had gestational diabetes during her pregnancy with AN. She is 35 years old and has a BMI of 35 kg/m^2 (obesity class II) and was recently told she has an elevated blood glucose level indicative of prediabetes. His father (age 36) has a BMI of 28 kg/m^2 (overweight). His maternal grandmother (age 65) is obese (BMI 32 kg/m^2) and has hypertension and type 2 diabetes; his maternal grandfather (age 67) had a myocardial infarction (MI) at age 53.

Social/Development/Puberty

AN's early childhood development is described as normal. He walked at age 15 months, was toilet trained at 3½ years. He is described as an average student. He admits that he feels uncomfortable with his stomach and does not want to take his shirt off in the summer when he goes swimming. He has friends but now prefers to spend most of his free time playing video games. AN denies smoking, alcohol, drugs, or sexual activity.

Social History

AN's mother works from 9 a.m. to 5 p.m. daily as a school administrator. AN's father works 8 a.m. to 6 p.m. as an optician. His parents divorced 4 years ago and he splits his time between his mother's and father's homes. AN is either alone in the afternoon or watched by his grandmother before either parent comes home from work. He is an only child.

Diet/Physical Activity History

AN's parents state that he has always had a "healthy appetite." When asked what he eats during the day (24-hour recall), mother states that at her house he usually eats scrambled eggs, bacon, toast, and orange juice for breakfast, and at father's house he eats a donut or a bagel with cream cheese, and drinks orange juice. Both parents pack a sandwich for lunch at school (peanut butter and jelly with cookies, juice or chocolate milk, or turkey with mayonnaise on white bread). AN usually augments what his parents provide at the school cafeteria with either a slice of pizza or some chips or pretzels. When he comes home from school he will usually have a snack of more chips or a grilled cheese sandwich and orange juice. He will eat fruit when his parents provide it. Mom or dad each eat out with AN once a week where he orders two slices of pizza or a bacon cheese burger with fries and a soda).

At home, they make baked chicken or burgers, potatoes or rice, and broccoli or string beans. While salad is usually served, he does not eat it. He drinks whole milk with dinner. AN's parents state that he is active with soccer and baseball during the year but they have noticed that his performance seems to be suffering as he can sometimes not keep up with the other boys. AN goes to bed between 9:30 and 10:00 p.m. and generally sleeps at least 9 hours. AN's parents report that he does snore and occasionally naps during the day.

Review of Systems

Skin: No history of rashes

Neurologic: No headaches, tremors, seizures

Endocrine: No polyphagia, polydipsia, or polyuria

Pulmonary: Regular snoring noted. Some decreased in exercise tolerance noted with weight gain

Joints: No swelling; complains that his legs hurt if has to walk for a long distance

Physical Examination

Vital Signs

Temperature: 99 °F (37 °C)

Heart rate: 95 BPM

Respiratory rate: 26 BPM

Blood pressure: 130/80 mm Hg (~90–95th percentile for age, sex, and height)

Current weight: 75 kg (165 lb) (95th percentile for age)

Current height: 160 cm (63″) (25th percentile for age)

BMI: 29.3 kg/m^2 (>95th percentile for age)

Weight history:

9 y/o: 28 kg (50th percentile for age)

11 y/o: 35 kg (50th percentile for age)

13 y/o: 60 kg (90th percentile for age)

Exam

General: Overweight teenage boy in no acute distress, no hirsutism, no edema, no

Cushingoid features

Skin: Wrinkled, hypertrophied skin with increased pigmentation at base of neck

HEENT: No abnormalities noted

Neck: Non-palpable thyroid

Eyes: EOMI, PERRL, normal disc margins

Abdomen: BS (+), soft, no masses or organomegaly palpable, liver span by percussion 8 cm, stretch marks noted

Cardiac: Regular rate and rhythm, S1, S2, no murmurs

Chest: Clear

Genitalia: Tanner 2 boy, phallus moderately obscured by fat pad, testes normal

Neurologic: Alert, strength 5/5, DTR +2 upper and lower extremities, normal tone

Orthopedic: Wide-based gait without a limp, mild bowing of lower aspect of legs bilaterally, full range of motion in both hips

Laboratory Data

Patient's Fasting Values	**Normal Values**
Glucose: 92 mg/dL	70–99 mg/dL
Insulin: 28 μU/mL	<20 μU/mL
HbA1C: 5.7%	<3–6%
Total cholesterol: 212 mg/dL	desirable <200 mg/dL
Triglycerides: 145 mEq/L	desirable <120 mg/dL
LDL-C: 105 mg/dL	desirable <130 mg/dL
HDL-C: 38 mg/dL	desirable ≥40 mg/dL
ALT: 37 U/L	10–30 U/L
AST: 55 U/L	10–30 U/L

Patient's Fasting Values	Normal Values
TSH: 2.3 µU/L	0.5–5.0 µU/L

Case Questions

Describe methods that can be used to assess AN's weight.

Describe the risk factors and health consequences associated with being an overweight child or adolescent.

What additional information should be asked regarding AN's increasing weight over the past 4 years?

How can AN's and his family's readiness to change be assessed and how should this treatment process be explained?

What are the appropriate medical nutrition therapy and physical activity recommendations for AN and his family?

What type of behavior modification techniques can be used to help AN and his family implement these dietary and lifestyle suggestions?

Answers to Questions: Case 1

Part 1: Diagnosis

1. Describe methods that can be used to assess AN's weight.

In the current CDC growth charts, which include BMI growth curves for children and adolescents, overweight is defined as a BMI between the 85th and 95th percentile, and obesity is defined as BMI greater than the 95th percentile. However, BMI is only a screening tool and the patient's degree of overweight must be confirmed on physical examination. Such screening is necessary to identify those who require intervention. The goal of intervention may be weight loss, or weight stabilization depending on the specific circumstances. Decreasing the rate of weight gain while a child is growing will help decrease ultimate gain in relative weight. AN's BMI of 29.3 kg/m^2 is >95th percentile for BMI for his age and sex. This places him in the obese category (see Table 4-1).

It is apparent from his weight history that AN was not always an overweight child, but began to gain weight rapidly over the past few years, crossing percentiles from 50th, 75th to 90th percentile for weight-for-age. It is common that overweight pre-pubertal children are taller than their normal weight counterparts, thus further

evaluation of short obese children and adolescents should be considered to assess for inherited syndromes (e.g., Prader–Willi syndrome) or medical conditions (hypothyroidism or other endocrine disorders) that may be associated with slower growth and excess weight gain. AN's stature-for-age plots him at the 25th percentile. As part of his further evaluation, bone X-rays revealed a delayed bone age. No other abnormalities were identified in the assessment. The delayed bone age suggests AN still has significant growth potential, which is supported by his Tanner stage that places him early in puberty. This may help support any planned weight management program, as he still has the potential to "grow into his weight" somewhat, if his rate of weight gain is at least stabilized (in other words, a weight loss diet may not be necessary at this time).

2. Describe the risk factors and health consequences associated with being an overweight child or adolescent.

Overweight children and adolescents are at risk for similar health problems as adults who are overweight or obese, including type 2 diabetes, hypertension, dyslipidemia, sleep apnea, asthma, gall bladder disease, orthopedic problems, and non-alcoholic fatty liver disease. AN's dyspnea on exertion is likely due to poor cardiovascular fitness. Cardiac problems in an

adolescent would be very rare, though the dyspnea could be a sign of undiagnosed exercise-induced asthma. An appropriate program for AN's fitness level should be recommended with the goal to improve his overall cardiovascular fitness level, which will help support overall weight management efforts.

Sleep Apnea Upon further questioning about his sleep patterns, AN and his parents indicate that he is a restless sleeper who snores loudly and sometimes has daytime sleepiness. These symptoms may be consistent with sleep apnea. AN should be referred to a pulmonary specialist for further evaluation and possibly a formal sleep study.

Diabetes Recently, there has been a dramatic increase in the prevalence of type 2 diabetes in children and adolescents, especially in African–American, Hispanic, and other minority populations. This may be explained, in part, by the parallel increase in the prevalence of overweight among children and teenagers. A positive family history of type 2 diabetes is associated with an increased risk of insulin resistance (insulin resistance is thought to be part of the etiology of type 2 diabetes). AN's grandmother has diabetes, and the mother's history of gestational diabetes and current elevated glucose level suggest she has insulin resistance and is at risk of developing type 2

diabetes. The increased skin pigmentation that AN demonstrates could be acanthosis nigricans, which is associated with insulin resistance. Since AN is obese, has a strong family history of type 2 diabetes and cardiovascular disease, and has acanthosis nigricans and prehypertension, he meets the criteria to be screened for diabetes. Thus a fasting serum glucose, insulin, and hemoglobin A1C were obtained. AN has a high normal glucose (92 mg/dL) and hemoglobin A1C (5.7 percent), with an elevated insulin level (28 mIU/mL), which is consistent with insulin resistance. However, in the evolution of type 2 diabetes, post-prandial glucose increases earlier than fasting glucose, therefore, determining plasma glucose 2 hours after a standard glucose load as part of an oral glucose test or 2 hours after a meal should be considered, along with further evaluation by an enodcrinologist.

Heart Disease/Hypertension As AN has multiple risk factors for adult cardiovascular disease (family history of heart disease, obesity, elevated blood pressure), a fasting lipid panel was ordered. These results, when compared to the age appropriate percentiles, indicate that AN has elevated triglyceride levels, and a reduced HDL-C level. Hypertriglyceridemia and low HDL-C are the most common lipid abnormalities associated with insulin resistance. AN's blood pressure is elevated. Further evaluation to confirm these levels

should be undertaken. Weight management and dietary change would be the first recommended intervention, and ANs blood pressure should be monitored at least every 6 months.

Non-Alcoholic Fatty Liver Disease (NAFLD) Overweight children may present with increased liver enzymes [alanine amino transferase (ALT) and aspartate amino transferase (AST)], which may be indicative of hepatic fat infiltration. Abnormal liver function tests have been described in 6 to 10 percent of obese adolescents. This condition, know as non-alcoholic fatty liver disease (NAFLD), has been described to progress to cirrhosis and liver failure in adults and in rare cases in children. Obesity-associated NAFLD is commonly associated with insulin resistance. Other than weight loss, there is currently no accepted therapy for NAFLD. Persistent elevations in liver enzymes should be evaluated further.

3. What additional information should be asked regarding AN's increasing weight over the past 4 years?

AN's 24-hour recall reveals that a lot of calories, sugar, and fat could be coming from meals eaten away from home, such as pizza, burgers, fries, and soda. It would be especially helpful to determine the portion sizes of meals and drinks when he eats out, as well as when AN was eating “on his own” at camp and at home in the

afternoon. Since AN is drinking juice at home with meals and snacks, it is also important to probe for the size of these drinks. Though juice contains more nutrients than soda, juice and other sugar containing beverages can provide a lot of calories. AN is doubling up on his lunches when in school and although after school snacks for growing adolescents may be appropriate, the caloric density of the foods consumed must be considered. When assessing dietary intake, it is important to note that dietary information provided for obese individuals tends to be under-reported. Studies suggest that obese adolescents under-report their caloric intake by as much as 40 to 60 percent, and that obese individuals under-report to a greater degree than non-obese individuals.

Further questioning reveals AN eats at least two slices of pizza and a large soda or an adult bacon cheese burger with large fries and a large soda when eating out and at least 12 ounces of orange juice at each meal or snack at home. During school, after AN eats his packed lunch, AN will also purchase a bag of chips or an ice cream dessert. After school he spends most days with his grandmother, who serves him a bag of chips and a grilled cheese sandwich with chocolate milk at 3:30 p.m. for a snack, after which time he does his homework and plays video games until dinner. After dinner, AN also enjoys either ice cream and a few chocolate chip

cookies or an 8 ounce (240 mL) glass of whole milk with peanut butter crackers before bed.

Physical Activity AN's parents stated that he is active with soccer in the fall and baseball in the spring. He usually has one game each week and plays goalie or a defensive position where there is very little running involved. As both teams have many players, AN never plays more than half a game or about 25 minutes. Following the game AN's family often go to a fast food restaurant. AN is sedentary during the winter months.

Sedentary Activity Detailed questioning about AN's television, video, and computer game usage reveals that on weekdays, on average, he watches 3 hours of screen time per day. On weekends AN watches television, plays video or computer games, or "surfs the web" for up to 6 hours per day.

4. How can AN and his family's readiness to change be assessed and how should this treatment process be explained?

Prior to recommending any dietary or lifestyle suggestions, it is very important to assess both AN's and his family's interest in making changes, which will need to be consistent at both his mother's and father's houses. It is best to directly address the motivation and willingness to change with AN and his parents. Some families may express significant interest

in changing, yet will be unable to identify concrete changes they are willing to undertake. It is also important to assess other potential environmental obstacles (e.g., uncooperative family members like AN's grandmother).

Motivational interviewing strategies use a ladder or Likert scale to determine how important the issue is to address and how competent each family member is in being able to institute needed changes. This conviction and confidence model has been used with success in many behavior change studies. AN's parents stated in the initial work-up that he has gained a lot of weight since last year so they seem to realize that there may be a problem with his weight. However, the fact that they blame his activities at teen travel camp and do not recognize the contribution of his sedentary lifestyle and increased caloric intake as a problem suggests some denial, or lack of willingness to change. Because AN says he does not like they way his stomach looks and admits that he feels embarrassed to take his shirt off at the pool, suggests that he has some interest in changing. However, the fact that he is becoming more and more withdrawn may suggest depression or other psychosocial issues that may be necessary to address before weight management interventions can be successful.

When explaining the process of weight management and the implications of excessive

weight gain, it is useful to review the child's growth curve with the family. The specific medical issues affecting the child should also be discussed. In AN's case, his insulin resistance, acanthosis nigricans, snoring indicating possible apnea, elevated blood pressure, and dyslipidemia are all partially related to his obesity. The family history of insulin resistance, diabetes, and premature heart disease should also be noted as additional reasons for increased vigilance. Explaining to parents and other family members that improved diet and increased physical activity with weight stabilization or weight loss can decrease AN's risk of developing diabetes and cardiovascular disease, may help motivate them to support him and potentially to join him in making changes.

In general, the initial goals of a pediatric weight management program are to decrease the rate of weight gain, aiming to keep weight stable while the child grows to decrease relative weight. In this case, given AN's continued growth potential, weight stabilization is an important first goal. With significant obesity, weight loss may be appropriate in children, and can be safely implemented with appropriate supervision.

5. What are the appropriate medical nutrition therapy and physical activity recommendations for AN and his family?

The most important dietary change that should be recommended for AN is to control portion sizes, reduce snacking, and limit calories from beverages, such as soda and orange juice. Specific recommendations could include changing to a bowl of low-sugar cereal (Multigrain Cheerios or Life) with low-fat milk, and fruit or a slice of toast with peanut butter and jelly and a glass of low-fat milk for breakfast. AN's juice intake is contributing over 800 calories per day and should be reduced to less than 6 ounces (180 mL) per day. Lunch could remain the same, with the substitution of fresh fruit, carrot sticks, and a Greek-style strawberry/banana yogurt to discourage him from buying dessert or other snacks. Both parents could send him to school with a bottle of water, which he can refill during and after school.

AN's grandmother should be included in these discussions since she is his after-school caregiver. Because she has type 2 diabetes, she may be receptive to the idea of prevention for her grandson. Healthy after-school snack suggestions for AN include fruit, low-fat yogurt, low-fat granola bar, microwave “lite” popcorn, or a frozen fruit bar. Snacks are a normal and important part of a child's diet; however, choices should not be high in calories. Given that AN was eating a full meal as an afternoon snack, providing guidance regarding an

appropriate serving size for a snack would be important.

Beverage choices are another common problem with overweight children. Efforts should be made to limit the intake of all sugar containing beverages including juices. Many families feel that since juices are “natural,” their intake should not be limited. It is not unusual to see a child ingest 500 to 1000 calories a day in juice, soda, and other sugar-sweetened beverages. Eliminating or significantly limiting juice, soda, and sports drinks, and switching to low-fat milk will likely reduce weight gain. Dinner meals seem to be the healthiest and could remain the same, except for the whole milk. In addition to healthy food choices and meals, children and families should be instructed on proper serving sizes for children for meals and snacks.

AN's family should provide ample opportunities for him to eat fruits and vegetables and low-fat dairy products. They should limit the availability of salty snacks and prepared foods as these are sources of excess sodium intake, which has been linked to blood-pressure elevation and to increased consumption of sugar-sweetened beverages. His relatively high saturated fat intake may also be contributing to his blood pressure elevation and would be a secondary goal.

Parents and families should assess and plan opportunities for increased physical activity.

Find activities that the child enjoys (i.e., do not expect a child to regularly use a treadmill). Parents need to provide an environment where being active several times a week is normal and expected. Parents should be role models and participate in activities with their children. They should not assume children are active during school recess as time for physical education has been consistently decreased and often eliminated from school curricula. Parents should also monitor and set daily limits for sedentary activities, such as watching TV and playing computer and video games. The American Academy of Pediatrics suggests screen time be limited to less than 2 hours per day. According to the Centers for Disease Control and Prevention (CDC), children and adolescents should engage in at least one hour of physical activity every day. AN's family should have a concrete discussion on goals for decreasing screen time and increasing physical activity with methods for monitoring progress and consequences for non-adherence.

6. What type of behavior modification techniques can be used to help AN and his family implement these dietary and lifestyle suggestions?

It is important to assess the child's and family's psychosocial well-being before initiating a behavior modification program. For example, if the child is depressed, the depression will

probably make weight management more difficult. In some cases, it may be best to defer the weight management program until the psychological or psychiatric issues are directly addressed. Similarly, significant family difficulties, such as a family member with anorexia or a substance abuse problem, should be identified and addressed. In this case, the potential of emotional issues related to the parent's divorce should be considered.

The issues surrounding eating and weight are complex and frequently emotionally charged. As few families will have the ability to address these issues as a “self-help” program without outside assistance, it is important to institute a behavior modification program with the guidance of a behavioral specialist. Little research has directly assessed the efficacy of different behavioral components of a weight management program. However, there are several factors that are commonly included in most weight management programs. These include the following:

Motivation It is important to assess the child's and family's motivation to participate in the weight management program. Experience suggests that in addition to an interested and motivated participant, children do better when a parent is also an active and supportive participant in the program. Using the transtheoretical model and the concept of

stages of change to assess a family's readiness and to plan an appropriate intervention program should be considered.

Stepwise Approach Even motivated children and families should not be overwhelmed with too much change at once. Initial goals should be chosen as ones that can be achieved relatively easily to allow the child and family to experience early success and build self-esteem. Additional and more challenging goals should then be added over time.

Stimulus Control and Environmental Modification It is important to limit the opportunities for children to deviate from their plan. Provide an environment that includes only healthy choices. Trying to restrict a child from eating certain foods (e.g., chips, soda) while these foods are still in the house may be counterproductive. The school environment is not as easily controlled.

Role Modeling It is important to have as many people as possible, and hopefully the whole family, act as role models in all aspects of the behavior modification program. Though all family members may not have a weight problem, the environmental and lifestyle changes recommended for the targeted child are part of an overall healthy lifestyle appropriate for everyone.

Positive Reinforcement and Parenting Skills Parents should be instructed in appropriate parenting skills, including methods of positive reinforcement and appropriate limit setting.

Self-Monitoring Parents and children should be instructed in methods of self-monitoring (keeping a diet diary, keeping an activity log), generally focusing on dietary intake and physical activity. Experience suggests that persons who self-monitor significantly decrease caloric intake and generally do much better in weight management programs.

Case 2 Malnutrition and Refeeding Syndrome in Children

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Objective

Describe the physiologic and metabolic adaptations that occur during starvation.

Describe the physiologic processes that occur when refeeding an undernourished patient.

Identify potential clinical manifestations of the refeeding syndrome and explain the most common laboratory abnormalities that may occur during refeeding.

Summarize the clinical recommendations for minimizing or avoiding the complications associated with refeeding.

RD is an 8-year-old boy of Liberian descent who lives in the United States with his parents. In October, RD and his family flew to Liberia to spend a few months with their extended family. Several weeks after his arrival, political unrest erupted. RD and his family were forced from their homes at gunpoint, taken to a university, and held against their will in overcrowded, unsanitary conditions. Medical and food supplies were scarce. Food was provided by soldiers outside the camp who lowered buckets of rice and occasionally fish over the barbed-wire fences. Daily tea was also provided. Many of the hostages died from starvation. RD and his family escaped after 3 months of captivity and sought refuge in the American Embassy. From there, they were airlifted to a neighboring country. Shortly thereafter, RD returned to the United States.

Vital Signs (United States Embassy)

Temperature: 97 °F (36 °C)

Heart rate: 45 BPM

Respiratory rate: 18 BPM

Blood pressure: 100/80 mm Hg

After 3 months of virtual starvation, the family reported that RD ate "everything he could get his hands on." Upon follow-up with his local physician in the United States, RD was immediately referred to the local emergency room for evaluation of malnutrition.

Anthropometric Data

	Height		Weight		BMI	
Date	(cm) (in)	Percentile	(kg)(lb)	Percentile	kg/m²	Percentile
1/7*	127 (50″)	50th	19 (42)	<5	11.8	<5th
1/10	127 (50″)	50th	22 (48)	10–25	13.6	<5th

*At initial presentation to the emergency room.

Past Medical History

RD tested positive for malaria in the past; no other problems were noted. On admission, he was not taking any medications or vitamins. RD has no known food allergies. He was having 4 to 5 loose stools per day.

Social/Diet History

By report, prior to his imprisonment in the refugee camp, RD's food supply met 100 percent of his needs. While in the refugee camp,

his estimated intake amounted to only 250 to 300 kcal/day, with 30 g of protein per week. Four days after he escaped, his intake rose to an estimated 2500 to 3000 kcal/day, with 80 to 90 g of protein per day.

Further evaluation in the hospital produced the following clinical picture.

Physical Examination

Vital Signs

Temperature: 101.8 °F (38 °C)

Heart rate: 120 BPM

Respiratory rate: 30 BPM

Blood pressure: 80/50 mm Hg

Exam

General: Eight-year-old boy who appears apathetic and emaciated

Skin: Dry, scaly dermatitis

Head: Alopecia, thinning hair lacking in luster

Abdomen: Mildly distended

Extremities: Bipedal edema; and muscle wasting

Laboratory Data

Date	Ca (mg/dL)	PO_4 (mg/dL)	Mg (mg/dL)	K (mEq/L)	Albumin (g/dL)
1/7*	8.0	3.0	1.8	3.6	2.7
1/10	6.3	1.0	0.9	2.0	2.4
Normal	(9–11)	(2.5–4.6)	(1.8–2.9)	(3.5–5.3)	(3.5–5.8)

*At initial presentation to the emergency room.

Case Questions

What nutrition-related changes in body function probably occurred during the past 3-month period of starvation?

Based on the physical examination and laboratory data, what clinical and biochemical manifestations of malnutrition does RD exhibit?

What metabolic and physiologic changes occur as RD begins to eat again? Why are his electrolyte abnormalities of primary concern?

Based on RD's physical examination and laboratory data, what complications of refeeding does he exhibit?

How could the complications of refeeding that RD experienced have been minimized or avoided?

Part 1: Physiology

1. What nutrition-related changes in body function probably occurred during the past 3-month period of starvation?

The body's systems adapt to calorie and protein deficits in a complex manner. Chronic nutritional deprivation results in a mildly catabolic state. The body's compensatory mechanisms involve changes in energy metabolism and hormone regulation. Fat from adipose tissue and protein from muscle mass are mobilized and converted to energy via glucose and ketones. The brain increases its use of free fatty acids replacing glucose as an energy source. The catabolism of fat and protein results in a loss of lean body mass, electrolytes, and water. The basal metabolic rate (BMR) decreases to conserve energy; the body becomes hypothermic, hypotensive, and bradycardic; and physical activity decreases. Growth hormone and thyroid hormone regulation decrease or stop growth, which helps to lower the BMR. Production of insulin, which promotes anabolism of catecholamines, cortisol, and glucagon, also decreases. The net effect facilitates survival by decreasing the BMR and promoting conservation of protein and organ function.

Overall decreases in cellular mass may eventually result in functional loss of vital organs. Respiratory muscle loss may lessen respiratory efficiency. Myocardial atrophy may reduce cardiac output. Decreased intravascular fluid volume results in decreased cardiac output.

Gastrointestinal (GI) atrophy slows motility and gastric acid secretion and causes thinning of the mucosa, villous atrophy, and decreased production of digestive enzymes. These effects reduce GI function and can result in malabsorption and diarrhea, further exacerbating the malnutrition and increasing susceptibility to infection. Liver wasting causes altered metabolism and decreased protein synthesis. The kidney's ability to concentrate urine decreases causing diuresis.

2. Based on the physical examination and laboratory data, what clinical and biochemical manifestations of malnutrition does RD exhibit?

Specific manifestations include wasting and apparent emaciation (depleted somatic protein and subcutaneous fat stores) due to protein-energy malnutrition. Though protein status may be depleted at initial presentation, serum albumin and protein values are commonly normal due to the decreased blood volume (hemoconcentration). However, as the child is refed, the total blood volume increases, and albumin and protein concentrations may decrease (hemodilution). The changes in calcium, phosphate, magnesium, and potassium levels may be associated with his malnutrition as well as his rapid refeeding. Bradycardia, hypothermia, and a decreased respiratory rate are common bodily defense

mechanisms in malnutrition that result in decreased energy needs. In addition, RD exhibited signs and symptoms of vitamin and mineral deficiencies, such as dry scaly dermatitis (essential fatty acids, vitamin A, niacin); alopecia (protein, biotin); and thinning, lusterless hair (essential fatty acids, zinc, protein). Non-specific manifestations include decreased growth rate and physical activity. The child generally appears apathetic with a flat affect.

RD presents with severe wasting demonstrated by his low body mass index (BMI) and weight change, suggesting acute malnutrition. If RD's starvation had continued, he would have manifested stunted or slowed height growth. His low serum albumin level suggests depleted visceral protein status as well, although most children with marasmus will have normal albumin levels.

Part 2: Initiating Refeeding

3. What metabolic and physiologic changes occur as RD begins to eat again? Why are his electrolyte and mineral abnormalities of primary concern?

Refeeding syndrome (RFS) is a term used to describe the broad range of metabolic abnormalities and physiologic consequences that can occur during aggressive oral feedings in a severely malnourished person. These

changes can lead to significant pathologic consequences, including death. Awareness of the physiologic adaptation and metabolic changes with fluid and electrolyte shifts with refeeding is of primary concern. It is important to note that these changes can occur, to a greater or lesser degree, in every pediatric or adult patient who has been deprived of adequate nutrients. Pediatric patients with the conditions listed in Table 4-10 are at particular risk for refeeding syndrome.

Table 4-10 Conditions of Pediatric Patients at Risk for Refeeding Syndrome

Source: John A. Kerner and Jo Ann T. Hattner. 2014. Used with permission.

Protein-calorie malnutrition (e.g., refugees or famine victims)
Chronic conditions causing malnutrition (uncontrolled diabetes mellitus, cancer, congenital heart disease, chronic liver disease, and neglect)
Malabsorptive sydromes (including inflammatory bowel disease, cystic fibrosis, chronic pancreatitis, and short bowel syndrome)
Morbid obesity with massive weight loss of 10% within the past 2 months

IV hydration without provision of sufficient calories and protein for 10–14 days

Anorexia nervosa

Patients <80% of ideal body weight (defined as 50% weight for stature)

Dysphagia caused by neuromuscular diseases (e.g., cerebral palsy)

When refeeding is initiated in the undernourished patient, anabolism begins almost immediately. A rapid alteration in hormonal levels – primarily an increase in insulin production – occurs, as the shift from fat to carbohydrate metabolism occurs and glucose becomes the predominant fuel. The glucose load with corresponding insulin release results in cellular uptake of glucose, phosphate, potassium, magnesium, and water, as well as protein synthesis. At this time the basal metabolic rate increases. Anabolism requires energy, nutrients, and enzymes as intermediate compounds to act as building blocks for regrowth. Increased requirements for anabolism may cause or unmask deficiencies, including life-threatening imbalances, thus inhibiting anabolism.

The cardiovascular adaptations of malnutrition, including myocardial atrophy and volume contraction, must also be considered when refeeding an undernourished patient. A rapid

alteration in calories, fluid, and particularly sodium intake may cause fluid shifts and intravascular volume overload, causing the patient to go into congestive heart failure.

The most common laboratory abnormalities encountered when refeeding undernourished patients involve serious deficiencies in potassium, phosphate, magnesium, and calcium. The etiologies of each of these abnormalities include the following:

Potassium Insulin, secreted in response to the increased glucose load during refeeding, causes glucose and potassium to enter the intracellular space. This increased cellular uptake of potassium may result in a rapid fall in serum potassium. Hypokalemia may alter nerve and muscle function resulting in weakness, respiratory failure, cardiac arrhythmias, and possibly cardiac arrest. A potassium concentration of less than 3.0 mEq/L is considered severe hypokalemia.

Phosphate Hypophosphatemia is the predominate feature of the refeeding syndrome. As anabolism increases, the need for phosphorylated intermediates also increases. Phosphate bound to these compounds is, in effect, “trapped” intracellularly. The resulting imbalance may cause severe hypophosphatemia, which may lead to cardiac, neuromuscular, hepatic, hematologic, and

respiratory dysfunction and, ultimately, organ failure.

Because phosphorus plays such a major role in the metabolic consequences of refeeding, hypophosphatemia is known as the “hallmark sign” of refeeding syndrome.

Magnesium Refeeding syndrome is associated with hypomagnesemia and the mechanism is probably multifactorial. Intracellular movement of magnesium into cells with carbohydrate feeding, and preexisting magnesium status, are two of the possible factors. Magnesium is also a cofactor for many enzyme systems and many biochemical reactions, including those involving ATP production. As the metabolic rate increases, magnesium demands rise. Thus, hypomagnesemia may cause hypokalemia likely due to impaired sodium/potassium-ATPase activity. In addition, magnesium is also required for normal parathyroid function. Hypomagnesemia may cause hypocalcemia likely due to impaired parathyroid function.

Calcium As growth is initiated, calcium requirements increase. Maintenance of calcium levels may be affected if hypomagnesemia is present. Serum levels of calcium are maintained in such cases at the expense of bone deposits. Thus, chronic malnutrition alters bone mineralization. Hypocalcemia may also alter muscle and myocardial function, causing tetany and cardiac arrhythmias.

Sodium Retention Sodium retention is also seen in refeeding syndrome. The infusion of carbohydrates leads to increased insulin secretion. Insulin causes decreased renal excretion of sodium and water. Patients may then develop fluid overload, pulmonary edema, and congestive cardiac failure. Low serum albumin may also contribute to edema during refeeding as a result of low oncotic pressure.

Thiamin Vitamin deficiencies also occur because of inadequate intake. Deficiency in thiamin (vitamin B_1) has important consequences during refeeding. It is an important cofactor for enzymes needed in carbohydrate metabolism, and it is rapidly consumed in glycolysis during refeeding. Deficiency can occur in less than 28 days, because its half-life is 9.5 to 18.5 days. Low levels of thiamin impair glucose metabolism and result in lactic acidosis. Further, thiamin deficiency may result in Wernicke's encephalopathy or Korsakoff's syndrome. Wernicke's encephalopathy is manifested by ataxia, confusion, hypothermia, ocular abnormalities, and coma. Korsakoff's syndrome is associated with amnesia and confabulation. Of note, adequate magnesium levels are required for the active form of thiamin.

4. Based on RD's physical examination and laboratory data, what complications of refeeding does he exhibit?

RD exhibits fluid overload, as evidenced by the edema. This condition could be exacerbated by his low albumin level as fluid leaks from the capillaries because of decreased oncotic pressure. In addition, he may be in congestive heart failure because of his decreased cardiac output secondary to loss of heart muscle function from protein catabolism. The stress of a restored blood volume on a depleted cardiac muscle could result in cardiac decompensation. Furthermore, his myocardial function may be altered by electrolyte imbalances, putting him at greater risk for cardiac arrhythmia.

RD demonstrated dangerously low serum calcium, phosphate, magnesium, and potassium levels after refeeding due to rapid utilization of depleted mineral stores to initiate anabolism. Additional clinical signs and symptoms of refeeding syndrome are shown on Table 4-11.

Table 4-11 Clinical Signs and Symptoms of Refeeding Syndrome

Hypophosphatemia	Hypokalemia	Hypomagnesemia	Vitamin/Thiamine Deficiency	Sodium Retention	Hyperglycemia
Cardiac Hypotension Decreased stroke volume Respiratory Impaired diaphragm contractility Dyspnea Respiratory failure Neurologic Paresthesia Weakness Confusion Disorientation Lethargy Areflexic paralysis Seizures Coma Hematologic Leukocyte dysfunction Hemolysis Thrombocytopenia Other Death	Cardiac Arrhythmias Respiratory Failure Neurologic Weakness Paralysis Gastrointestinal Nausea Vomiting Constipation Muscular Rhabdomyolysis Muscle necrosis Other Death	Cardiac Arrhythmias Neurologic Weakness Tremor Tetany Seizures Altered mental status Coma Gastrointestinal Nausea Vomiting Diarrhea Other Refractory hypokalemia and hypocalcemia Death	Encephalopathy Lactic acidosis Death	Fluid overload Pulmonary edema Cardiac compromise	Cardiac Hypotension Respiratory Hypercapnea Failure Other Ketoacidosis Coma Dehydration Impaired immune function

Source: Fuentebella J., Renner JA., Refeeding syndrome. *Pediatr Clin North Am.* 2010;57(5):1201–1210. Used with permission.

5. How could the complications of refeeding that RD experienced have been minimized or avoided?

The following treatment recommendations will help to avoid or minimize the complications of refeeding in children and adults:

Refeed slowly, with gradual increases in fluid, salts, and calories. Begin with 25 to 75 percent of resting energy expenditure (predicted or measured). Increase calories 10 to 25 percent each day or over 4 to 7 days until calorie goal is met while closely monitoring lab values, specifically calcium, phosphate, sodium, glucose, potassium, and magnesium, and the patient's overall clinical state. Consider stopping or slowing the advancement of calories if fluid overload, congestive heart failure, or electrolyte imbalance develops.

Provide multivitamin and mineral supplements.

Provide additional thiamin supplementation over and above the multivitamin supplement with the initiation of carbohydrate feedings. Thiamin is an important cofactor in carbohydrate metabolism and malnutrition can result in depleted stores.

Correct electrolyte abnormalities prior to initiation of enteral or parenteral nutrition support and monitor serum levels.

Monitor vital signs closely during refeeding to detect changes in cardiorespiratory function

early. Continuous electrocardiographic monitoring may be appropriate.

Monitor fluid intake and output carefully to avoid stressing the undernourished cardiorespiratory system and to avoid potential fluid overload.

Monitor daily weight gain. Excessive weight gain suggests fluid retention.

Case 3 Eating Disorders in Adolescent Athletes

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Objective

Recognize how rapid growth during puberty alters adolescents' nutritional requirements.

Identify teenagers at risk for eating disorders and determine appropriate interventions.

Assess the nutrient intake of adolescent athletes and their risk of developing nutritional deficiencies.

Outline the time sequence of the adolescent growth spurt and the stages of pubertal development described by Tanner.

AB is a 15-year-old female who recently began high school and started running for the school's cross country team. She presents to her physician after an episode of fainting while she was competing in a 5-kilometer race. Prior to fainting she felt dizzy, but she has denied heart palpitations, shortness of breath, or visual changes. She reports drinking her normal water prior to starting the race. Of note, AB does state that she has experienced episodes of muscle cramping and headaches over the past 2 weeks.

History of Present Illness

AB was in her usual state of health until about 6 months ago when she reported abdominal pain and a burning sensation in her chest. Her symptoms subsequently improved with the use of antacids and a change in her eating pattern by consuming smaller, more frequent meals. According to her medical records, AB was at the 50th percentile for her weight-for-age on the growth charts until last year. She has lost 15 pounds (6.8 kg) during the past year and is

currently at the 5th percentile for weight-for-age (see Figure 4-1).

Past Medical History

AB's history is negative for heart disease, asthma, epilepsy, or diabetes. She has no previous history of fainting. AB takes antacids occasionally, but she is not taking any over-the-counter supplements, medications, vitamins, or minerals. She has no known allergies.

Social/Development

AB has just started high school and has always been a high achieving student. Her current circle of friends includes mostly school athletes. Upon further questioning, AB expresses concern over recent changes in her body, such as breast development and widening hips. She wants to maintain a trim, muscular physique and fears excessive weight gain will affect her speed and athletic agility. She denies smoking, alcohol, drugs, or sexual activity.

Diet History

To prepare herself for the race, AB had been consuming a high-protein (80 to 100 g/day), low-fat, low-carbohydrate diet for the past few weeks. Further investigation of her diet history reveals that the average meal consists of 8 ounces of chicken or fish, two cooked eggs, two

servings of fruits or vegetables, and one glass of skim milk. She usually eats only one of these meals a day but may add a second if her mother is cooking; otherwise she admits she does not eat much due to her busy schedule. Twenty-four hours prior to the race, she consumed two high-carbohydrate meals.

AB states that she enjoys eating, but follows a low-fat regimen with no red meat to minimize weight gain so she can be more competitive on the varsity track team. On occasion, she indulges in high-fat or high-sugar foods. She admits to small weight fluctuations during the past year, but she cites the increases in the intensity of her exercise routine to keep her weight at 90 pounds (41 kg). She denies vomiting or abuse of laxatives, enemas, or diuretics. AB frequently skips meals and compensates by snacking. During the interview, she frequently expresses concern that she is overweight and not muscular enough for long-distance running. Based on a 24-hour dietary recall, AB consumes approximately 900 to 1000 kcal per day.

Menstrual History

Menses started when AB was 12 years of age. She reports a normal cycle every 30 days until 8 months ago, when menses abruptly ceased.

Physical Examination

Vital Signs

Temperature: 96 °F (35.6 °C)

Heart rate: 68 BPM

Respiratory rate: 14 BPM

Blood pressure: 90/62 mm Hg

Height: 162 cm (64 inches) (50th percentile for age)

Current weight: 41 kg (90 lb) (5th percentile for age)

Ideal weight: 53 kg (117 lb) (50th percentile for age)

BMI: 15.6 kg/m^2

Exam

General: Thin, muscular female appearing sad, anxious, and younger than her age

HEENT: Pale face, pale conjunctiva; no palpable goiter, dental erosions, gag reflex somewhat diminished; enlarged salivary glands

Cardiac: Normal rate and rhythm

Breasts: Elevation of breast mound with areola, Tanner 3

Genitalia: Coarse pubic hair with sparse distribution, Tanner 3

Neurologic: Reflexes slightly decreased in upper and lower extremities

Extremities: Dry, coarse skin at dorsum of hand

Laboratory Data

Patient's Lab Values	Normal Values
Sodium: 142 mEq/L	133–143 mEq/L
Potassium: 2.5 mEq/L	3.5–5.3 mEq/L
CO_2: 32 mmol/L	24–32 mmol/L
Calcium: 8.2 mg/dL	9–11 mg/dL
Phosphate: 4.2 mg/dL	2.5–4.6 mg/dL
Albumin: 3.5 g/L	3.5–5.8 g/L
Hemoglobin: 10.8 g/dL	11.8–15.5 g/dL
Hematocrit: 33.4%	35-45%
MCV: 72 fL	80–100 fL
TIBC: 494 mg/dL	260–470 mg/dL
Ferritin: 10 ng/mL	12–160 ng/mL
Transferrin: 378 mg/dL	200–360 mg/dL
B12: 514 pg/mL	300–900 pg/mL
Folate: 7.1 ng/mL	2.7–17.0 ng/mL

Case Questions

What clues in AB's medical history and physical examination indicate that she may have an eating disorder?

Based on AB's laboratory values, what are the possible causes of her fainting spell, muscle cramps, and headaches?

Is AB's Tanner staging appropriate for her age?

Is AB's current diet appropriate for her age and physical activity level?

What nutrient deficiencies is AB at risk for developing?

What treatment recommendations are appropriate for AB at this time?

What would your new diet recommendations be for AB?

Answers to Questions: Case 3

Part 1: Diagnosis

1. What clues in AB's medical history and physical examination indicate that she may have an eating disorder?

There are several clues in AB's past medical history that may lead the clinician to suspect she has an eating disorder. The history of a burning sensation in her chest and abdominal

pain that responded to antacids signals possible esophagitis, which may be secondary to self-induced vomiting, or purging. Purging behavior may be associated with both anorexia nervosa and bulimia nervosa. The hallmark of anorexia nervosa is an altered perception of body image with resulting restriction of calories and body weight maintained significantly below normal weight for age and height (less than 85 percent expected weight) (Tables 4-12 and 4-13). Bulimia nervosa is a disorder characterized by frequent episodes of binge eating followed by purging (self-induced vomiting or ingestion of laxatives or cathartics to induce vomiting). Patients with bulimia nervosa tend to be of normal or increased weight.

Table 4-12 Diagnostic Criteria for Bulimia Nervosa

Source: American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC, American Psychiatric Association, 1994. Reprinted with permission Copyright 1994 American Psychiatric Association.

Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:
Eating in a discrete period of time (e.g., within any 2-hour period), an amount of

food that is definitely larger than most people would eat during a similar period of time in similar circumstances; and A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating).
Recurrent inappropriate compensatory behavior in order to prevent weight gain, such as self-induced vomiting; misuse of laxatives, diuretics, or other medications; fasting; or excessive exercise.
The binge eating and inappropriate compensatory behaviors occur, on average, at least twice a week for 3 months.
Self-evaluation is unduly influenced by body shape and weight.
The disturbance does not occur exclusively during episodes of anorexia nervosa.
TYPES
Purging type The person regularly engages in self-induced vomiting or the misuse of laxatives or diuretics.
Non-purging type The person uses other inappropriate compensatory behaviors, such as fasting or excessive exercise, but does not regularly engage in self-induced vomiting or the misuse of laxatives or diuretics.

Table 4-13 Medical Complications of Anorexia Nervosa and Bulimia Nervosa

Source: Reprinted with permission from Devlin MJ, Walsh T. Anorexia nervosa and bulimia nervosa. In *Obesity*. Bjorntorp P, Brodoff BN, eds. Philadelphia: Lippincott, 1992.

Anorexia nervosa	**Bulimia nervosa**
Physical Signs and Symptoms	
Cachexia, body fat depletion	Ulceration or scarring of knuckles (due to abrasions received while inducing vomiting)
Bradycardia, hypotension, hypothermia	
Salivary gland hypertrophy	Salivary gland hypertrophy
Lanugo hair	Dental enamel erosion, tooth decay
Amenorrhea	Oligomenorrhea or amenorrhea
Edema	Enlarged parotids
Constipation	Loss of gag reflex
Polyuria	Esophagitis
	Constipation/diarrhea
	Peripheral edema
	Irregular menses

Anorexia nervosa	Bulimia nervosa
Laboratory Findings	
Anemia, leukopenia	Electrolyte abnormalities (hypokalemic alkalosis)
Elevated liver enzymes	Elevated serum amylase
Hypoglycemia	Metabolic alkalosis/ acidosis
Increased serum cholesterol	Hypoglycemia
Hypothalamic/ pituitary/endocrine	Hypocalcemia
gland abnormalities	Dehydration
Delayed gastric emptying	
Cortical atrophy on computed tomography	
Complications	
Sudden death possibly related to the presence of prolonged QT interval	Pancreatitis Ipecac-induced cardiomyopathy
Acute gastric dilatation	Esophageal or gastric rupture
Osteoporosis	Pneumomediastinum

Anorexia nervosa	Bulimia nervosa
	“Cathartic colon”

AB's presentation is consistent with anorexia nervosa, purging type. She is preoccupied with her body image, expresses an intense fear of gaining weight and not maintaining her former physique, and exercises vigorously to maintain herself at a low weight. Her fear about the body changes of puberty, her change in scenery with recently starting high school, and her use of exercise to control her weight are also clues. Despite her degree of malnutrition, AB views herself as overweight, unable to acknowledge the seriousness of her condition, which is likely secondary to the physical changes her body has undergone through puberty. These symptoms are typical of the anorexia nervosa diagnosis. Her physical examination with BMI of 15.6 kg/m^2, current weight in the 5th percentile for age, loss of dental enamel, enlarged salivary glands, along with the coarse skin on the dorsum of her hand are consistent with the purging.

AB's medical problems could be explained by her eating disorder. Although she denied vomiting, her possible esophagitis and electrolyte abnormalities (hypokalemia and alkalosis) suggest vomiting in an effort to keep her weight down. It is not unusual for patients

who purge food to deny vomiting or laxative abuse.

AB's low body weight and low body fat cannot support normal menstrual cycles, resulting in secondary amenorrhea, defined as an absence of menses for 6 months or for three usual cycle intervals following previous normal menstruation. Amenorrhea is more common among female athletes than in the general population; amenorrhea does not confirm an eating disorder but may be considered part of the diagnostic criteria (Tables 4-12 and 4-13).

Eating disorders primarily occur in adolescents and college-aged women, and it is estimated that the lifetime prevalence of anorexia nervosa, bulimia nervosa, and binge eating disorder for women are 0.9%, 1.5%, and 3.5%, respectively. Eating disorders are more often found in industrialized cultures, and occur in all socioeconomic levels and across all major ethnic groups. Given the emphasis on weight, certain athletes are at higher risk for the development of eating disorders. Those especially at risk include dancers, long-distance runners, figure skaters, actors, models, wrestlers, gymnasts, and jockeys.

2. Based on AB's laboratory values, what are the possible causes of her fainting spell, muscle cramps, and headaches?

Electrolyte abnormalities are probable causes of AB's fainting spells, dizziness, and muscle cramps. AB's low potassium level and metabolic alkalosis, indicated by an elevated carbon dioxide level (characteristic of base excess), are probably due to losses of potassium and hydrogen ions during self-induced vomiting. Low serum potassium and/or low serum calcium levels can lead to muscle cramps, headaches, dizziness, and abnormal heart rhythms, some of which may be life-threatening. Her low serum calcium level may be secondary to insufficient intake of calcium or vitamin D deficiency.

AB is at risk for dehydration if she has been inducing vomiting without orally replacing her fluid loss. During a race, she will lose additional free water, sodium, and potassium from sweating. Dehydration can cause headaches and weakness. Also, depletion of glycogen reserves, due to inadequate consumption of energy and carbohydrates, may result in poor muscle endurance and cramping. AB's low hemoglobin, low ferritin, low mean corpuscular volume (MCV), high total iron binding capacity (TIBC), and high transferrin levels, are diagnostic for iron deficiency anemia, which may also contribute to her early fatigue and muscle weakness due to her diminished capacity to transport oxygen (Table 4-13).

3. Is AB's Tanner staging appropriate for her age?

AB demonstrates an arrest of her pubertal development. Puberty starts in girls at an earlier age than in boys. Girls usually demonstrate acceleration of linear growth at the onset of puberty and reach peak growth velocity early, at Tanner stage 2 or 3, whereas boys reach peak growth velocity when genital and pubic hair are at Tanner stage 4 or 5. In healthy females, menarche usually occurs 1 year after their growth peak after the rise in estrogen stimulates closure of their growth plates. In normal females, hypothalamic hormones signal release of pituitary gonadotropins, prompting physical and sexual development; in AB's case, however, her malnutrition interferes with this cycle, arresting her development. Females typically reach their maximal growth velocity (a rate of 9.0 cm/year) at a mean age of 12.5 years. AB's height is already at the 90th percentile for her age, and she has experienced menarche. Therefore, her Tanner stage should be more advanced, but being undernourished and having a reduced amount of body fat prevents an appropriate hormonal milieu to support the progression of puberty.

Part 2: Nutrition Assessment

4. Is AB's current diet appropriate for her age and physical activity level?

No. AB's diet is inadequate to meet her needs, as she is consuming less than 1000 kcal per day and frequently skips meals. A sufficient diet would not normally maintain an adolescent at only 90 pounds (41 kg). Growing adolescents have increased energy requirements to support their rapid growth (calories per kg). In addition, vigorous exercise, such as running, further increases energy requirements 30 to 50 percent above basal metabolic needs. In AB's case, she needs to greatly increase her number of total calories, especially the number of carbohydrates she consumes, to be able to provide her body with the fuel it needs to perform. Furthermore, she should increase her meat and bean consumption to improve her body's iron stores to correct her iron-deficiency anemia. Her restriction of the variety and quantity of food she consumes places her at risk for several vitamin and mineral deficiencies as described subsequently.

5. What nutrient deficiencies is AB at risk for developing?

AB is at risk for developing a calcium deficiency. The highest requirements for calcium are during infancy and adolescence. Adolescent's high calcium requirements are due to increased bone modeling with calcium deposition, promoted by the hormonal changes associated with puberty and the associated growth peak (1300 mg/day). Maximal bone

mass during skeletal maturation is achieved by adolescence or early adulthood and provides the best protection against bone loss after menopause (osteoporosis). However, according to the NHANES III, only 20 percent of teenage girls meet the RDA for calcium. AB intentionally avoids dairy products such as cheese and ice cream because they are high in fat, but she could eat low-fat or fat-free sources and calcium fortified foods or drinks.

AB also most likely has iron-deficiency anemia, as seen by her abnormal hemoglobin, hematocrit, MCV, ferritin, TIBC, and transferrin. Adolescents also require increased dietary iron to support growth. Foods rich in iron, which include liver, red meat, legumes, dried fruits, and green vegetables, are often lacking in an adolescent's diet.

6. What treatment recommendations are appropriate for AB at this time?

A team approach that combines medical management, cognitive–behavioral intervention, and nutritional rehabilitation and counseling is important in the treatment of patients with eating disorders. Eating disorders are viewed as psychiatric conditions but these patients must be followed medically since there is a significant morbidity and mortality associated with these conditions. Potential medical complications can include delayed gastric emptying, heart failure, pancreatitis,

diarrhea, osteopenia, and life-threatening electrolyte disturbances. Patients with anorexia may also experience cognitive deficits secondary to malnutrition or the subsequent refeeding process.

Psychotherapeutic assessment and intervention are crucial in establishing a diagnosis, evaluating the risk of suicide, and assessing the severity of the psychological symptoms as well as other co-morbid conditions such as depression, anxiety, substance abuse, or personality disorders. If AB's prognosis is to improve, she needs to recognize her problem, improve her perceived body image, and set and achieve nutritional and weight goals. In addition to psychiatric/psychological and medical intervention, a dietitian should provide guidance for nutritional rehabilitation and education.

7. What would your new diet recommendations be for AB?

The initial goals of medical nutrition therapy for AB should be to gain control over her purging behavior, stop her caloric restriction, and support steady weight gain. Increases in caloric intake should be gradual to avoid refeeding syndrome. Efforts to help AB accept a healthier weight goal should be undertaken, such as seeing a school or personal therapist. If purging continues despite psychological intervention, medication may reduce her

binging and purging. Psychopharmacologic interventions (antidepressants and neuroleptics) have been less successful with anorexia nervosa than with bulimia nervosa.

Treatment for eating disorders can usually be initiated as outpatient therapy as long as the patient is medically and psychiatrically stable. Those who are 25 to 30 percent below their ideal weight are often hospitalized because the severity of their malnutrition is life-threatening. Since AB is only 90 pounds (41 kg), she will require close monitoring by her physician, and she may need to be hospitalized if her weight does not increase in the next few weeks.

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5
Older Adults

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Objectives*

Describe the physiological changes associated with aging and describe their impact on nutrient requirements, absorption, and metabolism.

List common factors associated with poor nutritional status in older adults.

Identify differences in the RDA for micronutrients and minerals for adults ≥51 years of age.

Understand the instruments utilized for nutritional assessments in older adults.

*Source: Objectives for chapter and cases adapted from the NIH Nutrition Curriculum Guide for Training Physicians. (www.nhlbi.nih.gov/funding/training/naa)

Introduction

Approximately one in eight Americans is over the age of 65. By 2030, 72.1 million Americans will be 85 years or older, representing 19 percent of the population. Women will continue to out number men and by 2030, Hispanics, Asians/Pacific Islanders, Native Americans, and African-Americans are projected to represent approximately 25 percent of the elderly population. Specific nutrition concerns for older adults include eating habits, eating ability, managing meals, relationships, culture, financial resources, and social support. Nutrition-related problems stem from chronic diseases, depression, dementia, dysphagia, obesity, cachexia, and frailty. Nutrition programs will have to become more diverse and flexible to meet the needs of this ever-growing older population. This chapter reviews the impact of aging on nutritional needs and outlines appropriate interventions for many important nutrition-related concerns for the older adult. The following section discusses the concerns of older adults, including fluid and hydration status, health literacy issues, social, cultural, and economic considerations, and physiological and metabolic changes needed to meet nutritional requirements.

Alterations in Nutritional Needs
Alterations of nutritional needs of older adults are related to the physiological and metabolic

changes associated with aging. Healthy Eating Index Scores among adults 60 years of age and over have demonstrated that only 17 percent had diets that were rated “good”, while 67 percent consumed diets that “needed improvement” and approximately 14 percent reported diets rated “poor”. Caloric needs decline with age due to reductions in resting metabolic rate. Therefore, consumption of nutrient dense foods becomes critically important. A comprehensive nutritional assessment, including past medical history, vital signs, review of systems, physical exam, and biochemical data, is critical to identify those at nutritional risk, as outlined in Chapter 1. Table 5-1 highlights age-related physiological changes and their potential nutrition-related consequences.

Table 5-1 Age-Related Physiologic Changes with Potential Nutrition-Related Outcomes

Source: Nutrition Screening Initiative. 2626 Pennsylvania Ave. NW, Suite 301, Washington, DC 20037. Used with permission.

Organ System	**Change**	**Potential Outcome**
Body composition	↑ Fat	↓ Basal metabolic rate
		↑ Fat-soluble drug storage,

Organ System	Change	Potential Outcome
		with prolonged half-life
	↓ Body water	↑ Concentration of water-soluble drugs
Gastrointestinal	↓ Gastric acid secretion	↓ Absorption of folate, protein-bound vitamin B_{12}
	↓ Gastric motility	↓ Bioavailability of minerals, vitamins, protein
	↓ Lactase activity	Avoidance of milk products, with reduced intake vitamin D and calcium
Hepatic	↓ Size and blood flow	↓ Albumin synthesis rate
	↓ Activity drug-metabolizing enzymes	Poor or delayed metabolism of certain drugs
Immune	↓ T-cell function	Energy
		↓ Resistance to infection

Organ System	Change	Potential Outcome
Neurologic	Brain atrophy	↓ Cognitive function
Renal	↓ Glomerular filtration rate	Reduced renal excretion of metabolites, drugs
Sensory-perceptual	↓ Taste buds, papilla on tongue	Altered taste threshold, reduced ability to detect sweet/salt, increased use of salt/sugar
	↓ Olfactory nerve endings	Altered smell threshold, reduced palatability causing poor food intake
Skeletal	↓ Bone density	↑ Fractures

Fluid and Hydration Fluid and hydration are especially important to the health of older adults. Older adults often have a poor thirst response and therefore are at increased risk of dehydration or urinary tract infections as are individuals with impaired cognition. Therefore, it is imperative to teach patients to drink fluids on a regular basis. Six to eight glasses of liquids every day will provide sufficient hydration for

the healthy older adult; however, it is often difficult to reach this level. Additional drinks such as tea and juices, especially cranberry juice, may be helpful to older adults who need to consume more fluids. However, patients with certain conditions, such as chronic heart failure and kidney disease, may require fluid restriction. In addition, there are potential negative effects of excessive water consumption that can lead to dilutional hyponatremia (water intoxication) and increased nocturia. Due to its sugar content, cranberry juice may not be appropriate for patients with diabetes.

Health Literacy It is important for older adults to understand health information in order to navigate through the health system. To do this, patients need the capacity to process health information and understand the health services that are available. This allows them to make better judgments regarding health care services. Education does not guarantee the ability to read. Age-related cognitive decline and past learning experiences impact literacy and this may determine a patient's ability to interpret food labels, choose proper nutrients, take medications, and achieve better health outcomes. One way to address low literacy situations is through the use of illustrations to improve patients' understanding of health information and ensure greater adherence to health regimens. Setting up a medication schedule that is easier to follow will also ensure

greater compliance. Research shows that patients with low literacy rates do not use a standardized medication regimen even if they are taking medications up to 7 times/day. Studies also show that low health literacy is significantly associated with higher all-cause mortality in patients with heart failure.

Social and Economic Considerations Economic hardship may limit financial resources for adequate nutrition. Deficits in physical functioning contribute to food insecurity, defined as uncertain ability to acquire nutritionally adequate and safe foods, and/or lack of appropriate nutrition in older adults. Many older adults who eat alone make poor dietary choices and may eat the same foods day after day. Reduced social contact, eating meals alone, and inadequate assistance with shopping and preparing food can impact dietary intake. Total caloric intake may be insufficient to meet dietary needs, placing the individual at increased risk for malnutrition. These risk factors often go unrecognized by healthcare providers, family, and friends. Healthcare providers need to inquire about these issues and refer patients with social and economic challenges to social workers and community agencies prepared to intervene.

Cultural Issues Food habits in older adults are the product of ethnic origin and cultural norms imparted at an early age. Food

preferences can vary depending on where an individual grew up (e.g., in a rural or urban setting). Food habits develop over a lifetime of experiences and have a strong influence on nutrient intake. Food can provide a means for communication of love or disapproval in families. For older adults, dietary intake shaped by cultural values may be modified by economic decline, stressors, or chronic illness. Practitioners should consider these unique issues and the challenges they present when assessing an appropriate nutritional intervention.

Macronutrient Needs of Older Adults

Energy Body composition changes with age. Lean body mass declines, body fat mass increases, and a lack of physical activity results in lower energy expenditure, all leading to a reduction in metabolic rate (Table 5-1). Therefore, caloric needs typically decline as people advance in age, unless they remain physically active and maintain their muscle mass and hence, their metabolic rate. While obesity is a major problem in adults, later in life, negative energy balance (caloric malnutrition) may result due to changes in taste, dentition, cognitive impairment, and depression.

Protein The current recommended daily amount (RDA) for protein (0.8 g/kg per day) is the same for adults of all ages, although there is evidence that a higher protein intake could help counteract sarcopenia (loss of muscle mass) in the older adult by enhancing the hypertrophic response to strength conditioning. The oldest age groups are most at risk for protein deficiency especially when health problems or other stresses are manifested and when patients are institutionalized, hospitalized, or reside in long-term care facilities.

Lipids, Carbohydrates, and Fiber There is a decrease in the intake of fat and cholesterol with age. There is also a reduction in the percentage of calories coming from fat. While absolute intake of carbohydrate typically decreases with age, carbohydrate as a percentage of calories increases slightly due to the reduction of calories coming from fats. Most adults, including the elderly, consume less fiber than the recommended of 25 to 35 g/day. Increasing dietary fiber helps prevent or alleviate constipation and may contribute to the prevention of age-related chronic diseases, such as coronary heart disease, and is beneficial for those with diabetes, hyperlipidemia, and gastrointestinal conditions, as described in Chapters 8, 9, and 10.

Vitamin Needs of Older Adults

Vitamin A The RDA for vitamin A is 900 µg/day for men and 700 µg/day for women and requirements do not change with age. The tolerable upper intake level for adults is 3000 µg/day. Concentrations of vitamin A decrease with aging, and lack of dietary or supplemental intake of vitamin A may further exacerbate this deficiency. Often individuals who face economic hardship do not consume sufficient food sources of vitamin A. Retention of vitamin A seems to be enhanced in aging, especially in older adults who consume large amounts from supplements and fortified food. Studies suggest that vitamin A may be helpful in maintaining age-related immune function, and proper vision (Chapter 5: Case 2). Foods sources of vitamin A are listed in Appendix A.

Vitamin D The RDA for vitamin D in men and women 51 years and older is 600 IU/day, and for those over 70, requirements increase to 800 IU/day. In clinical practice, higher doses may be prescribed without apparent undue effects. The tolerable upper intake level for adults is 2000 IU/day. There is an increased need for vitamin D in older adults due to age-related changes, specifically less efficient skin synthesis of vitamin D. In North America, it is estimated that 50 percent of the older population is vitamin D deficient. Vitamin D status can also

be negatively impacted by the use of sunscreen, being home-bound, and northern latitude.

The NIH Office of Dietary Supplements defines serum levels of 25(OH)D of 30 to 50 nmol/L as inadequate for overall health. Vitamin D deficiency results not only in impaired bone metabolism, but also muscle weakness, predominantly in the proximal muscles group. Vitamin D supplementation in vitamin D-deficient older adults improved muscle strength, walking distance, and functional ability, and resulted in a reduction in falls and non-vertebral fractures. Studies also show a protective relationship between sufficient vitamin D status and lower risk of colorectal cancer.

Vitamin D status should be routinely assessed and supplements prescribed when food intake is inadequate to maintain optimal health status. Foods sources of vitamin D are listed in Appendix B. It is important to teach patients that sunlight (UVB) exposure from 5 to 15 minutes twice a week helps maintain appropriate levels of vitamin D (in light-skinned individuals). After 15 minutes of sun exposure, sunscreen can be used as a protective measure against skin cancer. This fact should be impressed upon the older adult patient, because the conversion in the skin to the active form of vitamin D from sunlight declines with age. Vitamin D insufficiency has

been found to be much more prevalent in darker-skinned populations.

Vitamin E The RDA for vitamin E in adults is 15 mg (22.4 IU) and does not change with age. Alpha tocopherol is the most bioavailable form of vitamin E. Vitamin E absorption and utilization does not change with age, but dietary intake of vitamin E has been shown to be below recommended levels in older adults. A possible explanation is a reduction in high-fat foods containing vitamin E, such as vegetable oils and nuts. For optimal antioxidant function, vitamin E dietary intake needs to be supported with adequate intake of vitamin C, niacin, selenium, and glutathione. However, obtaining vitamin E via supplementation is not recommended. A recent meta-analysis concluded that high doses of supplemental vitamin E, more than 150 IU /day, may be linked with increased all-cause mortality, and supplements exceeding this amount should be avoided. Foods sources of vitamin E are listed in Appendix C.

Vitamin C The RDA for vitamin C is 90 mg/ day for men and 75 mg/day for women and requirements do not change with age. The tolerable upper intake level for adults is 2000 mg/day. Intake of vitamin C is highly variable among older adults. While many older adults consume generous amounts of vitamin C and achieve nutritional adequacy, some groups have been identified as having an increased risk of

deficiency, especially those with dental problems, dementia, and those in hospitals and nursing homes. Aging does not alter the absorption or metabolism of vitamin C, so low levels are generally attributed to poor intake or increased requirements. The clinical significance of vitamin C deficiency, other than scurvy, has not definitively been established. However, one study found that severe or marginal vitamin C deficiency was significantly associated with all-cause mortality. A meta-analysis of individuals taking vitamin C supplements found that 500 mg daily of vitamin C for a minimum of 4 weeks was associated with a significant decrease in serum low-density lipoprotein cholesterol (LDL-C) and triglyceride concentrations. High-density lipoprotein cholesterol (HDL-C) levels remained unchanged with vitamin C supplementation. Foods sources of vitamin C are listed in Appendix E.

Thiamin, Riboflavin, and Niacin Thiamin (vitamin B_1), riboflavin (vitamin B_2), and niacin (vitamin B_3) function as coenzymes in energy metabolism. This may lead to the notion that requirements for these vitamins diminish with declining energy requirements in older adults. However, available evidence suggests that requirements for these nutrients are unchanged with age. Potential causes of low blood levels include chronic alcohol use (thiamin) and low consumption of dairy products (riboflavin).

Older patients with food insecurity have been reported to have low intake levels of B vitamins.

Folate The RDA for folate in men and women 51 years and older is 400 μg/day. The tolerable upper intake limit for folate has been set at 1000 μg/day. Requirements for folate do not change with age; however, inadequate folate status contributes to hyperhomocysteinemia, which may increase the risk of coronary disease and other chronic diseases common in older adults. Folic acid supplementation has not been shown to reduce the risk of coronary events. A reduction in stroke events was observed in the Heart Outcomes Prevention Evaluation-2 study, but there were no significant effects on death rates and non-fatal myocardial infarction in patients receiving folate supplements. A reduction in the stroke mortality rate was seen in North America after folic acid fortification. Folate intake has increased due to food fortification programs to the point of raising concerns about excessive intake in older adults who consume a large amount of fortified foods such as breakfast cereals, breads, and products made from enriched flours. There is concern that this level of fortification may mask a vitamin B_{12} deficiency, particularly in elderly individuals, allowing the neurological sequelae to progress even though the anemia associated with this deficiency resolves. Also, high folate levels may reduce the response to anti-folate drugs that are used in the treatment of

rheumatoid arthritis, psoriasis, malaria, and some forms of cancer. As a result, higher folic acid intake may not be appropriate for some patients. Foods sources of folate are listed in Appendix F.

Vitamin B_{12} The RDA for vitamin B_{12} for men and women 51 years and older is 2.4 μg/day. Requirements for vitamin B_{12} do not increase with age, but low stomach acid secretion, secondary to atrophic gastritis, may seriously impair the absorption of vitamin B_{12} in those over age 50. To assure nutritional adequacy, supplements containing vitamin B_{12} or good food sources of vitamin B_{12}, such as animal and dairy foods, as well as foods supplemented with vitamin B_{12} (soy milk), should be consumed daily. Widespread use of vitamin B_{12} injections, once quite popular, is no longer necessary if the free form of B_{12} is given as an oral supplement at 2000 μg/day. Patients taking metformin and those on acid-suppressant therapy have been shown to have poor vitamin B_{12} absorption. Serum and red blood cell vitamin B_{12} levels should be checked and vitamin B_{12} should be prescribed when levels are borderline or below normal.

Mineral Needs of Older Adults

Calcium The RDA for calcium in men and women 51 years and older is 1200 mg/day. The

tolerable upper intake level for calcium is 2000 mg/day. Osteoporosis is a major health risk for older women and men. Calcium recommendations are set at levels associated with maximum retention of body calcium since bones that are calcium rich are known to be less susceptible to fractures. Calcium supplements should be considered for those whose dietary intake of calcium is deficient. More than 70 percent of men and 78 percent of women may have low calcium intake. The disparity between the dietary requirement for calcium and the amount that is actually consumed by the older adult population is the most dramatic of any known essential nutrient, especially in older women. Foods sources of calcium are listed in Appendices G and H.

Iron The RDA for iron is 8 mg/day in both men and women 51 years and older. The tolerable upper intake level for both men and women in this age group is 45 mg/day. Iron is an important component of proteins that transport oxygen, so iron deficiency limits oxygen delivered to the cells. This results in a lack of energy and a decrease in immunity. An excess of iron can cause toxicity and death. Approximately 11 percent of men and 10 percent of women aged 65 and older in the United States are anemic. Rates of anemia rise to 50 to 60 percent in older adults who are living in nursing homes. Poor outcomes from

anemia include frailty, increased rates of falls, impaired cognition, and death.

Healthcare providers need to assess iron levels and encourage patients to increase their intake of protein, iron, and vitamin C to provide the nutrients needed for hemoglobin production. When dietary iron intake is inadequate, appropriate iron supplements should be prescribed and an adjunctive stool softener recommended if this causes constipation. Foods sources of iron are listed in Appendix L.

Magnesium The RDA for magnesium is 420 mg/day for men and 320 mg/day for women and requirements do not change with age. The tolerable upper intake level for magnesium supplementation is 350 mg/day, the upper limit for magnesium represents intake from a pharmacological agent only and does not include intake from food and water. Magnesium is an essential nutrient for bone health and functions in conjunction with vitamin D and calcium. It also serves other critical roles such as nerve and muscle function, since it is an integral component to the sodium/potassium pump and required for potassium to enter the cell. Magnesium status has been linked to bone mineral density in both men and women. With age, magnesium absorption decreases, urinary losses increase, and low magnesium intake is often observed. Magnesium supplements have been used to safely treat constipation. Since

older adults frequently complain of constipation, magnesium supplementation between 250 to 400 mg per day (taken in the evening) may be beneficial to achieve the recommended intake of magnesium and to relieve constipation. Food sources of magnesium are listed in Appendix K.

Zinc The RDA for zinc is 11 mg/day for men and 8 mg/day for women. The tolerable upper intake level for zinc is 40 mg/day. Aging effects on zinc requirements are not completely understood, but it is likely that zinc needs increase with age. Reduced zinc status in older adults has been linked with decreased immunity and poor response to vaccinations. Zinc supplementation reduces susceptibility to infections and has been shown to enhance wound healing. Studies show that aging is associated with oxidative stress and that zinc is an effective anti-inflammatory as well as an antioxidant. Supplemental doses of zinc should not exceed 40 mg/day unless patients are under regular medical supervision, as high doses can induce copper deficiency and/or immune suppression. Foods sources of zinc include oysters, wheat germ, red meats, liver, dark chocolate, and roasted pumpkin seeds.

Identifying Individuals at Risk for Malnutrition

It is a considerable challenge for practitioners to assist their older adult patients to achieve an optimal balance of nutrients. Older adults who are hospitalized for serious illnesses, nursing home patients, and homebound older adults are at risk for malnutrition. The prevalence of malnutrition increases for those over the age of 70 years and is more likely to occur in individuals living in an urban setting. Overweight and obesity also have pronounced detrimental effects on the health and quality of life of older adults. Evidence is growing that nutritional interventions can improve overall function and quality of life for older adults. Healthcare providers need to appropriately screen, diagnose, and treat malnutrition in older adults in order to minimize the risk for malnutrition and optimize nutritional needs.

Etiology of Malnutrition Decreased oral intake may result from poverty, poor dentition, gastrointestinal pathology, pain, anorexia, dysphagia, depression, social isolation, and pain during chewing or swallowing. Increased nutrient losses can occur secondary to glycosuria, bleeding in the digestive tract, diarrhea, malabsorption, nephrosis, draining fistula, or protein-losing enteropathy. Additionally, any hypermetabolic state (e.g., inflammatory process or cancer) or excessive

catabolic process can result in increased nutrient requirements. Surgery, trauma, fever, wound healing, burns, severe infection, malabsorption syndromes, and critical illness can also dramatically increase nutrient requirements.

Nutrition Assessment of Older Adults

The purpose of a brief nutrition assessment is to identify patients at risk for poor or excessive nutritional intake. Nutrition assessment includes the past medical, family, and social history, diet and exercise history, vital signs, review of systems, physical examination, and biochemical data and should be incorporated into routine primary care visits (Chapter 1). The importance of nutritional screening is paramount when caring for older patients because culturally, older adults do not typically express their nutritional concerns. This lack of communication may be related to their loss of independence, fear of dementia, or shame associated with their chronic disease.

Recognizing individuals at risk for malnutrition is a greater challenge than actually diagnosing the condition once it occurs. Various screening tools have been developed to help clinicians identify patients at risk for malnutrition. The Nutrition Screening Initiative (NSI) can be filled out by the patient and used not only to

identify those at risk, but also identify potential contributing factors for malnutrition (Figure 5-1). NSI is a broad, inter-professional effort of the American Academy of Family Physicians, *the Academy of Nutrition and Dietetics*, and a coalition of more than 25 national health, aging, and medical organizations with the goal of promoting the integration of nutrition screening and intervention into the health care for older adults.

The Warning Signs of poor nutritional health are often overlooked. Use this Checklist to find out if you or someone you know is at nutritional risk.

DETERMINE YOUR NUTRITIONAL HEALTH

Read the statements below. Circle the number in the "yes" column for those that apply to you or someone you know. For each "yes" answer, score the number in the box. Total your nutritional score.

	YES
I have an illness or condition that made me change the kind and/or amount of food I eat.	2
I eat fewer than 2 meals per day.	3
I eat few fruits or vegetables or milk products.	2
I have 3 or more drinks of beer, liquor or wine almost every day.	2
I have tooth or mouth problems that make it hard for me to eat.	2
I don't always have enough money to buy the food I need.	4
I eat alone most of the time.	1
I take 3 or more different prescribed or over-the-counter drugs a day.	1
Without wanting to, I have lost or gained 10 pounds in the last 6 months.	2
I am not always physically able to shop, cook and/or feed myself.	2
TOTAL	

Total Your Nutritional Score. If it's –

0-2 **Good!** Recheck your nutritional score in 6 months.

3-5 **You are at moderate nutritional risk.** See what can be done to improve your eating habits and lifestyle. Your office on aging, senior nutrition program,senior citizens center or health department can help. Recheck your nutritional score in 3 months.

6 or more **You are at high nutritional risk.** Bring this Checklist the next time you see your doctor, dietitian or other qualified health or social service professional. Talk with them about any problems you may have. Ask for help to improve your nutritional health.

Remember that Wa rning Signs suggest risk, but do not re p resent a diagnosis of any condition. Tu rn the page to learn more about the Wa rnings Signs of poor nutritional health.

These materials are developed and distributed by the Nutrition Screening Initiative, a project of:

AMERICAN ACADEMY OF FAMILY PHYSICIANS
THE AMERICAN DIETETIC ASSOCIATION
THE NATIONAL COUNCIL ON THE AGING, INC.

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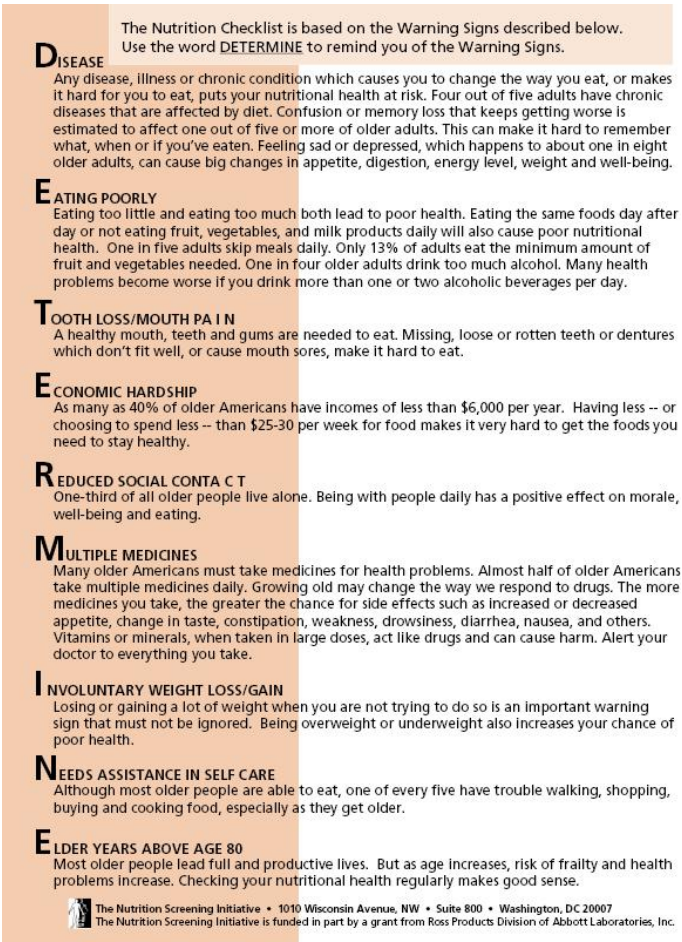
The Nutrition Screening Initiative is funded in part by a grant from Ross Products Division of Abbott Laboratories, Inc.



The Nutrition Checklist is based on the Warning Signs described below.
Use the word DETERMINE to remind you of the Warning Signs.

DISEASE
Any disease, illness or chronic condition which causes you to change the way you eat, or makes it hard for you to eat, puts your nutritional health at risk. Four out of five adults have chronic diseases that are affected by diet. Confusion or memory loss that keeps getting worse is estimated to affect one out of five or more of older adults. This can make it hard to remember what, when or if you've eaten. Feeling sad or depressed, which happens to about one in eight older adults, can cause big changes in appetite, digestion, energy level, weight and well-being.

EATING POORLY
Eating too little and eating too much both lead to poor health. Eating the same foods day after day or not eating fruit, vegetables, and milk products daily will also cause poor nutritional health. One in five adults skip meals daily. Only 13% of adults eat the minimum amount of fruit and vegetables needed. One in four older adults drink too much alcohol. Many health problems become worse if you drink more than one or two alcoholic beverages per day.

TOOTH LOSS/MOUTH PA I N
A healthy mouth, teeth and gums are needed to eat. Missing, loose or rotten teeth or dentures which don't fit well, or cause mouth sores, make it hard to eat.

ECONOMIC HARDSHIP
As many as 40% of older Americans have incomes of less than $6,000 per year. Having less -- or choosing to spend less -- than $25-30 per week for food makes it very hard to get the foods you need to stay healthy.

REDUCED SOCIAL CONTA C T
One-third of all older people live alone. Being with people daily has a positive effect on morale, well-being and eating.

MULTIPLE MEDICINES
Many older Americans must take medicines for health problems. Almost half of older Americans take multiple medicines daily. Growing old may change the way we respond to drugs. The more medicines you take, the greater the chance for side effects such as increased or decreased appetite, change in taste, constipation, weakness, drowsiness, diarrhea, nausea, and others. Vitamins or minerals, when taken in large doses, act like drugs and can cause harm. Alert your doctor to everything you take.

INVOLUNTARY WEIGHT LOSS/GAIN
Losing or gaining a lot of weight when you are not trying to do so is an important warning sign that must not be ignored. Being overweight or underweight also increases your chance of poor health.

NEEDS ASSISTANCE IN SELF CARE
Although most older people are able to eat, one of every five have trouble walking, shopping, buying and cooking food, especially as they get older.

ELDER YEARS ABOVE AGE 80
Most older people lead full and productive lives. But as age increases, risk of frailty and health problems increase. Checking your nutritional health regularly makes good sense.

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Figure 5-1 Determine Your Nutritional Health
Source: Nutrition Screening Initiative Washington, D.C. Nutrition Screening Initiative: Warning Signs.

Functional Status

More than half of older Americans report some degree of disability, and over one-third report severe disability. Activities of Daily Living (ADLs) reflect an individual's capacity for self-care and Instrumental Activities of Daily Living (IADLs) reflect more complex tasks that enable a person to live independently in the community (Table 5-2). Even after controlling for demographic, socioeconomic status, gender, and ethnicity, level of disability predicts mortality risk in older adults. It is imperative that when taking a medical history of older adults, questions regarding functional capacity be included.

Table 5-2 Commonly Used Measures of Functional Capacity

Activities of Daily Living (ADLs)*	**Instrumental Activities of Daily Living (IADLs)†**
Bathing	Telephone use
Dressing	Walking
Toileting	Shopping: groceries/ clothes
Transferring	Meal preparation
Continence	Housework/laundry
Feeding	Home maintenance/repair
	Take medicines

Activities of Daily Living (ADLs)*	Instrumental Activities of Daily Living (IADLs)†
	Manage money

*ADLs reflect capacity for self-care

†IADLs reflect capacity for independent living

Oral Health Assessment

Oral health assessment is integral to the nutritional status of older adults. Factors that can contribute to oral health problems include tooth decay, ill-fitting dentures, endentulism, pain, disease states, and medications which may alter taste. There is a strong connection between oral health and a person's general health status. An association has been noted between periodontal disease and myocardial infarction. It has also been reported that endentulous older adults consume fewer servings of fruits and vegetables and more soft foods, often leading to decreased fiber intake. There is a growing need for a community-based coalition of healthcare providers to ensure adequate oral health care for older adults in assisted living facilities, nursing homes, and those visited by home health agency staff. A number of these facilities have on-site dentists and dental hygientists to improve the oral health of their residents. The Kayser-Jones

BOHSE oral screening instrument is an appropriate tool to utilize for the oral assessment of older adults (Figure 5-2). Table 5-3 lists soft foods to suggest for patients with chewing difficulty.

try this: general assessment series
Best Practices in Nursing Care to Older Adults
From The Hartford Institute for Geriatric Nursing, New York University, College of Nursing

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Editor-in-Chief: Sherry A. Greenberg, PhD(c) MSN, GNP-BC
New York University College of Nursing

Oral Health Assessment of Older Adults: The Kayser-Jones Brief Oral Health Status Examination (BOHSE)

By: Leslie-Faith Morritt Taub, DNSc, A/GNP-BC, CDE, C. BSM, FAANP
New York University College of Nursing

WHY: The bidirectional effects of systemic diseases such as cardiovascular disease, cerebrovascular accident (CVA), human immunodeficiency virus (HIV), diabetes, and pneumonia on oral health in older adults is well recognized (IOM, 2011). Almost 70% of Americans 65 and older have no dental coverage (McGinn-Shapiro, 2008) and by the time they enter nursing homes this unmet need for dental care may take back seat to the myriad of other demands imposed by comorbid conditions. The Institute of Medicine's report (2011) Improving Access to Oral Health Care for Vulnerable and Underserved Populations recognizes the barriers to oral care in the current health system and supports training nondental health professionals such as nurses to perform oral disease screening.

BEST TOOL: In a systematic review of oral health assessment by nurses and others in the care of cognitively impaired institutionalized residents, the Kayser-Jones Brief Oral Health Status Examination (BOHSE) was found to be the most comprehensive, validated and reliable screening tool (Chalmers & Pearson, 2005). The 10-item examiner-rated BOHSE catalogues oral health problems with a higher score identifying more problems. The BOHSE assessment begins with observation and palpation for enlarged cervical lymph nodes and includes a complete oral cavity evaluation. Using a pen light, tongue depressor, and gauze, the conditions of the oral cavity, surrounding tissues, and natural/artificial teeth are examined and categorically graded from 0 (normal) to 2 (significantly problematic).

TARGET POPULATION: The BOHSE was designed to evaluate the oral condition of nursing home residents, with and without cognitive impairment, by those providing nursing care. The BOHSE has been employed in a variety of populations including community-dwelling and hospitalized older adults, nursing home residents, and individuals with cognitive impairment (Chalmers, Spencer, Carter, King, & Wright, 2009; Chen, Chang, Chyun & McCorkle, 2005; Lin, Jones, Godwin, Godwin, Knebl, & Niessen, 1999; Yu, Lee, Hong, Lau, & Leung, 2008).

VALIDITY AND RELIABILITY: Statistically significant test-retest reliability (r=.83-.79), inter-rater reliability (r=.68-.40), and content validity have been established by six field experts (Kayser-Jones, et al, 1995).

STRENGTHS AND LIMITATIONS: The BOHSE is a screening tool with demonstrated reliability and validity that should be used by nursing personnel in residential settings. Systematic use of this tool at scheduled times can facilitate the oral health triaging of residents to allow for timely care provided by the dentist.

FOLLOW-UP: Although the cumulative score is helpful, individuals who score on items with an asterisk that are underlined should be referred for a dental evaluation and exam and follow-up immediately. In general, a semi-annual checkup is recommended by a dentist for oral health assessment.

MORE ON THE TOPIC:

Best practice information on care of older adults: www.ConsultGeriRN.org.

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The Kayser-Jones Brief Oral Health Status Examination (BOHSE)

Resident's Name _____ Date _____

Examiner's name _____ TOTAL SCORE_____

CATEGORY	MEASUREMENT	0	1	2
LYMPH NODES	Observe and feel nodes	No enlargement	Enlarged, not tender	Enlarged and tender*
LIPS	Observe, feel tissue and ask resident, family or staff (e.g. primary caregiver)	Smooth, pink, moist	Dry, chapped, or red at corners*	White or red patch, bleeding or ulcer for 2 weeks*
TONGUE	Observe, feel tissue and ask resident, family or staff (e.g. primary caregiver)	Normal roughness, pink and moist	Coated, smooth, patchy, severely fissured or some redness	Red, smooth, white or red patch; ulcer for 2 weeks*
TISSUE INSIDE CHEEK, FLOOR AND ROOF OF MOUTH	Observe, feel tissue and ask resident, family or staff (e.g. primary caregiver)	Pink and Moist	Dry, shiny, rough red, or swollen*	White or red patch, bleeding, hardness; ulcer for 2 weeks*
GUMS BETWEEN TEETH AND/OR UNDER ARTIFICIAL TEETH	Gently press gums with tip of tongue blade	Pink, small indentations; firm, smooth and pink under artificial teeth	Redness at border around 1-6 teeth; one red area or sore spot under artificial teeth*	Swollen or bleeding gums, redness at border around 7 or more teeth, loose teeth; generalized redness or sores under artificial teeth*
SALIVA (EFFECT ON TISSUE)	Touch tongue blade to center of tongue and floor of mouth	Tissues moist, saliva free flowing and watery	Tissues dry and sticky	Tissues parched and red, no saliva*
CONDITION OF NATURAL TEETH	Observe and count number of decayed or broken teeth	No decayed or broken teeth/roots	1-3 decayed or broken teeth/roots*	4 or more decayed or broken teeth/roots; fewer than 4 teeth in either jaw*
CONDITION OF ARTIFICIAL TEETH	Observe and ask patient, family or staff (e.g. primary caregiver)	Unbroken teeth, worn most of the time	1 broken/missing tooth, or worn for eating or cosmetics only	More than 1 broken or missing tooth, or either denture missing or never worn*
PAIRS OF TEETH IN CHEWING POSITION (NATURAL OR ARTIFICIAL)	Observe and count pairs of teeth in chewing position	12 or more pairs of teeth in chewing position	8-11 pairs of teeth in chewing position	0-7 pairs of teeth in chewing position*
ORAL CLEANLINESS	Observe appearance of teeth or dentures	Clean, no food particles/ tartar in the mouth or on artificial teeth	Food particles/tartar in one or two places in the mouth or on artificial teeth	Food particles.tartar in most places in the mouth or on artificial teeth

Upper dentures labeled: Yes _____ No _____ None_____ Lower dentures labeled: Yes _____ No _____ None _____

Is your mouth comfortable? Yes _____ No _____ If no, explain: _____

Additional comments: _____

Underlined* -refer to dentist immediately

Kayser-Jones, J., Bird, W.F., Paul, S.M., Long, L., & Schell, E.S. (1995). An instrument to assess the oral health status of nursing home residents. *The Gerontologist, 35*(6), 814-824. Figure 2, p. 823.

The Hartford Institute for Geriatric Nursing would like to acknowledge the original author of this issue: Cheryl Chia-Hui Chen, DNSc, APRN, GNP, National Taiwan University School of Nursing, Taipei, Taiwan.

Figure 5-2 Oral Health Assessment Tool
Source: The Gerontological Society of America.

Table 5-3 Soft Foods to Suggest for Patients with Chewing Problems

Source: Lisa Hark, PhD, RD, 2014. Used with permission.

Apple sauce
Baked beans
Boiled vegetables
Broiled fish
Canned fruit in natural juice
Chopped and pureed foods
Cooked prunes
Cottage cheese
Ground meat
Ice cream
JELLO
Juices
Mashed potatoes
Oatmeal
Pudding
Potato salad
Scrambled eggs
Shakes
Soft bread with melted cheese
Soups
Tuna fish
Yogurt

Physical Examination (also see Chapter 1)

It is important for healthcare providers to begin a physical exam by measuring the height and weight of all patients. This allows calculation of the body mass index (BMI) (weight [kg]/height $[m]^2$), which reflects weight in relationship to height. The association between BMI and mortality follows a U-shaped curve, with increased mortality being associated with BMIs both above and below the ideal range. The nadir of the U-shaped curve increases with age, with the best BMI for older adults ~25. A BMI of less than 22 kg/m^2 indicates that an older patient is underweight and further assessment is warranted. Obtaining a correct BMI may be difficult due to alterations in height caused by kyphosis or the inability to stand for measurement. Patients can therefore be measured in bed in a supine position using a tape measure or lower leg length can be used as a substitute. This possibility makes it important to systematically monitor a patient's weight over time.

Percent Weight Change Weight loss is common in patients who are hospitalized or who reside in nursing homes. Weight loss is also frequently seen in older adults with significant changes in appetite due to acute illness, chronic disease, or gastrointestinal

problems secondary to surgery, chemotherapy, or radiation (Chapters 12 and 13). It is important to take a diet history and determine the percent weight change using the patient's current weight and usual weight. Malnutrition is diagnosed by clinically significant, unintentional weight loss of 5 percent weight change in a 1-month period or 10 percent weight change over 6 months. This is generally considered a significant weight change that needs further evaluation.

Other Signs and Symptoms Other aspects of the physical exam may reveal many conditions that can contribute to malnutrition, as well as frank malnutrition, for example muscle wasting, in particular temporal muscle wasting (sunken temples), ill-fitting dentures, and mouth sores or abscesses that limit oral intake. It is particularly important to examine patients with cognitive impairment, since they may not be able to verbally report conditions such as constipation, urinary retention, or abdominal discomfort. A brief cognitive screening test, such as the Mini-Mental Status Exam, will help uncover cognitive deficits that may be contributing to poor dietary intake and malnutrition. Figure 5-3 provides an algorithm for assessing, identifying, and treating unintentional weight loss in older adults.

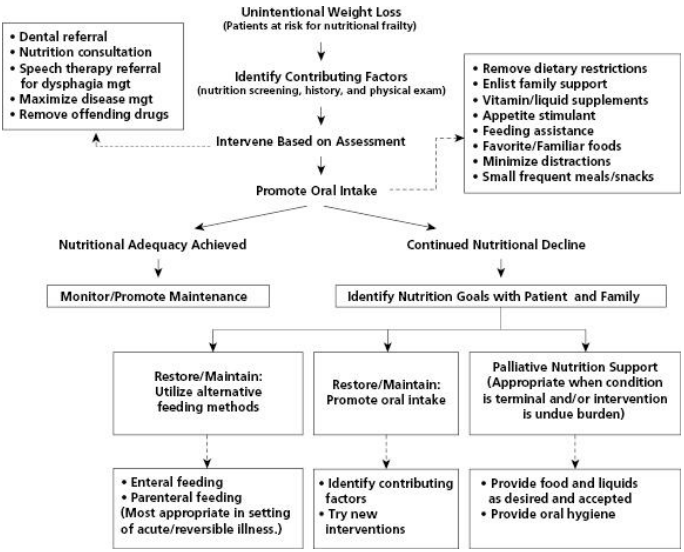

Figure 5-3 Algorithm to identify, assess, and treat weight loss in older adults

Source: Connie Bales, PhD, RD. 2014. Used with permission.

Nutritional Frailty Nutritional frailty is a condition that occurs in older adults and is characterized by low functional reserve, decreased muscle strength, and increased susceptibility to diseases. This is due to sarcopenia (loss of lean muscle mass), which reflects a progressive decrease in anabolism, increased catabolism, and a reduced muscle generation capacity. These changes lead to decreased overall physical functioning, increased frailty, fall risk, and eventually loss of independence. Disease processes, medications, and physical de-conditioning can play a role in

the development of nutritional frailty. These factors are elucidated in Figure 5-4.

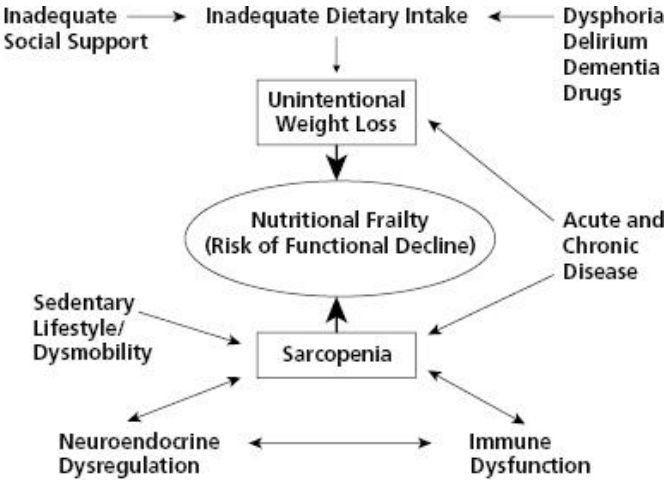

Figure 5-4 Dimensions of Nutritional Frailty

Source: Connie Bales, PhD, RD. 2014. Used with permission.

Chronic Diseases

Chronic disease is an important risk factor for malnutrition. However, it is important to recognize and address malnutrition as a separate treatable condition from chronic illness. Cancer cachexia has been largely related to the effects of pro-inflammatory cytokines on metabolic processes, causing excessive muscle turnover and wasting syndromes. Reversal of these processes is often difficult, even with adequate nutritional support. Tumor burden, including location and size, can cause

symptoms such as dysphagia, early satiety, abdominal pain, and intestinal obstruction that negatively impact nutritional status. Cardiac cachexia is marked by the loss of lean muscle mass and metabolic disturbances that may result from altered cytokine levels.

Weight loss is a common clinical feature of chronic obstructive pulmonary disease (COPD). This is likely related to increased resting energy expenditure from the increased work load of breathing and total daily energy expenditure, despite the inactivity associated with the disease process. Similarly, those with cancer, cardiac cachexia, and COPD can have elevated cytokine levels and catabolic processes that lead to muscle wasting. Symptoms such as dyspnea and fatigue may also interfere with caloric intake. Corticosteroids used in the treatment of COPD contribute to reduced muscle mass, reduced bone density, and negative nitrogen balance. Patients with chronic illness may also experience depression. Rates of major depression are particularly high among hospitalized patients with acute illness or those living in nursing homes. Depression often goes unrecognized and untreated, and can affect nutritional status either by an increasing or decreasing appetite.

Cognitive dysfunction is another important cause of unintentional weight loss and malnutrition among older adults. Numerous

studies have confirmed the tendency for patients with Alzheimer's disease to lose weight early in the disease process. Weight loss and subsequent malnutrition can lead to serious consequences, including increased mortality. There are two primary physiologic mechanisms that might explain anorexia and therefore decreased caloric intake in Alzheimer's disease: taste and smell dysfunction, and the effect of inflammatory mediators (e.g., cytokines) on appetite.

Medications Medication can have a profound impact on nutritional status. Many older adults take multiple medications both prescribed and non-prescribed. Multi-drug regimens are even higher among nursing home residents. Medications can alter nutritional status in a variety of ways, including alteration or loss of taste and smell, nausea, anorexia, dry mouth, diarrhea, reduced feeding ability or increased appetite. Non-prescription and recreational drugs should not be overlooked, since they can contribute to the overall problem.

Dietary Modifications When calorie and protein intake are inadequate, it is appropriate to remove traditional dietary restrictions related to disease processes, a position strongly supported by the Academy of Nutrition and Dietetics. For example, low sodium and low cholesterol diets have a profound negative impact on the taste and smell of food, and limit

overall food intake. On a positive note, flavor and caloric enhancement, such as butter, margarine, oil, and powdered milk, have been shown to increase food intake and maintain weight in nursing home residents. Additionally, having someone to eat with has been shown to significantly increase food consumption among homebound older adults. Some facilities offer older adults a glass of wine before dinner to help stimulate their appetite and provide a social event such as "happy hour." Table 5-4 lists key points to tell older adult patients to improve over intake and appetite.

Table 5-4 Key Points to Improve Appetite

Source: Lisa Hark, PhD, RD, 2014. Used with permission.

Make Eating an Enjoyable Experience
Eat by the window or outside
Light a few candles
Make the food look good by varying colors and textures
Put flowers on your table
Set the table with placemats
Use your holiday place settings
Use good china and silverware
Invite Company or Engage In Group Activities

Go out for dinner weekly

Invite someone over for a meal

Join senior citizen groups

Take part in senior activities and gatherings

Talk to your neighbors

Make Eating a Priority and as Easy as Possible

Cook in quantity and pack/freeze the leftovers for later

Eat at appropriate times to avoid missing meals

Keep frozen vegetables on hand for quick side dishes

Keep meal time consistent and eat something even if you are not hungry

Try to include all food groups at lunch and dinner

Learn how to use the microwave

Dysphagia Dysphagia can contribute to weight loss among frail older adults. Many neurological conditions effect the enervation of muscles which control swallowing and cause dysphagia. Esophageal muscle dysphagia is more often due to mechanical abnormalities such as strictures, webs, carcinoma, or extrinsic compression. Symptoms of dysphagia usually include coughing, coryza, and aspiration

pneumonia. It is important to ask about difficulty swallowing, as well as coughing or watering of the eyes with meals and intolerance to solids or liquids.

For optimal patient care, referral to a speech pathologist for swallowing studies can assist in diagnosing dysphagia, developing a treatment plan, and educating patients and caregivers. In older adults diagnosed with dysphagia, altering food and liquid consistency can minimize the risk of aspiration and reduce weight loss. Techniques to minimize the risk of aspiration include positioning the patient upright during mealtime and for 30 minutes after meals, tucking the chin during swallowing, and swallowing multiple times with each bolus.

Interventions for Malnutrition and Nutritional Frailty

Much of the research and guidelines for assessing and managing frailty in older adults have been done in the context of nursing home patients. In the nursing home environment, it is easier to monitor nutritional status closely and the resources to intervene are at hand, including the availability of dietitians. Many of the interventions applied in nursing homes can be applied in out-patient primary care settings. It is important for clinicians caring for older adults in out-patient settings to be

knowledgeable about the potential benefits, risks, and costs of specific interventions.

Supplements for Nutritional Frailty

When adequate nutrition cannot be achieved from *ad libitum* (self-regulated) meals, commercially prepared (usually liquid) nutritional supplements are often prescribed to increase total nutrient and caloric intake. These products provide a good source of shelf-stable nutrients in appropriate amounts. However, some products may be low in protein and/or fiber content and they may be misused as meal replacements rather than as supplements to a meal. Timing of liquid nutrition supplements can be a major determinant of their effectiveness. These drinks should not be given with meals, but in between meals and/or at bedtime. The chance of electrolyte and carbohydrate overload in chronic renal insufficiency and diabetes should be considered.

A meta-analysis of 55 supplementation trials showed that hospitalized patients (more than 65 years of age) and/or malnourished patients benefited the most and had fewer complications and decreased mortality from using these supplements. In the community setting, liquid protein/calorie supplements may benefit those patients with limitations in their oral food

intake, such as food intolerances, and inability, or unwillingness to eat, and the more severely malnourished.

Appetite Stimulants and Antidepressants

Orexigenic agents are often considered in the treatment of unintentional weight loss and malnutrition in older adults. In an effort to enhance food intake, megestrol acetate has been studied in undernourished older adults as a means to improve oral nutrition. The effects of megestrol take several months to impact appetite and weight status. Side effects include adrenal suppression, fluid retention, deep vein thrombosis, confusion, and impotence. Other agents that have been used to stimulate appetite include cyroheptadine, dronabinol, testosterone, growth hormone, oxandrolone, and steroids, but there insufficient evidence regarding their use.

The disease process is also important to consider when deciding to prescribe these medications, since benefits may be less in conditions such as advanced dementia than in other disease processes where the improved sense of well-being can be a meaningful and measurable outcome. Patients with advanced dementia or terminal cancer are not likely to benefit. In the situation of otherwise unexplained weight loss, the diagnosis of

depression must be considered. Even when the diagnosis is uncertain, a trial of an anti-depressant medication may be reasonable.

While tricyclic anti-depressants may result in weight gain in younger patients, they typically are not associated with weight gain in frail older adults. However, side effects including constipation, dry mouth, orthostatic hypotension, and urinary retention, make tricyclic anti-depressants less desirable than the selective serotonin reuptake inhibitors (SSRIs, e.g., sertaline and citalopram). Initial concern that SSRIs may produce weight loss in older adults has not been substantiated. In many instances of depression, weight gain may represent improvement in depression.

Conclusion

Healthcare providers are in a unique position to influence the health and well-being of their older adult patients by recognizing threats to nutritional adequacy and maximizing nutritional health. Healthcare providers should be able to identify, screen, inform, and intervene, as well as refer patients to registered dietitians when appropriate. Alterations in nutrient requirements for older adults should be discussed with patients and family members to optimize nutrient intake and avoid excessive consumption of calories. The status of hydration, protein, carbohydrate, lipid, and

fiber needs cannot be assumed or ignored, especially in frail older adults with multiple chronic illnesses. A multidisciplinary team of physicians, nurses, dietitians, social workers, speech pathologists, dentists, and pharmacists can assist patients in setting realistic goals for their nutritional health (see Table 5-5).

Table 5-5 Roles of the Health Professional

Source: Cecilia Borden, EdD, MSN, RN and Lisa Hark, PhD, RD, 2014. Used with permission.

Assess dietary intake for adequacy of energy, protein, fiber, vitamins, and minerals.
Assess nutritional status to diagnose overweight, underweight, and malnutrition.
Evaluate the potential benefit or harm regarding vitamins and herbal supplements.
Evaluate food/medication interactions and over the counter medications.
Recommend nutritional supplements when food intake is inadequate.
Counsel patients regarding the benefit of healthy eating and fortified foods.
Refer to registered dietitians for additional guidance and follow-up.

Case 1 Malnutrition and Depression

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Objectives

Identify common risk factors for poor nutritional status in older adults.

Describe the effects of malnutrition on physiologic function in geriatric patients.

Develop a nutritional care plan for an older adult with poor nutritional status and weight loss secondary to altered living situation.

Provide nutritional counseling appropriate to the physiologic, emotional, social, and financial changes that occur with aging.

Recognize the unique contribution of different members of a health care team including social workers, home health aides, and community volunteers in the effort to

improve the nutritional status of older people.

ML is an 80-year-old African–American widow who was brought to the office of her primary care physicianby the local Older Americans Transportation Service. She had missed two prior scheduled office visits due to the recent death of her husband and a subsequent fall, which resulted in an intertrochanteric fracture of her right hip.

On presentation, ML appeared withdrawn and much frailer than on previous visits. She answered in a monotone with terse, non-spontaneous speech, and she lacked expression. Her chief complaint, aside from pain with ambulation, was nocturnal leg cramps ("charlie-horses"). When asked about how she had been coping after the loss of her husband, she became tearful. She admitted that in addition to the loss of companionship, she has realized how much she relied on him to take care of the day-to-day chores, like shopping.

Past Medical History

ML tripped on the steps in her house 2 months ago and fractured her right hip. She underwent an open reduction/internal fixation surgery to repair the fracture and the operation went well. There were no serious operative complications,

but she lost approximately 350 cm^3 of blood during the procedure (1 unit = 500 cm^3). ML underwent inpatient rehabilitation for 10 days after discharge from the surgical service and then returned home, where she lives alone. She ambulates slowly with a cane and can climb stairs but with some difficulty.

During her inpatient rehabilitation stay, she was diagnosed with depression and was started on a selective serotonin reuptake inhibitor (SSRI) antidepressant. She has a history of hypertension, stage 2 chronic kidney disease, and osteoporosis, the latter discovered at the time of her hip fracture 2 months ago. ML had an appendectomy at age 46 and bilateral cataract surgeries 3 years ago. She has no previous history of pneumonia, tuberculosis, hepatitis, or urinary tract infection.

Medications

ML currently takes hydrochlorothiazide 25 mg daily for hypertension, fluoxetine (Prozac) 20 mg daily for depression, and an iron supplement for anemia three times per day. She also self-medicates with over-the-counter acetaminophen 500 mg three times a day, and frequently uses laxatives and glycerin suppositories for constipation, which she attributes to the iron tablets. Due to her kidney disease, she has been warned to avoid over-the-counter analgesics that might contain

non-steroidal anti-inflammatory medications, but she nevertheless takes occasional doses of ibuprofen 200 mg for pain. She does not take a multi-vitamin, calcium, or vitamin D supplement. She has no known food allergies.

Social History

ML lives alone in the small three-story row-home she has occupied since she married 58 years ago. Her son and daughter both live out of state. Although they call her every few weeks, they have not visited since her husband's death. ML states that she used to attend church and visit the local senior center regularly with her husband, but has not been to either lately. ML explains that she has no energy to “get up and go” anymore and she falls asleep in front of the television. She also reports being constipated and that her food does not have much taste. She avoids alcohol and tobacco and drinks one cup of coffee and two cups of tea daily.

ML's 24-Hour Dietary Recall

At her physician's request, ML provided the following 24-hour dietary recall, stating that this represents her usual daily intake:

Breakfast (home)	
Jelly doughnut	1 whole
White toast	1 slice

Breakfast (home)	
Jelly	2 Tbsp.
Coffee	1 cup
Lunch (home)	
Butter cookies	2 each
Chicken and rice soup	1 cup
Saltine crackers	6 each
Tea	2 cups
Dinner (home)	
White bread	1 slice
Jelly	2 Tbsp.
Peanut butter	2 Tbsp.
Butter cookies	2 each

Total calories: 1270 kcal

Protein: 25 g/day (8% of calories)

Fat: 42 g (30% of calories)

Carbohydrate: 201 g (63% of calories)

Calcium: 153 mg

Iron: 6 mg

Review of Systems

General: Weakness, fatigue, weight loss, and depression

Mouth: Food lacks taste (hypogeusia); dry, "thick-feeling" tongue; reddened fissures at the corners of mouth

GI: Poor appetite, constipation

Extremities: Hip pain when climbing stairs, some tenderness at old incision site, chronic low back pain, and troublesome episodes of nocturnal leg cramps that awaken her from sleep

Physical Examination

Vital Signs

Temperature: 97.0 °F (36 °C)

Heart rate: 88 BPM

Respiration: 18 BPM

Blood pressure: 130/80 mm Hg

Height: 5′6″ (168 cm)

Current weight: 110 lb (50 kg)

Usual weight: 140 lb (64 kg)

BMI: 18 kg/m^2

Weight 6 months ago prior to surgery: 125 lb (57 kg)

Percent weight change: 12% [(125 – 110/125) × 100]

Exam

General: Thin, frail-appearing elderly African–American woman who is appropriately conversant but withdrawn. She is well groomed, but her clothes are loose fitting

Skin: Warm to touch, "ashy"-appearing patches of dryness and flaking to elbows and lower extremities

HEENT: Temporal muscle wasting, no thyroid enlargement

Mouth: Ill-fitting dentures, sore beneath bottom plate; cracks/fissures at corners of mouth (angular chelitis), tongue is dry and pale without ulcers or plaques

Cardiac: Regular rhythm at 88 beats per minute, soft systolic murmur

Abdomen: Well-healed appendectomy site scar, no enlargement of liver or spleen, diffusely diminished bowel sounds

Extremities: Well-healed cicatrix overlying right hip with slight surrounding erythema, no sores on feet, trace pretibial edema to both lower extremities

Rectal: Hard stool in vault, stool test for occult blood negative

Neurologic: Alert, good memory, no evidence of sensory loss, slight psychomotor retardation evident

Gait: Slightly wide-based with decreased arm swing, antalgic and tentative but with safe, appropriate use of cane

Laboratory Data

Patient's Lab Values	Normal Values
Albumin: 2.5 g/dL	3.5–5.8 g/dL
Hemoglobin: 11.0 g/dL	11.8–15.5 g/dL
Hematocrit: 33.0%	36–46%

Case Questions

What information from the case history raises concern over ML's functional status?

Based on that information, what medical, environmental, and social factors could lead to nutritional problems in this patient?

What do ML's BMI and percent weight change indicate about her nutritional status?

What are ML's calorie and protein requirements for repletion? What general conclusions can you draw regarding ML's diet?

How can ML's diet be improved to meet her increased requirements, achieve weight gain, and relieve her constipation?

What specific recommendations would you offer to improve ML's nutritional status?

Part 1: Assessing Activities of Daily Living

1. What information from the case history raises concern over ML's functional status?

ADLs Although ML can feed herself, she has trouble chewing because of her loose dentures and a sore in her mouth. She has insufficient money for a visit to the dentist. ML also exhibits poor mobility; she walks with a cane, has difficulty with stairs, and fears falling since her hip fracture. Although she is mobile, she reports pain with movement and moves slowly about the house. Finally, ML dislikes eating alone, which may negatively impact her food intake.

IADLs Since her injury, ML has been afraid to go outside, which may be due to fear of falling or lack of energy. Because she does not drive and is unaccustomed to using public transportation, she has difficulty shopping for food and other necessities. ML reports a very limited social life; since her husband's death she has avoided church, community programs, and the senior center. Her reported dislike of cooking for one person most likely will have a negative effect on the quality and quantity of her food intake. She denies difficulty with dressing, grooming, or toileting, and feels that if her husband were alive she would resume cooking meals.

2. Based on that information, what medical, environmental, and social factors could lead to nutritional problems in this patient?

ML's ill-fitting dentures and hypogeusia may lead to decreased intake and malnutrition. Depression over the loss of her husband may decrease her appetite. The prevalence of depression in community-dwelling elders was noted by Sachs-Ericsson et al. to range from 8 to 16 percent. A study by Cabrera et al. found depression in 24.3 percent of elderly subjects, and noted a significant association ($p < 0.001$) between depression and nutritional deficit even after adjusting for variables such as low educational and socioeconomic level, and smoking.

ML lives alone in a three-story row-home and is not interested in cooking for herself since her husband died. Her impaired ambulatory function and limited funds for assistance with household tasks have negatively affected her dietary intake. She is also homebound, and therefore at risk of vitamin D deficiency due to inadequate sunlight exposure. Furthermore, she no longer participates in community activities that could provide support, meals, and social interaction. Her children have not visited recently or provided any assistance.

Several authors have noted that malnutrition in older persons is multifactorial and relates to the

presence of other geriatric syndromes, and psychological and functional impairments. ML's ambulatory dysfunction following her hip fracture is compounded by the problem of depression.

Part 2: Nutrition Assessment

3. What do ML's BMI and percent weight change indicate about her nutritional status?

Note that in this case the value used for ML's usual weight is 125 pounds (57 kg), as it was 6 months earlier prior to surgery (rather than her usual weight of 140 pounds prior to her husband's death). Her percent weight change in a period of 6 months represents a clinical indicator for malnutrition. Weight loss is not a normal part of aging and frequently represents an underlying disease process, such as depression, pulmonary or renal disease, or occult malignancy. Most nutrition experts currently consider satisfactory weight for those aged 65 and older as BMI between 24 and 27 kg/m^2. ML's BMI of 18 kg/m^2 clearly indicates that she is underweight and based on the overall assessment, she is at risk for malnutrition.

4. What are ML's calorie and protein requirements for repletion? What general conclusions can you draw regarding ML's diet?

ML's total estimated daily calorie requirements, based on the DRI, are calculated using the equation below:

$$354 - (6.91 \times \text{age}) + \text{physical activity coefficient} \times (9.36 \times \text{weight in kg}) + (726 \times \text{height in meters})$$

$$354 - (6.91 \times 80) + 1.12 \times (9.36 \times 50\ \text{kg}) + (726 \times 1.68\ \text{m}) = 1545\ \text{kcal/day}.$$

The estimated total daily protein requirements are 1.5 g/kg of weight:

$$(50\ \text{kg}) \times (1.5\ \text{g/kg}) = 75\ \text{g/day}.$$

ML's usual daily intake provides 1270 calories and 25 g of protein. Her diet is low in calories due to her poor appetite. ML's limited consumption of meats and poultry products, resulting in a poor overall protein and iron intake, is probably due to her low-income status and poor dentition. Because ML stopped drinking milk many years ago and does not shop for dairy foods regularly, her diet is deficient in calcium and vitamin D. Fruits, vegetables, and fluids also seem to be below acceptable limits in ML's diet.

Part 3: Medical Nutrition Therapy

5. How can ML's diet be improved to meet her increased requirements, achieve weight gain, and relieve her constipation?

Constipation, which is very common in older adults, can often be corrected by increasing fiber and fluid intake and physical activity. Examples of high-fiber foods include fruits, vegetables, bran cereals, and whole-grain products such as whole-wheat bread and brown rice. One bowl of raisin bran cereal or oatmeal every day would most likely be sufficient to achieve bowel regularity. If these measures are not sufficient, fiber supplements can be recommended. She should be advised to drink at least 6 glasses (8 ounces each) of water daily, and preferably more if tolerated to help alleviate constipation. The elderly, however, are prone to hypodypsia (blunted thirst response), which leads to inadequate fluid intake. Older adults may require prompting or frequent reminders to ensure adequate fluid intake. In light of her weight loss and inadequate dietary intake, ML's diet clearly needs to be higher in calories, protein, and calcium to fulfill her current requirements. She should also be asked whether she is taking her iron supplements, as older adults tend to discontinue these if constipation occurs.

High-Calorie, High-Protein Dietary Recommendations

Breakfast (home)	
Coffee	8 ounces (240 mL)

Instant oatmeal	1 package
Lactose-free 2% milk	6 ounces (180 mL)
Orange juice	4 ounces (120 mL)
Lunch (senior center)	
Chicken drumstick	3 ounces (85 g)
Baked potato	1 medium
Margarine	2 Tbsp.
Green beans	1/2 cup
Snack (senior center)	
Lactose-free 2% milk or yogurt	8 ounces (240 mL)
Canned peaches	1/2 cup
Dinner (home)	
Tuna salad	4 ounces (113 g)
Saltine crackers	6 each
Tomatoes	3 slices
Vanilla pudding	1/2 cup
Snack (home)	
Applesauce	1/2 cup

Total calories: 1540 kcal

Protein: 72 g (19% of calories)

Fat: 57 g (33% of calories)

Carbohydrate: 190 g (49% of calories)

Calcium: 974 mg

Iron 15 mg

6. What specific recommendations would you offer to improve ML's nutritional status?

In addition to the recommended dietary modifications, ML and/or her primary care physician should take the following steps to ensure her continued well-being:

Contact her children and other family members for support and to help her arrange to move to an apartment or a smaller, single-story home.

Contact her other healthcare providers, specifically her psychiatrist or psychologist, regarding recommended changes in medications and make arrangements to have her dentures properly adjusted. It is clear that Prozac has not effectively relieved ML's depressive symptoms and, because SSRI's may cause nausea, may be contributing to her anorexia. Probably the most effective and safest intervention for depression for ML is to get her activated and engaged in life activities. If an antidepressant is necessary, Remeron (mirtazapine) may be a better choice because it stimulates appetite. Consider utilizing the Council on Nutrition Appetite Questionnaire (CNAQ – Table 5-6) at quarterly evaluations to assess ML's appetite. Wilson et al. have shown

that the CNAQ is a short, simple appetite assessment tool that predicts weight loss in community dwelling adults and long-term care residents.

Drink high-calorie, high-protein liquid supplements or suggest adding non-fat powdered milk to puddings to increase her intake of calories, protein, vitamins, and minerals.

Prescribe a multivitamin and mineral supplement with 100 percent of the RDA for older adults and calcium (600 mg BID) with at least 1000 IU vitamin D.

Use a microwave oven to prepare convenience foods and decrease cooking time.

Contact a social worker to help ML get in touch with the area Council on Aging, Meals on Wheels, and other community resources.

Consider a home health aide to monitor ML's weekly weight and food intake and assess whether her ambulatory status is improving or whether she is at increased risk of falling again.

Utilize church, synagogue, and community volunteers to shop for food or contact a grocery store that delivers.

Undergo further rehabilitation and exercise therapy to increase her diminished mobility.

Contact a neighbor with whom ML could share meals or travel to the senior center daily for a hot lunch.

Table 5-6 Council on Nutrition Appetite Questionnaire

Source: Wilson MM et al. *Am J Clin Nutr* 2005;82:1074–1081.

A. My appetite is:	**B. When I eat, I feel full after:**
1. Very poor	1. Eating only a few mouthfuls
2. Poor	2. Eating about a third of a plate/meal
3. Average	3. Eating over half of a plate/meal
4. Good	4. Eating most of the food
5. Very good	5. Hardly ever
C. I feel hungry:	**D. Food tastes:**
1. Never	1. Very bad
2. Occasionally	2. Bad
3. Some of the time	3. Average
4. Most of the time	4. Good
5. All of the time	5. Very good

E. Compared to when I was 50, food tastes:	**F. Normally, I eat:**
1. Much worse	1. Less than one regular meal a day
2. Worse	2. One meal a day
3. Just as good	3. Two meals a day
4. Better	4. Three meals a day
5. Much better	5. More than three meals a day (including snacks)
G. I feel sick or nauseated when I eat:	**H. Most of the time my mood is:**
1. Most times	1. Very sad
2. Often	2. Sad
3. Sometimes	3. Neither sad nor happy
4. Rarely	4. Happy
5. Never	5. Very happy

Scoring:

Total the score by adding the numbers associated with the patient's response. A score of less than 28 is cause for concern. If the total is:

8–16 The patient is at risk for anorexia and needs nutrition counseling.

17–28 The patient needs frequent reassessment.

>28 The patient is not at risk at this time.

Case 2 Macular Degeneration

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Objectives

Describe the risk factors, prevalence, and pathogenesis of age-related macular degeneration.

Recommend dietary modifications to reduce the risk of progression of age-related macular degeneration.

Understand the mechanism through which diet may modify age-related macular degeneration.

CW is a 77-year-old Caucasian woman with a recent diagnosis of advanced non-neovascular

age-related macular degeneration (AMD) in both eyes. Ten years ago, she had perfect 20/20 vision and did not notice vision changes. Since then, her vision has slowly decreased to 20/60 in both eyes and she now complains of blurry vision and loss of central vision. She now has difficulty reading, driving, and recognizing faces.

Past Medical History

Hypertension: 13 year history. Treated with hydrochlorothiazide 25 mg daily.

Family History

CW has a family history of hypertension, stroke, and AMD. CW's mother and father both had AMD and hypertension. CW's father died of a stroke at age 72 years.

Social History

CW currently smokes cigarettes. She has a 20 pack per year history over the last 40 years. She drinks two glasses of wine a week. Her physical activity is limited as she dislikes exercise and is fearful of falling. She worked as a school teacher and retired 15 years ago. Her husband passed away a few years ago and she now lives with her daughter.

CW's 24-Hour Dietary Recall

Breakfast	
Coffee	12 ounces
Half and half cream	1 ounce
Onion bagel	1 small
Cream cheese	1 Tbsp.
Lunch	
Ham and cheese sandwich	1 large
Coca-cola	12 ounces
Snack	
Soft pretzel	1 small
Mustard	2 Tbsp.
Lemonade	15 ounces
Dinner	
Angel hair pasta	1 cup
Tomato sauce	1 cup
Roasted chicken	4 ounces
Light butter	1/2 Tbsp.
Red wine	6 ounces
Vanilla ice cream	1/2 cup

Total calories: 1874 kcal

Protein: 68.2 g (14.6% of calories)

Fat: 42.7 g (20.5% of calories)

Saturated fat: 16.4 g (8.0% of calories)

Monounsatured fat: 12.8 g

Cholesterol: 221 mg

Carbohydrates: 270.5 g (57.75% of calories)

Dietary fiber: 9.7 g

Sodium: 2265 mg

Calcium: 468 mg

Review of Symptoms

Remainder of review of symptoms is unremarkable.

Physical Examination

Vital Signs

Temperature: 98.6 °F (37 °C)

Heart rate: 74 BMP

Blood pressure: 145/93 mm HG

Height: 5′5″ (165 cm)

Weight: 135 lb (61.4 kg)

BMI: 22.5 kg/m^2

Waist circumference: 28 inches (71 cm)

Exam

General: Well-appearing female

HEENT: Normocephalic, atraumatic

Neurologic: Alert and oriented. Motor and sensory exams grossly intact. Deep tendon reflexes are symmetric

Cardiovascular: Normal rate and rhythm; no murmur

Pulmonary: Clear to auscultation bilaterally

Extremities: Trace pretibial pitting edema bilaterally

Laboratory Data

Patient's Values	Normal Values
Hemoglobin A1C: 6.2%	<6.5%
Fasting blood glucose: 97 mg/dL	70-99 mg/dL
Cholesterol: 190 mg/dL	Target <200 mg/dL
Triglycerides: 177 mEq/L	Target <120 mg/dL
HDL-C: 51 mg/dL	Target >50 mg/dL
Calculated LDL-C: 120 mg/dL	Target <130 mg/dL

Case Questions

Define AMD and describe its prevalence.

Describe the pathogenesis of AMD.

What factors put CW at increased risk for AMD?

How do these factors increase CW's risk for AMD?

What lifestyle and dietary modifications would you recommend to slow CW's progression of AMD?

Are there any vitamin or mineral supplements that should be recommended to CW?

Describe the mechanism through which dietary interventions may affect AMD.

Part 1: Age-related Macular Degeneration (AMD)

1. Define AMD and describe its prevalence.

AMD is the number one cause of blindness in developed countries and the third leading cause of blindness internationally. The macula contains the most densely packed area of photoreceptors, which allows for the majority of functional vision. Degeneration of the macula can cause central blind spots, visual blurring and distortion, which can lead to reduced quality of life due to decreased ability to read, drive, or function (Figure 5-5).

Figure 5-5 Vision loss due to AMD
Source: National Eye Institute.

The two major forms of AMD are non-neovascular (also known as "dry" or atrophic) and neovascular (also known as "wet"). The non-neovascular form of the disease accounts for 90 percent of all AMD cases and is characterized by yellowish deposits of extracellular material called drusen in the retina and degeneration of the photoreceptors. Non-neovascular AMD usually progresses slowly over many years and seldom causes severe vision loss. The neovascular form is characterized by growth of abnormal blood vessels in the retina that leads to leakage of blood, fluid, and lipids, causing fibrous scars to form in the retina (Figure 5-6). While neovascular AMD only accounts for approximately 10 percent of AMD cases, more than 80 percent of severe vision loss is due to the neovascular form of the disease.

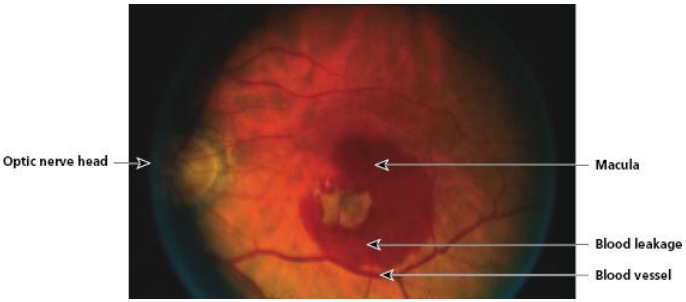

Figure 5-6 Fundoscopic photograph of the retina of a patient with neovascular AMD.

Source: Wills Eye Hospital. 2014. Used with permission.

Only 1 percent of the population under 75 years of age has AMD, 5 percent age 75 to 84, and 13 percent over 85 years. In the United States, over 9 million people have AMD and the prevalence increases dramatically as people age.

2. Describe the pathogenesis of AMD.

The pathogenesis of AMD is not entirely understood but recent evidence has shown that chronic inflammation and vascular endothelial growth factor (VEGF) play important roles in the disease. The clinical hallmark of AMD is the appearance of drusen, white or yellow deposits of protein and lipid in the retina. Small drusen in one eye are not considered pathologic as they are common in individuals over 50 years old. However, numerous intermediate to large-sized

drusen are an independent risk factor for visual loss in patients with AMD.

The histopathology of drusen has helped clarify the pathogenesis of AMD. Drusen are made up of acellular debris, consisting predominantly of cholesterol, vitronectin, and apolioproteins. Additionally, multiple complement proteins and immunoglobulin light chains have been found in drusen, highlighting the pivotal role of inflammation and the compliment system in the disease. Geographic atrophy is a common sign of late stage AMD and indicates areas of photoreceptor degeneration often overlying drusen deposits.

VEGF, a signal protein released by cells, causes the growth of new blood vessels and plays a critical role in neovascular AMD. Treatments targeting VEGF have become the standard of care for wet AMD and have revolutionized patient care. Uninhibited VEGF leads to growth of new vessels, vascular leakage and hemorrhage, all of which contribute to the rapid decrease in vision. New vessels can also lead to retinal detachment and fibrotic scars with severe vision loss.

Part 2: Nutritional and Risk Factor Assessment

3. What factors put CW at increased risk for AMD?

CW's strongest risk factors for AMD are her advancing age, cigarette smoking, white ethnicity, and family history of AMD. Age is the strongest risk factor for AMD, with people over 80 years having approximately 25 times the risk of developing AMD compared to people younger than 70. Cigarette smoking has been consistently associated with AMD and is the strongest modifiable risk factor. Current smokers have at least three times the risk of AMD compared to non-smokers. White and Asian ethnicity has also been associated with an approximate threefold increase in risk compared to blacks. Finally, epidemiologic and twin studies have consistently shown genetics to influence the incidence of developing AMD.

Dietary and exercise factors also affect AMD incidence and progression. Low consumption of fish, vegetables, and antioxidants including vitamin C, vitamin E, and zinc are associated with increased risk of AMD. Low consumption of carotenoids, particularly lutein and zeaxanthin both found in green leafy vegetables, has been associated with increased risk for the disease. Lack of physical activity has been associated with AMD, as individuals participating in high levels of activity have significantly lower risk than individuals with low activity levels. Several other risk factors including obesity, hypertension, and history of cardiovascular disease have shown a moderate

association with development and progression of AMD.

4. How do these factors increase CW's risk for AMD?

The risk factors mentioned earlier are thought to influence AMD by affecting chronic inflammation, in part by activating the complement system. The complement system is part of the innate immune system used to attack foreign pathogens. Enzymes and regulatory proteins make up the complement system and balance activation for phagocytosis and inactivation for self-protection. A number of the risk factors for AMD, including smoking, hypertension, and obesity have been shown to activate the complement system leading to increased levels of C-reactive protein, a marker of inflammation.

Part 3: Medical Nutrition Therapy

5. What lifestyle and dietary modifications would you recommend to slow CW's progression of AMD?

CW should be encouraged to stop smoking as this is the greatest modifiable risk factor for AMD. Given the epidemiologic association of AMD with low dietary intake of omega-3 fatty acids, fish, lutein, zeaxanthin, and vegetables, it is reasonable to recommend an increase in fish, nuts, fruits, and vegetables. Foods with a high

content of omega-3 fatty acids include oily fish such as salmon, sardines and mackerel, as well as walnuts, flaxseeds, and chia seeds. Lutein and zeaxanthin are found in green leafy vegetables such as collard greens, spinach, and kale, as well as broccoli, zucchini, brussel sprouts, eggs, and corn. While no prospective studies have conclusively shown these dietary interventions to affect AMD, they can be recommended based on their general health benefits and associations with AMD.

6. Are there any vitamin or mineral supplements that should be recommended to CW?

Given her advanced AMD, CW should be prescribed the Age-Related Eye Disease Study 2 (AREDS-2) formulation of 500 mg vitamin C, 400 IU vitamin E, 80 mg zinc oxide, 2 mg copper, 10 mg lutein, and 2 mg zeaxanthin. The original AREDS formula consisted of the previously mentioned formulation with beta-carotene in place of lutein and zeaxanthin. The landmark study was the first randomized controlled trial to demonstrate the effectiveness of vitamin and mineral supplementation to prevent the progression of AMD. The amount of antioxidants found in the AREDS formula are considerably higher than those found in daily multivitamin supplements and are difficult to reach with diet alone. The study showed that high antioxidant supplementation can result in

a 25 percent decreased risk of AMD progression in people with intermediate or advanced AMD.

Since the original AREDS, beta-carotene has been found to be associated with a significantly increased risk of lung cancer, particularly among smokers. Consequently, the AREDS-2 investigated whether the antioxidants of lutein and zeaxanthin could be used in place of beta-carotene with similar outcomes. Additionally, the AREDS-2 evaluated whether the addition of supplemental omega-3 fatty acids, in the form of 350 mg docosahexaenoic acid and 650 mg eicosapentaenoic acid, decreased the risk of disease progression. The study found that lutein and zeaxanthin could replace beta-carotene with no difference in progression of AMD. However, supplemental omega-3 fatty acids had no significant impact on AMD.

7. Describe the mechanism through which dietary interventions may affect AMD.

Antioxidant supplementation is thought to prevent damage to the retina by limiting the harmful effects of free radicals produced in the process of light absorption. Lutein and zeaxanthin are found in high concentration within the macula. Dietary supplementation of these carotenoids has the potential to maintain their natural protective roles, which is thought to occur by filtering harmful short-wave blue

light and by preventing oxidative stress. Docosahexaenoic acid and eicosapentaenoic acid, which are omega-3 fatty acids, may promote healthy eye tissue by regulating inflammation and immune response in the retina and improving endothelial cell function.

Case 3 Menopause and Weight Gain

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Objectives

Define the clinical characteristics of perimenopause and menopause.

Identify medical nutrition therapy appropriate for women during menopause.

List the benefits of exercise for women during perimenopause and menopause.

Identify vitamin, mineral, and herbal supplements that may improve symptoms associated with menopause.

MK is a 52-year-old Caucasian woman who presents to her family physician with a history of a 30 pound weight gain over the past 3 years. She complains of constant fatigue, sleep disturbance, constipation, memory, mood changes, and depression. She describes frequent hot flashes and night sweats which have increased during the past few months. She has not had a period in over a year. MK admits to being more irritable and sometimes feeling sad, but attributes this to her lack of sleep.

Past Medical History

No past history of cardiovascular disease or abnormal blood sugars. MK had two uncomplicated deliveries. She is not taking any medications, vitamins, or herbal supplements.

Family History

MK's 78-year-old mother has hypertension and is overweight. She experienced menopause at age 53. Her father had a heart attack when he was in his early 70s but is doing fine on his current regimen. MK's younger sister, who is 48-years-old, had a lumpectomy 5 years ago. She was treated with radiation and has been cancer free since that time. Her brother is

overweight and has hypertension and type 2 diabetes.

Social History

MK separated from her husband 3 years ago. She has two children, age 15 and 13 who live with her. MK's full-time job allows her to work from home. She quit smoking over 10 years ago. MK states she is a social drinker and tries to limit herself to no more than two drinks per day. Lately, she has been having a glass of wine with dinner to help her relax and sleep.

For breakfast she eats a bagel with cream cheese or a large muffin, an 18 ounce cup of coffee with half and half and artificial sweetener. Lunch at home consists of leftovers or a frozen microwaveable meal. For dinner she consumes pasta with Alfredo or pesto sauce or breaded chicken cutlets and Caesar salad which she prepares for her family. MK snacks on granola bars, pretzels, and chips whenever she is hungry and drinks several cups of coffee throughout the day to stay awake. She rarely eats fruits or vegetables.

MK does not go out with friends because she is usually too exhausted. Her hot flashes and night sweats frequently wake her up during the night so she does not often get a good night's sleep.

Review of Systems

General: Fatigue, hot flashes, and weight gain

Endocrine: Increased appetite

Genitourinary: Last menstrual period was 1 year ago

Neurological: Mood swings, but no headache, change in vision, numbness, or tingling in extremities; she admits to emotional eating when she feels depressed

Vision: No changes

Gastrointestinal: Constipation

Physical Examination

Vital Signs

Temperature: 98.6 °F (37.1 °C)

Heart rate: 85 BPM

Respiration: 17 BPM

Blood pressure: 140/90 mm Hg

Height: 5′6″ (168 cm)

Weight: 197 lb (89.4 kg)

Body mass index (BMI): 31.2 kg/m^2

Waist circumference: 37 inches (94 cm)

Weight history: MK describes a weight gain of approximately 30 lb within the past 3 years

Exam

General: Obese female in no acute distress

HEENT: Normal, visual acuity 20/20 bilaterally, normal funduscopic examination

Neck: No carotid bruits, thyromegaly, or lymphadenopathy

Lungs: Clear bilaterally

Heart: Regular rate and rhythm, no murmurs

Abdomen: Obese, non-tender without organomegaly; no femoral bruits

Pelvic: Normal sized uterus, no adnexal masses or tenderness

Genitourinary: Normal introitus and labia, no lesions noted, positive for dry, thin vaginal mucosa

Laboratory Data (Fasting)

MK's Lab Values	Normal Lab Values
Glucose: 99 mg/dL	70-99 mg/dL
Hemoglobin A1C: 5.5%	4–6%

MK's Lab Values	Normal Lab Values
Cholesterol: 220 mg/dL	Desirable <200 mg/dL
HDL-C: 48 mg/dL	Desirable >50 mg/dL
LDL-C: 140 mg/dL	Desirable <100 mg/dL
Triglycerides: 160 mg/dL	Desirable <150 mg/dL
Thyroid stimulating hormone: 2.5 μIU/mL	0.4–4.0 μIU/mL
Hemoglobin: 13.1 mg/dL	12.0–16.0 mg/dL
Follicle stimulating hormone: 60 mIU/ml	<30 mIU/ml
Creatinine: 0.8 mg/dL	0.6–1.1 mg/dL for women
DEXA scan: –1.5	–1.0 to +1.0

Mammogram shows no changes from baseline.

Based on her history and laboratory data, MK's problem list includes:

Depression

Osteopenia

Hypertension

Hyperlipidemia

Obesity

Menopause with hot flashes and sleep disturbance

Constipation

Case Questions

What is the definition of menopause and how common are these symptoms?

What clinical characteristics are associated with menopause?

What is the definition and age of onset of perimenopause?

What nutrition-related issues are important to assess during perimenopause and menopause and why?

Why is daily exercise important for women during perimenopause and menopause?

What exercise recommendations are appropriate for MK and why?

What are the key dietary recommendations for MK at the present time?

What are the appropriate treatment recommendations for depression and hot flashes?

What vitamin, mineral, and herbal supplements could be recommended to MK

based on her history and the results of her DEXA scan?

Answers to Questions

Part 1: Diagnosis and Pathophysiology

1. What is the definition of menopause and how common are these symptoms?

Menopause is defined as cessation of menses for 1 year brought about by a normal, progressive reduction in estrogen and progesterone production. Failure to produce estrogen may begin as early as age 30 but remains asymptomatic until a woman makes the transition from less ovarian function to ovarian failure by age 50 to 55. Normal physiologic cessation of menses in menopause is thought to be due to the depletion of follicle units within the ovary, mainly via apoptosis of oocytes. This process begins before birth and continues until all oocytes are exhausted, depleting a much greater number of follicles than those lost to ovulation alone. Removal of the ovaries, radiation to the abdomen, chemotherapy, premature ovarian failure, and other idiopathic causes can also result in the cessation of menstruation but are not normal physiologic processes and therefore not included in the diagnosis of menopause.

The average age for the onset of menopause is approximately 51 years with a range between 44

and 56 years in 95 percent of women. Many women remain asymptomatic even after the loss of menstrual bleeding for over 1 year. Up to 85 percent of menopausal women experience vaginal dryness and discomfort, hot flashes, sweating, and insomnia. In most cases, symptoms subside after approximately 5 years; however, some women continue to experience persistent symptoms beyond this 5-year window. While lack of menstruation, or amenorrhea, loss of fertility, and symptoms are aspects of menopause, the specific diagnosis is based on failure to produce hormones. Thus, when serum follicle stimulation hormone (FSH) is measured, levels are greater than 30 mIU/ml, combined with these symptoms, confirm a woman is experiencing menopause.

2. What clinical characteristics are associated with menopause?

The severity of menopause varies from woman to woman and can include none or many of the following conditions:

Vaginal atrophy Symptoms include vaginal dryness and itching, pain with intercourse.

Uroepithelial atrophy Symptoms include cystitis, urethritis, urinary frequency, urgency, and incontinence.

Hot flashes A sudden sensation of intense body heat, often with profuse sweating and reddening of the head, neck, and chest.

These symptoms can be accompanied by mild to severe palpitations, anxiety, irritability, and, in rare cases, panic. Perspiration and a rapid heat loss may also lead to chills. These vasomotor symptoms can be objectively measured and should *not* be considered psychosomatic. Hot flashes occur in 50 to 80 percent of women during menopause and are more frequent at night. Intensity and frequency vary with each woman and can last weeks, months, or years. The exact cause is not known but there are several triggers, many of which can be managed by lifestyle changes. Hot flashes can also be aggravated by hypothyroidism, prescription medications such as raloxfen or tamoxifen, some over-the-counter supplements, such as niacin, or foods such as hot peppers and certain spices.

Coronary artery disease (CAD) The risk of CAD doubles for women after menopause. Estrogen is thought to have a cardio-protective effect before menopause but the safety and efficacy of hormone replacement therapy (HRT) during or after menopause has been seriously questioned after the results of the Women's Health Study.

Osteoporosis This is a decrease in bone mineral density leading to an increased risk of fractures. A score of less than −2.5 on a Dual Energy X-ray Absorptiometry (DEXA)

scan indicates osteoporosis, where as a score of –1.0 to –2.5 indicates osteopenia. Osteopenia is a lesser degree of bone loss with less fracture risk. Estrogen may play a role in the intestinal absorption of calcium and bone remodeling, but the exact mechanism of its role in bone health remains unclear; 75 percent of bone loss in women occurs within the first 15 years after menopause.

Mental health Many neurological disorders have been described during menopause including headaches, brain fog, memory loss, and confusion. Changes in mood and behavior may also be attributed to many other causes, including sleep disturbance and hormonal changes.

3. What is the definition and age of onset of perimenopause?

Perimenopause is a period of transition into menopause during which a woman experiences increased irregularity of her menstrual cycle due to shifting hormonal levels. The cycle may lengthen, causing an increase in the number of days between each period, or a woman may skip periods. Perimenopause usually begins in the mid to late 40s as the patient approaches the average age of menopause but can start in the 30s as well. This time period can last only a few months, or several years, with 4 years being the average length of time for perimenopause.

During perimenopause, women continue to ovulate, but FSH levels begin to rise. Inhibin, a hormone that inhibits the release of FSH, also begins to decline during this time. Some women experience headaches, mood changes, and weight gain during this time as well. Although there is a decline in fertility during perimenopause, ovulation continues irregularly and women can still become pregnant.

Part 2: Nutrition Assessment

4. What nutrition-related issues are important to assess during perimenopause and menopause and why?

Nutrition plays an important role in managing symptoms associated with perimenopause and menopause. Assessing dietary intake, including consumption of meals, snacks, sweets, fruits, vegetables, beverages, and caffeine will help to understand where changes can be made. As women age and go through menopause, metabolism slows down, muscle mass diminishes, and changes in hormone levels often cause disturbances in sleep patterns, mood, and nutritional needs. MK's weight gain of 30 pounds over the past 3 years and constipation are likely due to increasing consumption of high-calorie and high-fat foods and beverages, low intake of fruits and vegetables, and sedentary lifestyle. Based on the brief diet history, she is likely consuming at

least 2500 calories per day and her diet is lacking in important nutrients such as fiber, vitamins A, E, D, C, calcium, magnesium, beta-carotene, iron, zinc, and phytonutrients.

Changes in sleep patterns due to hot flashes can increase cortisol levels and cause an increase in appetite and blood sugar levels. Sleep deprivation can interfere with metabolism of carbohydrates, causing an increase in fat storage. Interfering with sleep for as little as two nights or getting fewer than 7 hours of sleep each night can increase ghrelin levels which increase appetite and decrease leptin levels which promote satiety. Since her weight gain coincides with her separation and divorce, helping her to understand this connection and exploring her feelings associated with the divorce may be helpful.

Assessing intake of beverages, specifically water, sugar-sweetened drinks, milk, coffee, and alcohol will provide insight into her calorie, calcium, and vitamin D intake. MK rarely drinks water and may be losing water during night sweats and hot flashes. Inadequate water consumption and dehydration can also lead to constipation, increased hot flashes, dizziness, and sagging skin. Caffeine and alcohol may also trigger hot flashes. Since MK is having trouble sleeping and complains of chronic fatigue, her caffeine intake needs to be assessed. MK drinks coffee throughout the day to battle her fatigue.

Since caffeine can take up to 6 hours to leave the system, MK should be advised to cut down and eventually avoid coffee and any caffeinated beverages. Suggest MK reduce her coffee intake and switch to decaffeinated coffee and herbal tea to alleviate her night sweats and improve her sleep pattern. While alcohol may help MK fall asleep, studies show it can disrupt sleep habits, compromise deep REM sleep, and lead to insomnolence, or waking up in the early morning hours and feeling tired.

Because MK complains of constipation, her fiber intake should also be assessed. The average American consumes less than 15 g of fiber per day, which is below the American Cancer Society's recommendation of 25 to 35 g. Increasing fiber will improve bowel integrity and help with satiety. The best sources are whole grains such as barley, quinoa, millet, oatmeal, or whole grain breads, vegetables, and fruits. If she still complains of constipation, adding a magnesium supplement (250 to 400 mg/day), taken in the evening, will help her sleep and have normal bowel movements in the morning.

5. Why is daily exercise important for women during perimenopause and menopause?

Regular physical activity plays a role in weight management, improving mood, and preventing the onset of diseases such as diabetes, heart

disease, hypertension, and osteoporosis. As metabolism slows down during menopause, muscle mass diminishes, and weight gain is common. Physical activity can offset the metabolic changes associated with aging, improve blood flow to the brain, improve mental sharpness, promote weight loss, and reduce blood pressure as well as abdominal fat. Exercise can also build muscle mass which helps the body burn excess calories that otherwise would be stored as fat. Regular exercise can also combat depression, reduce hot flashes, and improve sleep, all of which can benefit MK.

Part 3: Medical Nutrition Therapy

6. What exercise recommendations are appropriate for MK and why?

MK should be informed of the benefits of exercise and recommended to start a walking program or join a gym. The minimum requirement is walking at least 30 minutes most days of the week. It is best to start any exercise program gradually and then add resistance for bone health. Exercise can reduce both the frequency and severity of her hot flashes, improve her mood, increase blood flow to her brain, reduce stress, and help her to lose weight. MK could also take a break in her work schedule and include a half hour walking program or use a home exercise video. If she did not want to exercise alone, suggest joining a

gym or a dance, yoga or aerobics class. Regular exercise will also be helpful in lowering MK's blood pressure and achieving her weight loss goals.

Weight bearing exercise has been shown to help maintain bone integrity. Walking, jogging, dancing, cycling, and weight lifting are good example of weight bearing exercises which not only maintain bone strength but also helps to restore bone as well. There are no age limits when it comes to exercise. Women in their 80s and 90s have demonstrated an improvement in bone strength when exercises targeted the muscles that support the spine. Exercise also improves balance, which may prevent falls associated with bone fractures.

7. What are the key dietary recommendations for MK at the present time?

Since MK has gained 30 pounds in the past 3 years, it is most appropriate to help her understand how to reduce her caloric intake by reducing portion sizes, limiting her snacking, preparing healthier foods at all meals, and incorporating more fruits and vegetables into her diet on a daily basis. MK's diet is currently lacking fruits and vegetables which are high in antioxidants, phytonutrients, vitamins, and minerals which are important to strengthen her immune system. Determining which fruits and vegetables she enjoys and suggesting she take

time to purchase fresh and frozen varieties every week will allow her to have the foods available to cook for her family.

She should also be advised to use heart healthy olive and canola oils instead of butter and salad dressing to reduce her saturated and *trans* fat intake. The American Heart Association (AHA) states that during menopause, the protective HDL-C levels start to decline as blood pressure and LDL-C level increase. According to the AHA, following a healthy lifestyle, eating a diet rich in vegetables, fruit, and fiber, exercising 30 minutes daily and avoiding smoking will lower a woman's risk of heart disease.

MK should be encouraged to purchase, prepare, and eat more fish, white meat chicken and turkey, and lean meats and less processed foods. The sample meal plan below would provide MK with approximately 1800 calories and enough food choices to make this a meal plan she could follow. Her exercise program would help reverse the weight gain she has recently experienced. Establishing set meal times and snacks would make it easier for MK to stay on track. If wine is still a part of MK's diet, a spritzer would reduce the calories and allow her to stay within her 1800 calories. Water should be encouraged throughout the day via a large water bottle by her disk while she works.

Breakfast (home)

Whole grain toast	1 slice
Smart Balance margarine	1 Tbsp.
Omelet	3 egg white
Shredded carrots or tomatoes	½ cup
Decaffeinated coffee with low-fat milk	
Morning snack (home)	
Fat free greek yogurt	6 ounces
Slivered almonds	10 each
Raspberries	½ cup
Lunch (home)	
Homemade chicken salad with chopped celery	3 ounces
Lite mayonnaise	1 Tbsp.
Low calorie whole wheat bread	2 slices
Apple	medium - gala
Afternoon snack (home)	
Grapefruit	½
Almond milk	1 cup
Dinner (home or restaurant)	
Baked salmon	6 ounces
Steamed broccoli	1 cup

Baked sweet potato	½ medium
Smart Balance margarine	1 Tbsp.
Tossed salad	2 cups
Dressing made balsamic vinegar and olive oil	1 Tbsp.
Decaffeinated green tea	1 cup
Evening snack (home)	
Frozen fruit bar	1 bar

Total calories: 1760 kcal

Protein: 125 g

Fat: 44 g

Cholesterol: 395 g

Sodium: 1320

Fiber: 32 g

Calcium: 1310 mg

8. What are the appropriate treatment recommendations for depression and hot flashes?

Although a hot flash is harmless, it can disrupt sleep patterns, memory, and quality of life. Other tips suggested to MK were drinking a glass of cold water at the first sign of a flash, or running cool water over her wrists. Since MK works at home she could easily keep her windows open or keep her thermostat at a

comfortable 68 to 70 °F during the day and 60 to 62 °F at night. She could also try wearing loose-fitting cotton clothing which is more comfortable and cooling. MK could also document when and where she has hot flashes to help her pinpoint triggers. She could add this to her food log which she was keeping to help her lose weight.

Very low doses of HRT have traditionally been used to reduce hot flashes. Several studies have been published indicating an increased risk of cancer when using HRT, therefore many women have opted not to use these medications. Selective serotonin reuptake inhibitors (SSRI) such as Zoloft, Prozac, or Effexor have been very successful in treating women with hot flashes. Herbal remedies, such as black cohosh (*Cimicifuga racemosa*), red clover (*Trifolium pratense*), wild yam, evening primrose oil (*Oenothera biennis*), Maca (*Lepidium meyenii*), dong quai (*Angelica sinensis*), vitamin E (400 IU/day), flax seed (2 Tbsp./day), and whole soy foods (tofu, soymilk, edamame, roasted soy nuts, tempeh) have been recommended to reduce hot flashes. Valerian *(Valeriana officinalis)*, ginsing (*Panax ginseng* or *Panax quinquefolius*) and magnesium (400 mg/day) have been prescribed to enhance sleep. Acupuncture and yoga may also be helpful to ease menopausal symptoms. MK declined hormone therapy because of a family history of breast cancer but is willing to try acupuncture

and take a yoga class once a week. Since the black cohosh was not successful, she was placed on an SSRI for a 6-month period. MK was informed that it may take several weeks before the SSRI would take full effect.

9. What vitamin, mineral, and herbal supplements could be recommended to MK based on her history and the results of her DEXA scan?

Menopausal women are vulnerable to osteoporosis not only because of the loss of estrogen which prevents bone breakdown but also from a history of low calcium and vitamin D intake throughout their life. The risk of a woman having a hip fracture is equal to her combined risk of breast, uterine, and ovarian cancers. As women age, the risk of dying 1-year after a fracture is up to 40 percent.

MK is already experiencing a decline of bone mass and will need to increase her calcium intake. Calcium is important not only for MK's bones but she also needs it for her muscles and nerve health. The best sources of calcium are low-fat dairy foods such as milk, yogurt and cottage cheese. In addition, calcium is also found in kale, bok choy, broccoli, spinach, firm tofu, sardines and canned salmon bones, legumes, and calcium fortified beverages (Appendices G and H). MK's choice of half and half and cheese sauces are high in fat and calories and have minimal calcium and protein.

By replacing the cream cheese with a spreadable cheese made with skim milk and substituting her creamer with almond milk, MK could increase her calcium intake and decrease her total calories.

Vitamin D is also crucial for bone health and needed to improve calcium absorption. Higher vitamin D serum levels are associated with improved bone health and reduced risk of some cancers, heart disease, and infectious diseases. Sun exposure for 20 to 30 minutes per day can achieve this goal. Healthy food sources for both calcium and vitamin D can be found in low-fat dairy products, fatty fishes like salmon, tuna, and mackerel, and egg yolks. The current vitamin D recommendations for menopausal women are 400 to 600 IU/day (Appendix B).

Other key nutrients necessary for bone health are phosphorus, magnesium, and vitamins K and C.

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Part III
Integrative Systems and Disease

6
Cardiovascular Disease

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Objectives*

Identify patients at risk for coronary heart disease including identification of risk factors, assessment of abdominal obesity by waist circumference, and use of a nutrition history that targets dietary components relevant to atherosclerosis, hypertension, and/or heart failure.

Propose an optimal set of goals for nutritional risk factor reduction, given a patient's medical history and laboratory data, by using the American Heart Association and American College of Cardiology guidelines for nutrition and exercise.

Discuss issues related to vitamin supplementation for prevention or treatment of cardiovascular disease.

Summarize the dietary parameters of the DASH diet for the hypertensive patient.

Prioritize nutritional goals for the patient with heart failure.

*Source: Objectives for chapter and cases adapted from the *NIH Nutrition Curriculum Guide for Training Physicians*. (www.nhlbi.nih.gov/funding/training/naa)

Introduction

According to the National Center for Health Statistics and the American Heart Association (AHA), about one-third of Americans (32 percent) have cardiovascular disease (CVD), accounting for 1 of every 3 deaths in the United States. Approximately 34 percent of the deaths from CVD occurred in people before they reached 75 years of age. Nutrition plays a key role in the prevention and treatment of various types of cardiovascular disease, particularly the most common forms in the American population – coronary heart disease (CHD) and hypertension. Updated 2013 guidelines for assessment of CV risk, lifestyle modifications to reduce CV risk, and management of blood

cholesterol, overweight and obesity in adults have been developed by the American College of Cardiology (ACC) and the AHA Task Force on Practice Guidelines. Advising patients to consume a healthy diet, exercise regularly, maintain desired body weight, avoid smoking, and drink alcohol in moderation are critical to reducing CV risk.

Evidence Base for Diet and Heart Disease

Strong evidence indicates that diet, largely through its effect on serum lipids, influences the incidence of heart disease. Intake of saturated fat increases low-density lipoprotein cholesterol (LDL-C) levels, thereby increasing the risk for CHD. Large-scale clinical trials have conclusively shown that reducing serum LDL-C levels reduces the number of acute cardiac events and deaths from CHD both in patients with existing disease and those at risk due to elevated lipids. Angiographic studies have demonstrated that LDL-C reduction slows the progression of atherosclerosis in patients with known disease. Atherosclerosis is now viewed, not simply as the deposition of lipid in the artery, but as a complex inflammatory response to damage to the endothelial lining of arteries.

Dietary Lipids

An understanding of the basic biochemistry of fat and fatty acids is needed to address the role of dietary fat in the prevention and treatment of heart disease. Dietary fats are composed chiefly of three fatty acids attached to a glycerol molecule. All fats are a combination of saturated, monounsaturated, and polyunsaturated fatty acids. Fat is the most calorically dense nutrient, supplying 9 calories/g. Therefore, a diet high in fat is generally high in calories. Reducing total fat intake and adhering to an exercise program can help an individual lose weight. A summary of dietary recommendations based on CVD risk factors are summarized in Table 6-1.

Table 6-1 Summary of Lifestyle Recommendations Based on CVD Risk Factors

Source: Lisa Hark, PhD, RD and Fran Burke, MS, RD, 2014. Used with permission.

Risk Factor	Recommendation
Elevated LDL-C	↓ Saturated fat, ↓ soluble fiber, weight loss, Avoid trans fat
Low HDL-C	↑ Exercise, weight loss
Diabetes and insulin resistance	Weight loss, ↓ blood pressure, ↓ carbohydrates, ↑ exercise

Risk Factor	Recommendation
Elevated triglycerides	↑ Fish oils, weight loss, ↓ alcohol, ↓ carbohydrates
Obesity (BMI >30)	Weight loss, ↑ exercise, ↓ portion sizes
Hypertension	↓ Sodium, ↑ fruits and vegetables, ↓ alcohol, weight loss, ↑ exercise
Metabolic syndrome	Weight loss, ↑exercise, customized recommendations for total fat, carbohydrate and calorie intake

Saturated Fats

Saturated fats are fatty acids with no double bonds. With the exception of palm and coconut oil, foods high in saturated fat are solid at room temperature and are primarily from animal sources.

Major Contributors of Saturated Fat

Meats/Poultry: brisket, regular ground beef, sausages, hot dogs, sausage, bacon, fatty luncheon meats (pastrami, corned beef, salami, tongue), pâté, spare ribs, lamb, lard, poultry skin, chicken fat, beef fat and fried foods.

Dairy Products: butter, stick margarine, coffee creamer, whole milk, 2% milk, heavy

cream, half-and-half, whipped cream, full-fat yogurt, whole milk cottage and ricotta cheeses, ice cream, hard cheeses, cream cheese, and sour cream.

Breads/Snacks: potato chips, croissants, butter or sweet rolls, quick breads, and biscuits.

Desserts/Sweets: donuts, cakes, candy, pies, pastries, and cookies.

The ACC/AHA report suggests that given the current average intake of saturated fat at 11 percent, it would be beneficial to decrease saturated fat intake to 5 to 6 percent of calories for those who need to lower LDL-C levels.

Saturated fatty acids, when contrasted with unsaturated fatty acids, decrease synthesis and activity of LDL-C receptors, promoting an increase in serum LDL-C, thereby contributing to atherogenesis. An increase of 1 mg/dL in serum LDL-C increases CHD risk by 1 percent. A meta-analysis of dietary studies concluded that for every 1 percent increase in calories from saturated fat, serum LDL-C increases approximately 2 percent. Consuming a diet rich in vegetables, fruits, low-fat dairy products, poultry, fish, beans, legumes, nuts, whole grains, and vegetable oils; and limited in sweets, sugar-sweetened beverages, and red meat can help patients lower their saturated fat intake.

Polyunsaturated Fats

Two major categories of polyunsaturated fats (PUFA) are omega-3 and omega-6 fatty acids. Vegetable oils such as corn, canola, sunflower, safflower, cottonseed, peanut, and soybean contain omega-6 fatty acids. Omega-6 fatty acid (linoleic acid), an essential fatty acid, cannot be synthesized by the body and is required in the diet. Arachidonic acid, which is synthesized from linoleic acid, is the major omega-6 fatty acid found in cell membranes and the precursor of prostaglandins. The Dietary Reference Intake for linoleic acid is an Adequate Intake of 17 g/day for men and 12 g/day for women. Substitution of dietary sources of PUFA for saturated fat lowers LDL-C and reduces risk for CHD.

Omega-3 fatty acids include the very long chain eicosapentanoic acid (EPA) and docosahexenoic acid (DHA), as well as the 18-carbon alpha-linolenic acid, another essential fatty acid. The long-chain omega-3 fatty acids decrease serum triglycerides, platelet aggregation, and inflammation, and may therefore provide cardiac benefits. Dietary sources are listed in Appendix M and include canola oil, walnuts, flax seed, chia seeds, salmon, sardines, tuna, and herring. Epidemiologic studies suggest that healthy individuals who consume 7 ounces of fish per week are 30 to 40 percent less likely to die from

a cardiac event than those who do not regularly consume fish. The AHA recommends consumption of fish at least twice a week to reduce CVD risk.

In patients with heart disease, some studies indicate a benefit of omega-3 fatty acids. Clinical trials suggest an intake of approximately 1 g/day of EPA/DHA can reduce death from cardiac events. Other studies indicate a trend toward less restenosis after angioplasty for patients receiving omega-3 dietary supplements. Doses of 3 to 4 g/day can be prescribed to lower serum triglyceride in hypertriglyceridemic patients. Although omega-3 fatty acids lower triglycerides, they also slightly increase LDL-C. As research continues, it is appropriate to encourage a dietary pattern that incorporates omega-3 fatty acids, especially from fatty fish, but the benefit of oral supplements is less definitive.

The role of fish oil supplements is more controversial. High doses (3 to 4 g/day) have a definite role in treating hypertriglyceridemia, but the potential for CV benefits and other uses are not clear. One gram of fish oil daily failed to reduce heart disease deaths in an Italian population with multiple CVD risk factors. This dose is low in relation to what might be recommended (1 to 3 g/day) and the population studied already was on a diet higher in monounsaturated fats than the typical United

States diet. Therefore, it is difficult to draw firm conclusions about the potential effectiveness of fish oil for CVD prevention from this negative result.

Monounsaturated Fats

Monounsaturated fats (MUFA) contain one double bond; oleic acid is the most common dietary form. Oils high in oleic acid include canola and olive oil. Other dietary sources of MUFA include avocados, almonds, pistachios, peanuts, and pecans. Epidemiologic and clinical evidence from the Mediterranean region, report a lower incidence of CHD when a diet high in MUFA from olive oil is consumed. Shorter-term clinical trials of a Mediterranean style diet have shown improvement in a number of risk factors, including lowering serum triglyceride. Substitution of oleic acid for saturated fatty acids reduces LDL-C levels. A diet high in MUFA lowers LDL-C and serum triglycerides without lowering high-density lipoprotein cholesterol (HDL-C). Provision of some calories from MUFA, which might otherwise be provided from carbohydrate, can lower LDL-C without lowering HDL-C or raising triglyceride levels.

When a reduction in saturated fat intake is recommended to reduce LDL-C, favorable effects on lipid profiles are greater when saturated fat is replaced by polyunsaturated fatty acids, followed by monounsaturated fatty

acids, and then carbohydrates. Substitution of saturated fat with whole grains is preferable to refined carbohydrates.

Trans Fatty Acids

Hydrogenation – the addition of hydrogen atoms to an unsaturated fat – can change a fatty acid double bond from a *cis* to *trans* configuration. The major source of *trans* fatty acids is partially hydrogenated vegetable oils found in coffee creamers, canned frosting, microwave popcorn, and some foods served in restaurants. Food manufacturers have used this process to prolong the shelf-life of foods such as crackers, cookies, potato chips, and puddings. Randomized clinical trials indicate that *trans* fatty acids raise LDL-C levels when compared with naturally occurring *cis* fatty acids; they also decrease HDL-C levels. The structural similarity of *trans* fat to saturated fat may explain the detrimental effects. Although margarines contain *trans* fatty acids, use of a soft or liquid margarine maintains a lower LDL-C than does a comparable diet containing butter (a source of saturated fat and cholesterol). *Trans*-free tub margarines can be recommended. Recent changes in the formulations of fats used in baked goods and frying oils have reduced the *trans* fat intake in the United States.

The Institute of Medicine has concluded that there is no safe level for consumption of *trans*

fats and a Food and Drug Administration (FDA) regulation will ban all artificial *trans* fats from the American food supply. This recommendation aims to save thousands of lives and potentially billions of dollars in medical and economic costs a year. The FDA's proposal aims to eliminate a loophole that allowed manufacturers to label their products as containing zero grams of *trans* fats per serving if they contain less than half a gram.

Dietary Cholesterol

Although saturated fat and *trans* fats are perhaps the major dietary factor responsible for raising serum LDL-C levels, a high intake of cholesterol in the diet can also increase serum LDL-C. Animal foods are sources of cholesterol, with the highest being egg yolk and organ meats. Meat and dairy sources of saturated fat, such as cheese, cream, and fatty meats, also contain substantial amounts of cholesterol.

Hyperlipidemia

Hyperlipidemia, the clinical term used to describe elevated cholesterol, LDL-C, or triglyceride levels, increases the risk of atherosclerosis. An estimated 31.9 million adults 20 years of age and older have total serum cholesterol levels greater than 240 mg/dL, for a prevalence of 13.8 percent. When atherosclerosis proceeds to occlusion or rupture

of a blood vessel, myocardial infarction, stroke, or peripheral vascular disease can result (depending upon the affected site). Various lipoproteins transport cholesterol and triglycerides in the blood. The majority of cholesterol is carried in the blood by LDL-C and transported into cells via LDL-C receptors. Low-density lipoproteins are the major atherogenic lipoproteins. In contrast, cholesterol carried by HDL-C represents cholesterol being released by cells. The majority of serum triglyceride is present in very low-density lipoproteins (VLDL). A fasting lipid profile of the patient's LDL-C, HDL-C, and triglyceride levels is now recommended by the ACC/AHA Guidelines for assessing patient risk of CVD.

Secondary Causes of Hyperlipidemia

Note that hyperlipidemia may also be caused by some underlying “non-lipid” etiology rather than a primary disorder of lipid metabolism. Secondary causes of dyslipidemia include type 2 diabetes mellitus, hypothyroidism, excessive alcohol consumption, cholestatic liver diseases, nephrotic syndrome, chronic renal failure, cigarette smoking, obesity, and certain medications.

Assessment of the Hyperlipidemic Patient

The ACC and AHA collaborated with the National Heart, Lung, and Blood Institute (NHLBI) to develop clinical practice guidelines for assessment of CV risk, lifestyle modifications to reduce CV risk, and strategies for the management of blood cholesterol, overweight and obesity in adults which builds on the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults – Adult Treatment Panel (ATP).

The clinical approach to the hyperlipidemic patient outlined in the ACC/AHA guidelines is built upon evidence from numerous randomized clinical trials. A heart healthy diet was an underlying principle within these trials. With the goal of reducing atherosclerotic events, moderate or high-intensity statin therapy is prescribed based on an algorithm that considers the patient's LDL-C level, presence of atherosclerosis and/or diabetes, and in some patients, estimation of 10-year risk. While a heart healthy diet can lower LDL-C by about 10 percent, moderate-intensity statin therapy lowers LDL-C by 30 to 50 percent and high-intensity statin therapy lowers LDL-C by more than 50 percent. The treatment plan is based on an assessment of atherosclerotic cardiovascular disease (ASCVD) risk (defined as first occurrence non-fatal and

fatal myocardial infarction (MI), and non-fatal and fatal stroke).

Assessing Risk

The updated guidelines recommend a comprehensive assessment of the estimated 10-year risk for an ASCVD event that includes both CHD and stroke. This is in contrast to the use of an estimated 10-year risk for hard CHD (defined as non-fatal MI and CHD death). This guideline recommends using the new Pooled Cohort Risk Assessment Equations developed by the Risk Assessment Work Group to estimate the 10-year ASCVD risk for the identification of candidates for statin therapy (http://my.americanheart.org/cvriskcalculator). These equations use age, smoking status, total cholesterol, HDL-C, and presence of hypertension and/or diabetes to estimate risk based on race and gender. They can be used to predict stroke as well as CHD events in non-Hispanic Caucasian and African–American women and men aged 40 to 79 years with or without diabetes who have LDL-C levels 70 to 189 mg/dL.

Metabolic Syndrome

Recent attention regarding risk for CHD has focused on a constellation of characteristics termed metabolic syndrome. Metabolic syndrome includes (1) insulin resistance, (2)

pre-hypertension, (3) dyslipidemia that can include elevated serum triglycerides, low HDL-C, and small, dense LDL-C, (4) a prothombotic state, and (5) a proinflammatory state. Although measurement of insulin resistance can strengthen the diagnosis of metabolic syndrome, a series of simple measurements shown in Table 6-2 provide a reliable means of clinical identification of individuals at risk for metabolic syndrome. The presence of abdominal obesity is a valuable clue to metabolic syndrome. It can easily be assessed by measuring the patient's waist circumference, which is described in detail in Chapter 1, Case 1.

Table 6-2 Diagnostic Criteria for Metabolic Syndrome

Source: ACC/AHA Guidelines. 2013. Used with permission.

3 or More of the Following 5 Criteria:	
Abdominal obesity	Waist circumference: Men > 40 inches Women > 35 inches
High blood pressure	BP ≥ 130/≥85 mm Hg or documented use of antihypertensive therapy
High fasting blood glucose (FBG)	FBG ≥ 100 mg/dL

3 or More of the Following 5 Criteria:	
High triglycerides	≥ 150 mg/dL
Low HDL-C	Men < 40 mg/dL Women < 50 mg/dL

The increasing prevalence of metabolic syndrome has amplified the importance of nutrition in CHD due to the potential for morbidity and mortality from heart disease. The association of obesity with the development of hypertension, type 2 diabetes, and consequent CVD further heightens the need for all healthcare workers to be educated in the role of nutrition in health promotion and disease prevention.

Medical Nutrition Therapy for Hyperlipidemia and Metabolic Syndrome

Diet and exercise are cornerstones of the effective treatment of hyperlipidemia and metabolic syndrome. The ACC/AHA guidelines for lifestyle modifications to reduce CV risk in adults emphasizes intake of:

vegetables, fruits, and whole grains,

low-fat dairy products, poultry, fish, legumes, non-tropical vegetable oils, and nuts,

limit intake of sweets, sugar-sweetened beverages, and red meats.

The dietary pattern should provide appropriate calories while considering personal and cultural food preferences, and nutrition therapy for other medical conditions (including diabetes mellitus). This pattern can be achieved using the Dietary Approaches to Stop Hypertension (DASH) dietary pattern, the USDA My Plate (www.choosemyplate.gov), or the AHA/ Therapeutic Lifestyle Changes Diet. Implementation of any of these patterns should include:

reduction of percent of calories from saturated fat to 5 to 6 percent,

reduction in percent of calories from *trans* fat.

(Dietary patterns that limit saturated fat to 5 to 6 percent of calories, generally provide total fat within the range of 25 to 30 percent of calories.)

Other therapeutic options that may be added for further LDL-C lowering include:

intake of 2 g of plant stanol/sterol esters per day,

increasing viscous fiber intake to 10 to 25 g/day.

For patients with hypertriglyceridemia, the proportion of dietary carbohydrate and fat can be shifted such that dietary fat is at the upper end of the allowed range, while calorie intake is

adjusted for either weight loss or weight maintenance. Adopting lifestyle changes that incorporate new long-term dietary habits demands an investment of time and family support. Referral to a registered dietitian for medical nutrition therapy allows for a comprehensive assessment of nutritional status, development of negotiated, tailored behavior change goals, and strategies to achieve these goals. The dietitian can assist patients with problem areas such as portion size, eating out, and tips for food purchasing and preparation. Continued reinforcement and monitoring of behavior change by healthcare professionals is important for achieving and maintaining lifestyle changes. Many lipid centers have dietitians on staff who routinely counsel patients and work closely with the healthcare team.

Other Nutritional Components

Stanol/Sterol Esters

Plant sterols and their chemically modified counterpart, plant stanols, have been esterified and incorporated into a growing number of products, such as margarine, yogurt, and orange juice. Consuming 2 tablespoons/day of sterol-fortified spread can provide 2 to 3 g of sterol/stanol esters per day and lower LDL-C levels by 7 to 15 percent. In the gastrointestinal tract, sterol/stanol esters compete with

cholesterol for incorporation into micelles and thus absorption. Two possible concerns regarding use of plant sterol/stanol fortified margarines are: (1) caloric adjustment to maintain energy balance if margarine use is increased; (2) adequate intake of fruits and vegetables to compensate for the reduced absorption of dietary carotenoids.

Dietary Fiber

Inclusion of viscous or soluble fiber in the diet can decrease LDL-C levels. Based on evidence from a meta-analysis of over 50 clinical trials, ACC/AHA recommends inclusion of at least 5 to 10 g/day of viscous fiber, with the option of greater intakes in the range of 10 to 25 g/day. The 5 to 10 g/day has been shown to reduce LDL-C by about 5 percent. The hypocholesterolemic effect of soluble fiber results from its ability to form a gel-like substance in the gut, which binds and removes bile acids from the body through the stool before they are reabsorbed. Hepatic conversion of cholesterol into new bile acids reduces serum cholesterol. Total fiber intake is recommended at 25 to 35 g/day. Dietary sources of soluble and total fiber are shown in Table 6-3.

Table 6-3 Food Sources of Soluble and Total Fiber

Source: Wahida Karmally, DrPH, RD, CDE, CLS, FNLA. 2014. Used with permission.

Food	Soluble Fiber (g)	Total Fiber (g)
Cereal grains (1/2 c)		
Barley	1	4
Oatmeal	1	2
Oatbran	1	3
Seeds		
Psyllium(1tbs)	5	6
Fruit (1 medium)		
Apple	1	4
Bananas	1	3
Blackberries (1/2 c)	1	4
Pears	2	4
Prunes (1/4 c)	1.5	3
Food	**Soluble Fiber (g)**	**Total Fiber (g)**
Legumes (1/2 c cooked)		
Black beans	2	5.5
Kidney beans	3	6
Lima beans	3.5	6.5
Lentils	1	8

Food	Soluble Fiber (g)	Total Fiber (g)
Black eyed peas	1	5.5
Vegetables (1/2 c)		
Broccoli	1	1.5
Brussel sprouts	3	4.5
Carrots	1	2.5

Fruits and Vegetables

The evidence for inclusion of fruits and vegetables is summarized in a meta-analysis that concluded that each additional portion of fruit and vegetable consumed daily decreased the risk of CHD by 4 percent. Generous intake of fruits and vegetables is reflected in the DASH dietary pattern, as well as the Mediterranean diet. Practical advice to the patient is to cover half of the plate with fruits and non-starchy vegetables.

Supplemental Vitamins

Although supplementation with antioxidants and B vitamins was common in the 1990s as a strategy to reduce atherosclerosis, clinical trials did not demonstrate significant benefits. In fact, use of an antioxidant "cocktail" of vitamins C and E, beta-carotene, and selenium actually

lowered the beneficial sub-fraction HDL_2 cholesterol in patients receiving simvastatin and niacin treatment; it also reduced the stenosis lowering effect of the medical treatment. One meta-analysis of antioxidant supplementation trials reported a slight increase in mortality among subjects receiving vitamin A or E supplements. Beyond use of a daily multivitamin supplement, patients should be encouraged to obtain antioxidants and other vitamins from a diet rich in colorful fruits and vegetables and grains, rather than through supplements. It should be noted that that there is controversy regarding the benefits of even a daily multivitamin supplement.

Medical Nutrition Therapy for CHD (Chapter 6: Case 1)

Nutrition issues should be addressed with patients who have hyperlipidemia, CHD, or a family history of heart disease during most routine primary care visits. Attention to calorie balance is important for most patients primarily for weight control. Fostering control of caloric intake and encouraging increased physical activity are key to promoting weight maintenance and weight reduction. Weight reduction in overweight patients improves parameters associated with metabolic syndrome, including reducing LDL-C and triglycerides, increasing HDL-C, reducing blood

pressure, and normalizing elevated serum glucose levels. In many cases, as little as 7 to 10 percent weight reduction alone can eliminate the need for drug therapy in this clinical syndrome.

Conversely, it is possible that the initiation of a lipid-lowering medication prompts patients to feel attention to diet is no longer needed. Failure to follow appropriate diet when drugs are used can limit their effectiveness or necessitate higher doses, increasing the potential for side effects. Therefore, health professionals should continue to emphasize the underlying benefit of a calorically balanced, low saturated fat diet when lipid-lowering drugs are used (Table 6-1).

Alcohol

In addition to the general lifestyle issues of diet and exercise, a specific issue often raised in patient conversations regarding heart disease is the consumption of alcohol. Alcohol, in relation to heart disease, has both positive and negative effects. A first step in advising patients regarding alcohol is to obtain an alcohol intake history. Although light-to-moderate intake of alcohol may reduce the risk of CHD, intake over 30 g/day (more than 2 drinks) is associated with an increased mortality due to hypertension, pancreatitis, hypertriglyceridemia, gastrointestinal malignancies, stroke, cardiomyopathy,

cirrhosis, accidents, and breast cancer. Moderate alcohol intake is defined as no more than 2 drinks per day for men and 1 drink per day for women. A drink is defined as 5 ounces of wine, 1.5 ounces of 80-proof liquor, or 12 ounces of beer.

In terms of benefits, alcohol may have cardioprotective effects by increasing HDL-C levels and reducing LDL-C oxidation via the antioxidant polyphenols (catechin, quercetin, resveratrol). A CHD patient can continue to drink alcohol in moderation if free of other medical, psychiatric, or social problems. However, it is *not* appropriate to recommend alcohol intake to a non-drinker for its cardioprotective effect, as there are many other effective non-pharmacological therapies.

Reversing Heart Disease

The early promise of atherosclerotic plaque regression through intensive lifestyle modification and dietary manipulation does not seem to have been reproduced in subsequent lipid-lowering studies. On the other hand, statin drugs have also been shown to have effects on the vascular endothelium beyond lipid lowering. The potential mechanisms of plaque regression are under active investigation.

Hypertriglyceridemia

Evidence from epidemiological and controlled clinical trials has demonstrated that triglyceride levels are markedly affected by body weight status and body fat distribution. Data from National Health and Nutrition Examination Survey (NHANES) supports a relationship between body mass index (BMI) and triglyceride levels, whereby 80 percent of participants who were overweight and obese had triglyceride levels above 150 mg/dL. The Framingham Heart Study also confirmed this strong association of triglyceride levels with both subcutaneous abdominal adipose tissue and visceral adipose tissue in men and women (mean age 50 years). A consequence of excessive fat combined with impaired clearance or storage of triglycerides in subcutaneous fat is ectopic fat deposition in skeletal muscle, liver, and myocardium, which may result in insulin resistance, non-alcoholic fatty liver disease, and pericardial fat.

Medical Nutrition Therapy for Hypertriglyceridemia

Weight Reduction

There is strong evidence that weight loss, reducing simple carbohydrates at the expense of increasing dietary fiber, eliminating *trans* fats, restricting fructose and saturated fats,

implementing a Mediterranean-style diet, and consuming marine-derived omega-3 PUFA can produce a marked triglyceride-lowering effect ranging between 20 and 50 percent. The AHA recommends 2 to 4 g/day of EPA plus DHA, provided as capsules under a physician's care, for patients who need to lower their triglyceride level. This recommendation is based on a large body of evidence showing triglyceride-lowering effects of marine-derived omega-3 PUFA.

Dietary practices or factors that are associated with elevated triglyceride levels include excess body weight, especially visceral adiposity; simple carbohydrates, including added sugars and fructose; a high glycemic load; and alcohol. Studies show that multiple dietary interventions can result in additive triglyceride-lowering effects. The magnitude of decrease in triglycerides is directly related to the amount of weight loss. Meta-analyses have reported that for every kilogram of weight loss, triglyceride levels decrease 1.9 percent, or 1.5 mg/dL. A weight loss of 5 to 10 percent results in a 20 percent decrease in triglycerides, a 15 percent reduction in LDL-C, and an 8 to 10 percent increase in HDL-C. The magnitude of decrease in triglycerides is directly related to the amount of weight loss.

Reducing Fat and Carbohydrates

The relationship between percent of total fat intake and change in triglyceride and HDL-C

concentrations was reported in a meta-analysis of 19 studies published by the Institute of Medicine. In this analysis comparing low-fat, high-carbohydrate diets versus higher-fat diets, for every 5 percent decrease in total fat, triglyceride level was predicted to increase by 6 percent and HDL-C to decrease by 2.2 percent. Epidemiological and clinical trial evidence suggests that the Mediterranean-style dietary pattern is associated with decreased triglyceride levels. In the Framingham Heart Study Offspring Cohort ($n = 2730$), subjects in the highest quintile for Mediterranean-style dietary pattern score had the lowest triglyceride levels (103 versus 114 mg/dL) over a 7-year follow-up. In addition, the lowest triglyceride levels were observed when added sugar represented 10 percent of total energy. Conversely, higher triglyceride levels (5 to 10 percent) were observed when added sugar represented a greater proportion of energy intake.

Physical Activity to Reduce the Risk of CVD

Regular physical activity is associated with reduced CVD with an inverse dose response. In essence, higher levels of activity are associated with lower rates of CVD. This reduction in CVD occurs at least in part through the effect of exercise on CV risk factors. The ACC/AHA Guidelines on Lifestyle conclude that both

aerobic exercise and resistance training have benefits on the serum lipid profile, as well as decreasing blood pressure. Unfortunately, one-third of Americans report that they do *not* engage in any aerobic leisure-time physical activity. The ACC/AHA Lifestyle Guidelines advise adults to engage in aerobic physical activity to reduce LDL-C and non-HDL-C for at least 3 to 4 sessions a week, lasting on average 40 minutes per session, and involving moderate-to-vigorous intensity physical activity.

Hypertension (Chapter 6: Case 2)

Approximately 78 million United States adults currently have hypertension, defined as greater than 140/90 mm Hg. This represents 33 percent of United States adults 20 years of age and older. Hypertension affects men and women in nearly equal proportions and African–Americans have among the highest prevalence of hypertension (44 percent) in the world. Hypertension is a major risk factor for the development of CHD, cardiomyopathy, and stroke. National guidelines recommend pharmacological treatment of hypertension based on patient age. For patients older than 60 years, treat medically when systolic blood pressure is greater than 150 mm Hg or diastolic blood pressure greater than 90 mm Hg. For the general population younger than age 60 years, treat when systolic blood pressure is greater

than 140 mm Hg or diastolic blood pressure greater than 90 mm Hg. Specific treatment goals vary with patient's age and diagnosis of kidney disease or diabetes.

Diet and other lifestyle factors have enormous potential for the prevention and treatment of hypertension and in some cases can obviate the need for drug therapy or lower the dose required. This is particularly evident in patients with blood pressure in the range of 120/80 to 130/89 mm Hg. Nutritional factors that may contribute to the development of essential hypertension include obesity, high sodium intake, low potassium and calcium intake, and excessive alcohol consumption. The DASH trial, the subsequent DASH-sodium trials, the PREMIER study, and the 2013 AHA/ACC lifestyle guidelines to reduce cardiovascular risk all have substantiated the benefit of a comprehensive dietary approach in the prevention and treatment of hypertension.

The DASH diet, outlined in Table 6-4, provides for a substantial intake of potassium and calcium through the inclusion of fruits and vegetables and low-fat dairy products. In addition, meat portions are limited and nuts are used to provide magnesium and additional fiber. This rather plant-based diet also limits saturated fat making it appropriate for those needing to lower LDL-C. Based on clinical trials, the DASH diet reduced diastolic blood

pressure by as much as 5 mm Hg, regardless of age, gender, ethnicity, or preexisting hypertension. The diet was more effective among African–American and hypertensive individuals. For patients with blood pressure in the range of 140/90 to 159/99 mm Hg, the diet lowered blood pressure similar to the effect of a single-agent anti-hypertensive therapy. *Your Guide to Lowering Your Blood Pressure With DASH* is available at http://www.nhlbi.nih.gov/health/public/heart/hbp/dash/new_dash.pdf.

Table 6-4 Dietary Approaches to Stop Hypertension (DASH Diet) Recommendations

Source: National Heart, Lung, and Blood Institute. Used with permission.

Food Group	Daily Servings	Serving Sizes
Grains and grain products	7–8	1 slice bread 1 cup dry whole grain cereal* ½ cup cooked rice, pasta, or cereal
Vegetables	4–5	1 cup raw leafy vegetable ½ cup cooked vegetable 6 ounces low sodium vegetable juice

Food Group	Daily Servings	Serving Sizes
Fruits	4–5	6 ounces fruit juice 1 medium fruit ¼ cup dried fruit ½ cup fresh, frozen, or canned fruit
Low-fat or fat-free dairy foods	2–3	8 ounces milk 1 cup yogurt 1½ ounces cheese
Meats, poultry, and fish	2 or less	3 ounces cooked meats, poultry, or fish
Nuts, seeds, and dry beans	4–5 per week	⅓ cup or 1½ ounces unsalted nuts 2 Tbsp or ½ ounce unsalted seeds ½ cup cooked dry beans
Fats and oils†	2–3	1 tsp soft margarine 1 Tbsp low fat mayonnaise 2 Tbsp light salad dressing 1 tsp vegetable oil
Sweets	5 per week	1 Tbsp sugar 1 Tbsp jelly or jam ½ ounce jelly

Food Group	Daily Servings	Serving Sizes
		beans 8 ounces lemonade

This DASH eating plan is based on 2000 calories daily. The number of servings may vary from those listed depending on caloric needs.

*Serving sizes may vary between ½ and 1¼ cups.

†Fat content changes serving counts for fats and oils: 1 Tbsp of regular salad dressing equals ½ serving; 1 Tbsp of fat-free dressing equals 0 servings.

1. Following the advice to consume vegetables, fruits, and whole grains, low-fat dairy products, poultry, fish, legumes, non-tropical vegetable oils, and nuts within the DASH dietary pattern provides for reduced sodium intake compared to the average American diet. Patients with hypertension should also be advised to limit alcohol intake and work towards a healthy weight. Limiting sweets and sugar-sweetened beverages assists with weight management. 2. After the original trial, the DASH-sodium trial investigated the effect of the DASH diet combined with three different levels of sodium (3300 mg, 2400 mg, and 1500 mg). Reductions in blood pressure were proportional to the level of sodium restriction.

The high quality evidence from the DASH trials, as well as lower quality evidence of the benefits of the Mediterranean dietary pattern supports the benefit of frequent consumption of fruits and vegetables in reducing both hypertension and atherosclerosis. The benefit in lowering blood pressure has been demonstrated in those with and without hypertension, in men and women, in younger and older individuals, and in both African–Americans and non-African–Americans. This benefit is independent of weight or sodium intake. A wide variety of resources can assist in adaptation to personal and cultural preferences, including use of lacto-ovo vegetarian diets.

Obesity and Hypertension

Obesity is a major risk factor in the development of hypertension. It has been estimated that 60 percent of the hypertensive population are more than 20 percent overweight. A linear relationship exists between the degree of obesity and the severity of hypertension. The beneficial effect of weight reduction in hypertensive individuals has been clearly documented. Controlled dietary intervention trials estimate that a mean reduction in body weight of 20 pounds (9.2 kg) is associated with a 6.3 mm Hg reduction in systolic blood pressure and a 3.1 mm Hg reduction in diastolic blood pressure. The exact mechanism of obesity-induced hypertension is

unclear, but increased cardiac output, sodium retention, and increased sympathetic activity in response to elevated insulin levels are all thought to be significant contributors. Weight reduction should be the primary goal for the overweight hypertensive patient, since even a 10 percent change in body weight is sufficient to reduce blood pressure. Therefore, weight management is an important component to control blood pressure.

Lower Dietary Sodium Intake

Population studies have repeatedly demonstrated a relationship of hypertension to higher sodium intakes. Strong evidence from clinical trials consistently indicates that lowering sodium intake reduces blood pressure. This benefit is seen in those with and without hypertension, in African–Americans and non-African–Americans, and across various age groups.

The National High Blood Pressure Education Program, the American Society of Hypertension, and the *Dietary Guidelines for Americans* set an upper limit of 2300 mg of sodium per day for the general adult population. For high-risk groups including African–Americans, individuals ≥ 51 years of age, and individuals with hypertension, diabetes, or chronic kidney disease, the recommendation is to further limit sodium to

1500 mg per day. The AHA currently encourages of the goal of 1500 mg/day for both hypertensive and healthy adults.

In regard to sodium and blood pressure, the AHA/ACC Lifestyle Guidelines recommend:

no more than 2400 mg/day of sodium,

further reduction of sodium intake to 1500 mg/ day is encouraged,

reduction of sodium intake by at least 1000 mg/ day (that will lower BP, even if the desired daily sodium intake is not yet achieved),

combination of lower sodium intake with the DASH dietary pattern.

Reducing sodium intake can be challenging for an individual because of the ubiquitous nature of sodium in the American food supply. The typical American diet contains approximately 4 to 8 g of sodium per day. Table salt and foods high in sodium – such as salted, smoked, canned, and highly processed foods – should be limited. Educational materials with strategies to help patients lower sodium intake are provided by several Federal and private sources. The use of convenience foods, fast foods, and eating out all frequently contribute to higher sodium intakes among Americans. Key questions for patients with hypertension are:

Do you use a salt shaker at the table or in cooking?

Do you read labels for sodium content? (recommend <400 mg/serving)

How often do you eat canned, smoked, frozen, and processed foods?

In addition to individual lifestyle changes, changes in food manufacturing and processing are being implemented to reduce the sodium intake of Americans.

Both a healthy dietary pattern rich in fruits and vegetables and low fat protein sources as exemplified by DASH and a reduced sodium intake independently reduces blood pressure. However, the beneficial effect is even greater when these dietary changes are combined. In the 60 percent of United States adults with blood pressure above 120/80 mm Hg, simultaneously implementing both dietary recommendations can prevent and control HTN more than either intervention alone.

Increase Dietary Potassium Intake

Epidemiologic and observational studies have reported an inverse correlation between potassium intake and blood pressure, especially among African–Americans and individuals consuming a high-sodium diet. More recently, several small intervention studies have shown that potassium supplementation results in a modest hypotensive effect. Although the exact mechanism remains unclear, effects of potassium supplementation include natriuresis,

inhibition of renin release, and decreased thromboxane production. For practical purposes, increasing dietary intake of potassium may have a beneficial effect on blood pressure. Foods high in potassium include oranges, orange juice, potatoes (especially with the skins), and bananas. To maintain a high potassium intake, the DASH diet includes 8 to 10 servings of fruits and vegetables daily. Certain diuretic therapy, specifically loop diuretics, frequently induces potassium wasting. Increasing dietary potassium intake in these patients may obviate the need for synthetic potassium supplements, which require close monitoring.

Increase Dietary Calcium Intake

Calcium intake may be lower among hypertensive patients than among normotensive individuals. Increased dietary intake may reduce the incidence of hypertension and calcium supplements may produce a hypotensive effect in some patients. Although dietary calcium has been correlated with blood pressure, calcium supplementation has not been shown to significantly lower blood pressure. On the other hand, the inclusion of low-fat dairy food within the framework of the DASH diet did provide additional blood pressure lowering, as outlined in Tables 6-4 and 6-5, which advise two to three servings per day of fat-free or low-fat dairy food. (See

Appendices G and H: Dietary Sources of Calcium.)

Table 6-5 Diet and Lifestyle Interventions to Manage Hypertension

Source: Lisa Hark, PhD, RD and Fran Burke, MS, RD. 2014. Adapted from JNC-7.

Modification	Recommendations	Systolic Blood Pressure Reduction
Weight reduction	Maintain healthy body weight (BMI 18.5–24.9)	5–20 mm Hg for each 10 kg weight loss
Adopt DASH eating plan	Consume diet rich in fruits, vegetables, low-fat dairy products and low-saturated fat	8–14 mm Hg
Dietary sodium reduction	Reduce sodium intake to 2300 mg/day	2–8 mm Hg
Increase physical activity	Engage in regular aerobic physical activity such as walking 30 minutes at least 5 days a week	4–9 mm Hg
Moderate alcohol intake	Limit alcohol to no more than 2 drinks/	2–4 mm Hg

Modification	Recommendations	Systolic Blood Pressure Reduction
	day for men and 1 drink/day for women	

Reduce Alcohol Intake

Individuals who drink three or more alcoholic beverages per day account for 5 to 7 percent of those diagnosed with hypertension. Two or more drinks per day can lead to an increase in blood pressure. Although alcohol acts as a vasodilator, chronic alcohol ingestion is associated with increased formation of the vasoconstrictor thromboxane. Chronically increased levels of this prostaglandin metabolite may be partially responsible for the hypertensive effect of chronic alcohol ingestion. In controlled studies, reducing alcohol consumption in this population has been associated with a modest reduction in blood pressure.

Physical Activity Recommendations to Reduce Blood Pressure

As is true for other cardiovascular risk factors, adults with hypertension should engage in three to four aerobic activity sessions a week, lasting on average 40 minutes per session, and

involving moderate-to-vigorous intensity physical activity.

Heart Failure

Heart failure (HF), which affects nearly 5 million adults in the United States, is characterized by decreased cardiac output, venous stasis, sodium and fluid retention, and malnutrition. Example of signs and symptom of heart failure include shortness of breath (dyspnea); persistent coughing or wheezing; buildup of excess fluid in body tissues (edema); tiredness, fatigue, decrease in exercise and activity; and lack of appetite or nausea.

Reduced function of the left ventricle and accompanying neuro-hormonal changes promote accumulation of sodium and water and shortness of breath, fatigue, and inactivity result. Attention to medical nutrition therapy in the management of patients with HF is critical. Close monitoring, which includes surveillance by the patient and his or her family, can lead to the detection of changes in body weight or clinical status early enough to allow the patient or a healthcare provider an opportunity to institute treatments that can prevent clinical deterioration.

Causes of Malnutrition in Heart Failure

Cardiac cachexia is the wasting and malnutrition seen in patients with

long-standing HF. As myocardial function progressively deteriorates, patients present with the loss of adipose tissue and lean body mass secondary to poor nutritional intake and decreased activity. Upper-body and temporal wasting with lower-extremity edema are the hallmark features of this condition. The proposed mechanisms to explain cardiac cachexia include:

impaired cellular oxygen supply,

increased nutrient losses,

increased nutritional requirements,

decreased nutritional intake.

Impaired cellular oxygen supply Decreased cardiac output reduces oxygen delivery to cells, resulting in inefficient substrate oxidation and inadequate synthesis of high-energy intermediary metabolites.

Increased nutrient losses Hypoxemia and increased venous pressure causes bowel edema with subsequent fat and protein malabsorption. Decreased synthesis of hepatic bile salts and pancreatic enzymes caused by oxygen deprivation to the liver and pancreas may further contribute to this. Proteinuria, secondary to the reduced renal blood flow, is also a feature of HF.

Increased nutritional requirements Patients with HF have increased nutritional

requirements due to a hypermetabolic state caused by the increased work required for breathing, the mechanical work of the heart, and oxygen consumption related to alterations in neuroendocrine activity. If additional calories are not ingested to meet these increased demands, weight loss ensues.

Decreased nutritional intake Factors that may result in an inadequate food intake in patients with HF include one or all of the following:

hepatomegaly and ascites reduce functional gastric volume causing early satiety,

dyspnea and fatigue induced by eating,

unpalatable low-sodium diets,

anorexia, nausea, or vomiting from medications used to treat CHF.

Medical Nutrition Therapy for Heart Failure

Medical nutrition therapy for patients with HF is aimed at controlling blood pressure, sodium and fluid retention, restoring and maintaining body weight, providing adequate energy, protein, vitamins, and minerals, and repletion of protein stores in patients who have lost lean body mass. Providing practical information about eating a well-balanced diet, high in fruits and vegetables and low in saturated fats is critically important.

Lower Dietary Sodium Intake

Patients with HF retain sodium and fluid and therefore, dietary sodium restriction is a cornerstone of treatment. The level of sodium restriction may be individualized according to the severity of the HF. It is recommended that patients with symptomatic HF reduce dietary sodium intake to 2 to 3 g (2000 to 3000 mg) per day. Fewer research studies are available on the benefit of sodium restriction in heart failure, but based on the available studies and the potential influence on several mechanisms involved in treatment of heart failure, The Academy of Nutrition and Dietetics Evidence Analysis Library recommends restricting sodium intake to 2 g/day. Sodium restriction supports the effectiveness of diuretic agents in achieving negative sodium balance. One-fourth or more of hospital re-admissions for patients with HF are due to non-adherence with dietary sodium advice. Patients need more than to be told “stay away from salt.” They need to be able to state their recommended level of dietary sodium, use values on nutrition labels to guide their intake, and distinguish between very high and high sources of sodium.

A study in an urban heart failure clinic linked knowledge of dietary sodium sources with consumption of fewer high sodium foods. Another report indicated that 1 hour of education before hospital discharge decreased

likelihood of re-hospitalization by 35 percent and saved $2,823 per patient. Whether the patient is seen in the acute care or ambulatory setting, referral to a registered dietitian for assessment of their nutritional status and assistance in achieving the skills needed to manage a sodium restricted diet at home is appropriate for cost-effective management of HF. Salt substitutes are available to flavor foods, but many of them substitute potassium for sodium. Patients with renal failure or those taking potassium-sparing diuretics should avoid these products. (See Appendix I: Dietary Sources of High Sodium Foods.)

Lower Fluid Intake

Heart failure associated with dilutional hyponatremia may require restricting fluid intake to 1500 to 2000 mL/day. The fluid may be restricted slightly more in the hospital setting. Some suggest limiting daily fluid intake to an amount equal to the 24-hour urine output volume plus 500 mL. Traditional nutrition assessment parameters, such as actual body weight or weight change, may not accurately reflect nutritional status in HF patients. For example, cardiac cachexia may go undetected if body weight is normal or elevated because of sodium and water retention. In addition, serum protein levels, such as albumin, may be decreased secondary to either malnutrition or artificially as a result of dilution from fluid

overload. When HF appears well controlled with no evidence of edema or ascites, along with low serum BNP (B-type natriuretic peptide) levels, increase in weight is more likely dry weight gain.

Adequate Calories and Increased Protein

Daily caloric intake should be adequate to promote weight gain (if needed) in patients with HF. Research indicates HF patients generally need higher calories than a healthy control subject, but research to date has not determined how many calories most HF patients need. Some practitioners estimate dietary calories at 1.5 times the basal energy expenditure. Another set of recommendations suggests 28 to 30 kcal/kg of ideal body weight for weight maintenance and 32 to 35 kcal/kg actual weight for the malnourished patient.

Provision of 1.5 g/kg per day of protein can promote anabolism and achieve positive nitrogen balance in patients with cardiac cachexia. High-protein, high-calorie supplements are often necessary to achieve this level of intake, especially when the patient has a poor appetite. Nutritional supplements, both liquid and pudding forms, are available and provide a high concentration of calories and protein in a relatively small volume. The sodium and fluid content of HF supplements must be considered in the total daily sodium and fluid allowance. Small, frequent meals may

help HF patients achieve an adequate dietary intake. Patients who cannot meet their caloric and protein requirements orally may require enteral tube feeding (Chapter 12). Enteral feeding in a HF patient is precarious as it can result in overfeeding, which will aggravate the primary condition. Many patients with heart failure have obesity, which places additional strain on an already compromised heart.

Importance of Daily Weight Monitoring

Sudden weight gain or weight loss can be a sign of heart failure, worsening of the condition, and volume overload. Advise patients and their caregivers to measure body weight on a daily basis at the same time of day with similar clothing. Patients should track their weight and compare it to their "dry" weight without edema.

Other Nutrients and Supplements

Reduced food intake can reduce caloric intake and various nutrient levels. Thiamin deficiency has been noted more frequently among heart failure patients. Daily intake of a multivitamin can improve micronutrient status and reduce the possible detrimental effects of thiamine deficiency on the heart. Although a number of additional supplements have been tested, there is limited evidence of benefit to date. A few small trials have shown improved exercise tolerance and quality of life for heart failure patients receiving coenzyme Q10.

Alcohol Alcohol consumption should be limited in order to maintain blood pressure in target range or avoided if the patient has a history of alcoholic cardiomyopathy.

Smoking Cessation Smoking is considered a modifiable risk factor associated with heart failure; it is appropriate to recommend smoking cessation interventions, such as referral to a Quitline and/or pharmacological therapy.

Case 1 Disorders of Lipid Metabolism

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Objective

Identify cardiac risk factors for coronary artery disease in obese patients without known disease.

Describe other physical examination findings and screening and laboratory measurements relevant in a patient with disorders of lipid metabolism.

Describe the science-based nutritional and lifestyle recommendations for patients with disorders of lipid metabolism.

Apply the current AHA/ACC guidelinesfor screening, evaluation, and treatment of disorders of lipid metabolism.

Recognize the importance of medical nutrition therapy and lifestyle recommendations for treatment and prevention of cardiovascular disease.

JT is a 52-year-old Hispanic man who consults a new physician for a routine physical examination because his employer has recently changed their health insurance plan. He has not seen a physician for the past 3 years.

Past Medical History

JT has no prior history of hospitalizations or chronic illnesses. He is not taking any medications or over-the-counter dietary or herbal supplements, and he has no known food allergies.

Family History

JT's family history is positive for heart disease. His father had a fatal heart attack at age 54, and his father's brother had a heart attack at age 55. JT's uncle is currently being treated for hypercholesterolemia. There is no family history of hypertension, diabetes, or obesity.

Social History

JT works as an accountant and reports a high stress level both at work and at home. His work commitments do not allow him much free time so he frequently orders lunch in and eats at his desk. After a long day at work and his 45-minute commute home, JT feels too tired to exercise. Over the past 3 years he has experienced a 12-pound weight gain. JT attributes this to his sedentary, high-stress lifestyle, and to dining out with clients on average 2 to 3 nights per week. JT is a non-smoker. He drinks a 20-ounce (600 mL) cup of regular coffee every morning and two alcoholic beverages every evening. JT is married and has one daughter who is currently in her junior year of college.

Dietary Intake Using the 24-hour recall method, JT's physician obtained the following information about his typical diet.

Breakfast (office)	
Bagel	1 large (4 ounces/113 g)
Cream cheese	2 Tbsp.
Coffee	20 ounces (600 mL)
Half-and-half	2 ounces (60 mL)
Lunch (restaurant)	
Pizza with cheese	2 slices
Soda (cola)	12 ounces (360 mL)

Breakfast (office)	
Snack (office)	
Jelly beans	1 ounce (28 g)
Evening (restaurant)	
Hamburger	6 ounces (170 g)
Bun	1 large
French fries	1 cup
Vanilla ice cream	1 cup
Beer	24 ounces (720 mL)

Total calories: 2730 kcal

Protein: 106 g (16% of total calories)

Fat: 108.5 g (33.5% of total calories)

Saturated fat: 47 g (15.5% of total calories)

Monounsaturated fat: 36 g (12% of total calories)

Polyunsaturated fat: 10 g (3% of total calories)

Trans fat: 6.0 g (2% of total calories)

Cholesterol: 313 mg

Carbohydrate: 299 g (44% of total calories)

Dietary fiber: 11 g

Soluble fiber: 5 g

Sodium: 2680 mg

Review of Systems Noncontributory

Physical Examination

Vital Signs

Temperature: 98 °F (37 °C)

Heart Rate: 76 BPM

Respiration: 20 PM

Blood pressure: 139/88 mm Hg

Height: 5′10″ (178 cm)

Current weight: 212 lb (96 kg)

BMI: 30.4 kg/m^2

Weight 2 years ago: 200 lb (91 kg)

Waist circumference: 42 inches (107 cm)

Exam

General: Obese male in no acute distress

Remainder of physical examination was normal and unremarkable

Laboratory Data

JT's lipid profile, after a 12-hour overnight fast, provided the following laboratory values:

Patient's Lab Values	Normal Values
Total cholesterol: 260 mg/dL	desirable <200 mg/dL
HDL-C: 32 mg/dL	desirable ≥40 mg/dL

Patient's Lab Values	Normal Values
LDL-C: 158 mg/dL	desirable <100 mg/dL
Triglycerides: 350 mg/dL	desirable <150 mg/dL
Lp(a): 11 mg/dL	<20 mg/dL
Plasma glucose: 95 mg/dL	70 to 99 mg/dL

Framingham Point Score: 10-year risk for Coronary Heart Disease (CHD) is 16 percent based on total cholesterol level.

Case Questions

What additional questions should be asked of all patients during the general health maintenance screening?

What physical examination findings should one look for in a patient suspected of having disorders of lipid metabolism?

How should JT's lipid profile, waist circumference, and blood pressure be interpreted, based on the AHA/ACCGuidelines?

Based on JT's medical history, physical examination, and laboratory data, how would you classify and diagnose his lipid disorder?

What is the patient's stage of behavior change? And what would you say to encourage him? What are some of his barriers to change?

What is the currently recommended treatment and follow-up for JT's dyslipidemia?

Is JT's current nutrient intake within the recommended guidelines?

What are the best lifestyle approaches for this patient?

How can JT translate the recommended dietary guidelines into food choices?

Should JT receive a lipid-lowering medication at this time?

Answers to Questions: Case 1

Part 1: Screening, Risk Assessment, and Diagnosis

1. What additional questions should be asked of all patients during general health maintenance screening?

During the general health maintenance screen, a thorough history should include questions related to cardiac risk factors. Traditional risk factors for coronary artery disease in this patient include elevated total cholesterol, LDL-C and triglyceride levels, age (men >45),

family history of heart disease, low HDL-C, obesity (BMI ≥30 kg/m^2), increased waist circumference (>40 inches), and smoking habits. Nutrient intake, average weekly alcohol consumption, alternative medicine (dietary supplements such as botanicals, fish oil, etc.) use, exercise habits, and stress levels are also important areas to explore. The physician should also consider any diseases in the patient's past medical history that directly increase cardiovascular risk (e.g., diabetes) or any secondary medical disorder that could be contributing or causing the disorder of lipid metabolism

2. What physical examination findings should one look for in a patient suspected of having disorders of lipid metabolism?

In addition to general health screening, patients suspected of having dyslipidemia should undergo an examination of pulses (palpation of all pulses, and auscultation for bruits in the carotid and femoral arteries), thyroid palpation (hypothyroidism is a possible secondary cause of hypercholesterolemia), an eye examination for corneal arcussenilis, and a tendon and skin examination for xanthelasmas or xanthomas.

3. How should JT's lipid profile, waist circumference, and blood pressure be interpreted, based on AHA/ACC guidelines?

The current recent AHA/ACC guidelines focus on LDL-C but recommend a complete lipoprotein profile (total cholesterol, LDL-C, HDL-C, and triglycerides) as the preferred initial laboratory test.

LDL-C can be calculated using the following equation. Techniques for measuring LDL-C directly also are available:

$$\text{Total cholesterol} = \text{HDL-C} + \text{LDL-C} + \text{VLDL-C or}$$

$$\text{LDL-C} = \text{Total cholesterol} - (\text{HDL-C} + \text{VLDL-C})$$

$$\text{VLDL-C} = \frac{\text{Triglyceride level}}{5}$$

In dyslipidemic states, a triglyceride level greater than 400 mg/dL invalidates the results of this equation. In addition to the screening tests described above, Lp(a) was measured because of JT's family history of premature heart disease.

In addition the new guidelines identify four groups of subjects who should be considered for statin treatment:

Individuals with clinical ASCVD

Individuals with primary elevations of LDL-C >190 mg/dl

Individuals with diabetes, aged 40–75 years, with LDL-C 70–189 mg/dL

Individuals without ASCVD or diabetes, with LDL-C 70–189 mg/dL, and estimated 10-year ASCVD risk of ≥7.5%.

To rule out secondary or contributory causes of dyslipidemia, fasting serum glucose should also be measured to diagnose impaired glucose tolerance, prediabetes, or diabetes mellitus. Thyroid-stimulating hormone should also be measured to rule out hypothyroidism. If lipid-lowering drug therapy is required, baseline liver transaminases (ALT and AST) and uric acid levels may be helpful in choosing the appropriate type of drug therapy. A urine test should be done for protein and signs of glomerular disease.

Although metabolic syndrome was a central component of the ATP III guidelines, it was not at all a focus of the new ones. However, even if the presence of metabolic syndrome will not affect treatment approaches, if the new AHA/ACC guidelines are followed, its presence does indicate a high risk for future diabetes as well as the potential for significant benefit of lifestyle intervention across several risk factors. Patients with abdominal obesity should be evaluated for metabolic syndrome. Each of the five clinical criteria for metabolic syndrome can be obtained using a focused medical history, brief physical examination, and fasting laboratory data. Recent estimates suggest that 34 percent of the United States population meets the criteria for

metabolic syndrome. Metabolic syndrome should be a secondary target of therapy in dyslipidemic patients. JT has four out of the five criteria for metabolic syndrome, including abdominal obesity, elevated triglycerides, low HDL-C, and elevated blood pressure:

prehypertension: 139/88 mm Hg,

abdominal obesity: waist circumference 42″,

low HDL-C: 32 mg/dL,

elevated triglycerides: 350 mg/dL.

4. Based on JT's medical history, physical examination, and laboratory data, how would you classify and diagnose his lipid disorder?

This type of lipid disorder is called dyslipidemia since both JT's total plasma triglycerides and LDL-C concentrations are elevated and HDL-C is low. Although it is likely that a variety of combinations of regulatory defects in lipid metabolism account for a significant number of individuals with this phenotype, familial clustering of dyslipidaemia has been identified in which members of the same family may have both elevated LDL-C and triglycerides, only hypertriglyceridemia, or only elevated LDL-C concentrations.

The type of dyslipidemia that JT has seems to be associated with the secretion of increased numbers of very-low-density lipoprotein

(VLDL) particles. Once these individuals assemble and secrete increased numbers of large triglyceride-rich VLDL, their plasma triglyceride concentrations depend on their ability to hydrolyze VLDL triglycerides with lipoprotein lipase and, to a lesser degree, with hepatic lipase.

The ability to hydrolyze VLDL triglycerides also regulates the generation of LDLs in the plasma. Thus subjects with FCHL (familial combined hyperlipidemia) who have very high VLDL triglyceride concentrations (and are not able to efficiently catabolize VLDLs) might have normal or reduced numbers of LDL particles in the circulation and thus a normal LDL-C concentration. If these same individuals were able to efficiently catabolize the increased numbers of VLDL particles that were entering the plasma, they would generate increased numbers of LDL particles and have both hypertriglyceridemia and high LDL-C levels. Patients with dyslipidemia who synthesize only normal quantities of triglycerides and secrete increased numbers of VLDLs carrying normal triglyceride loads would generate increased numbers of LDL particles and have elevated plasma LDL-C concentrations only.

5. What is the currently recommended treatment and follow-up for JT's dyslipidemia?

Although JT has significant hypertriglyceridemia and low levels of HDL-C, with a high non-HDL-C, the new AHA/ACC guidelines tell us to focus on his LDL-C after assessing his CHD risk. JT does not have an LDL of more than 190, does not have CHD, and is not diabetic, so we need to calculate his 10-year risk. Using the new risk calculator from the AHA/ACC panel (http://my.americanheart.org/cvriskcalculator and http://www.cardiosource.org/science-and-quality/practice-guidelines-and-quality-standards/2013-prevention-guideline-tools.aspx for risk equations) JT's 10-year risk for CHD (fatal or non-fatal MI, fatal or non-fatal stroke) is 10.4 percent, which is greater than the 7.5 percent level the new guidelines suggest as a cutpoint for initiation of statin treatment. We will discuss medical therapy further in this chapter.

The presence of the metabolic syndrome indicates that intense lifestyle approaches have the potential to benefit him significantly. Particularly, he needs intensification of weight management, and increased physical activity. However, the new guidelines do not provide any goals for either statin or lifestyle therapy; there are clearly no HDL-C or triglyceride targets.

Part 2: Medical Nutrition Therapy

6. What is the patient's stage of behavior change? And what would you say to

encourage him? What are some of his barriers to change?

JT admitted early in his visit that he feels hopeless about his weight. Now he tells the doctor that he knows he has to lose weight and wants to know how much. He also tells his doctor that he needs to get educated on choosing low-fat foods. JT has probably already been thinking about making a change (Contemplation) – and perhaps he is now moving into the Preparation stage (Table 6-6). The role of the clinician is to confirm that weight loss would be slow, provide some guidance on how much weight loss to aim for (e.g., a loss of 10 percent of body weight is often achievable over 6 to 12 months). Barriers to weight loss that JT may encounter:

Stress at work. He orders his "usual" high-fat meal without looking for opportunities to find lower fat alternatives.

There may be social meetings on two to three nights that include excessive eating and drinking.

He may be unaware of opportunities for increased daily physical activity at work.

He is overwhelmed with work and does not feel that he can add physical activity into his routine.

His wife may not understand the seriousness of his health and may not be supportive by cooking healthy meals when he eats at home.

Table 6-6 Stages of Change Processes of the Transtheoretical Model

Source: Finckenor MA, Byrd-Bredbenner C. *J Am Diet Assoc*. 2000;100:335–342.

Stages of change	**Appropriate Advice for Each Stage**
Precontemplation Not interested in change	Should receive brief advice and offer of future help
Contemplation Thinking about making a change	Advise patient and assist to reduce obstacles to change
Preparation Is getting ready to change	Advise and provide assistance and follow-up as needed
Action Is working on the change	Follow-up, support, and encouragement as needed
Maintenance Trying to maintain the change	Follow-up, support, and encouragement as needed

7. Is JT's current nutrient intake within the recommended guidelines?

The key elements of the diet include:

saturated fat below 5 to 6% of calories; (avoid *trans* fat),

dietary cholesterol intake below 200 mg/day.,

an increase of viscous (soluble) fiber to 10–25 g/day,

intake of 2 g/day of plant sterols/stanols daily,

weight management,

increased physical activity.

JT's current diet is not within these recommended guidelines. According to the nutritional analysis of his current intake, JT's saturated fat intake is about 16 percent of his caloric intake (<5 to 6 percent is recommended), *trans* fat intake is 3 percent of calories (needs to be avoided) and cholesterol intake is 313 mg (<200 mg/day is recommended). Significant sources of saturated fat in JT's diet come from high-fat dairy foods including half and half cream cheese, mozzarella cheese, and ice cream as well as the ground red meat. His caloric intake is approximately 2700 calories per day. This excessive calorie intake combined with his sedentary lifestyle will continue to promote weight gain unless he reduces total calories and routinely participates in some physical activity. In order to lose 1 to 2 pounds of body weight per week (which is the recommended rate of weight loss), JT must reduce his weight maintenance caloric needs by at least 500

calories and increase activity by 250 calories daily. Alternatively, JT may choose to exercise more rather than eat less to achieve the targeted weight loss.

JT's typical diet is deficient in fruit and vegetables, which are generally low in calories and are nutrient dense. The DASH diet has been found to be very effective in lowering blood pressure and can also be recommended to JT. The DASH diet especially emphasizes greater intake of vegetables, fruits, and whole grains. The DASH diet includes 7 to 8 servings of whole grains; 4 to 5 servings of vegetables; 4 to 5 servings of fruits; 2 to 3 servings of non-fat dairy products; 2 or less servings of meats; 2 to 3 servings of fats/oils on a daily basis. It also limits sodium to less than 3 g/day; and encourages 4 to 5 servings of unsalted nuts/ week. JT's diet contains only 11 g of dietary fiber/day and g of soluble fiber/day, compared to the TLC diet, which recommends 10 to 25 g of soluble (viscous) fiber/day as adjunctive therapy to reduce LDL-C.

8. What are the best lifestyle approaches for this patient?

JT's modifiable risk factors include obesity, high-saturated fat diet, sedentary lifestyle, and excessive alcohol consumption. Implementing a number of lifestyle and behavioral changes should improve JT's risk profile significantly.

The first line of therapy for all lipid and non-lipid factors associated with the metabolic syndrome is weight reduction and increased physical activity. Overweight and obesityarerecognized as major underlying risk factors for coronary heart disease. Regular physical activity is a component in the management of dyslipidemia.

In order to make dietary recommendations, it is necessary to first define the desired endpoint or goal for each individual. Is the goal to reduce triglycerides and LDL-C with/without weight reduction? For JT the goal is to lower total cholesterol, LDL-C, and triglycerides, raise HDL-C levels, and reduce weight. He can achieve this by adhering to the DASH diet and reducing his total caloric intake by self-monitoring. Monounsaturated fat and omega-3 fatty acids should be favored in place of both saturated and omega-6 fatty acids, while keeping total fat to a maximum of 35 percent of total calories.

The specific dietary recommendations include reducing total calories and saturated fat intake (less than 6 percent), avoiding *trans* fat, increasing monounsaturated fat (up to 20 percent), and reducing alcohol intake.

9. How can JT translate the recommended dietary guidelines into food choices?

A hypocaloric diet, which favors monounsaturated fat, is recommended for JT. Sources of monounsaturated fats are canola oil, olive oil, pistachios, almonds, hazelnuts, pecans, unsalted peanuts, peanut butter,avocado, and high oleic acid safflower oil and sunflower oils. The main sources of omega-3 fatty acids are fatty fish such as salmon, mackerel, herring, sardines, and plant foods such as flax seeds, chia seedsand walnuts. The main sources of *trans* fat are the French fries and pizza crust made with partially hydrogenated oils. He can substitute with a baked potato or brown rice or barley. JT should eat more vegetables, fruits, whole grains, and beans, only non-fat or very low-fat dairy products, and chicken without skin, fish, or lean meats limited to 5 to 6 ounces per day. If he enjoys eggs, he can include two large egg yolks per week. Egg whites have protein and no fat or cholesterol.

His fiber intake would be significantly increased with the recommended servings of fresh fruits, vegetables, and whole grains containing fiber. Therapeutic options for enhancing LDL-C reduction include increased intake of viscous (soluble) fiber (10 to 25 g/day) from oats, psyllium, dried beans, and fruits such as strawberries, apples, and vegetables such as okra and eggplant. Fat spreads containing plant stanol/sterols (2 g/day) could be included to further lower LDL-C in place of other spreads

the patient may currently be using. Two grams of stanol/sterols can reduce LDL-C by 7 to 15 percent. Plant stanols/sterols containing products are available in the supermarkets, It is important to note that these products have calories and should replace other fat sources, such as margarine or cream cheese. JT will benefit from a reduction in alcohol and sodium intake. Alcohol adds calories to JT's diet and can raise triglycerides and blood pressure.

JT's Recommended Modified Fat Diet

Breakfast	
Oat cereal	2 cups
Skim milk	1 cup
Orange, navel	1
Lunch	
Tuna, canned, water pack	0.5 cup
Whole wheat bread	2 slices
Tomato	1/2 medium
Carrot	1/2 cup
Mayonnaise or olive oil	1 Tbsp.
Non-fat flavored yogurt	1 cup
Dinner	
Chicken breast, baked	3 ounces (85 g)
Noodles, cooked	1 cup
Broccoli/eggplant	2 cup

Breakfast	
Romaine lettuce	2 cups
Olive oil	1 Tbsp.
Vinegar	1 Tbsp.
Banana	1 small
Snack	
Apple	1 small
Peanut butter	2 Tbsp.
Skim milk	6 ounces (180 mL)

Total calories: 1960 kcal

Protein: 107 g (22% protein calories)

Total fat: 62 g (29% fat calories)

Saturated fat: 12 g (6% SFA calories)

Polyunsaturated fat: 19 g (9% PUFA calories)

Monounsaturated fat: 27 g (12% MUFA calories)

Cholesterol: 163 mg

Carbohydrate: 229 g (47% carbohydrate calories)

Fiber: 31 g

Soluble fiber: 10 g

Sodium: 2,172 mg

Part 3: Lipid Lowering Medication

10. Should JT receive a lipid-lowering medication at this time?

JT may require drug therapy at some point in the future, but only after an adequate trial of lifestyle modification has been undertaken. It should be emphasized, however, that if pharmacologic intervention becomes necessary it should be thought of as an adjunct to reducing lipid levels, and not as a substitute to lifestyle modification.

The physician needs to set the stage for medical nutrition therapy and encourage increases in physical activity. The physician's positive attitude toward lifestyle changes can influence the patient's attitude and success toward making these changes. An explanation of the positive effects that lifestyle modification can have on JT's prognosis should be highlighted. These benefits include lower LDL-C and triglyceride levels, increased HDL-C levels (usually only modestly), decreased blood pressure, increased cardiac output, increased collateral blood supply, and stress relief. Regardless of age, patients should begin any exercise program gradually and include 5 to 10 minutes of warming up at the beginning of exercise and cooling down at the end. The ultimate goal is to increase the total workout to 30 minutes daily. JT would need a stress test

(>40 years of age) before he starts an exercise program.

Referring the patient to a registered dietitian/ nutritionist often helps to facilitate dietary changes. The patient's readiness to make behavioral changes needs to be assessed. Most patients are not ready to make significant changes in their lifestyle habits during the first meeting. Assessment of the patient's compliance is essential to determine if the diet changes are optimal to maximize their effects on lipid metabolism. Diet instruction may require several follow-up visits. Early initial follow-up (every 4 to 6 weeks) is important because it affords opportunities to verify adherence to, and provide support for, diet and exercise changes. The patient can be monitored at intervals deemed appropriate to reinforce diet recommendations and to check lipid levels. In a patient such as JT, lifestyle changes should be attempted for 3 months before considering drug therapy, because they may bring about a significant decrease in lipid parameters, thereby obviating the need for drug therapy.

Drug Treatment

Based on the new guidelines, one can consider JT for statin treatment based on his 10-year risk of 10.4%. Because of the presence of metabolic syndrome and his primary prevention status, a reasonable trial of diet and exercise, should be initiated. If he responds, particularly in terms of

weight loss, his triglyceride levels should fall and his HDL-C level should increase. However, he would still need a dramatic fall in his LDL-C to reach a 10-year risk of less than 7.5.

The following drugs may be considered:

Statins are the recommended treatment for JT according to the new guidelines. Since the guidelines do not have LDL-C targets for treatment, the patient and his physician would have to choose between high intensity statin (about 50 percent reductions in LDL-C) and moderate intensity statin (35 to 45 percent reductions in LDL-C). Because several randomized trials and a regression of all the statin trials support greater intensity therapy and a way to maximally reduce CHD risk, this approach would seem reasonable. If JT could not tolerate high intensity statin treatment, adjustment to moderate intensity would follow. Additionally, if JT's LDL-C dropped significantly with lifestyle changes, moderate intensity might be adequate from the start. Statins can lower triglycerides at higher doses, adding to their potential efficacy in JT.

There are no specific recommendations in the new guidelines for adding non-statin drugs once statin therapy has been optimized. However, the guidelines acknowledge that doctors may want to try drugs that lower LDL-C on top of statins in patients with very high initial LDL-C levels (>190 mg/dl). The

guidelines also note that there are non-statin drugs that lower triglyceride levels and raise HDL-C levels, but point out the lack of randomized control trials (RCT) data supporting their use in combination with statins.

Nicotinic Acid (Niacin) lowers LDL-C and triglyceride levels and raises HDL-C. It can also increase insulin resistance; this would be less of a risk if JT loses weight concomitantly.Recent studies, however, have raised doubt about the efficacy of niacin when added to statin therapy.

Fibric Acid Derivatives lower triglyceride and raise HDL-C; can have a modest (about 6 percent) LDL-C-lowering effect.A recent study, however, has raised doubt about the efficacy of fibrate when added to statin therapy.

Omega-3 fatty acids At doses of 2–4 g/day, omega-3 fatty acids lower triglyceride without significant effects on LDL-C or HDL-C. There is mixed evidence regarding the cardioprotective effects of omega-3 fatty acids.

Case 2 Hypertension and Lifestyle Modifications

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Objectives

Define pre-hypertension and discuss the rational for this diagnosis.

List the diet and lifestyle factors that may contribute to the development of hypertension.

Describe the parameters of the DASH diet for the treatment of hypertension.

Prioritize medical nutrition therapy and exercise goals for patients with hypertension.

RF is a 36-year-old African-American man with pre-hypertension. During his last visit to his family doctor, his blood pressure (BP) was elevated and he complained of occasional heartburn after meals. His physician recommended a 24-hour ambulatory BP monitor, Prilosec to treat heartburn, and diet and lifestyle changes aimed at weight reduction. RF is to return in 6 weeks to review his results.

Past Medical History

RF has no significant past medical history. He describes a gradual weight gain over the past 15 years, with his current weight being his highest. He was a college-level football player weighing around 200 pounds at the time. Following his college graduation, he slowly gained approximately 40 to 50 pounds.

Family History

RF has a positive family history of obesity, heart disease, and hypertension. His mother and brother are obese. His mother has hypertension and is currently being treated with antihypertensive medications. Paternal grandfather had a myocardial infarction (MI) at age 62 and his father has high cholesterol.

Medications

RF takes no medications or over-the-counter dietary supplements.

Social/Diet History

RF lives with his wife and two children and works as a corrections officer in a local prison. He eats three meals a day. RF typically eats fast food for breakfast and lunch and enjoys snacking after dinner. He does not engage in regular physical activity and has not done so for the past 10 years. He denies any recreational drug use and drinks one beer a day with dinner.

RF smoked two packs of cigarettes per day for 18 years (36 pack/year history). He quit smoking 2 years ago.

RF's Usual Diet

Breakfast	
Bagel	1 large
Cream cheese	2 Tbsp.
Orange juice	12 ounces
Lunch	
Roast beef hoagie	10 inch size
Russian dressing	2 Tbsp.
Potato chips	2-ounce bag
Regular soda	20 ounces
Snack	
Cheese/peanut butter crackers	1 package (6 crackers)
Dinner	
Baked chicken	1 breast and thigh with skin
Baked potato	1 large
Butter	1 Tbsp.
Green salad	2 cups
French dressing	2 Tbsp.
Beer	12-ounce bottle

Breakfast	
Snack	
Salted nuts	4 ounces
Regular soda	12 ounces

Total calories: 4117 kcal

Protein: 158 g (15% of total calories)

Fat: 185 g (41% of total calories)

Saturated fat: 46 g (10% of total calories)

Monounsaturated fat: 57 g (12% of total calories)

Polyunsaturated fat: 25 g (5% of total calories)

Cholesterol: 334 mg

Carbohydrate: 450 g (44% of total calories)

Dietary fiber: 23 g

Soluble fiber: 1 g

Sodium: 6319 mg

Calcium: 476 mg

Review of Systems

General: Denies sleep problems

Gastrointestinal: Occasional GERD after eating

Neurologic: No headaches, tremors, seizures, or depression

Musculoskeletal: No muscle or joint pain, no swelling or redness

Pulmonary: Short of breath when climbing stairs

Physical Examination

Vital Signs

Temperature: 98.4 °F (36.8 °C)

Heart rate: 65 BPM

Respiratory rate: 12 BPM

Blood pressure: 140/92 mm Hg

Height: 5′10″ (178 cm)

Current weight: 248 lb (110 kg)

BMI: 35.5 kg/m^2

Waist circumference: 42″

Exam

General: Obese male in no acute distress

HEENT: Nonpalpable thyroid; no hirsutism or striae; no acanthosis nigricans

Cardiac: S1 and S2 normal, regular rate and rhythm; no murmurs or gallops

Chest: Clear to percussion and auscultation

Abdomen: Obese non-tender, no masses, no abdominal bruit

Extremities: No edema

Neurologic: Alert and oriented to person, place, and time, intact memory

Laboratory Data

Patient's Fasting Lab Values	Normal Values
Glucose: 99 mg/dL	70–99 mg/dL
Potassium: 3.8 mEq/L	3.5–5.3 mEq/L
Serum cholesterol: 210 mg/dL	<200 mg/dL
Triglycerides: 175 mg/dL	<150 mg/dL
HDL-C: 41 mg/dL	>40 mg/dL
LDL-C: 134 mg/dL	near optimal <130 mg/dL
	optimal <100 mg/dL

Follow-Up Description

RF returned in 6 weeks for his follow-up doctor's appointment. His 24-hour BP monitor confirmed a diagnosis of stage 1 hypertension with a 24-hour mean BP of 139/88 mm Hg (hypertension defined as >135/85) and a systolic BP load of 72% (hypertension >40%). RF reported that the Prilosec alleviated his heartburn.

Case Questions

What is the difference between pre-hypertension and clinical hypertension?

What are the medical risks associated with high blood pressure?

What role does sodium play in the pathogenesis of high blood pressure and what are the current United States dietary recommendations for sodium?

What are the effects of diet and lifestyle factors on blood pressure control?

How does RF's lifestyle contribute to his high blood pressure?

What evidence-based diet and lifestyle recommendations would you counsel RF on given his current diagnosis?

What factors would help to increase adherence in hypertensive patients?

Answers to Questions: Case 2

1. What is the difference between pre-hypertension and clinical hypertension?

According to the most recent national survey data (2007–2010), 33 percent of United States adults ≥20 years of age have hypertension, and another one-third have prehypertension. In the United States the prevalence of hypertension

among blacks is 40 percent, which exceeds the rate of hypertension among whites (27 percent) and Hispanics (26 percent). Among hypertensive adults, increases have been seen over the past 10 years in awareness, treatment, and control of their condition; however, only 82 percent are aware of having hypertension, 76 percent are treated, and 53 percent are well-controlled. Blood pressure rises slowly with age and in adults, systolic BP rises by approximately 0.6 mm Hg per year.

The prevalence of pre-hypertension is strongly correlated with increasing body mass index (BMI) and waist circumference for both sexes; however, it is more common in men than women and is similar in both blacks and whites. According to longitudinal data from the Framingham Heart Study, BP values of 130–139/85–89 mm Hg (now considered pre-hypertensive) are associated with a more than two-fold increase in relative risk of cardiovascular disease (CVD) compared to BP levels below 120/80 mm Hg. The term prehypertension is defined as a systolic blood pressure (SBP) of 120 to 139 mm Hg and/or diastolic blood pressure (DBP) of 80 to 89 mm Hg. It was established to focus attention on those individuals who were at higher than normal risk of CVD and in whom lifestyle approaches to prevent or delay the onset of hypertension would be beneficial. The decision

to establish this new BP category was based on the following factors:

BP increases with age.

~90 percent of individuals age 55 years or older with normal BP ultimately develop hypertension during their lifetime.

Observational studies in adults between the ages of 40 and 80 years have demonstrated with each incremental rise in BP of 20/10 mm Hg, starting at 115/75 mm Hg, the risk of CVD doubles.

Primary hypertension accounts for about 95 percent of all hypertension cases, and is defined as having a SBP of 140 mm Hg or greater, having a DBP of 90 mm Hg or greater, or taking anti-hypertensive medications. Elevated BP is the result of both genetic and environmental factors and their interactions. Dietary and lifestyle factors have a significant role in lowering blood pressure especially in hypertensive individuals, but have also been shown to lower blood pressure or prevent hypertension in normotensive individuals. Populations who eat a plant-based diet and those whose sodium intake is low have virtually no increase in blood pressure with age.

2. What are the medical risks associated with high blood pressure?

Analyzed dichotomously, hypertension compared to normotension is associated with a

3- to 4- fold increased risk of stroke and heart failure, and a 2-fold increased risk of coronary artery disease. Hypertension is a major contributor to the burden of disease and this relationship is strong, consistent, and continuous. It is a leading cause of preventable deaths, accounting for 13 percent of deaths worldwide. Hypertension frequently coexists with other CVD risk factors including obesity, dyslipidemia, insulin resistance, and glucose intolerance. Anti-hypertensive therapy has been associated with mean reductions of 35 to 40 percent in stroke incidence, 20 to 25 percent in myocardial infarction, and more than 50 percent in heart failure in clinical trials.

3. What role does sodium play in the pathogenesis of high blood pressure and what are the current United States dietary recommendations for sodium?

Sodium is the nutrient most widely investigated for its effect on blood pressure. Both observational and RCTs have documented that a high sodium intake raises blood pressure. The International Study of Electrolyte Excretion and Blood Pressure (INTERSALT), a large observational trial which included 10,079 participants from 32 countries in 52 centers, showed that over a wide range of sodium intake, populations with a low sodium intake have lower BP than those with high intakes. Populations with very low sodium intake (<55

mmol) had low blood pressure and little or no increase in blood pressure with age. Numerous RCTs have consistently shown a reduction in blood pressure with sodium restriction. A recent meta-analysis of trials, at least 4 weeks in duration, showed that a reduction in sodium by 75 mmol per day (equivalent to 4.4 g salt/day) decreased SBP and DBP on average by 5 mm Hg and 3 mm Hg, respectively, in hypertensive participants and by 2 mm Hg and 1 mm Hg, respectively, in normotensive participants regardless of sex and ethnicity.

Several physiological mechanisms have been proposed to explain the relationship between sodium and hypertension. Increased cardiac output associated with extracellular fluid volume expansion is one postulated mechanism for the effect of sodium excess on blood pressure; however, increased sodium intake does not raise blood pressure in all individuals. Those that are most susceptible to dietary sodium intake are considered “salt sensitive,” which is associated with low plasma renin levels (effective plasma renin activity <0.65 ng/mL per hour) and several demographic characteristics such as older age, black ethnicity, weight, and resistant hypertension. It is also believed that a high sodium intake over time may impair the structure and function of the heart and kidney leading to clinical disorders in cardiac, vascular, and renal

function, such as those experienced in patients with long-standing hypertension.

The actual sodium intake in the United States currently exceeds recommendations and is estimated to be about 3600 mg/day. Based on the belief that lowering sodium intake should reduce CVD, the National High Blood Pressure Education Program, the American Society of Hypertension, and the *2010 United States Dietary Guidelines* set an upper limit of 2300 mg of sodium per day for the general adult population. For high-risk groups including African–Americans, individuals ≥51 years of age, and individuals with hypertension, diabetes, or chronic kidney disease, the recommendation is to further limit sodium to 1500 mg per day. In 2010, The American Heart Association also lowered its recommendation to 1500 mg of sodium per day for all adults.

Maintaining a daily sodium intake of 1500 mg will be challenging for many individuals since their preference for sodium has likely developed over years of exposure. Studies, however, have shown that a decreased preference for salty foods can take as little as 3 to 4 weeks. Approximately 10 percent of dietary sodium comes from natural sources and another 5 to 10 percent added during cooking or at the table. The remaining 80 percent of dietary sodium in the United States comes from packaged, processed, and restaurant foods. Strategies to

lower dietary sodium must include public health awareness campaigns to help individuals choose less processed and more fresh and reduced sodium foods, and an overall voluntary reduction in sodium content in the food supply.

4. What are the effects of diet and lifestyle factors on blood pressure control?

DASH Diet: www.nhlbi.nih.gov/health/health-topics/topics/dash/

Two landmark trials have provided evidence that a diet rich in fruits, vegetables, whole grains, and low-fat dairy products and reduced in saturated fat, sodium, and refined carbohydrates can lower blood pressure either alone or in combination with other lifestyle changes. These include the Dietary Approaches to Stop Hypertension (DASH) and the DASH-Sodium trials, both funded by the National Heart, Lung, and Blood Institute (NHLBI) to assess the effects of a combination diet on blood pressure. Participants with a BP <160/80–95 mm Hg were randomly assigned to a control diet typical of the average United States diet or a combination diet and were provided with all meals and snacks for the duration of the trials.

The DASH diet emphasizes eating more fruits, vegetables, low-fat dairy products, whole grains, poultry, fish, and nuts and limits intake

of fats, red meat, sweets, and sugar-containing beverages. This dietary pattern is rich in potassium, magnesium, calcium, and fiber, and low in total and saturated fat and cholesterol. The DASH trial found that adherence to this combination diet led to a mean reduction in SBP of 5.5 mm Hg and 3.0 mm Hg in DBP for all participants compared to the control group. Among hypertensive participants enrolled in the trial, the mean reduction in SBP was 11.4 mm Hg and 5.5 mm Hg in DBP, reductions equivalent to single antihypertensive drug therapy. The greatest change in BP was seen in African–Americans, who experienced a 13.2 mm Hg mean reduction in SBP and 6.1 mm Hg in DBP.

The subsequent DASH-Sodium trial looked at the effect of limiting dietary sodium intake and showed step-wise decreases in blood pressure in both the DASH and control diet groups following a typical American diet. Reductions in sodium intake from 150 mmol/day (3450 mg) to 100 mmol/day (2300 mg) resulted in a 1.3 mm Hg reduction in SBP, and a further dietary sodium reduction to 50 mmol/day (1150 mg) resulted in an additional decrease of 1.7 mm Hg while following the DASH diet. Compared to the control diet, the combined effect of the DASH diet and lowest sodium intake was a reduction of 8.9 mm Hg in SBP and 4.5 mm Hg in DBP. These trials provided evidence that a low-sodium, combination-based diet can lower

blood pressure in individuals without hypertension and therefore reduce the risk of related adverse health outcomes.

Weight Reduction Body weight is another strong determinant of blood pressure. Data from the most recent National Health and Nutrition Examination Survey (NHANES) show that the prevalence of hypertension is 42.5 percent among obese individuals with a BMI ≥30 kg/m^2 compared to 15.3 percent for those with a BMI <25 kg/m^2. Several postulated mechanisms have been proposed for the obesity-related hypertension, although the exact mechanism is unknown. Obesity is commonly associated with increases in both sympathetic nervous system (SNS) activity and insulin resistance. Increased SNS activity increases catecholamine production, which may adversely affect BP through vascular effects. Weight gain has also been shown to increase BP by increasing plasma renin activity.

The results of a meta-analysis of 25 clinical trials indicate that an average weight loss of 5.1 kg results in a mean drop in SBP of 4.4 mm Hg and 3.6 mm Hg in DBP. Other studies have documented that weight loss can prevent the development of hypertension by 20 percent in individuals who are overweight and prehypertensive. The JNC-7 also reports a reduction in SBP of approximately 5 to 20 mm Hg for each 10 kg weight loss. More research is

needed to evaluate whether or not sustained weight loss can prevent the age-related rise in BP.

Physical Activity Epidemiologic studies have shown an inverse relationship between physical activity and blood pressure. Participating in moderate aerobic physical activity five times a week for at least 30 minutes, results in significant reductions in blood pressure, from 8 to 11 mm Hg in SBP and 7 to 8 mm Hg in DBP. A reduction in SBP of approximately 4 to 9 mm Hg with increased physical activity is reported in the JNC-7. Research has also suggested an added benefit of including resistance training, in addition to aerobic exercise, as a part of routine physical activity. Recent studies have demonstrated a reduction of as high as 13 mm Hg for both SBP and DSP in patients with previously diagnosed hypertension. Significant decreases have been found after as little as 4 weeks after the commencement of resistance training. The American Heart Association has prescribed 3 days of resistance training per week (2 days for beginners) with exercises targeting a mixture of the major muscle groups.

Alcohol A direct relationship between alcohol use and blood pressure has been well documented. This effect is particularly evident with alcohol intakes of more than 2 drinks per day (a drink is defined as 12 ounces beer, 5 ounces wine, or 1.5 ounces spirits). A

meta-analysis of 15 randomly controlled trials found that reduction of alcohol intake resulted in a decrease in SBP of 3.3 mm Hg and DBP of 2.0 mm Hg. It was also found that the greater the reduction in alcohol intake, the greater the reduction of BP. From these studies it was suggested that for each reduction of one alcoholic drink per day, a reduction in both systolic and DBP of 1 mm Hg resulted.

Table 6-5 summarizes the average reduction in systolic blood pressure expected from the diet and lifestyle interventions described in this case.

5. How does RF's lifestyle contribute to his high blood pressure?

RF's current diet is sub-optimal and lacks many of the major components recommended by the DASH diet. By favoring fast food restaurants and eating foods high in salt (processed meats, cheese, and salty snacks), he is increasing his consumption of sodium significantly above the recommended limits (>6000 mg/day). His intake of fruits, vegetables, and dairy foods is low, while intake of foods high in saturated fat, including cream cheese, butter, fatty lunchmeats, and chicken skin, is high. Overall, his typical dietary intake is low in both calcium (476 mg/day) and potassium, and high in sodium, fat, and calories.

RF's weight and lack of physical activity also contribute to his high blood pressure. His current BMI of 35.5 kg/m^2 places him in the Class II obesity category, well above the recommended 24.9 kg/m^2. An initial weight loss of 20 pounds would have a significant effect on reducing his blood pressure. RF's daily intake of alcohol, fruit juice, and sugar-sweetened soda provides an excessive amount of calories, which can promote weight gain and prevent weight loss in a sedentary individual. RF states that he has not routinely exercised in 10 years, which is another lifestyle factor contributing to his high blood pressure.

6. What evidence-based diet and lifestyle recommendations would you counsel RF on given his current diagnosis?

RF should be counseled to follow the diet and lifestyle recommendations outlined in the both the DASH-Sodium and PREMIER trials. The PREMIER study investigated the effects of the DASH eating plan with concurrent lifestyle interventions to lose weight (goal was at least 15 pound weight loss), increase physical activity (goal was at least 180 minutes per week of moderate-intensity physical activity), reduce sodium intake (no more than 2300 mg per day), and reduce alcohol intake (no more than 2 drinks per day for men and 1 drink per day for women) but participants were responsible for their own meals and snacks. The mean

reduction in blood pressure when all conditions were followed was 4.6 mm Hg in SBP and 2.1 mm Hg in DBP at 6-month follow-up, and 2.1 mm Hg SBP and 1.0 mm Hg DBP at 18-month follow-up. The BP response was less than in the original DASH trials and believed to be due to poorer dietary compliance.

Patients with hypertension, or who are at risk for hypertension, should consume diets high in fruits and vegetables (8 to 10 servings/day) and low-fat dairy products (2 to 3 servings/day), and low in sodium (2300 mg/day). One serving of a fruit or vegetable is equivalent to a half cup cooked or 1 cup fresh and one serving of a low-fat dairy product is equivalent to 1 cup of low-fat or non-fat milk or yogurt or 1 ounce of low-fat cheese.

RF can increase his fruit and vegetable intake by eating a banana at breakfast with a high-fiber cereal, choosing a raw vegetable such as carrot sticks at lunch with a sandwich on whole grain bread, and preparing a large salad with dinner along with a cooked vegetable. RF should limit his morning intake of 100 percent orange juice to no more than 4 ounces per day. He can try mixing the juice with water if he finds this is not a sufficient quantity (see Appendix O: Food Sources of Dietary Fiber).

Snacks are an especially good place for RF to increase his intake of DASH-recommended foods; all that is required is a little advance

planning. Bringing a low-fat cheese stick, a 4-ounce 1 percent cottage cheese snack pack, a fat-free yogurt, or an apple with him to work will provide a readily accessible snack, rather than choosing an item from the vending machine. Another strategy would be for RF to purchase multiple pieces of fruit at the start of the week and keep them at his desk so that he will have a healthy snack available for the rest of the week.

Eating more fish is beneficial as it is a very low calorie source of protein when prepared by grilling or baking, low in saturated fat and contains omega-3 fatty acids, which are cardioprotective. Whole grains can be easily incorporated into dinner. Brown rice and whole-wheat pasta are two substitutions (for white rice and white flour pasta) that RF can make immediately. Quinoa has become a popular side dish and RF should be encouraged to try this and other whole grain products.

These dietary changes should result in weight reduction for RF and increase his motivation to adhere to a heart healthy diet. A discussion about gradually increasing his aerobic activity to 30 minutes, 5 days a week should also occur at the physician visit. Approaching the subject with activities RF enjoys may help to get him engaged in performing this activity regularly. Given RF's background as a football player, he might be interested in resuming weight lifting

and resistance training, activities that he most likely participated in as a college athlete. Combining aerobic activity with strength training is an ideal way for RF to improve his health.

7. What factors would help to increase adherence in hypertensive patients?

Dietary and lifestyle changes are successful only if they are followed. A study based on the 1999 through 2004 NHANES data found that only 19 percent of patients with hypertension actually follow the DASH diet. Specifically, adherence was lowest among African–Americans and individuals with a BMI of 30 kg/m^2 or higher – two groups who could benefit the most from following the DASH diet. Cultural influences on food choices, preferences, and food preparation, such as increased consumption of fried and highly seasoned foods, may make it more difficult particularly for African–Americans to adhere to the DASH diet. Lack of family support and lack of access to fresh fruits and vegetables may also be a significant factor in DASH adherence, especially in urban areas where there is often limited availability and higher cost of healthy food. Canned fruits and vegetables are generally more available and less expensive but also very high in sodium and sugar content. Patients need to be instructed to rinse canned foods thoroughly before eating, purchase canned

fruits packed in “light” syrup, and to look for “no salt added” products whenever possible.

Various strategies have been proposed to help increase adherence. The primary means that a patient has for receiving information about the DASH diet (both how to follow it, and why it is so important) comes from the primary care physician. Therefore, it is essential that patients be given instruction during office visits; yet one study reported that only one-third of patients with hypertension received dietary counseling during office visits. Limited time to educate patients about how to properly follow the diet may reduce the potential benefits of dietary and lifestyle interventions. Physicians should make in-office instruction a priority, or if this is not possible, the patient should be referred to a dietitian or nurse educator. Furthermore, continual follow-up support from healthcare providers is greatly beneficial for increasing long-term maintenance of lifestyle modification.

A lower level of education is also associated with decreased adherence to the DASH diet, and this may be linked to a lack of “functional health literacy” in certain populations. This refers to the patient's ability to understand and act on the health information provided, which is necessary for the implementation of a lifestyle or dietary modification. A patient who is illiterate, for example, will be unable to follow

written guidelines for the DASH eating plan. Patients should be provided with examples of specific foods that may meet requirements for the DASH diet, as well as help in learning how to implement appropriate lifestyle strategies.

Case 3 Metabolic Syndrome and Lp(a) Genetic Defect

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Objectives

Identify risk factors for coronary heart disease and describe the increased cardiovascular risk that is specific to the Asian–Indian population.

Identify the criteria for metabolic syndrome and understand the disorder's impact on cardiovascular health.

Discuss why it is important to understand how cultural and ethnic factors play a role in treatment recommendations.

Discuss the medical workup of a patient with cardiovascular risk factors, with particular emphasis on the appropriate utilization of

inflammatory markers and advanced lipoprotein testing, such as lipoprotein(a).

Provide a diet and physical activity plan for an Asian-Indian patient at risk for coronary heart disease.

MG is a 32-year-old Asian–Indian man who is self-referred to the Preventive Cardiology Clinic because he is concerned about his family history of heart disease. He is seeking ways in which to avoid developing heart disease. During the initial visit he states that he does not want to take medication and prefers to focus on changing his diet and lifestyle. He is evaluated and referred to a nutritionist for counseling. His electronic health record is used to provide historical data from his last health maintenance visit 3 years before.

Past Medical History

MG has no current symptoms relevant to cardiac risk, he has had no prior hospitalizations or chronic illnesses. He has never had any surgeries. He is not taking any medications or over-the-counter dietary or herbal supplements. He has no known food or drug allergies.

Family History

MG has a family history of heart disease. His father suffered a heart attack at age 45 and died of heart disease last year at age 57. His mother has type 2 diabetes mellitus.

Social History

MG immigrated to the United States 11 years ago to attend college and he is now an engineer. He reports being very busy with work and rarely finds time to exercise. He married 2 years ago and has a 1-year-old daughter. After his father died, MG's mother moved in with his family. She does most of the cooking. MG does not smoke, drink alcohol, or use any recreational drugs.

Diet History

The nutritionist in the Preventive Cardiology Clinic determines that MG is a vegetarian. Since moving to the United States, he eats a combination of American and Indian foods. His typical diet consists of the following:

Breakfast	
Skips	
Lunch (work)	
Cheese sandwich	2 slices white bread
American cheese	2 slices

Breakfast	
Mayonnaise	1 Tbsp.
Potato chips	2 ounce bag
Soda (cola)	12 ounces (360 mL)
Snack (office)	
Whole milk yogurt	8 ounce (240 g)
Evening (home)	
Samosa (stuffed potato, fried)	1 large
Curried vegetables	2 cups
Spinach panier (cheese)	1/2 cup
Chickpeas	2 Tbsp.
White rice	1 cup

Total calories: 2976 kcal

Protein: 88 g (12% of total calories)

Fat: 143 g (43% of total calories)

Saturated fat: 32 g (10% of total calories)

Monounsaturated fat: 13 g (4% of total calories)

Polyunsaturated fat: 3 g (1% of total calories)

Trans fat: 0 g

Cholesterol: 147 mg

Carbohydrate: 336 g (45% of total calories)

Dietary fiber: 8 g

Soluble fiber: 0.1 g

Sodium: 3857 mg

Review of Systems

Noncontributory

Physical Examination

Vital Signs

Temperature: 98 °F (37 °C)

Heart Rate: 78 BPM

Respiration: 21 RPM

Blood pressure:

135/85 mm Hg (previous exam, 3 years ago)

150/86 mm Hg (current visit)

	Previous Exam	**Current Visit**
Weight:	167 lb (76 kg)	182 lb (83 kg)
Height:	5′6″ (168 cm)	—
BMI:	27 kg/m^2	29 kg/m^2
Waist circumference:	36″	39″

Exam

General: Overweight male in no acute distress

Remainder of physical examination was normal and unremarkable

Laboratory Data

	Previous Exam	Current Visit	Normal Values
Fasting glucose:	100	122	≤99 mg/dL
Total cholesterol:	190	230	desirable <200 mg/dL
Fasting triglyceride:	210	250	desirable <150 mg/dL
HDL-C:	40	35	desirable >40 mg/dL (for men)
Non-HDL-C:	150	195	desirable <160 mg/dL
LDL-C:	108	145	desirable <130 mg/dL
Lp(a):	112	—	desirable <30 mg/dL
hsCRP:	2.1	2.5	desirable <1.0 mg/L
apoB:	100	105	desirable <90 mg/dL

Case Questions

Is MG at higher risk of heart disease compared with age-matched peers and how does his ethnic background affect his risk?

Why are apoprotein B, high-sensitivity C-reactive protein, and lipoprotein(a) helpful to informing MG's management?

What factors have contributed to the change in MG's risk factor profile? What are some potential solutions?

How does MG's ethnic background affect his dietary habits and lifestyle?

Based on MG's current lab results, what are the most appropriate next steps in his management?

Answers to Questions: Case 3

Part 1: Risk Factors and Laboratory Assessment

1. Is MG at higher risk of heart disease compared with age-matched peers and how does his ethnic background affect his risk?

MG currently has three major risk factors for the development of cardiovascular disease: low HDL-C, hypertension, and a family history of premature coronary disease. Based on the 2013 ACC/AHA guidelines discussed earlier in this chapter, he does not fall into a high risk category. His young age precludes estimation of a 10-year ASCVD risk since the Pooled Cohort Risk Assessment Equations are only valid in individuals aged 40 to 79 years of age. However, this same risk calculator can be used to calculate MG's estimated lifetime risk of having an ASCVD event. MG's lifetime ASCVD risk based on his current blood pressure and lipid values is quite high at 46%. If all of his risk factors were optimal, this risk would be only 5%. Therefore, MG is at significant lifetime risk of ASCVD if his risk factors are not modified. In addition, MG's actual risk may be even higher since his family history of premature CHD is not factored in to this risk calculation. MG also currently meets all five criteria for metabolic syndrome: abdominal obesity, elevated

triglycerides, low HDL-C, elevated systolic blood pressure, and elevated fasting blood glucose (Table 6-2). Multiple studies have demonstrated that the presence of metabolic syndrome puts MG at an increased risk of developing diabetes as well as an increased lifetime risk of CHD. Several of MG's laboratory values also indicate a higher CHD risk than age-matched controls. His elevated levels of high-sensitivity C-reactive protein (hsCRP) and lipoprotein (a) (Lp(a)) also put him at higher cardiovascular risk. The combination of elevated Lp(a) elevated LDL-C level and low HDL-C level, reflect even greater CHD risk. Putting all of these factors together, MG is at very high long term risk for developing ASCVD, an assessment that could only be made after looking at multiple variables and risk factors, as no single method can comprehensively predict CHD risk.

MG's Asian–Indian descent also increases his CHD risk compared with other ethnicities, as the disease in Asian–Indians tends to manifest 5 to 10 years earlier than in other populations. This increased risk is largely attributable to higher rates of metabolic syndrome, insulin resistance, and diabetes, which often present at earlier ages. Asian–Indians are also at increased risk for ischemic heart disease and cardiovascular disease at elevated Lp(a) levels, compared to other ethnicities.

Conventional criteria from the NCEP ATP III have been shown to underestimate the prevalence of metabolic syndrome by 25 to 50 percent in Asian–Indians, as this ethnic group develops metabolic abnormalities at a lower BMI and waist circumference compared to other populations. Therefore, several national and international organizations have recommended using the International Diabetes Federation ethnic and gender waist circumference criteria for central obesity when diagnosing metabolic syndrome in these patients (Table 6-7).

Table 6-7 Ethnic and Gender Waist Circumference (WC) Criteria for Central Obesity

Source: International Diabetes Federation. www.idf.org.

	Men (inches)	**Women (inches)**
European	>37	>32
Sub-Sahara Africa	>37	>32
Middle eastern	>37	>32
South Asian	>35	>32
South/Central American	>35	>32
Japanese	>33	>35
Chinese	>35	>32

2. Why are apoprotein B, high-sensitivity C-reactive protein, and lipoprotein(a) helpful to informing MG's management?

In appropriate patient populations, apolipoprotein B (apo B), hsCRP, and Lp(a) have been demonstrated to be valuable predictors of CHD risk. First, the measurement of apo B is only warranted in patients at intermediate or high CHD risk, which includes those, like MG, with a family history of premature CHD. An elevated apo B level is a better predictor of CHD risk than LDL-C. Importantly, one-third of all Asian–Indians will have elevations in apo B. Additionally, in patients started on statin therapy, apo B provides a more direct assessment of residual atherogenic particle number, which could guide therapeutic decision-making.

Evaluation of hsCRP, a marker for inflammation, is also considered most valuable in patients with intermediate cardiovascular risk, and is especially beneficial in men older than 50 years and women older than 60 years with normal LDL-C levels but one additional major CHD risk factor. While MG does not strictly meet these criteria, his positive family history and metabolic syndrome make evaluation of hsCRP reasonable. Highly-sensitive CRP predicts future vascular events independent of LDL-C level and can

guide decisions on if or when to begin lipid-lowering therapy.

Finally, screening for Lp(a) is recommended for patients with intermediate or high risk of CHD (Table 6-8). In MG's case, screening was performed not because of his ethnicity, but because of his family history of premature CHD. There is a strong positive, continuous, association between Lp(a) levels and both cardiac and peripheral vascular disease. This association is independent of LDL-C, non-HDL-C, and the presence of other cardiovascular risk factors. Lp(a) is a modified form of LDL-C with an additional protein moiety, apolipoprotein(a). Like LDL, Lp(a) penetrates the arterial wall, but is more strongly retained in the wall than LDL. In addition, Lp(a) is approximately 80 percent structurally similar to plasminogen, but has no thrombolytic activity. Therefore, by competing with plasminogen for fibrin and cell surface binding, Lp(a) also demonstrates antifibrinolytic properties. Recent studies suggest that Lp(a) primarily promotes atherosclerosis rather than thrombosis, though both mechanisms are believed to play a role in Lp(a)'s cardiovascular effects. In adults, Lp(a) levels are genetically determined and vary widely (<0.2 to >250 mg/dL); they are similar in men and women. The median level varies by ethnicity and is lowest in non-Hispanic Caucasians (median = 12 mg/dL) and highest in

African–Americans (median = 39 mg/dL), with levels in Asian–Indians falling between these two populations. Studies show that the risk of CHD is increased when the levels of Lp(a) are more than 30 mg/dL and there is a 2- to 3-fold increased risk of myocardial infarction at Lp(a) levels more than 50 mg/dL (80th percentile for plasma levels). Recent studies indicate that CHD risk is much greater when elevated Lp(a) levels are accompanied by low HDL-C versus high LDL-C levels.

Table 6-8 Recommended Screening for Lipoprotein(a)

Source: Nordestgaard BG, Chapman MJ, Ray K, et al. *Eur Heart J*. 2010; 31:2844–2853.

Measure once in subjects at intermediate or high risk of CHD who present with:
Premature CHD
Familial hypercholesterolemia
Family history of premature CHD and/or elevated Lp(a)
Recurrent CHD despite statin therapy
≥3% 10-year risk of fatal CHD (European guidelines)
≥10% 10-year risk of CHD (United States guidelines)

Repeat measurement of Lp(a) levels in patients is only necessary if treatment was initiated and evaluation of therapeutic response is desired. This is because Lp(a) is a very stable parameter, largely unaffected by diet and most drugs. As MG was screened for Lp(a) at his initial visit, he did not require repeat testing at his follow-up visit 3 years later.

Part 2: Nutrition Assessment and Cultural Issues

3. What factors have contributed to the change in MG's risk factor profile? What are some potential solutions?

Through a therapeutic physician–patient relationship, MG can be helped to identify the factors in his life that have negatively contributed to his current health status. More importantly, a supportive and non-judgmental approach to caring for MG will motivate his lifestyle changes. The factors in MG's life that have contributed to his risk profile change and possible solutions to these barriers are given here.

Lifestyle MG has a full-time job and a young child, which results in a busy schedule that precludes time to exercise. As he would greatly benefit from a regular exercise program, a discussion to determine how to make exercise a part of his daily agenda should be held. For example, he could take his child for a walk in a

stroller when he comes home from work, allowing him to spend time with his family while getting valuable exercise. An exercise prescription should be written and his schedule and leisure activities should be discussed. A recommendation to purchase a pedometer to help quantify his activity could be beneficial.

Stress The death of his father and pressure at work has placed significant stress on MG, potentially causing him to overeat, exercise less, and forget about the importance of his own health. MG could be educated on the benefits of meditation, yoga, and massage therapy as approaches to stress reduction and to help him re-gain perspective on what he values in life.

Preparation of Family Meals MG's mother now lives with him and his family and cooks all their meals. As a result, he has less control over his diet, which may have contributed to the decline in his health. It is imperative that MG's mother participates in the nutritional counseling sessions, as the lifestyle changes MG must make will be nearly impossible without family support and changes in shopping and cooking.

4. How does MG's ethnic background affect his dietary habits and lifestyle?

Nutritional interventions for the prevention and treatment of CHD must maintain compatibility with patients' cultural beliefs and values. It is

very important that MG maintain his cultural identity, particularly with regard to his diet. By providing culturally appropriate recommendations targeted to MG's Asian–Indian heritage, the goal of positive lifestyle change without violating cultural foundations will be possible. Health professionals must recognize the importance of specific foods within cultures, while not making generalizations about dietary patterns based solely on the basis of race, ethnicity, or geographic origin. This is because food choice diversity is common among all cultures and racial groups. Therefore, the most effective strategy for nutritional intervention focuses on each family's unique dietary history.

Many Asian–Indians follow a vegetarian diet for both cultural and religious reasons. Rice and wheat are staples of the Indian diet, whereas fruit and vegetable intake can be low. Many vegetarian foods and baked goods are prepared with coconut and palm oil, butter, ghee (clarified butter), vanaspati (hydrogenated fat), and coconut milk, which are very high in saturated and *trans* fats. Asian–Indians living in the United States tend to have a high carbohydrate consumption, which is associated with elevated triglyceride levels. These populations may also have a low dietary intake of omega-3 fatty acids.

Part 3: Medical Treatment and Nutrition Therapy

5. Based on MG's current lab results, what are the most appropriate next steps in his management?

The management plan should utilize a multidisciplinary approach with both medical and nutritional interventions. First, MG should be educated on the significance of his current laboratory results and physical exam findings. He should be told of his increased risk of CHD based on his family history, laboratory values, and diagnosis of metabolic syndrome. He should also be counseled on his risk for the development of diabetes, based on his current fasting glucose level and maternal family history. Such discussions must emphasize that most of his risk factors are modifiable, with the exception of his family history of premature CHD and diabetes and his elevated Lp(a) level. The conversation must also highlight the dietary and lifestyle factors that have contributed to his current state. An assessment of MG's willingness to change is an important next step, as his stage of change will guide advice and management (Table 6-6). Assuming that MG is motivated to change, the next step would be to create a nutritional treatment strategy with the help of a nutritionist. As MG's mother is the primary cook for the household,

she should be included in these counseling sessions.

MG would benefit from a diet low in saturated fats, devoid of *trans* fats, and restricted in total calories to achieve weight loss and improve in his cholesterol level. He should be recommended to substitute lower fat dairy products for those that are high in saturated fat, such as cheese and whole milk yogurt. Increasing his total and soluble fiber intake by substituting whole grain starches for white bread and white rice would also be advantageous. The predominant cooking oil used in food preparation should be high in monounsaturated fat such as olive or canola oil. He should make other dietary substitutions that would align his diet with the 2013 ACC/AHA guidelines on lifestyle management to reduce cardiovascular risk or the Mediterranean style diet, if culturally acceptable. An effort should be made to increase his fruit and vegetable intake, as this would increase his fiber consumption, decrease the energy density of his diet, and help him to control his weight. Finally, MG should be counseled to avoid drinking sugar-sweetened beverages such as regular soda and fruit juice. These beverages, which contain refined sugars, contribute to increased calories, triglyceride and glucose levels, and risk of CHD and diabetes. As his cholesterol levels are elevated, a dietary portfolio of cholesterol-lowering foods could also be recommended because it has been

shown to improve lipid profiles. Food items included in the portfolio plan include plant sterols, viscous fibers from oats, barley, and psyllium, soy from soymilk and tofu, and nuts. Consumption of peas, beans, and lentils should also be encouraged. MG and his mother should also be provided recipes for healthier versions of their traditional Asian–Indian cuisine (Table 6-9).

Table 6-9 Healthier Versions of Traditional Asian Indian Cuisine

Source: Wahida Karmally, DrPH, RD, CDE, CLS, FNLA. 2014. Used with permission.

Traditional Food	**Healthier Way of Eating**
Meat, poultry, fish, and eggs fried in ghee, butter, coconut oil, palm kernel oil, or hydrogenated fats and oils.	Bake, roast, broil, grill, or sauté. Remove skin from chicken before eating. Fry with canola, olive, or corn oil instead. Limit to ¼ cup oil.
Legumes and vegetables prepared with oil, butter, or cream yogurt to enhance flavor.	Use almond paste or non-fat yogurt in place of cream and butter. Season with onion, garlic, spices, or

Traditional Food	Healthier Way of Eating
	low-sodium chicken broth to enhance flavor.
Rice (white) dishes or wheat (refined) preparations deep fried or prepared with large amounts of ghee, butter, and hydrogenated fats (vanaspati) containing *trans* fatty acids.	Use brown rice and whole grain wheat. Boil or bake instead of frying. Fry with canola, olive, or corn oil or *trans*-free margarine instead of solid or hydrogenated fat. Limit to ¼ cup oil.
Whole milk/cheese/ cream/yogurt used to prepare rice dishes, vegetables, desserts, and shakes. Yogurt cheese (panir) prepared with whole milk.	Substitute low-fat or non-fat milk, milk powder, cheese, cream, yogurt, buttermilk, or soymilk instead.
Omelets and desserts prepared with egg yolks.	Substitute egg whites for whole eggs.
Snacks such as fried legumes.	Snack on fruits, rice cakes, and puddings made

Traditional Food	Healthier Way of Eating
	with low-fat milk instead. Use oat and whole wheat cereal to prepare savory snacks.
Salt used to enhance flavor.	Use herbs (e.g., cilantro, mint), spices (e.g., cumin, black pepper, cardamom, cinnamon), or flax seed powder to enhance flavor.

As MG's blood pressure is in the hypertensive range, he should also be counseled to follow the Dietary Approaches to Stop Hypertension (DASH) diet to aid in blood pressure control (Tables 6-4 and 6-5). MG should be counseled on daily physical activity to reduce his risk for CHD and diabetes. He should undertake a minimum of 150 minutes of moderate-intensity aerobic activity, such as brisk walking, every week and would benefit from some regular resistance exercise as well.

In addition to the nutrition and lifestyle changes recommended above, MG should be considered for medical therapy. As this patient

has expressed his wishes to start with lifestyle changes, he should be given a brief trial period before cholesterol-lowering medication is prescribed. However, initiation of an HMG CoA reductase inhibitor, or statin medication, would be reasonable based on multiple factors. First, MG's LDL-C is elevated above the target of <130 mg/dL, which is based on his having two or more major risk factors. Secondly, studies have demonstrated a reduced incidence of major cardiovascular events in patients, like MG, with hsCRP levels above 2.0 mg/L who are treated with statin therapy. As MG's triglyceride level is above his goal, it could be recommended that he begin taking fish oil supplements. Additionally, an antihypertensive medication, such as an angiotensin converting enzyme inhibitor (ACE-Inhibitor), should be considered to control his elevated blood pressure. Finally, low-dose aspirin could be considered for MG to reduce his cardiovascular risk, although the largest benefit is generally seen in men over the age of 45.

The management of MG's elevated Lp(a) level is a secondary priority after maximally lowering his elevated LDL-C. Additionally, treatment should only be considered in patients with levels greater than 50 mg/dL. Currently, niacin is the only agent shown to consistently reduce Lp(a) levels. Dosing at 1 to 3 g/day can reduce Lp(a) levels by 30 to 40% in a dose-dependent manner while also reducing LDL-C, total

cholesterol, and triglycerides and raising HDL-C levels. However, it is unknown if lowering Lp(a) with niacin leads to improved CHD outcomes and caution must be used as niacin can raise glucose levels.

Before a decision on medical treatment is made, a discussion with MG about his wishes for such medication is warranted. As he voiced a preference not to take medications on his initial clinic visit, his current wishes should be revisited. Follow-up appointments with both the physician and registered dietitian should be scheduled for 8 to 12 weeks to monitor changes in serum lipids, glucose, blood pressure, and weight and to reassess his medications and dietary adherence. Lastly, MG should complete a food and activity log that can be reviewed by the physician/nutritionist at subsequent appointments to identify both progress and areas needing improvement.

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7
Gastrointestinal Disease

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Objectives*

To increase healthcare providers' knowledge on the role of nutrition therapy in gastrointestinal diseases.

To incorporate nutrition into the medical history, review of systems, and physical examination of patients with gastrointestinal diseases.

To identify the causes of malnutrition in inflammatory bowel disease, liver diseases, and malabsorption syndrome.

To describe why sodium and fluid restriction may be necessary for patients with liver disease.

To explain the association between diet and lower esophageal sphincter pressure in patients with gastroesophageal reflux disease.

*Source: Objectives for chapter and cases adapted from the *NIH Nutrition Curriculum Guide for Training Physicians*. (www.nhlbi.nih.gov/funding/training/naa)

Introduction

Digestive disorders are often complex illnesses requiring a multi-faceted approach. Rarely is there one solution that will work for all patients. In addition to medical treatment of the underlying disease, nutrition therapy can improve gastrointestinal (GI) symptoms. The impact of dietary manipulations, such as dietary fiber in irritable bowel syndrome or a gluten-free diet in celiac disease, demonstrates the intricate role that nutrition therapy plays in the management of chronic digestive disorders. GI complaints, even seemingly mild, can negatively impact patients' quality of life. Healthcare providers often evaluate and treat digestive disorders, and patients seek care for various symptoms from food intolerances to chronic digestive diseases. Clinicians must determine whether symptoms such as abdominal pain, nausea, and altered bowel

habits are caused by dietary intolerance, underlying GI pathology, or anxiety. The role of the health professional is to differentiate between more benign versus potentially life-threatening GI symptoms. Once a diagnosis is found, the patient becomes a partner in the management of his/her GI problem. Depending on the diagnosis and the severity of disease, the patient may need a referral to a specialist such as a gastroenterologist or hepatologist. Management of these disorders frequently includes some degree of dietary manipulation. Some dietary guidelines, such as a diet rich in whole grain foods, can be useful across the spectrum of most GI symptoms, whereas certain disorders require specific nutritional modifications. Clinicians with a strong understanding of the role of nutrition in GI illnesses will be well suited to optimize disease management and improve patients' quality of life.

Digestion and Absorption

Nutrient digestion requires a controlled process of mechanical and chemical breakdown, with subsequent enzymatic and secretory responses that facilitate nutrient absorption. Carbohydrate digestion requires adequate amylase to convert starches into disaccharides, which then undergo further hydrolysis into monosaccharides. Monosaccharides are absorbed through a process of either diffusion

or active transport. Dietary fats require the action of lipase, which results in the hydrolysis of free fatty acids from triglycerides. Once hydrolyzed, monoglycerides, glycerol, and fatty acids, as well as fat-soluble vitamins, undergo emulsification by bile acids in order to promote diffusion across the cell membrane of the enterocyte. Protein digestion requires adequate gastric acidity, which activates pepsin and other proteases, allowing breakdown of proteins into peptides and amino acids. Defects in any of the mechanical, chemical, or secretory processes involved in digestion can result in nutrient maldigestion and malabsorption.

Malabsorption

Inadequate nutrient absorption can occur as a result of many diseases of the digestive system. In order to effectively treat the symptoms of malabsorption, one must first identify the cause, after which appropriate treatment can be implemented. The management of disorders of carbohydrate, protein, and fat malabsorption can often be improved with appropriate nutrition therapy.

Carbohydrate Malabsorption

Lactose intolerance is the most common form of carbohydrate malabsorption and has been estimated to affect approximately 70 to 75 percent of the world's population. Lactose is a

disaccharide sugar that requires hydrolysis by the enzyme lactase into glucose and galactose for absorption. Lactose malabsorption or intolerance is usually caused by suboptimal activity or deficiency of lactase. Characteristic symptoms of lactose intolerance include bloating, abdominal pain, flatulence, borborygmi, nausea, or diarrhea after consumption of dairy foods. These symptoms are caused by the passage of undigested lactose into the colon where it is metabolized by colonic bacteria, producing excess fluid and gas in the bowel. In some cases, individuals will have delayed GI motility possibly due to the result of methane production. These patients will often present with constipation. The diagnosis of lactose intolerance can frequently be made by improvement or resolution of symptoms after temporary avoidance of dairy foods. It is sometimes necessary to confirm the diagnosis with a lactose tolerance test or lactose hydrogen breath test if symptom etiology is present, as other GI disorders, such as irritable bowel syndrome, inflammatory bowel disease, or celiac disease may be suspected.

Lactase production naturally declines as one ages. Lactose expression on the mucosal surface of the human enterocyte is at its peak at 34 weeks gestation, and begins to decline within the first few months of life. Thus, while lactase deficiency may be pathological in infants, it is normal in most teens and adults. Secondary

lactase deficiency can occur as a result of certain GI disorders including bacterial overgrowth, mucosal injury, or inflammatory bowel diseases. Effective treatment of these underlying disorders may improve lactose tolerance.

The prevalence of lactase deficiency among populations suggests a certain genetic predisposition. Lactose malabsorption occurs in approximately 5 to 20 percent of Caucasians, but may be as high as 50 to 80 percent in Latinos, 60 to 80 percent among African–Americans and Ashkenazi Jews, and nearly 100 percent among Asians and American Indians. The goal of treatment for lactose intolerant individuals is to improve symptoms while preventing secondary bone disease by supporting adequate calcium intake. Lactose-free dairy foods and lactase supplements make it possible for individuals with lactose intolerance to consume adequate dietary calcium from dairy foods. For patients with lactose intolerance, the severity of symptoms is often related to the quantity of lactose consumed. Given the high calcium and vitamin D content in dairy foods, all individuals, regardless of lactose malabsorption, should be encouraged to include three servings of low-fat dairy foods in their diet every day.

Lactose hydrolyzed products can be well tolerated in those patients who are lactose intolerant. In addition, fermented dairy foods such as yogurt, fermented cheese, and fermented milk contain lactic acid bacteria, which improve tolerance and result in decreased symptoms related to lactose malabsorption. There may be some benefit from probiotics in patients with lactose malabsorption, possibly because microbial lactase is present within lactic acid bacteria in the probiotics themselves; however, research is ongoing in this area. In addition, non-dairy foods and beverages enriched with calcium, such as soy, hemp, almond, coconut and rice milk, and yogurt are good options for patients who are lactose intolerant. Ingredients that may not be well tolerated by persons with lactose intolerance include:

whey or lactose,

non-fat milk solids, buttermilk, or malted milk,

margarine or sweet or sour cream.

Lactose intolerant patients who are unable to tolerate adequate intake of dairy foods should be encouraged to consume calcium-fortified foods or take a 1000 mg calcium supplement once a day to ensure adequate recommended intake. The DRI for men and women age 19 to 50 is 800 mg/day and 1000 mg/day for those over 51 years of age. Table 2-2 identifies the recommended daily intake of calcium for all age

groups. Food sources of calcium are shown in Appendices G and H.

Protein Malabsorption

Celiac disease, also termed gluten intolerance, is a small bowel absorption disorder characterized by chronic inflammation of small bowel mucosa, villous atrophy, and crypt hyperplasia. It is caused by intolerance to gliadin, the protein fraction of wheat, rye, and barley in genetically predisposed individuals. The prevalence of celiac disease is approximately 1 percent in the general United States population. However, the disorder remains largely under-diagnosed. Frequently there are delays in diagnosis even after a patient seeks medical care for symptoms. Currently the only treatment for celiac disease is a life-long adherence to a gluten-free diet. Disease presentation is variable and onset of celiac disease can occur at any age. Presenting symptoms of celiac disease can be GI in nature (diarrhea, weight loss, vomiting, abdominal pain, bloating, distension, anorexia, and constipation) or may be less specific and include iron deficiency anemia, folic acid or vitamin B_{12} deficiency, osteoporosis or osteomalacia, infertility, or elevated transaminases. Neurological symptoms, such as ataxia, have also been traced to gluten intolerance. In recent years “silent” celiac disease or “non-celiac” gluten sensitivity has

been described. Patients may present with non-specific symptoms, such as those associated with irritable bowel syndrome, or extra-GI symptoms such as headaches (Chapter 7: Case 3).

Testing for celiac disease should be pursued in patients with persistent GI symptoms, such as chronic diarrhea, malabsorption, weight loss, or abdominal distension. Testing should also be considered in patients with unexplained iron deficiency anemia, vitamin deficiencies, infertility, or elevated transaminases. Recent research suggests a higher prevalence of celiac disease among patients with osteoporosis but conflicting data have been presented. High-risk populations for celiac disease include those with autoimmune endocrinopathies (especially type 1 diabetes mellitus), first and second-degree relatives of persons with celiac disease, and Turner syndrome. The diagnostic evaluation of celiac disease should occur while the patient is on a gluten-containing diet and should include serologic testing followed by a small bowel biopsy if serologic testing is positive. The National Institutes of Health (NIH) consensus statement on celiac disease recommends the IgA antihuman tissue transglutaminase (TTG) and IgA endomysial antibody immunofluorescence (EMA) tests to avoid false negative results in IgA deficient patients. Positive results warrant small bowel biopsies for histologic confirmation.

Recommendations for people with celiac disease are shown in Table 7.1.

Table 7-1 Key Recommendations for Celiac Disease

Consultation with a registered dietitian specializing in celiac disease
Education about the disease
Lifelong adherence to a gluten-free diet
Identification and treatment of nutritional deficiencies
Access to an advocacy group
Continuous follow-up by a multidisciplinary team

Clinical evaluation should include an assessment for vitamin and mineral deficiencies. Initial blood work should include liver function tests, serum iron or ferritin, serum or red blood cell folate, vitamin B_{12}, calcium, and vitamin D. A DEXA scan should also be considered in patients diagnosed with celiac disease to screen for osteoporosis. In addition, serum albumin levels should be tested, as low levels may reflect small bowel protein loss. Serum albumin can also serve as one component of the overall assessment of nutritional status and be used as a baseline to monitor improvement as treatment progresses. Identified deficiencies should be replenished,

but long-term supplementation is likely not required once the disease is under control. Annual evaluation of vitamin status should be done as deficiencies of folate and vitamin B_6 have been documented in patients on long-term, gluten-free diets.

The gluten-free diet excludes all foods containing wheat, rye, and barley. Recent evidence suggests that patients can safely consume small amounts of oat-containing foods and gluten-free labeled oatmeal; however, questions about safety remain with an oat-containing, gluten-free diet. Some patients report worsened GI symptoms when including oats in the diet, even if mucosal integrity is maintained. the principles of a gluten-free diet are described in Table 7-2. Patients should be advised to look for the many "gluten-free" products, which are increasingly available in supermarkets and natural foods stores.

Table 7-2 Gluten-Free Diet Guidelines

Source: The Celiac Disease Foundation and the Gluten Intolerance Group.

Celiac disease, sometimes called gluten intolerance, is a disorder that prevents wheat products from being properly digested. Gluten is found in most grain products, including wheat, barley, and rye. The list below provides basic guidelines for a gluten-free diet. It is important to get additional education from a

nutritional professional who specializes in celiac disease.

Allowed Foods

Allowed grains/flours: rice, corn, soy, potato, tapioca, beans, garfava, sorghum, quinoa, millet, buckwheat, arrowroot, amaranth, tef, nut flours, pure uncontaminated oats, and flax.

Plain meat, chicken, fish, fruits and vegetables do not contain gluten and can be safely consumed.

Foods Not Allowed

Grains/flours: wheat (including durum, semolina, kamut, spelt), rye, barley, triticale in any form, graham, farina, matzoh, couscous, commercial oats may not be recommended. Versions of oats that are gluten free are available and may be more safe.

Foods that often contain gluten: breading and coating mixes, broth or soup bases, communion wafers, croutons, imitation bacon or seafood, marinades or sauces, salad dressings, processed meats, self-basting poultry, soy sauce, stuffings, thickeners.

Read ingredient lists on all food labels. The following list includes ingredients which may contain gluten: brown rice syrup, caramel color, dextrin, flour or cereal products, malt or malt flavoring, malt vinegar, modified food starch, soy sauce or soy sauce solids.

Check with your pharmacist about gluten content of medications or products like mouthwash.

After diagnosis, patients should always be referred to a registered dietitian for assessment of nutritional deficits, degree of malnutrition, and education on a gluten-free diet. In addition, information on patient resources and support groups should be provided. Some studies examining the nutritional quality of gluten-free diets demonstrated that despite adherence to dietary restrictions, overall diet quality tends to be poor. The majority of women consume sub-optimal intakes of whole grain foods, fiber, calcium, and iron. While men were more likely to consume adequate amounts of fiber and iron, diet choices remained low in calcium and whole grain foods. In addition, gluten-free diets tended to be higher in concentrated sweets and soft drinks. Some studies have even shown a trend towards increased BMI, rather than weight loss, after the gluten-free diet has been implemented, but this may be due to improved calorie and nutrition absorption. This data has lead some healthcare professionals to question the long-term adequacy of the gluten-free diet and the potential impact it may have on chronic medical conditions such as heart disease and diabetes mellitus. It should also be noted that while most wheat-based products in the United States are fortified with vitamins and minerals,

gluten-free products are usually not. To improve diet quality, patients with celiac disease should be encouraged to consume 6 to 11 servings of whole grain or enriched gluten-free grains and three servings of gluten-free dairy foods per day. In addition, gluten-free vitamins are commercially available, and these may aid those with celiac disease in meeting daily vitamin and mineral requirements. All healthcare providers, in partnership with gastroenterologists and dietitians, should reinforce the need for life-long diet adherence to the gluten-free diet in patients with celiac disease, particularly after symptom resolution.

Fat Malabsorption

Fat malabsorption is associated with many GI disorders and frequently presents with symptoms of steatorrhea. Fat malabsorption may occur in cases of impaired luminal transport of products of digestion, and is often seen in disorders causing widespread mucosal injury, such as celiac disease, inflammatory bowel disease, and bacterial overgrowth. In such cases, management of the underlying mucosal disorder is the treatment of choice. Steatorrhea can also be caused by maldigestion of fats, due to lipase deficiency or a lack of emulsification, as seen in chronic pancreatitis, cystic fibrosis, and bile salt deficiencies. In addition, fat malabsorption can be seen in

wasting syndromes, such as HIV wasting, or can be iatrogenic in nature, such as post-gastric bypass or extensive resection of the small bowel, particularly the terminal ileum. Untreated fat malabsorption may result in weight loss, failure to thrive, osteomalacia, bone pain, infertility, dysmenorrhea, and amenorrhea. In addition, fat-soluble vitamin deficiencies (A, D, E, and K) may occur.

Adoption of a low-fat diet may aid in symptom management. Patients following a low-fat diet may have difficulty consuming adequate calories to maintain weight. Additional calories can be added to the diet with the use of medium chain triglycerides (MCT). These provide 115 calories per tablespoon. MCT oil is rapidly hydrolyzed and absorbed directly into portal circulation and therefore does not require bile salts or micelle formation for digestion. Factors limiting the use of MCT oil include poor palatability and possible side effects such as nausea and vomiting; therefore, patients are typically unable to consume more than 3 to 4 tablespoons per day. Oral nutrition supplements with added MCT oil are commercially available and may provide some benefit. Unfortunately, these products tend to be very expensive and they are often not covered by medical insurance. For patients with pancreatic exocrine insufficiency, supplemental pancreatic enzymes may be necessary. Recent evidence suggests that patients with chronic

pancreatitis may benefit from early screening for fat malabsorption. These patients may present with post-prandial abdominal pain resulting in reduced caloric intake even in the absence of clinically significant steatorrhea. Conjugated bile acids may improve digestion of fat in patients with a history of ileal resection.

Fat malabsorption places patients at risk for vitamin and mineral deficiencies, specifically fat-soluble vitamins (vitamins A, D, E, and K). Monitoring for fat-soluble vitamin deficiencies should occur on an annual basis, with aggressive repletion as needed. Provision of fat-soluble vitamins in a water-miscible form may allow patients to have better vitamin absorption. Deficiencies of calcium, magnesium, zinc, and iron may also be present due to impaired absorption and increased intestinal losses and should be aggressively repleted.

Gastric Disorders

Gastroesophageal Reflux Disease (GERD)

Gastroesophageal reflux disease (GERD) is characterized by a burning sensation in the substernal area caused by abnormal reflux of acidic gastric contents into the esophagus. This condition has been reported to affect up to 20 percent of the population. As many as one in

seven persons may suffer from daily symptoms of “heartburn”, which can negatively affect patients' quality of life. Although the underlying causes of GERD are not known, the pathogenesis has been related to altered and intermittent relaxation of the lower esophageal sphincter. Over the long term this can result in esophageal mucosal damage and erosion, and may increase risk of complications, such as peptic stricture, chronic esophagitis, Barrett's esophagus, and development of esophageal adenocarcinoma.

Obesity is considered a significant risk factor for development of GERD. Increasing abdominal circumference is associated with increased intra-abdominal pressure and lower esophageal sphincter relaxation, which may contribute to the development of GERD. The risk of GERD increases with increasing BMI. Other lifestyle factors that have been positively associated with the incidence of GERD include poor quality of sleep, regular use of non-steroidal anti-inflammatory drugs (NSAIDs), heavy alcohol intake, and irregular dietary habits. Recent evidence has also suggested a possible association by *Helicobactor pylori* infection and gastroesophageal reflux symptoms.

Specific dietary factors have been evaluated as a cause of reflux disease. Although limited data are available, spicy foods, acidic foods, high-fat

foods, chocolate, mint, and caffeine (coffee, tea, cola) have been associated with GERD symptoms. High-fat intake, particularly saturated fat, has also been found to increase the risk of GERD. High-fat foods or large meals delay gastric emptying time, which can lead to increased reflux of gastric contents. There is some evidence that increasing dietary fiber may have a protective effect against reflux. The mechanism is unclear, but may be related to fiber's role as a nitrite scavenger in the gut as nitrites have been implicated in contributing to decreased lower esophageal sphincter tone.

Nutrition therapy for patients with GERD should be focused on minimizing reflux symptoms. Patients may have varying degrees of sensitivity to different high-risk foods. The goals of therapy should be to prevent relaxation of the lower esophageal sphincter, reduce volume of gastric acid, and prevent esophageal irritation. In addition, encouraging patients to gradually increase their intake of whole grain foods may reduce their reflux symptoms. Table 7-3 lists dietary recommendations for patients with GERD.

Table 7-3 Key Dietary Recommendations for Gastroesophageal Reflux Disease

Source: Lisa Hark, PhD, RD and Darwin Deen, MD, 2014. Used with permission.

Limit intake of high fat, high calorie meals.

Avoid large meals during a single sitting.

Eat smaller meals more frequently during the day.

Drink most fluids between meals rather than with meals.

Increase intake of high fiber foods (fruits, vegetables, and whole grains).

Sit up or take a walk after eating rather than lying down.

Avoid eating at least 2 hours before bedtime if possible.

Limit foods that worsen symptoms, such as alcohol, chocolate, coffee, or caffeine-containing beverages, mints, citrus fruits, tomato products, spicy foods, or carbonated beverages.

Peptic Ulcer Disease

The management of peptic ulcer disease (PUD) has changed significantly in recent decades. Early treatment of PUD included a bland diet as a mainstay of treatment. It is now understood that most gastric and duodenal ulcers are caused by damage to the gastric mucosa, and the most common causative agents are the bacteria *Helicobacter pylori*, and the overuse of NSAIDS. Treatment of the underlying cause of

PUD may result in resolution of symptoms of PUD.

Gastric acid secretion occurs as a result of vagal stimulation of the parietal cells by the sight or taste of food. Although gastric acid is no longer thought to be responsible for ulcer development, reduction in gastric acid may facilitate healing and decrease abdominal discomfort. Certain foods are known to increase gastric acid secretions including coffee, tea, colas, and alcohol. No differences have been found in randomized controlled trials that compared restricted diets with unrestricted diets in the resolution of ulcers. The focus of nutrition therapy should be based on individual tolerance and patients should be encouraged to avoid their individual triggers. Foods that are often poorly tolerated include coffee, orange juice, fried foods, spicy foods, and fruits. After treatment of a *Helicobactor pylori* infection, improved tolerance of these trigger foods has been demonstrated. There is some evidence that malabsorption of certain vitamins and minerals may occur in patients with peptic ulcer disease. Specifically, intestinal absorption of iron, vitamin B_{12}, folic acid, and vitamins A, C, and E have been reported to be reduced. This may be due to modified intragastric pH seen in PUD. The clinical significance of this is uncertain. However, the clinician should consider possible testing for these deficiencies in patients with PUD who demonstrate clinical

symptoms of vitamin and mineral deficiencies. Table 7-4 outlines key dietary recommendations for symptom management of PUD.

Table 7-4 Key Dietary Recommendations for Peptic Ulcer Disease

Source: Lisa Hark, PhD, RD and Darwin Deen, MD, 2014. Used with permission.

Limit intake of caffeine-containing beverages and foods including coffee, tea, iced tea, colas, and chocolate.
Avoid alcohol, especially on an empty stomach.
Eat three small meals per day.
Don't skip meals.
Avoid eating spicy foods, fried foods, and citrus fruits as these foods may worsen symptoms.
Avoid other foods or drinks that cause discomfort.

Small and Large Bowel Disorders

Diarrhea

Diarrhea is characterized by increased frequency of loose or watery stools, and may be acute or chronic in nature most often due to

self-limited viral or bacterial infections. Acute diarrhea often resolves on its own, whereas chronic diarrhea lasts for more than 4 weeks. Up to 5 percent of the population may suffer from chronic diarrhea. Chronic diarrhea occurs in many underlying GI illnesses, and therefore appropriate evaluation of symptoms is vital. Malabsorptive disorders, such as lactose intolerance, celiac disease, or inflammatory bowel disease may result in chronic diarrhea. Assessment should identify the frequency of stools, duration of symptoms, and potential weight loss. Stool characteristics (i.e., watery, mucousal, or fatty) can aid in further evaluation of the pathogenesis of diarrhea. Secretory diarrhea occurs as a result of a disruption in electrolyte transport within the epithelium with resultant diarrhea. It may be caused by enterotoxins, intestinal resections or mucosal disease, or mesenteric ischemia due to atherosclerosis. Osmotic diarrhea occurs after ingestion of poorly absorbed cations and anions, such as sorbitol or sugar alcohols, magnesium sulfate, or phosphate, or may be related to deficiencies of disaccharidases, as in lactase deficiency.

In patients with chronic diarrhea, a comprehensive evaluation is necessary to determine the underlying cause. Management of diarrhea to prevent electrolyte abnormalities and potential weight loss is vital. Adequate fluids are also necessary to prevent

dehydration, and oral rehydration solutions are beneficial to compensate for electrolyte losses. While diarrhea may be worsened by the intake of insoluble dietary fibers, soluble fibers may aid in improvement as they form a gel within the intestinal lumen, thus slowing intestinal transit. Sources of soluble and insoluble dietary fiber are reviewed in Table 7-5. After diarrhea resolves, patients may tolerate gradual reintroduction of insoluble dietary fiber, such as whole grain breads and cereals. Other foods that may worsen diarrhea, such as lactose-containing foods or high-fat foods, should be avoided until diarrhea begins to resolve. Evidence suggests that incorporating functional foods containing live, active bacterial cultures, such as yogurt, or probiotic supplements may be helpful in treating diarrhea associated with antibiotic use, acute infectious diarrhea, travelers' diarrhea, and diarrhea-predominant irritable bowel syndrome. The most studied probiotic strains are *Lactobacillus, Bifidobacterium*, and *Saccharomyces*. However, recent studies have shown adverse outcomes associated with administration of probiotics to critically-ill hospitalized patients. The use of probiotic supplementation in this population is not recommended.

Table 7-5 Dietary Sources of Soluble and Insoluble Fiber

Source: Lisa Hark, PhD, RD and Darwin Deen, MD, 2014. Used with permission.

Soluble Fiber	**Insoluble Fiber**
Apples Citrus fruits Strawberries Carrots Oats Beans Legumes Barley Fiber supplements: Psyllium (Metamucil) Guar gum (Benefiber)	Whole wheat flour Bran Vegetables Whole grains Wheat Fruits with edible seeds (strawberries, blueberries, etc.)

A thorough medication history can identify potential drugs that may exacerbate diarrhea. Sorbitol or lactulose-containing medications should be adjusted if possible. Significant amounts of sorbitol and other sugar alcohols found in low carbohydrate or sugar-free foods can also play a role. Patients should be encouraged to eliminate these foods temporarily and assess for symptom resolution.

Constipation

Constipation is a common complaint with prevalence estimates of 12 to 19 percent in North America. Risk factors for constipation include advancing age and female gender, with women being twice as likely as men to report symptoms. Constipation is defined as less than two to three bowel movements per week and can be classified as primary constipation, which is caused by disordered movement of stool in the colon, or secondary constipation, which is caused by various systemic disorders or medications. Because the causes of constipation are varied, it is important to rule out structural causes of constipation as well as organic disease.

Nutrition therapy for constipation focuses on increasing fluid intake and gradually increasing fiber intake. It is important that patients are instructed to make gradual dietary changes, as rapid fluctuations in dietary fiber can worsen symptoms of constipation and abdominal discomfort. There is some debate over the efficacy of fiber in treatment of constipation. Recent studies have not shown an association between increasing fiber intake and improvement in symptoms of constipation. Some studies have even shown an increase in abdominal discomfort, such as bloating and distention, with an increase in fiber. This has lead healthcare professionals to recommend a

moderate fiber intake in the form of soluble fiber for patients with constipation, in order to avoid a worsening of abdominal symptoms. Regardless of this recent debate, *United States Dietary Guidelines* recommend 25 to 35 g of fiber daily including fruits, vegetables, whole grains, legumes, and nuts. Clinicians should base their recommendations for fiber intake on individual patient tolerance. Treating constipation in the elderly, another high-risk group, should also involve dietary management that promotes appropriate increases in fluid and fiber intake. Assessment for other contributing factors including co-morbid conditions, decreased mobility, and inability to sit on the toilet should be considered (in the case of bed-bound patients) and should be evaluated by healthcare professionals (see Appendix O for high fiber foods).

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD), including both Crohn's disease and ulcerative colitis, are idiopathic, chronic, inflammatory conditions affecting the GI tract. Crohn's disease can involve any part of the digestive tract, while ulcerative colitis primarily involves the colon. Because of the chronic involvement of the GI tract, many patients with IBD, particularly those with Crohn's disease, are at risk for specific nutritional deficiencies and malnutrition. Enteral nutrition may also be

employed as a primary treatment modality for individuals with Crohn's disease. Therefore, careful attention to diet and in-depth involvement of a gastroenterologist and registered dietitian are important components of the care of individuals with IBD. Dietary interventions in IBD should focus on maintaining or improving nutritional status through adequate intake, and avoiding foods that worsen symptoms. Table 7-6 outlines nutritional concerns, which should prompt involvement of a registered dietitian experienced in the management of individuals with IBD.

Table 7-6 Nutritional Concerns in Patients with Inflammatory Bowel Disease

Source: Julie Vandelpool, RD, 2014. Used with permission.

Weight loss, growth failure (weight), short stature (height).
Pregnant women not gaining weight appropriately.
Following low-residue diet for more than 6 weeks.
Presence of comorbidities (diabetes, celiac, CAD, liver disease).
Suspected or confirmed eating disorder.
Poor appetite.

Meal planning assistance.

Has or is at risk for nutrient-deficiencies due to malabsorption (especially fat) , restriction of a specific food group, or medication (e.g. prednisone, proton pump inihibitor).

Excessive weight gain secondary to medication (prednisone).

Protein-calorie malnutrition is common among patients with IBD and correlates with disease activity, which may be mediated by pro-inflammatory cytokines such as IL-1, IL-6, and tumor necrosis factor alpha. Nutrition assessment is essential because of the severe consequences of malnutrition, including growth failure and developmental impairment in children and teenagers, impaired wound and intestinal healing, weight loss with loss of muscle mass, metabolic bone disease, and increased susceptibility to infection in children and adults. In addition, a malnourished patient with IBD may present with defects in GI function that further limit the absorption and utilization of nutrients.

Causes of Malnutrition

Malnutrition occurs in patients suffering from IBD as a consequence of decreased dietary intake, increased nutrient losses, and increased nutrient requirements.

Decreased Dietary Intake

Inadequate dietary intake and poor appetite are the most important factors contributing to poor nutritional status in patients with IBD. GI symptoms such as nausea, diarrhea, and recurrent abdominal pain may lead to a decrease in appetite and a fear of eating. Disease-specific complications such as oral aphthous ulceration, gastritis, small intestinal inflammation, or intestinal strictures, may also contribute to inadequate dietary intake or increased symptoms. For example, patients with Crohn's disease may experience impaction of high-fiber foods in an inflamed or fibrotic section of bowel, which can precipitate an obstruction. High-fat foods or spicy foods may worsen diarrhea. Some medications that may be used to treat IBD such as metronidazole, methotrexate, or sulfasalazine, may also decrease appetite. To maximize nutrient intake, unwarranted dietary restrictions should be avoided.

Increased Nutrient Losses

In patients with Crohn's disease, small and large bowel inflammation, and/or multiple bowel resections can decrease the absorptive surface area of both the small and large intestine and cause malabsorption of essential nutrients. Resection of the ileum can cause bile salt deficiency, resulting in steatorrhea or fat malabsorption and subsequent deficiency of

fat-soluble vitamins A, D, E, and K. Small intestinal bacterial overgrowth may also interfere with nutrient utilization.

Vitamin B_{12} is coupled with intrinsic factor, which is secreted by the parietal cells of the stomach. Because the vitamin B_{12}–intrinsic factor complex is absorbed in the terminal ileum, complete ileal resection or prolonged inflammation of the terminal ileum may result in a vitamin B_{12} deficiency that requires treatment via subcutaneous or intramuscular injections, nasal spray, or sublingual vitamin B_{12}.

IBD also can result in a protein-losing enteropathy through excessive intestinal transudate (movement of protein rich fluids through the inflamed bowel wall). In the case of Crohn's disease, protein-rich fluid can also be lost through fistulas, particularly high-output fistulas. Severe diarrhea causes depletion of electrolytes, minerals, and trace elements, such as zinc. GI bleeding can also contribute to iron deficiency. Prednisone, which is frequently used during IBD flares, reduces calcium absorption and increases protein breakdown.

Increased Nutrient Requirements

The inflammatory process of IBD may increase resting energy expenditure, thereby contributing to weight loss and depletion of fat stores when patients do not consume adequate

calories and protein. Patients with fever, infection, sepsis, and those undergoing surgery also have greater dietary requirements compared to patients who are less severely ill. Increased intestinal cell turnover can also raise nutrient requirements in patients with IBD.

Nutrition and Pathogenesis of IBD

With an observed increase in incidence of IBD, the potential role of diet in the pathogenesis of IBD has gained increasing attention. Recent studies have focused on dietary fat intake and the risk of IBD development. In a recent prospective study from Europe, individuals with a higher intake of linoleic acid had an increased risk of developing ulcerative colitis. Linoleic acid is metabolized to arachadonic acid, which can then be used to generate pro-inflammatory mediators. Linoleic acid is present in various dietary sources, including red meat, cooking oils, and margarines. A separate European study has illustrated that a diet high in animal protein is associated with an increased risk of development of IBD. Dietary sources including meat and fish, but not eggs or dairy products, was associated with an increase in development of IBD.

Nutrition Therapy for IBD

While dietary factors may play into the risk of development of IBD, no specific diet has been shown to prevent or treat IBD. However, some

diet strategies help control symptoms. Nutritional recommendation must take into account the patient's digestive and absorptive capabilities. They also depend on whether the patient is hospitalized in an acute flare-up or asymptomatic. Therefore, goals of nutrition therapy for patients with IBD are shown in Table 7-7.

Table 7-7 Nutrition Therapy Goals for Patients with IBD

Source: DeLegge.

Prevent symptoms associated with malabsorption, such as diarrhea.
Correct and prevent nutritional deficiencies.
Promote healing of the intestinal mucosa.
Minimize stress on inflamed or narrowed segments of intestine (Crohn's disease).
Promote normal growth and development in children and teenagers.

Oral nutritional repletion may be difficult to achieve during symptomatic flares of active IBD since most patients' symptoms worsen both during and following meals. To decrease both the symptoms associated with eating and bowel activity during the healing process, patients hospitalized for IBD are sometimes placed on bowel rest. Prolonged bowel rest without nutrition support can lead to nutritional

depletion. Any hospitalized patient on bowel rest who is not anticipated to resume oral repletion within 7 days should be considered for total parenteral nutrition (TPN) (Chapter 13).

An oral diet may be tolerated when active IBD is less severe. To control diarrhea and malabsorption, a low-fat, low-fiber, low-lactose diet is often prescribed. Small, frequent feedings may help to limit GI secretions as well as reduce the volume of food that the damaged bowel must handle at any one time. During a flare, the diet should be individualized according to the patient's clinical condition and food tolerances. While the dietary composition of fat and protein may serve as a risk factor for initial development of IBD, there is no data to suggest that specific dietary triggers can result in flare of established IBD. While certain foods have been associated with causing increased GI pain or other symptoms, they are not believed to cause disease relapses. Restriction of diet when individuals do not have active IBD is not encouraged because it can further limit nutrient intake unnecessarily (unless there is fixed narrowing in the lumen of the GI tract). General dietary recommendations for patients with IBD are listed in Table 7-8.

Table 7-8 Key Dietary Guidelines for Patients with Active IBD

Source: Brown.

Eat small meals/snacks often throughout the day (6 small meals or eat every 3–4 hours).

Increase fluid intake to a minimum of eight 8 ounce glasses (2000 ml) per day if loose stools persist. Include rehydration beverages.

Incorporate a chewable multivitamin and mineral supplement daily.

Eat foods high in potassium.

Eat foods high in probiotics and prebiotics.

Limit lactose based on symptoms. Add milk back slowly to monitor tolerance when bowel movements normalize and when the patient is feeling better. Low-fat yogurt and cheese are better tolerated than milk.

Avoid fried and high-fat meats, highly marbled or tough meats. Try lean meat such as skinless poultry, baked or broiled fish.

Limit high fiber grains such as whole grain breads/cereals/pasta with greater than 2 g of dietary fiber per serving

Avoid raw vegetables. Try well-cooked, skinless vegetables.

Avoid dry fruit and raw fruit with peels or skins. Try juice, bananas, melon, and canned fruits. Dilute juice with water if they are not tolerated at full strength.

Limit fats and oils to 40 ml per day.

Avoid caffeine (coffee, tea, cola, chocolate).

Avoid alcohol.

Avoid artificial sweeteners (sorbitol, mannitol, xylitol).

Avoid concentrated sweet

Patients should be advised to eat foods based on tolerance; however, there are certain foods that can be discouraged because they offer few redeeming nutritional qualities and have been associated with intestinal distress (e.g., popcorn, seeds). This can also allow patients to feel they have more control over their disease. For those who are symptomatic, the goal is to liberalize the diet as much as possible after symptoms have subsided, under the guidelines of a dietitian and gastroenterologists.

Alcohol and caffeine can trigger diarrhea because they stimulate the GI tract; which often occurs within 30 minutes of consumption. Similarly, diet foods and beverages containing sugar alcohols, such as sorbitol, xylitol, and mannitol, can also cause intestinal discomfort and diarrhea, and patients should be encouraged to read labels and avoid these items. Though controversial, heavily spiced foods, fried foods, and concentrated sweets have also been associated with inducing diarrhea. Individuals who experience intense GI pain after eating, benefit from keeping a food

diary to determine if any specific foods or beverages they consume may act as a GI irritant. A food diary is essential for patients to gain a better understanding of what foods they can or cannot tolerate. Food diaries can be simple and could include columns in a notebook for:

type of food or beverage consumed,

amount of the food or beverage consumed,

where it was consumed (home, car, restaurant),

time of day,

symptoms.

Calories

In adults, ingested calories should be provided in amounts sufficient to maintain or restore bodyweight. In children, the amount of ingested calories should be adequate to support growth and development, as measured on the pediatric growth charts. Active disease and complications, such as fevers, infection, sepsis, and high output fistulas may increase caloric requirements in adults to as high as 35 to 45 kcal/kg per day, or approximately 1.5 to 1.7 times the basal energy expenditure. For example, a female patient with moderate to severe disease activity weighing 110 lb (50 kg) may require 1750 to 2250 kcal/day to maintain her weight. If a patient is severely malnourished and his or her calorie intake is low, the patient

should be assessed by a registered dietitian to help determine the most appropriate feeding plan. Usually 20 to 25 kcal/kg per day may be initially prescribed to help avoid complications of refeeding syndrome. Supplemental calories can be given in the form of whole protein, elemental or semi-elemental products, and easy to metabolize MCT oils that do not require bile salts for digestion.

Protein

Protein needs are often increased in patients with IBD due to intestinal inflammation or presence of complications, such as abscesses in patients with Crohn's disease. The majority of IBD patients have daily protein needs of 1.0 to 1.5 g/kg ideal body weight. For weight gain and to restore loss of lean body mass greater than 10 percent after an acute flare, protein needs may be increased up to 3.0 g/kg. Protein needs are also increased if the patient is taking prednisone.

Vitamins and Minerals

Patients with IBD are at higher risk for vitamin, mineral, and trace element deficiencies. Higher doses of specific nutrients are indicated if clinical or laboratory evidence identifies a deficiency due to possible poor absorption or increased requirements. Vitamin and mineral requirements for patients with IBD are described here and summarized in Table 7-9.

Patients with Crohn's disease who have extensive intestinal damage due to prolonged inflammation and/or have undergone resection of the terminal ileum are likely to suffer from inadequate vitamin B_{12} absorption. Small intestinal bacterial overgrowth may also occur in the setting of loss of the terminal ileum and ileocecal valve, and may predispose to vitamin B_{12} deficiency due to bacterial use of B_{12}. Patients with Crohn's disease may require supplementation with intramuscular, sublingual, or intranasal vitamin B_{12}, if they fail to improve B_{12} levels following oral supplementation.

IBD patients with persistent, watery diarrhea may have difficulty maintaining adequate zinc, potassium, and magnesium levels and may require supplementation.

Chronic blood loss and altered iron intake and absorption, frequently observed in patients with IBD, can cause iron deficiency anemia. However, oral iron may cause symptoms of nausea, constipation, and abdominal cramping. Slower iron supplementation, given with ascorbic acid, may be more effective as ascorbic acid enhances the absorption of iron by converting the ferric ions to the ferrous form, which is absorbed primarily in the duodenum. Only 25 to 50 mg of ascorbic acid is needed daily to enhance the absorption of iron. Intravenous iron should be considered in

individuals with severe anemia (hemoglobin < 10 g/dL), intolerance to oral iron supplementation, lack of improvement in hemoglobin (normalization or improvement in hemoglobin by 2 g/dL within 4 weeks), or severe intestinal inflammation.

Patients treated with sulfasalazine (Azulfidine) should receive oral folate supplements, 1 mg/day, because this medication inhibits folate absorption by competitive inhibition of the enzyme folate conjugase in the jejunum. Mexthotrexate also requires folate supplementation at 1 mg daily because it is a folate antagonist (it inhibits the enzyme dihydrofolate reductase) and folate deficiencies may lead to stomatitis and anemia.

If a patient is taking a bile salt sequestrant used to treat bile salt-induced diarrhea, fat-soluble vitamin deficiency (A, D, E, and K) may develop. Folate and magnesium absorption can also be impaired by bile salt sequestrants.

Table 7-9 Vitamin and Mineral Requirements for Patients with IBD

Source: adapted from Eiden.

Nutrient	Recommended Daily Requirements	Recommended Replacement for Deficiency (Oral Dose)
inc	15 mg	50 mg elemental/day
Iron	10–15 mg	300 mg 3times/ day
Vitamin B_{12}	3 μg	1000 μg /day
Calcium	800–1500 mg	1500–2000 mg/ day
Magnesium	400 mg	150 mg elemental 4 times/day
Vitamin D	1000 IU	50,000 IU once weekly × 8 weeks

Vitamin D and IBD

Vitamin D deficiency and bone demineralization is common in adults and children with IBD. Factors contributing to this include reduced dietary intake, infrequent sunlight exposure, and limited physical activity. Corticosteroid use contributes to bone demineralization, while decreasing calcium absorption and increasing calcium excretion. Research has also recently focused on a potential role for vitamin D in control of disease

activity through immunomodulation and modification of the risk of IBD-associated malignancy. Serum concentration of 25-OH vitamin D should be monitored at least yearly in individuals with IBD, with a serum level of 32 ng/mL considered as a minimum level of sufficiency. Replacement strategies are listed in Table 7-9, with 50,000 IU of vitamin D given weekly for individuals with 25-OH vitamin D levels less than 20 ng/mL. Individuals with 25-OH vitamin D levels between 20 and 32 ng/mL may improve vitamin D levels with supplementation of 1000 to 2000 IU/day, but should be followed for normalization of vitamin D status.

Fiber

A low-fiber diet is often prescribed for patients with narrowed sections of bowel to decrease the possibility of intestinal obstruction, minimize physical irritation to the inflamed bowel, reduce stool weight and frequency, and slow the rate of intestinal transit. The diet consists of white bread and refined cereals and avoidance of high-fiber fresh fruits and vegetables, nuts, skins, and seeds. The benefit of a low-fiber diet in managing symptoms or affecting the course of IBD remains unclear. Diets should be recommended based on a patient's individual tolerance and intolerance; intake of fiber-rich, nutrient-dense foods can generally be encouraged in the absence of bowel strictures

and if there is no discomfort. A fiber rich diet should not be prescribed in patients with strictures (Crohn's disease), as this could potentially contribute to a small bowel obstruction.

Fat

Decreased fat intake may help control the symptoms of steatorrhea, especially in patients with Crohn's disease involving the small bowel. However, fats serve as a form of concentrated calories, which are needed to promote weight gain in underweight or malnourished patients. Dietary fats are also essential for the absorption of vitamins A, D, E, and K. In order to decrease diarrhea related to fat malabsorption, MCT oil can be substituted as it is more easily absorbed. MCT oil can be added to other foods, but this may change the palatability of the food. Doses should be given in less than 15-g amounts. Referral to a registered dietitian is essential for all patients requiring weight gain who present with fat malabsorption.

Inflammatory versus Anti-Inflammatory Fatty Acids

It has been demonstrated that gene mutations that affect the immune system, causing inflammation, are associated with IBD. Consequently, it has been hypothesized that the ratio of different polyunsaturated fats in the diet may play a role in helping to control

inflammation. Western diets are often high in dietary intake of omega-6 fats (vegetable oils) compared to omega-3 fats. An increase in consumption of omega-3 fats and a decrease in omega-6 fats results in reduced arachidonic acid and it is hypothesized that reducing omega-6 fat sources and increasing omega-3 fatty acids results in a reduction of inflammation. However, there are insufficient data to recommend the use of omega-3 fatty acids in treatment of active IBD or in maintenance of remission in IBD. While research has not demonstrated that supplementation with omega-3 is beneficial in helping to sustain remission, food sources of omega-3 fats should be incorporated into a recommended balanced diet. Dietary sources of omega-3 fats include fatty fish, walnuts, soy, flaxseed, canola oil, and in small amounts, certain leafy greens and are listed in Appendix M.

Oxalate

Calcium oxalate kidney stones are a common complication in patients with Crohn's disease who undergo intestinal surgeries such as ileal resection, or diverting ileostomy which can lead to bile salt malabsorption. Malabsorbed fat then binds intraluminal calcium, decreasing the amount of calcium bound to oxalate and an increase in intestinal and colonic absorption of free oxalate. Low levels of urinary magnesium

and citrate may also contribute to a tendency to develop oxalate stones. Dietary modifications to prevent oxalate stones aim to increase intake of fluid, dietary calcium, potassium, magnesium, and phytates. Calcium supplementation may be given in forms of calcium carbonate or calcium citrate, as supplemental calcium will help bind intestinal oxalate; calcium citrate may also improve urinary citrate excretion (as urinary citrate inhibits stone formation). Dietary measures should also include reduced intake of oxalate and dietary fat. Oxalate rich foods to avoid include beets, turnip greens, rhubarb, strawberries, sweet potatoes, wheat bran, chocolate, tea, spinach, nuts, and citrus juices.

Prebiotics and Probiotics

Probiotics

The joint Food and Agriculture Organization (FAO) and World Health Organization (WHO) report on the evaluation of probiotics in food defines probiotics as "live microorganisms which when administered in adequate amounts confer a health benefit on the host." While many products are labeled as probiotics, few of the commercially available products have been studied within a controlled experimental design. This concept is important, as the majority of probiotic effects are thought to be strain specific and should not be extrapolated from one strain to another, regardless of how

closely related. The rationale for the use of probiotics in IBD stem from the thought that alteration in the intestinal microbiome predisposes one to IBD, and animal models which show anti-inflammatory properties of specific probiotic strains or soluble proteins from specific probiotic cultures. Despite this, clinical trials of probiotics in treatment of IBD have been mixed. Caution should be taken when prescribing probiotics to patients, as complications have been described in patients who are immunocompromised, have surgical short bowel syndrome, and patients who are critically ill.

Ulcerative colitis Various probiotic strains have shown promise in treatment of mild/ moderate ulcerative colitis, largely in conjunction with standard medical therapy. However, studies are often limited by small sample sizes and various strains and dosing regimens of probiotics used. Two probiotic strains that have shown promise in induction and/or maintenance of remission of ulcerative colitis include VSL3 (probiotic preparation including four *Lactobacillus* species, three *Bifidobacterium* species, and one strain of *Streptococcus* species) and *E. coli* Nissle 1917.

Crohn's disease Currently, there is insufficient evidence to support the use of probiotics in induction of remission or maintenance of remission in Crohn's disease.

Existing clinical trials are small and are limited by study design and various preparations and dosing regimens used.

Prebiotics

Prebiotics are non-digestible carbohydrates that upon reaching the colon undigested, may stimulate the growth of healthy bacteria found in the gut and may improve gut health. More studies are needed to support prebiotic supplementation in IBD patients. Prebiotic supplements such as fructooligosaccharides (FOS), an insulin-type probiotic, must initially be started in small amounts and slowly increased as they may cause significant gas production. Recommended maximum FOS intake is 15 g/day.

Nutrition Support

Enteral nutrition support should be the primary source of nutrition if it is safe to provide and oral nutrition consumption is unable to meet nutritional demands. There is little randomized data to support a specific type of enteral formula in the nutritional rehabilitation of individuals with IBD. As such, standard polymeric formulas can be recommended, switching to a hydrolyzed or elemental formula in those who prove intolerant to standard formulas. Nutritional support of the pediatric patient with IBD, especially Crohn's disease, gains increasing importance as poor nutritional

status can predispose to growth failure and short stature.

Parenteral nutrition (PN) support is indicated only in severe cases of IBD when bowel rest is considered necessary and enteral nutrition (EN) support is not an option, as in cases of bowel obstruction or severe strictures, severe perianal or enterocutaneous fistulas that prohibit feeding, or in individuals with intestinal failure secondary to surgical short bowel syndrome. In individuals requiring PN secondary to severe malnutrition, PN should be introduced gradually and cautiously with close monitoring for refeeding syndrome.

Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is a functional GI disorder characterized by abdominal pain, altered bowel motility, and bloating or abdominal distension. The pathogenesis of irritable bowel syndrome is not well understood; however, genetic and environmental factors are thought to play a role. In addition, researchers have reported abnormal GI motility, visceral hypersensitivity, dietary intolerances, and psychological or emotional dysfunction in patients with IBS. No specific physiologic or psychologic abnormality has been shown to be absolutely indicative of this disorder.

The abdominal pain associated with IBS is variable, and can be mild to severe. Diarrhea and constipation may occur in varying degrees, and despite extensive research, no one predominant pattern of small bowel or colonic dysmotility has been found. IBS may present with diarrhea or constipation predominant symptoms; however, some patients have alternating diarrhea and constipation. An evaluation for organic causes of GI symptoms should be considered. Recent evidence suggests that carbohydrate malabsorption may precipitate symptoms of IBS. Testing for lactose or fructose malabsorption should be considered in patients with symptoms consistent with IBS. Based on patient symptoms and physical exam, diagnostic tests such as motility studies and manometry may or may not be performed. If IBS is diagnosed, treatment should focus on management of symptoms.

Nutrition Therapy for IBS

Nutrition therapy for IBS is variable, as many patients have specific food intolerances. Following a lactose-restricted diet may improve symptoms for some patients with IBS, particularly those with diarrhea-predominant IBS. In addition, reducing the amount of dietary fructose, found in fruits, fruit juices, and foods prepared with high fructose corn syrup may be beneficial as fructose is not absorbed well by some individuals and can contribute to

upset stomach and diarrhea. A high-fiber diet is often recommended, especially in patients with constipation-predominant IBS, as it aids in water absorption, promotes bulking of the stool, and can improve intestinal transit. There have been many studies examining the role of insoluble and soluble fibers in the treatment of IBS. The results of these studies have been mixed with many showing only marginal improvements in global symptoms of IBS. Some studies show that in patients with constipation-predominant symptoms, insoluble fiber caused their symptoms to worsen. This may be related to a functional decrease in small bowel, or colonic motility seen in some patients with IBS. These mixed results suggest that individualized dietary counseling and recommendations for fiber intake are needed in patients with IBS.

Because symptoms are variable, encouraging patients with IBS to keep a food diary may allow them to determine specific dietary triggers, and the foods identified as triggers should be limited or avoided. In addition, a trial high-fiber diet may produce symptomatic improvement in some patients, especially if their dietary intake of fiber is less than the recommended 25 to 35 g/day. Clinicians should be aware of what type of fiber patients are consuming, and encourage them to experiment with more or less insoluble and soluble fibers depending on their symptoms. High-fiber food

sources are shown in Appendix O. Patients should be instructed to increase fiber intake gradually, and to increase fluid intake as fiber intake increases. Avoidance of lactose- or fructose-containing foods, as well as gas-producing foods may reduce episodes of bloating and abdominal pain. Key recommendations to reduce gas and bloating are listed in Table 7-10. Patients who avoid dairy foods due to symptoms of lactose intolerance should be encouraged to consume other calcium-rich foods or calcium supplements to meet the recommended daily intake of calcium as shown in Appendices G and H.

Table 7-10 Key Recommendations to Decrease Gas and Bloating

Source: Lisa Hark, PhD, RD and Darwin Deen, MD, 2014. Used with permission.

Certain foods can produce excess gas during digestion and may worsen your symptoms of abdominal pain or bloating. Various foods affect people in different ways; avoid these foods if they cause you discomfort. The following diet tips may improve your symptoms. Foods that may cause gas: Beans, cabbage, cauliflower, brussel sprouts, broccoli, asparagus, peppers, cucumbers, onions, garlic, radishes, sauerkraut

Raw apples, avocado, melon
Eggs, fried and fatty foods, spicy foods, carbonated beverages
Swallowing air may also cause excess gas. To prevent this:
Eat slowly
Avoid chewing gum, drinking carbonated beverages, and smoking

Research examining a role for probiotics in IBS is ongoing. It is thought that alterations of normal GI flora may play a role in symptom expression, and some studies have shown decreased levels of the healthy bacteria lactobacilli and bifidobacteria in patients with IBS. It has been hypothesized that the restoration of normal gut flora may decrease abnormal gas production in some patients. In addition, it is thought that probiotics may decrease adherence of pathogenic bacteria to the GI mucosa, thereby decreasing symptoms of IBS. Additional research is needed to determine the ideal balance between diet, fiber supplements, and probiotics in the management of IBS.

Diverticulosis

Diverticulosis is a disorder of the colon, most often the sigmoid colon, caused by multiple potential factors including age-related changes

in the colonic wall, abnormal increases in colonic intraluminal pressure, and motor dysfunction. Inadequate fiber intake is thought to increase the risk for the development of diverticulosis. The incidence of diverticulosis increases with age. The prevalence of diverticular disease has been reported at 10 percent of the population, most often occurring after age 40. It has been estimated that more than 30 percent of patients over age 60 and 50 percent of patients over age 80 have evidence of diverticulosis.

Treatment of diverticulosis focuses on increasing dietary fiber intake via whole grain foods, fruits, and vegetables. Some studies have shown an improvement in symptoms of uncomplicated diverticular disease with a fiber intake of 25 to 30 g/day. The best results seemed to be obtained when a combination of soluble and insoluble fiber was included in the diet. Appendix O lists high-fiber food choices. It may be necessary to increase fiber intake with the use of soluble fiber supplements, such as psyllium or guar gum. Early recommendations for diverticular disease encouraged the elimination of foods containing nuts and seeds due to concerns that these items could become lodged within the diverticuli. However, new evidence from large cohort studies suggests that nuts, corn, and popcorn are safe for most patients, and exclusion in the diet should be based on individual patient intolerance. While

seeds have not been specifically assessed for tolerance in clinical trials, blueberries and strawberries have been included in studies and have not been found to be associated with increased risk of diverticulitis. The most current recommendations focus on increasing dietary fiber intake and do not recommend avoidance of nuts, seeds, and popcorn. It is important to advise patients to increase fluid intake as fiber intake is increased. Although no evidence is available to provide an exact recommendation for fluid intake, encouraging at least 64 ounces of fluids daily is reasonable.

Diverticulitis

Diverticulitis occurs when there is inflammation or perforation at the site of a diverticuli. Management focuses on resolution of inflammation. Bowel rest is often indicated with gradual diet advancement. As eating resumes, patients should maintain a low-fiber intake until the inflammation is resolved. The diet should be advanced slowly as tolerance permits, and fiber intake should be gradually increased. Eventual return to a high-fiber diet should be encouraged, as well as consumption of adequate fluids.

Liver Disease

Fatty Liver

The development of fatty liver can occur as a result of chronic alcohol use or as a side effect of many medications. Recently, much emphasis has been focused on the development of non-alcoholic fatty liver disease (NAFLD), which refers to the development of hepatic steatosis when no other causes for secondary hepatic fat accumulation are present. Two subsets of NAFLD include non-alcoholic steatohepatitis (NASH) and non-alcoholic fatty liver (NAFL). NASH is characterized by steatosis with inflammation, cellular ballooning, and fibrosis. Patients with NASH have the potential to progress to advanced cirrhosis and end-stage-liver disease. NAFL is characterized by steatosis with minimal inflammation. These patients are at less risk for disease progression. The worldwide prevalence of NAFLD is increasing, and has been found to be associated with the increase in the prevalence of obesity and type 2 diabetes. Patients at risk for NAFLD are those with aspects of metabolic syndrome, including central obesity, elevated triglycerides, low HDL-cholesterol, hypertension, and insulin resistance.

In patients who experience fatty liver as a result of alcohol use, abstinence from alcohol should

be strongly encouraged. Nutrition therapy of NAFLD is aimed at a gradual weight loss of 1 to 2 lb/week. Rapid weight loss may be associated with worsening of liver function and should be discouraged. The ideal dietary composition for patients with NAFLD is unclear, but reduction in total calorie and fat intake and increased dietary fiber intake will likely aid in weight loss and improve other symptoms associated with metabolic syndrome. Increased physical activity will aid in sustaining weight loss maintenance. Patients may benefit from referral to a registered dietitian or weight loss programs that offer a support component, either through local hospitals or programs such as Weight Watchers. Weight loss programs, involving intensive dietary counseling by an experienced dietitian or health educator, have been shown to improve biochemical and histologic liver disease markers.

Cirrhosis

Malnutrition and vitamin deficiencies are extremely prevalent in patients with cirrhosis because the diseased liver is no longer able to play a central role in the metabolism of carbohydrate, fat, and protein. It is estimated that protein calorie malnutrition affects between 50 and 90 percent of patients with liver disease, and may be more common in individuals with alcoholic liver disease compared to those with non-alcoholic liver

disease. Protein-calorie malnutrition is often considered a negative prognostic risk factor and is associated with poor outcomes and complications such as hepatorenal syndrome, refractory ascites, variceal hemorrhage, and spontaneous bacterial peritonitis. Causes of malnutrition in this population vary. There is impaired nutrient metabolism, causing patients to move more rapidly from a fed state to a fasting state. Malabsorption may occur as a result of diminished bile acid production. Calorie requirements may be increased acutely during complications of ascites or spontaneous bacterial peritonitis. GI symptoms, such as anorexia, nausea, and early satiety may impact the intake of adequate nutrients. In addition, highly restricted diets, lactulose therapy, frequent paracentesis, and diuresis are iatrogenic causes which may worsen malnutrition. Nutrient deficiencies, particularly the B vitamins (thiamin, folate, B_{12}), are often seen in patients with alcoholic cirrhosis, and supplementation is often necessary. Recommendations on the optimal macronutrient content of diets in patients with cirrhosis have varied historically. Insulin resistance and glucose metabolism defects are common in individuals with cirrhosis, and may occur with type 2 diabetes mellitus or secondary to cirrhosis itself. In this setting, carbohydrate intake may need to be modified and patients should be referred to an

experienced dietitian. Patients should be encouraged to increase consumption of whole grains and limit sweets. Fat intake should be adjusted based on symptoms of intolerance, particularly in cholestatic diseases. In patients with significant malnutrition and anorexia, increasing calorie intake by way of high-fat, energy-dense food choices may be helpful as long as they are not experiencing significant fat malabsorption. Protein restrictions have frequently been recommended in cirrhosis, especially with accompanying encephalopathy, often at levels of 40 g/day. However, it has been shown that excessive protein restriction can worsen outcomes in cirrhosis. Protein restrictions should be limited to periods of acute encephalopathy, but should be temporary and never less than 0.6 to 0.8 g/kg/day. Protein intake can then be liberalized after the cause of encephalopathy is determined and corrected. It is now recommended that patients with cirrhosis should consume 1.0 to 1.5 g of protein/kg/day to prevent muscle catabolism. Protein requirements should be based on the estimated dry weight. In addition, the increased fiber content of vegetable protein sources may facilitate desired nitrogenous losses in the stool. Avoidance of raw seafood and shellfish should be encouraged due to the risk of *Vibrio vulnificus* infections.

Individuals with persistently inadequate oral intake may benefit from oral liquid nutrition

supplements to increase calorie and protein intake. Oral supplements high in branched-chain amino acids (BCAA – isoleucine, leucine, and valine) have been developed for these patients. There is thought to be higher levels of aromatic amino acids in patients with liver disease with a decrease in levels of BCAAs. Normalization of this ratio was hypothesized to improve hepatic encephalopathy by competing with aromatic amino acids for transport across the blood–brain barrier, and decreasing the synthesis of false neurotransmitters seen in acute encephalopathy. However, data has not consistently shown a benefit to BCAA supplementation in improvement in hepatic encephalopathy. Improvements may be seen in overall nutrition status, hospitalizations, and quality of life. However, adherence is limited by expense and palatability of these supplements.

Many patients with cirrhosis will develop ascites, and therefore a low sodium diet is also indicated. Restriction of sodium to less than 2000 mg/day is often recommended. Further restrictions in sodium worsen the palatability of the diet and increase the risk of inadequate nutrient intake. Fluid restriction may also be indicated. In patients with significant steatorrhea, it may be necessary to provide additional supplementation of fat-soluble vitamins, preferably in a water-soluble form. Key nutrition recommendations for patients

with cirrhosis and advanced liver disease by the American Society of Parenteral and Enteral Nutrition are:

caloric intake goal of 30 to 35 kcal/kg dry body weight,

50 to 60 percent of calories from carbohydrate,

20 to 30 percent of calories from protein, or 1.0 to 1.5 g/kg dry body weight,

10 to 20 percent of calories from fats,

avoid dietary restrictions if possible,

provide small, frequent meals throughout the day and small snacks,

screen for vitamin and mineral deficiencies, particularly fat soluble vitamins (A, D, E, K), B vitamins (folate, B_{12}, thiamine), zinc, and calcium,

avoid alcohol.

Gallbladder Disease: Cholelithiasis

Cholelithiasis is caused by a combination of lithogenic bile, cholesterol crystallization, and gallbladder stasis. The majority of cases of gallstone disease are related to cholesterol stones. Female gender, pregnancy, age, obesity, and certain ethnic backgrounds have higher rates of cholelithiasis. Rapid weight loss, family history, and certain medications may also increase the risk of developing gallstones. Although there are no specific diet

recommendations for the management of gallstones, dietary factors may play a role in gallstone development. For example, excess energy intakes, as well as diets high in saturated fats and refined sugars, have been identified as risk factors for gallstone development. The combination of dietary factors that predispose patients to weight gain and obesity also predispose them to gallstone disease. Long-term population studies suggest that high-fiber diets may reduce risk of gallstone formation. In addition, there has been some evidence that diets high in polyunsaturated and monounsaturated fats reduce the risk of cholelithiasis in both men and women.

Patients who are at risk for the development of gallstone disease should be encouraged to adopt healthy lifestyle habits, including a diet low in saturated fats and refined sugars and high in dietary fiber. If weight loss is indicated, patients should be encouraged to make gradual changes to support weight loss of no more than 1 to 2 lb/ week. Rapid weight loss has been associated with gallstone formation. In patients with current gallstone disease, a diet that restricts fat to 25 to 30 percent of total calories is indicated. Further restriction of fat should be avoided, as it may prevent adequate stimulation of gallbladder contraction. Food intolerances may be reported, specifically with foods that cause gas and bloating. Avoiding these foods may aid in symptom control. If steatorrhea is reported,

supplementation of fat-soluble vitamins may be indicated.

Case 1 Alcohol and Vitamin Deficiencies

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Objectives

Explain how excessive alcohol consumption contributes to nutritional deficiencies.

Recognize the medical and societal costs of alcohol abuse.

Describe the biochemical and pathophysiologic abnormalities that occur with excessive alcohol intake.

Recognize the importance of assessing a patient's alcohol intake during a routine social history.

Describe the nutritional recommendations for patients who consume alcohol.

CT, a 52-year-old car salesman, presents to his family physician for his yearly physical examination reporting fatigue, burning in his feet, decreased memory, and heartburn. He has

also noticed a recent weight gain and increased waist circumference and complains of increase in abdominal girth in association with weight gain and decreased endurance when exercising. He denies blurred vision, headaches, night sweats, or hearing loss.

Past Medical History

CT has no prior history of heart disease, stroke, or peripheral vascular disease. He has been told in the past that his liver is "damaged," but he has never received specific treatment for this. He is not taking any medications and has no known drug or food allergies.

Social History

CT states that he usually consumes three "healthy" meals every day, but his appetite has been poor for the past week. He has smoked one pack of cigarettes per day for 30 years (30-pack year history).

Family History

CT's family history is negative for the presence of heart disease, stroke, cholesterol, and lipid disorders, or neurologic diseases.

Review of Systems

General: The patient reports lethargy, decreased appetite, and recent bloating; he

relates that his pants are tighter in the waist than usual

GI/abdomen: No vomiting or diarrhea

Neurologic: No history of seizures, no tinnitus, no syncope. He has reported some memory loss

Physical Examination

Vital Signs

Temperature: 98.2 °F (36.8 °C)

Heart rate: 104 BPM

Respiratory rate: 16 BPM

Blood pressure: 120/90 mm Hg

Height: 5′8″ (173 cm)

Current weight: 160 lb (73 kg)

Usual weight: (1 month ago): 150 lb (68 kg)

BMI: 24 kg/m^2

Exam

General: Well-dressed male who appears to be in mild distress

Skin: Jaundiced; spider angiomas on the upper chest (central blood vessels feeding small, dilated vessels, characteristic of chronic liver disease)

Eyes: Pale conjunctiva, sclera icteric; no ophthalmoplegia or nystagmus

Cardiac: Resting tachycardia; heart sounds are normal; no murmurs are present

Chest/Pulmonary: Lungs clear to auscultation and percussion bilaterally; mild gynecomastia (excessive development of male mammary glands)

Abdomen: Distended abdomen; presence of an abdominal fluid wave and shifting dullness, consistent with ascites (physical finding of fluid accumulation in the peritoneal cavity that can be associated with severe liver disease); enlarged liver size (14 cm span) with a firm, non-tender edge; no splenomegaly

Extremities: slight (1+) bilateral lower extremity edema

Neurologic: decreased vibratory sensation in the lower legs; bilaterally decreased knee reflexes; no asterixis; normal sensation and position sense in upper and lower extremities; cranial nerves II through XII grossly intact

Mental status: alert; oriented to time, place, and person

CT's Laboratory Data

Patient's Values	Normal Values
Red blood cells (RBC): 3.8 million/mm^3	4.3–5.9 million/mm^3
Hemoglobin: 10 g/dL	13.5–17.5 g/dL
Hematocrit: 35%	41–53%
Mean corpuscular volume (MCV): 104 fL	80–100 fL
Albumin: 2.8 g/dL	3.5–5.8 g/dL
Prothrombin time: 15 seconds	11.0–13.2 seconds
International Normalized Ratio (INR): 1.3	1.0
Total bilirubin: 5 mg/dL	0.1–1.0 mg/dL
Aspartate aminotransferase (AST): 140 IU/L	8–20 U/L
Alanine aminotransferase (ALT): 80 IU/L	8–20 U/L
Sodium: 135 mmol/L	133–143 mmol/L

Case Questions

What additional information is important to obtain from a patient who presents with these symptoms?

What are the biochemical consequences of excessive alcohol consumption?

What is the prevalence of alcoholism in the United States and what are the associated medical and societal consequences?

What are the nutritional consequences of excessive alcohol consumption?

What evidence from CT's history, physical examination, and laboratory data suggests complications of alcoholism and nutritional deficiencies?

What does CT's serum albumin level indicate?

What additional laboratory tests would you request before giving CT a folate supplement?

Answers to Questions: Case 1

1. What additional information is important to obtain from a patient who presents with these symptoms?

Assessment of a patient's alcohol intake should always be included in the social history because many people who actively drink alcohol may not voluntarily admit to having a drinking problem and at-risk alcohol consumption is often asymptomatic. Particular attention must be paid to those signs, symptoms, and lab tests that are likely to be abnormal in the alcoholic

patient. Neurologic signs, combined with fatigue, gynecomastia, ascites, enlarged liver, possible gastroesophageal reflux, anemia, cardiomyopathy and abnormal liver function tests all alert the clinician to probe for chronic alcohol ingestion. For patients who admit to drinking, specific information regarding quantity, type, frequency, and duration of consumption should be obtained.

CT has been drinking heavily for 10 years. His daily routine consists of two cocktails before dinner, a few glasses of wine with dinner, and two cocktails after dinner, totaling six drinks per day. Considering that CT is a heavy drinker, as evidenced by his consumption of 42 drinks per week, he is a candidate for a screening tool such as the CAGE test. The CAGE test was developed as a diagnostic tool for alcoholism. CT is asked the following questions, which are assigned a value of one point if answered “yes”.

Have you ever felt you should **C**ut down on your drinking? ____(Yes)

Have people **A**nnoyed you by criticizing your drinking? ____(No)

Have you ever felt bad or **G**uilty about your drinking? ____(Yes)

Have you ever had a drink the first thing in the morning (**E**ye opener) to steady your nerves or to get rid of a hangover? ____(No)

When interpreting the CAGE test, take into account the patient's answers to the preliminary questions about alcohol use. A key question is "When was the last time you had a drink?" Because CT reports drinking within the past 30 days and scored two on the CAGE test, he is very likely to have a current alcohol problem.

2. What are the biochemical consequences of excessive alcohol consumption?

Excessive alcohol consumption can cause metabolic acidosis by interfering with the oxidation of acetyl CoA in the TCA cycle. Ethanol is oxidized to acetaldehyde by the enzyme alcohol dehydrogenase, which also simultaneously reduces NAD^+ to NADH + H^+. Next, the enzyme acetylaldehyde dehydrogenase oxidizes acetaldehyde to acetyl CoA and reduces another NAD^+ to NADH + H^+. This enzyme requires NAD^+ to accept the hydrogen ions.

The increased ratio of NADH to NAD^+ in the presence of excess alcohol, called an altered redox state, drives pyruvate to lactate instead of to acetyl CoA. High levels of lactate generated from pyruvate suggest an abnormality in the recycling of NADH to NAD^+ caused by excessive alcohol ingestion. In addition, instead of entering the TCA cycle, where more NADH is produced, acetyl CoA is converted to ketone

bodies and fatty acids. As a result, a ketoacidotic state develops and fatty acids are converted to triglycerides. In turn, a significant rise in triglyceride levels can lead to fatty liver (Figure 7-1).

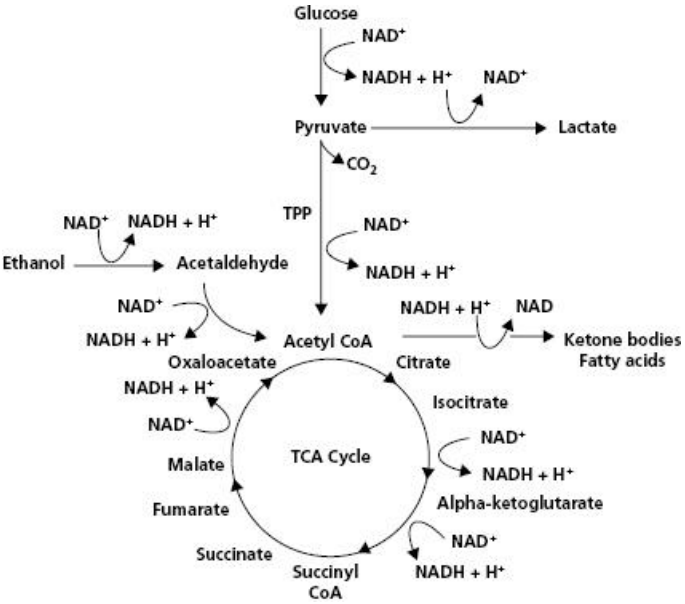

Figure 7-1 Alcohol Metabolism and the Altered Redox State

Source: Adapted from BergJM, Tymoczko JL, Stryer L. *Biochemistry*.Paperback Edition, WH Freeman: New York. 2008.

3. What is the prevalence of alcoholism in the United States and what are the associated medical consequences?

Alcoholism is a major problem in the United States. Each year, about 100,000 deaths in the

United States are related to alcohol consumption. According to the 2000 National Household Survey on Drug Abuse, almost half of Americans (46.6 percent) aged 12 and older reported being consumers of alcohol in some form or another. This translates into an estimated 103 million people. In addition, nearly 5.6 percent of people aged between 25 and 44 were heavy drinkers (five or more drinks per day) and 9% of American adults and 13% of those who drink alcohol, meet criteria for an alcohol-use disorder. Risk drinking is defined as having an average of 15 or more standard drinks in a week, or 5 or more on an occasion for men and 8 or more drinks weekly or 4 or more on an occasion for women. Continued drinking despite adverse consequences constitutes an alcohol-use disorder.

The harm associated with intake of large amounts of alcohol is well-documented. Alcohol intake over 3 g/day (more than 2 drinks) has been associated with increased mortality due to hypertension, pancreatitis, gastrointestinal malignancies, stroke, cardiomyopathy, cirrhosis, motor vehicle accidents, and breast cancer. However, even light drinking is associated with increased risk of esophageal, oropharyngeal, and breast carcinomas, as alcohol is a carcinogen. Alcoholics can also experience marital/family difficulties and also may lose their jobs as a result of work absenteeism. In addition, alcohol can interact

with many different medications affecting their potency.

4. What are the nutritional consequences of excessive alcohol consumption?

Chronic alcoholism is considered the most common cause of malnutrition in the western world. Alcohol provides 7 kcal/g, which can be utilized and metabolized when substituted for calories from food, but provides no protein, vitamins, or minerals. Patients with chronic alcohol consumption consume a disproportionate amount of calories from alcohol. Drinking causes a decrease in appetite that generally is proportional to the amount of ingested calories from alcohol and can significantly affect the nutritional adequacy of a patient's diet. In alcoholic liver disease (ALD), malnutrition is common and is multifactorial. The prevalence of protein-calorie malnutrition in patients with ALD has been reported to range from 20 to 60 percent in patients with alcoholic cirrhosis. High concentrations of alcohol can disrupt the gastric and duodenal mucosa, affect the digestive and absorptive processes, and as a consequence, significantly reduce the absorption of vitamins.

One of the most important vitamin supplements routinely given to alcoholics is thiamin, since alcohol interferes with thiamin absorption, even in healthy individuals. Thiamin is important in carbohydrate

metabolism. Its predominant form, thiamin pyrophosphate (TPP), functions as a coenzyme for pyruvate dehydrogenase, which converts pyruvate to acetyl CoA. Inadequate thiamin intake forces pyruvate to be converted to lactate, further contributing to the development of lactic acidosis (Figure 7-1). Thiamin deficiency manifests as anorexia, irritability, fatigue, and decreased memory. Later stages present with peripheral neuropathy, confusion, and tachycardia.

Chronic alcohol consumption has also been associated with folate deficiency; however, the etiology is unclear. Alcohol may affect folate levels by decreasing dietary intake, impairing absorption and metabolism, increasing urinary excretion of folate, and may also be directly toxic to bone marrow and other cells. Tetrahydrofolate (THF), the coenzyme derived from this vitamin, is involved in one-carbon-unit transfers including amino acid interconversions and purine and pyrimidine biosynthesis. The interconversion of homocysteine to methionine requires methyl tetrahydrofolate as the coenzyme for methionine synthase. Vitamin B_{12} also acts as a cofactor in the methylation of homocysteine to methionine, in which methyl tetrahydrofolate is converted to THF. As a result, in vitamin B_{12} deficiency, the demethylation of methyl THF is prevented, blocking folate metabolism, or trapping folate.

Folate is also required for normal purine and pyrimidine biosynthesis. The methylation of deoxyuridine monophosphate (dUMP) to thymidine monophosphate (dTMP,) catalyzed by thymidylate synthase, requires 5,10-methylene THF, which is synthesized from THF. Folate deficiency alters red blood cell production, resulting in enlarged, oval erythrocytes, manifested as megaloblastic anemia. It often cannot be distinguished from the anemia associated with a vitamin B_{12} deficiency. However, the neurologic abnormalities that occur with a vitamin B_{12} deficiency are rarely seen in folate deficiency.

5. What evidence from CT's history, physical examination, and laboratory data suggests complications of alcoholism and nutritional deficiencies?

Decreased lower extremity reflexes, decreased lower extremity vibratory sensation, and paresthesias are all neurologic signs and symptoms associated with thiamin deficiency due to prolonged alcohol abuse. The diagnosis of thiamin deficiency is highly likely because this patient has been drinking heavily for 10 years. This condition is considered a medical emergency because, if left untreated, it can progress quickly and cause irreversible damage.

This patient's hematology lab data reveal that anemia is present, which may explain his fatigue. An elevated mean corpuscular volume

(MCV) indicates the presence of large red blood cells, a characteristic finding in megaloblastic anemia. Megaloblastic anemia can be caused by either vitamin B_{12} or folate deficiency; however, alcoholics are not usually vitamin B_{12} deficient.

6. What does CT's serum albumin level indicate?

CT's serum albumin value may reflect moderately depleted protein status and overall nutritional status. Decreased albumin, however, may not accurately reflect protein status in patients with severe liver disease because albumin is synthesized in the liver and is also influenced by hydration status. Usually, the liver retains its capacity to produce albumin until end-stage liver disease. The liver also synthesizes the vitamin K-dependent clotting factors, which explains CT's prolonged prothrombin time, since the liver's ability to produce factors II, VII, IX, and X can be affected early in liver disease.

7. What additional laboratory tests would you request before giving CT a folate supplement?

Serum and RBC folate and serum vitamin B_{12} levels should be checked. Serum folate levels are greatly affected by current diet intake; however, RBC folate levels are a better measure of tissue folate status. Although alcoholics are not usually vitamin B_{12} deficient, it is important

to check CT for vitamin B_{12} deficiency because if CT's megaloblastic anemia is due to vitamin B_{12} deficiency, prescribing folate without vitamin B_{12} will improve the anemia but mask the vitamin B_{12} deficiency and its progression with the associated neurologic damage. It is important to remember that neurologic impairments due to vitamin B_{12} deficiency do not respond to folate supplementation alone and are not reversible; however, hematologic abnormalities respond to both folate and to vitamin B_{12}.

CT's results from the recommended tests support the diagnosis of folate deficiency.

CT's Values	**Normal Values**
Vitamin B_{12}: 520 pg/mL	220–960 pg/mL
Serum folate: 2 ng/mL	3.0–17 ng/mL
RBC folate: 90 ng/mL	280–903 ng/mL

Based on his clinical presentation and laboratory data, CT should receive thiamin, folate, and multivitamin supplements, especially if he continues to drink alcohol. CT should be advised to eliminate drinking alcohol and be referred to specialty treatment programs and mutual help groups. He should be followed closely and his healthcare provider should inquire at regular follow-up visits about his alcohol use.

Case 2 Malabsorption

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Objective

Evaluate the clinical, anthropometric, and laboratory data of a patient with malabsorption.

Explain how dietary factors affect a patient with malabsorption.

Identify nutrient deficiencies associated with malabsorption and develop a nutritional care plan to treat these problems.

JR, a 27-year-old graduate student, is referred to the GI clinic by his primary care physician because of persistent complaints of loose bowel movements. JR's history is significant for a gunshot wound to his abdomen 5 years ago, requiring intestinal resection of approximately 75 percent of his small intestine (the ileum and most of the jejunum) with anastomosis (surgical re-attachment) of the proximal jejunum to the cecum. Post-operatively he

noted about five liquid bowel movements daily, described as oily and foul smelling, which have persisted until the present time. After surgery he did not seek medical follow-up. JR takes no medications.

Social History

After surgery he was instructed to eat 5 to 6 small meals per day, to follow a high-calorie, high-protein diet with 5 to 10 g of soluble fiber and a limited intake of oxalates, and to take a daily multivitamin and mineral supplement. JR chose to discontinue the vitamin and mineral supplement 1 year ago. JR does not smoke cigarettes, but he reports drinking two beers per week and three cups of coffee daily. He states that he does not have the energy to exercise.

Diet History

JR reports the following recall as his "typical" intake.

JR's 24-Hour Dietary Recall

Breakfast (diner)	
Fried eggs	2 large
Margarine	1 Tbsp.
Bacon	3 slices
White toast	2 slices (enriched)
Butter	2 Tbsp.

Breakfast (diner)	
Cranberry juice	12 ounces
Coffee	1 6-ounce cup
Sugar	4 packets
Snack (food truck)	
Coffee	1 6-ounce cup
Sugar	4 packets
Jelly doughnut	1 regular
Lunch (fast-food)	
Double cheeseburger	1 large
French fries	1 large order
Chocolate milkshake	12 ounces (360 mL)
Dinner (home)	
Baked ham	8 ounces (227 g)
Baked potato	1 medium
Butter	2 Tbsp.
White bread	2 slices (enriched)
Butter	2 Tbsp.
Apple pie	? of 9 inch pie
Coffee	1 cup
Sugar	2 packets
Snack (home)	
Corn chips	3 ounces bag (85 g)
Beer	12 ounces (360 mL)

Total calories: 4462 kcal

Protein: 143 g (13% of calories)

Fat: 204 g (43% of calories)

Saturated fat: 85 g (17% of total calories)

Monounsaturated fat: 31 g (6% of total calories)

Polyunsaturated fat: 6 g (1.5% of total calories)

Cholesterol: 852 mg

Carbohydrate: 488 g (44% of calories)

Dietary fiber: 25 g

Sodium: 6902 mg

Calcium: 544 mg

Review of Systems

General: 27-year-old male who appears very thin and wears loose-fitting clothes; weight loss (10 lb or 4.5 kg) over the past year, fatigue, and weakness. Patient reports his appetite is good but that he must eat "twice as much food" as he did prior to his operation and he still continues to lose weight

Skin: Dry and scaly

Eyes: Difficulty driving at night due to poor night vision

GI: Five liquid bowel movements daily, described as oily and foul-smelling

Physical Examination

Vital Signs

Temperature: 98.0 °F (37 °C)

Heart rate: 80 BPM

Respiration: 16 BPM

Blood pressure: 94/60 mm Hg

Height: 5′10″ (178 cm)

Current weight: 125 lb (57 kg)

Usual body weight: 165 lb (75 kg); has lost 40 lb (18 kg) since surgery 5 years ago

BMI: 18 kg/m^2

Exam

General: Thin, underweight man in mild distress.

Skin: Flaky dermatitis, ecchymoses.

Head: Bilateral temporal muscle wasting.

Mouth: Glossitis, cheilosis.

GI/abdomen: Protuberant abdomen, bowel sounds with no activity, no hepatosplenomegaly.

Extremities: Skeletal pain, interosseous muscle wasting, subcutaneous fat wasting, skeletal muscle wasting.

Laboratory Data

Patient's Lab Values	Normal Values
Albumin: 2.5 g/dL	3.4–5.4 g/dL
Cholesterol: 120 mg/dL	desirable <200 mg/dL
Calcium: 5.5 mg/dL	8.7–10.2 mg/dL
Vitamin B_{12}: 100 pg/mL	279–996 pg/mL
Vitamin A: 13 µg/dL	20–100 µg/dL
25(OH)D: 5 ng/mL	30–100 ng/mL
Vitamin E	
Alpha tocopherol: 3 mg/L	4.6–14.5 mg/L
Beta/gamma tocopherol: 0.6 mg/L	1.4–4.8 mg/L
Prothrombin time: 16 seconds	<11–15 seconds
Parathyroid hormone: 50 pg/mL	8–51 pg/mL
Serum folate: 2.5 ng/mL	>5.4–18 ng/mL
Zinc: 300 mg/dL	550–1400 mg/dL
Magnesium: 1.2 mg/dL	1.5–2.3 mg/dL
Fecal fat (72 hours): 28 g	<7 g daily

Sources: Alexander, 2012 and Harrison's Principle Of Internal Medicine 18th edition.

Case Questions

Explain why JR continues to lose weight even though he eats a large volume of food.

What is the cause of JR's steatorrhea?

What are the causes and associated clinical signs or symptoms of each laboratory abnormality with which JR presents?

Using JR's actual body weight, calculate the percentage change from his usual weight and interpret these results.

What conclusions can you draw regarding the fat, calorie, vitamin, and mineral content of JR's diet?

How does JR's current caloric intake compare with his requirements?

JR notes that his symptoms worsen when he eats fried or fatty foods. What should be done to correct these symptoms and his laboratory abnormalities?

Answers to Questions: Case 2

Part 1: Diagnosis

1. Explain why JR continues to lose weight even though he eats so much food.

Weight loss may be a result of fat malabsorption (steatorrhea). Moreover, while luminal digestion of starch into oligosaccharides and proteins into oligopeptides should be unaffected, decreased small bowel surface area interferes with brush border and cytoplasmic digestion, as well as transport across enterocytes. Transit time through the small intestine is decreased in patients who have undergone partial resection. Therefore, reduced exposure of nutrients to the intestinal mucosa interferes with optimal absorption.

2. What is the cause of JR's steatorrhea?

JR does not have an ileum and thus is unable to reabsorb bile salts. Bile salts are essential for the absorption of fats and fat-soluble vitamins. Normally, bile salts are reabsorbed through the ileum, transported to the liver via the enterohepatic circulation, and recycled back to the intestinal lumen to meet the need for bile salts. Following ileal resection, bile salt loss through the stool increases because these salts are no longer being absorbed. The liver

increases bile salt production in an attempt to compensate for the losses, but often fails to adequately accommodate them. As a result, absorption of fat, fat-soluble vitamins (A, D, E, and K), calcium, and magnesium decreases as the bile salt pool becomes depleted. In spite of greatly increased hepatic synthesis of bile salts, a deficiency of conjugated bile salts may result.

The inability to reabsorb bile salts results in an increased rate of conversion of cholesterol to bile acids by the liver. Depletion of intracellular free cholesterol up regulates the low-density lipoprotein receptors in these cells, resulting in an elevated rate of removal of cholesterol from the blood. This could explain the relatively low serum cholesterol level in the face of a high cholesterol intake. However, the rate of conversion of cholesterol to bile acids is inadequate in this patient to prevent symptoms of steatorrhea.

Bile salt deficiency leads to impairment in the body's ability to incorporate ingested dietary lipids (primarily long-chain triglycerides) into the micellar phase. This inability leads to decreased mucosal absorption of ingested lipids and fat-soluble vitamins resulting in subsequent steatorrhea, a condition called cholerrheic enteropathy. The deficiency of bile acids/salts diminishes the emulsification needed for efficient digestion of triacylglycerols

to fatty acids by pancreatic lipase, due to the small surface area for enzyme attachment.

When treating patients who have undergone ileal resection, it is important to remember that although bile salt absorption occurs passively through the upper small intestine, active sodium-coupled uptake of bile salts in the ileum normally is responsible for retrieval of over 95 percent of the intraluminal bile salts.

Part 2: Laboratory Evaluation

Several laboratory abnormalities were observed in this patient. JR's nutritional problems reflect his decreased small bowel absorptive area, which renders him less able to absorb fat, protein, carbohydrate, vitamins, and minerals.

3. What are the causes and associated clinical signs or symptoms of each laboratory abnormality with which JR presents?

Albumin JR's value: 2.5 g/dL	Normal value: 3.4–5.4 g/dL

A serum albumin level of 2.1 to 2.7 g/dL is an indication of a moderate degree of visceral protein depletion caused by decreased protein absorption. Muscle wasting and weakness are signs of skeletal protein depletion.

Calcium JR's value: 5.5 mg/dL	Normal value: 8.7–10.2 mg/dL

Because calcium is bound to albumin, it is always important to determine the serum calcium corrected for the patient's albumin level to account for the ionized calcium in serum, which is determined by equilibrium between free calcium and calcium bound to serum protein. We use the following equation to determine the corrected calcium:

$$(\text{Normal albumin} - \text{serum albumin}) \times (\text{correction factor}) + \text{serum calcium}$$

$$\text{Correction factor} = 0.8 \text{ normal albumin} = 4.0 \text{ g/dL}$$

Therefore, in JR's case

$$\text{Corrected calcium} = (4.0 - 2.5)(0.8) + 5.5 = 6.7 \text{ mg/dL}$$

This calcium value of 6.7 mg/dL, corrected for JR's albumin level, still is not in the normal range of 8.7 to 10.2 mg/dL. The recommended calcium intake for 19 to 30 years of age is 1000 mg/day. Most calcium absorption occurs in the duodenum, but all small intestinal segments absorb calcium. When adjustments are made for transit time and the relative lengths of the different intestinal segments, both the jejunum and ileum contribute substantially to overall calcium absorption. JR's resection has reduced the available absorptive surface area of the small intestine and this accounts, in part, for his low serum calcium value.

A second cause for the low serum calcium seen in this patient is the reduction in the size of the bile salt pool with impairment of micellar solubilization. This condition leads to decreased calcium absorption due to intraluminal binding of dietary calcium to unabsorbed fatty acids (soap formation). Third, vitamin D malabsorption and deficiency also lead to calcium malabsorption. Lastly, increased levels of protein and sodium in the diet generally increase calcium excretion through kidneys. This effect is present especially in low calcium intake, which is the case with JR.

JR suffers from hypocalcemia, a low serum calcium level. Evaluation of ionized calcium would help in assessing the severity of calcium depletion. Clinical manifestations of calcium deficiency include skeletal pain, tetany, paresthesia, osteoporosis, and stunted growth in children. (See Appendices G and H for dietary sources of calcium.)

Vitamin B_{12} JR's value: 100 pg/mL	Normal value: 279–996 pg/ mL

After vitamin B_{12} combines with the binding protein, intrinsic factor (which is produced in the stomach), it is absorbed in the terminal ileum. Patients who have undergone removal of the terminal ileum cannot absorb vitamin B_{12} and require intramuscular injections of this nutrient to prevent long-term deficiency and

associated peripheral neuropathy, which generally first becomes apparent after 5 to 10 years. An intranasal form of vitamin B_{12} has gained favor as a supplement. Clinical manifestations of vitamin B_{12} deficiency include megaloblastic anemia, peripheral neuropathy, glossitis, and cheilosis. The only dietary sources of vitamin B_{12} are foods of animal origin such as meat, chicken, fish, eggs, dairy products, and fortified soymilk. Some breakfast cereals are also fortified with vitamin B_{12}. Since JR has no ileum, dietary sources are unimportant since absorption is not feasible.

Vitamin A JR's value: 13 μg/dL	Normal value: 20–100 μg/dL

Vitamin A, in the form of dietary retinyl ester, is a fat-soluble vitamin that is hydrolyzed to retinol by pancreatic and intestinal brush border esterases prior to uptake from the gut lumen. Absorption occurs in the proximal small intestine and is aided by the presence of bile salts. Another source of retinol is the vitamin precursor beta-carotene. After uptake and transport, vitamin A is stored in the liver cells called stellate cells. Clinical manifestations of vitamin A deficiency include xerophthalmia (with clinical findings ranging from night blindness to corneal ulceration and irreversible blindness), poor wound healing, and loss of epithelial integrity (in the skin, GI tract, and urinary and respiratory systems). Dietary

sources of vitamin A and beta-carotene are listed in Appendix A. These nutrients also are found in meats, wheat and rice germ, nuts, and legumes. Vitamin A absorption is also limited by fat malabsorption.

Vitamin D JR's value: 5 ng/mL	Normal value: 30–100 ng/mL

Vitamin D is a fat-soluble vitamin, naturally occurring in two forms, vitamin D_2 and vitamin D_3. Fat malabsorption conditions adversely affect vitamin D absorption. Once absorbed and transported to the liver as a component of the chylomicrons or bound to a serum carrier protein, vitamin D binding protein (DBP), vitamin D undergoes hydroxylation to 25-hydroxy vitamin D [25(OH)D] with further conversion to its physiologically active form, 1,25-dihydroxy-vitamin D [$1,25(OH)_2D$], in the kidneys. The synthesis and metabolism of vitamin D is closely coupled to calcium homeostasis. Therefore when calcium levels in the blood are low, the body releases parathyroid hormone (PTH), which stimulates the kidney to convert calcidiol to calcitriol (its active form). Elevations in $1,25(OH)_2$ D stimulate the gastrointestinal tract to increase calcium absorption from about 10 to 30 percent and phosphorous absorption from about 60 to 80 percent.

Vitamin D deficiency due to fat malabsorptive disorders can result in rickets in infants and children and osteomalacia (softening of the bones) in adults. Osteomalacia may lead to pain in the legs, ribs, hips, and muscles, and easily broken bones. Vitamin D promotes neuronal survival and has a neurosteriod-like role in the CNS. Also, vitamin D deficiency can cause seasonal mood disturbances in otherwise healthy adults and responds well on supplementation. In older adults, deficiency can also cause cognitive decline affecting daily functioning and also lead to depressive behavior. The recommended daily intake of Vitamin D is 400 IU up to the age of 70 years and maximum dose for adults should be 4000 IU per day. (See Appendix B for dietary sources of vitamin D.)

Parathyroid hormone (PTH) and vitamin D: Normal value: 8–51 pg/ mL	JR's PTH value: 50 pg/ mL

It is important to consider PTH levels in patients who have low vitamin D levels because it is likely that the upper limit of normal for the PTH range (especially in elderly subjects) is set too high. Low vitamin D levels will tend to raise PTH secretion and may affect the PTH reference range by reducing calcium absorption. PTH tends to increase as vitamin D levels fall below 10 to 15 ng/mL. Severe vitamin D deficiency is likely to raise PTH to levels

above the reference range (“secondary hyperparathyroidism”), irrespective of the plasma calcium or phosphate level. However not all patients with hypovitaminosis D will necessarily show “hyperparathyroidism”.

Vitamin E	JR's alpha tocopherol value: 3.0 mg/L
	Normal value: 4.6–14.5 mg/L
	JR's beta gamma tocopherol value: 0.6 mg/L
	Normal value: 1.4–4.8 mg/L

Vitamin E is absorbed passively in the proximal small intestine. Bile salts serve as an important factor in normal vitamin E absorption. Like other fat-soluble vitamins, vitamin E is packaged into chylomicrons and delivered into the mesenteric lymphatics. It is stored primarily in the liver and in adipose tissue. Thus, deficiency is secondary to fat malabsorption. Clinical manifestations of vitamin E deficiency occur many years after the onset of deficiency which include neurologic dysfunction in the form of cerebellar ataxia, loss of deep tendon reflexes, and diminished vibratory and position sense. Hemolytic anemia may also result from vitamin E deficiency. (See Appendix C for dietary sources of vitamin E.)

Vitamin K JR's PT (prothrombin time): 16 seconds	Normal PT: <11–15 seconds

Vitamin K is obtained from dietary sources and also produced by colonic flora. Absorption of vitamin K occurs primarily in the proximal small bowel and requires bile salts. Following intestinal absorption, vitamin K is taken up largely by the liver and accumulated in the microsomal fraction. In the liver, vitamin K is a required cofactor for the enzymatic gamma-carboxylation of glutamic acid on vitamin K–dependent coagulation proenzymes (factors II [prothrombin], VII, IX, and X) and other proteins involved in coagulation and fibrinolysis (proteins C, S, M, and Z). Clinical manifestations of vitamin K deficiency include prolonged clotting time resulting in bleeding problems (oral, genitourinary, gastrointestinal, and skin). Long-term use of antibiotics may eliminate bacterial production of vitamin K for patients, rendering them prone to clinical deficiency if they do not receive exogenous sources of vitamin K. (See Appendix D for dietary sources of vitamin K.)

Serum Folate JR's value: 2.5 ng/mL	Normal value: 5.4–18 ng/mL

The jejunum absorbs folate for subsequent delivery into the portal circulation. Following intestinal resection, the remaining portions of

the small intestine may increase their uptake of folate to compensate for poor absorption; however, JR's folate intake is low due to poor intake of fruits and vegetables. Serum folate levels reflect very recent dietary ingestion rather than total body folate stores. Therefore, a normal serum folate test does not exclude folate deficiency. A better reflection of total body folate stores would be an erythrocyte folate level. Clinical manifestations of folate deficiency include megaloblastic anemia and glossitis. (See Appendix F for dietary sources of folate.) Folate is easily destroyed in cooking or processing.

Zinc JR's value: 300 mg/dL	Normal value: 550–1400 mg/dL

Zinc absorption occurs throughout the small intestine, but its rate of absorption is greater in the jejunum than in the ileum or duodenum. In patients who have undergone intestinal resection, transit time and surface area for absorption decrease, especially for zinc absorption. Intestinal reabsorption of zinc is impaired further in these patients because the jejunum and ileum have been removed. Clinical manifestations of zinc deficiency include anorexia, hypogeusia, alopecia, delayed onset of puberty, dermatitis, and poor wound healing. Oysters, meats, nuts, and legumes are all excellent dietary sources of zinc.

Magnesium JR's value: 1.2 mg/dL	Normal value: 1.5–2.3 mg/dl mg/dL

Magnesium is absorbed primarily in the jejunum and ileum by a passive mechanism. In patients with steatorrhea, unabsorbed fatty acids inhibit Mg absorption by forming insoluble complexes in a reaction called chelation. Magnesium absorption is reduced in patients who have undergone small intestinal resections because of the decreased available surface area. Clinical manifestations of magnesium deficiency may include neuromuscular weakness, confusion, fatigue, tetany, and paresthesia. (See Appendix K for dietary sources of magnesium.)

Fecal Fat JR's value: 28 g over 72 hours	Normal <7 g/day

Normal fat excretion on a diet of 80 to 100 grams of fat is up to 6 grams of fat per day. A larger amount of fat excretion is associated with a disorder of fat digestion and/or fat malabsorption.

Part 3: Clinical Assessment

4. Using JR's current body weight, calculate the percentage change from his usual weight and interpret these results.

$$\%\text{Weight change} = \frac{\text{Usual weight} - \text{Current weight}}{\text{Usual weight}} \times 100$$

$$\%\text{Weight change} = \frac{165\ \text{lb} - 125\ \text{lb}}{165\ \text{lb}} \times 100 = 24\%$$

A value of this magnitude (24 percent weight change) indicates a clinically significant and severe weight loss.

5. What conclusions can you draw regarding the fat, calorie, vitamin, and mineral content of JR's diet?

According to JR's 24-hour dietary recall analysis, his diet is high in fatty and salty foods and sweets. He is consuming more than 200 grams of fat per day. JR's diet lacks foods from three major food groups: fruits, vegetables, and dairy products. The fact that he rarely selects foods from these food groups places him at high risk for vitamin and mineral deficiencies compounded by malabsorption of fat and several vitamins and minerals.

6. How does JR's current caloric intake compare with his requirements?

According to the Harris–Benedict equation or 35 kcal/kg estimate, JR should consume 2700 to 2800 kcal/day to achieve a weight of 166 pounds (75 kg). However, according to JR's actual intake, he is consuming 4462 kcal/day. Normally, fat weight gain can be expected even

when excess intake amounts only to a few hundred calories, but JR's significant malabsorption problem has resulted in weight loss instead.

Part 4: Treatment

7. JR notes that his symptoms worsen when he eats fried or fatty foods. What should be done to correct these symptoms and his laboratory abnormalities?

JR is experiencing fat malabsorption secondary to his surgery. JR should follow adaptive hyperphagia, as studies indicate that multiple small meals per day can help increase the net nutrient absorption in short bowel syndrome. He can thus increase his diet 50% more than typical diet to compensate the effects of malabsorption .Because his ileum was resected, JR cannot reabsorb the bile acids required for fat digestion. Thus his dietary fat intake, at 43 percent of total calories, far exceeds his ability to digest and absorb fat properly. Referral to a registered dietitian for individualized counseling and reinforcement of the following suggestions is highly recommended in JR's case.

Low-fat foods should be substituted for fried and fast foods. However, because JR may have difficulty g weight difficult if his diet is too low in fat, monitoring his weight carefully is

important. JR should be encouraged to eat small frequent meals. Not all patients with malabsorption require a low-fat diet. JR should consume a wide variety of foods and increase his intake of soluble fiber (e.g., legumes, fruits, and oats). Because many patients with malabsorption due to intestinal resection tend to be lactose-intolerant as a consequence of their reduced levels of lactase enzyme, a lactose-free diet may be beneficial. To avoid oxalate kidney stones, calcium citrate can be a useful preparation owing to its solubility and absorption.

Vitamin and mineral supplementation is indicated, since his surgery has significantly increased his intestinal motility and decreased transit time and the available absorptive area for the vitamins and minerals described previously. Especially for vitamin B_{12}, it is preferable to use liquid supplementation for better bioavailability of the vitamin. In addition, as a result of bile salt depletion, his absorption of fat and fat-soluble vitamins A, D, E, and K also has decreased. Other food factors that are troublesome in patients with resected small intestines include insoluble fiber (whole-wheat products), oxalates (chocolate, cocoa, coffee, strawberries and cranberries), most nuts (especially peanuts), beans, beets, bell peppers, black pepper, parsley, rhubarb, spinach, Swiss chard, summer squash, sweet potatoes, tea and concentrated sweets.

Case 3 Celiac Disease

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Objectives

Identify clinical features of celiac disease and gluten-sensitive enteropathy.

Describe the assessment of a patient with celiac disease with regard to history taking, physical exam, and diagnostic tests.

Describe the treatment of celiac disease.

Provide resources for patients following a gluten-free diet.

TG is a 28-year-old female accountant who presents with intermittent diarrhea, bloating, and diffuse lower abdominal discomfort over the past 7 years. Her symptoms had been episodic but have become more frequent and more severe during the past several months. She also complains of mild fatigue but she is able to work without significant limitation. While an undergraduate, she was seen in the

Student Health Clinic for these symptoms and was diagnosed with diarrhea-predominant irritable bowel syndrome. She was treated with anti-diarrheal and anti-spasmodic medications on an as needed basis which controlled her symptoms but did not prevent recurrences.

Past Medical History

Osteopenia. She underwent a bone density evaluation after her mother was diagnosed with osteoporosis. She has no prior history of hospitalization. She is not taking any medications or over-the-counter dietary or herbal supplements.

Family History

Her father has a history of hypertension, and her mother has a history of osteoporosis, migraine headaches, and irritable bowel syndrome. She has a 32-year-old brother who has no medical problems.

Social History

Her work requires minimal physical activity, but she does try to exercise fairly regularly. She participates in aerobic exercises 2 to 3 times a week at the gym for 30 to 60 minutes. She states she would like to exercise more; however, she often feels fatigued after work. She does not smoke or use recreational drugs. She drinks

socially, consuming approximately 2 to 3 alcoholic beverages per week.

Review of Systems

She has no complaints of sleep problems and has not noticed any changes in her hair or nails. No cough, shortness of breath, or dyspnea on exertion are reported. Her appetite is good and her weight is stable. She has no muscle or joint pain.

Physical Examination

Vital Signs

Pulse: 84

Temperature: 37.8 °C (100 °F)

Heart rate: 78 BPM

Respiration: 14 BPM

Blood pressure: 120/70 mm Hg

Height: 5′6″ (173 cm)

Current weight: 122 lb

Usual body weight: 122–126 lb

BMI: 19.7 kg/m^2

General: Well-developed young woman in no acute distress

Skin: No rashes or bruises

HEENT: Normal, no exophthalmos, pale conjunctiva

Chest: clear to percussion and auscultation

Breasts: no masses

Abdomen: flat, hyperactive bowel sounds, no masses palpated, diffusely tender without guarding or rebound

Extremities: no cyanosis, clubbing, or edema

Laboratory Data

Patient's values	**Normal values:**
Creatinine: 0.9 mg/dL	0.5–1.2 mg/dL
BUN: 7.0 mg/dL	7–20 mg/dL
Glucose: 83 mg/dL	70–110 mg/dL
Albumin: 3.1 g/dL	3.6–4.5 g/dL
Calcium: 7.5 mg/dL	8.5–10.5 mg/dL
ALT: 81 U/L	10–40 U/L
AST: 49 U/L	10–40 U/L
Alkaline phosphatase: 48 U/L	50–130 U/L
White blood cell: 5.0	4800–10,800 µL
Hemoglobin: 8.6 g/dL	12–16 g/dL
Hematocrit: 26.4%	37–47%
MCV: 68.2 μm^3	82–94 μm^3

Patient's values	Normal values:
Platelet: 421,000/mm^3	150,000–350,000/mm^3
IgA anti-tissue transglutaminase: 2	
Total serum IgA: 48 IgG anti-tissue transglutaminase: 14	

Diet

TG's 24-Hour Food Recall

Patient states that this is a typical eating pattern during the week.

Breakfast (office 8:00 a.m.)	
Bagel	1 plain (3.5″)
Cream cheese	2 Tbsp.
Orange juice	6 ounces
Banana	1 medium
Morning snack (office 10:00 a.m.)	
Licorice (black)	4 pieces
Pretzels, honey wheat	1 ounce
Lunch (office 12:00 p.m.)	
Deli turkey breast	6 thin slices (3 ounces)
Whole wheat bread, light	2 slices
Low fat mayonnaise	1 Tbsp.

Baby carrots	8
Apple	1 medium
Oatmeal cookie with raisins	2
Bottled water	16 ounces
Afternoon snack (office 3:30 p.m.)	
Latte with skim milk	12 ounces
Dinner (home 6:30 p.m.)	
Salmon, baked	3 ounces
Angel hair pasta	2 ounces dry
Marinara sauce, canned, no meat	¼ cup
Green salad	1.5 cup
Croutons, plain	2 Tbsp.
Light vinaigrette	2 Tbsp.
Steamed broccoli	½ cup
Biscotti, almond (from bakery)	1 pc.
Tea, herbal (no sweetener)	8 ounces

Total calories: 1958 kcal

Protein: 81.5 g

Total fat: 42 g

Saturated fat: 9.8 g (4.5% of total calories)

Cholesterol: 149 mg

Carbohydrate: 327 g

Dietary fiber: 30 g

Sodium: 2821 mg

Case Questions

What are the typical symptoms of a patient with celiac disease or gluten-sensitive enteropathy?

What are the appropriate diagnostic tests for celiac disease?

When should genetic testing be performed to assess a patient's risk for CD?

What is the appropriate management for CD and/or gluten-sensitive enteropathy?

Which cereal grains contain gluten?

Which foods are safe to eat on a gluten-free diet?

How would you modify this patient's diet to provide for relief of symptoms?

How does a patient identify foods, beverages, dietary and herbal supplements, and medications that contain gluten?

1. What are the typical symptoms of a patient with celiac disease or gluten-sensitive enteropathy?

In the past, celiac disease (CD) was considered a pediatric disorder with the “classic” patient

presenting with diarrhea, malabsorption, steatorrhea, growth retardation, and weight loss with failure to thrive. With the emergence of serologic testing, the variable nature of the symptoms seen in CD has been discovered. Other potential signs and symptoms include: abdominal pain, bloating, weight loss, bone loss, chronic fatigue, infertility, hypoproteinemia, metabolic and electrolyte imbalances, iron deficiency anemia, elevated liver enzymes, peripheral neuropathy, and dermatitis herpetiformis, a blistering rash that typically affects the extensor surfaces of the body. Several conditions are associated with an increased risk of CD, such as, Down's and Turner's syndromes, thyroid disease (e.g., Hashimoto's thyroiditis), autoimmune diseases (e.g., Sjögren's disease, immunoglobulin A nephropathy), type 1 diabetes mellitus, immunoglobulin (Ig) A deficiency, and irritable bowel syndrome.

2. What are the appropriate diagnostic tests for celiac disease?

Immunoglobulin A (IgA) anti-tissue transglutaminase (TTG) antibody is the recommended single test for detection of CD in patients older than 2 years. The sensitivity and specificity of TTG-IgA for the detection of untreated CD are both approximately 95 percent. A total serum IgA level should also be obtained due to the association of CD and

selective IgA deficiency. It is recommended to perform TTG-IgG- testing in cases of IgA deficiency, which should include both TTG-IgG and IgG-deamidated gliadin peptides (DGPs). IgA antiendomysial antibodies (EMA) have been shown to have high specificity for CD (nearly 100 percent); however, it is expensive and operator-dependent, and should be used only to confirm borderline positive TTG antibodies or in cases of suspected false positive TTG antibodies. TTG antibody and EMA testing are less sensitive in children younger than 2 years, so TTG should be combined with DGP testing in this population.

Upper endoscopy with multiple duodenal biopsies while on a gluten-containing diet is required to confirm the diagnosis of CD. Histologic findings of duodenal biopsies range from increased intraepithelial lymphocytes to complete villous atrophy with crypt hyperplasia in the presence of increased intraepithelial lymphocytes; however, CD is not the only potential explanation for these findings, so confirmation of a diagnosis of CD is made by a combination of symptoms, antibody testing, and histology.

3. When should genetic testing be performed to assess someone's risk for CD?

Genetic background is important in the predisposition of CD. Human leukocyte antigen

(HLA)-DQ heterodimers are present in essentially all patients with CD. HLA-DQ2 is present in 95 percent, and HLA-DQ8 is seen in the remaining 5 percent. Importantly, the HLA-DQ2 haplotype is seen in approximately 25 to 30 percent of the general population; therefore, HLA-DQ testing alone is not routinely performed in the diagnosis of CD due to very low positive predictive value. HLA-DQ testing is helpful, however, in several scenarios. HLA-DQ2 and HLA-DQ8 testing may be useful in cases of mild histologic findings or when there is a discrepancy with antibody testing and biopsy results. Also, it is not uncommon for patients to seek medical care after initiating a gluten-free diet (GFD), which typically leads to normalization of antibodies and histology after several weeks to several months. This is perhaps the most common indication for HLA-DQ testing. Because HLA-DQ is seen in up to a third of the population, a positive result is not reliable in making a diagnosis of CD; however, if HLA-DQ2 and HLA-DQ8 are not detected, this effectively rules out CD with a negative predictive value of >99 percent.

The presence of HLA-DQ is seen in approximately 70 percent of first-degree relatives with CD. Routine HLA-DQ testing is not generally recommended for asymptomatic first-degree relatives with negative antibody testing due to the high probability of a potential false positive result with the potential initiation

of a GFD with its associated effects on quality of life.

4. What is the appropriate management for CD and/or gluten-sensitive enteropathy?

The primary goal of medical nutrition therapy for CD is to eliminate all gluten-containing products from the diet, including wheat germ, wheat bran, and any products containing wheat flour. Grains that are safe to eat include rice, corn, millet, buckwheat, sorghum, quinoa, and amaranth. Oats are generally safe for patients with CD but many oat products are processed using equipment that is also used for wheat so CD patients should look for oat products specifically labeled "gluten-free". When following a GFD, individuals must learn to read food labels, identify sources of gluten in foods, beverages, and dietary supplements, and eliminate these items from their diet. When adhering to a GFD, most patients have substantial and rapid improvement of symptoms, including symptoms other than the typical ones.

5. Which cereal grains contain gluten?

Gluten-containing grains are listed in Table 7-11 and should be avoided.

Table 7-11 GFD Foods to Avoid

Barley, barley malt Bran Bulgur Couscous Curum Einkorn Emmer Farino Farro Graham Kamut	Malt/extract/flavoring Oats/oat bran/flavoring Orzo Rye Seitan (wheat gluten) Semolina Spelt Triticale Wheat: bran, germ, grass, starch “Sprouted grains” made from these sources

6. Which foods are safe to eat on a gluten-free diet?

Following a GFD is an opportunity to eat whole foods instead of packaged or processed foods. Table 7-12 lists the foods that are recommended in the daily diet of an individual who has been diagnosed with CD or gluten-sensitive enteropathy.

Table 7-12 Gluten-Free Diet Recommended Whole Foods

Fruit – fresh or frozen
Vegetables – fresh or frozen without sauces

Beans and legumes
Nuts and seeds
Meat, fish, poultry without breading or gravies
Eggs
Dairy/non-dairy alternatives such as soy, almond milk – also consider lactose intolerance
Fats and oils
Allowable grains/grain products – quinoa, rice without seasonings, amaranth, arrowroot, bean flour, buckwheat, corn, flax, millet, potato, tapioca, sorghum

When reading labels on foods, dietary supplements, and medications, avoid the items listed in Table 7-13 as these may be derived from wheat.

Table 7-13 Ingredients that may contain gluten

Artificial color	Mustard powder
Artificial flavoring	Soy sauce
Beer	Smoke flavoring
Brewer's yeast	Soba noodles
Caramel color	Starch
Dextrins	Stock cubes
Food starch	Vitamins

Gravy cubes	Wheat starch
Ground spice mixes	
Imitation seafood	
Maltodextrin	
Miso	
Modified starch	
MSG	

7. How would you modify this patient's diet to provide for relief of symptoms?

Based on this patient's 24-hour recall, she should eliminate the bagel, pretzels, whole wheat bread, oatmeal cookies, croutons, angel hair pasta, and biscotti. All of these items can be replaced with gluten-free products including breads, cookies, and pasta. In addition, she should carefully read food labels for wheat, wheat flour, and wheat gluten.

9. How does a patient identify foods, beverages, dietary and herbal supplements, and medications that contain gluten?

It is very important for patients with CD to read labels very carefully. Every ingredient should be reviewed, even if the product claims to be gluten-free or wheat-free. If the patient is unsure of a specific ingredient, that food should be avoided. The patient can document the

product in question and look it up later, or ask a trained professional. It may also be useful for a patient to carry around with them a list of foods that are forbidden and a list of those that are safe.

To make things safer for consumers, beginning January 2006, the Food Allergen Labeling & Consumer Protection Act required food manufacturers to identify major allergens on food labels. Beginning in January 2008, gluten labeling was required which includes sources of gluten in many products. Many grocery stores now have many gluten-free products and many restaurants offer gluten-free menu items.

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8
Endocrine Disease: Diabetes Mellitus

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Nutrition Concepts by Franz, Inc., Minneapolis, MN

Objectives*

Describe the most common macrovascular and microvascular complications associated with diabetes mellitus and describe the role of glycemic control, nutrition therapy, and physical activity in reducing these complications.

Summarize the current nutrition recommendations and interventions for diabetes, and compare and contrast the nutrition strategies for persons with type 1 vs. type 2 diabetes.

Complete a thorough food and nutrition history of a person with diabetes, including an assessment of the (a) family history of diabetes, (b) onset and duration of diabetes symptoms, (c) evidence of complications, (d)

weight history, (e) usual food intake, (f) frequency, intensity, and duration of physical activity, (g) use of medications, and (h) alcohol consumption. Identify any problem areas.

Recognize the central importance of medical nutrition therapy and physical activity in the maintenance of health, and demonstrate a commitment to support patient adherence to nutrition interventions that are proven to be effective.

*Source: Objectives for chapter and cases adapted from the *NIH Nutrition Curriculum Guide for Training Physicians*. (www.nhlbi.nih.gov/funding/training/naa)

Introduction

Diabetes mellitus is manifested in three primary forms: type 1 diabetes, type 2 diabetes, and gestational diabetes mellitus (GDM). Diabetes is a group of diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Pathogenic processes involved in the development of diabetes range from autoimmune destruction of the beta cells of the pancreas with resultant insulin deficiency – type 1 diabetes – to abnormalities that result in resistance to insulin

action and an inadequate compensatory insulin secretory response – type 2 diabetes.

Without sufficient insulin, hyperglycemia occurs, resulting in acute and long-term microvascular and macrovascular complications. Mild hypoglycemia may be inconvenient or frightening to patients with diabetes; more severe hypoglycemia can cause acute harm to the persons with diabetes or others, if it causes falls, motor vehicle accidents, or other injury. The stress of illness, trauma, and/or surgery frequently compromise glycemic control and may result in acute, life-threatening consequences of uncontrolled hyperglycemia such as ketoacidosis and non-ketotic hyperosmolar syndrome. Long-term complications of hyperglycemia include retinopathy, nephropathy, and peripheral and autonomic neuropathy. Patients with diabetes are also at high risk for atherosclerotic, cardiovascular, peripheral arterial, and cerebrovascular disease. Hypertension and lipoprotein abnormalities are other common problems. Therefore, it is essential that effective therapy to achieve normal glycemia levels be initiated early to prevent the deleterious effects of hyperglycemia. Treatment for lipid disorders and hypertension is also essential.

Prevalence

In the United States, 25.8 million people of all ages are reported to have diabetes; 8.3 percent of the population. Of these 18.8 million who are diagnosed, 7.0 million remain undiagnosed. Diabetes prevalence increases with increasing age, affecting 10.9 million or 26.9 percent of those 65 years of age or older and is particularly prevalent in ethnic populations, including African-American, Latino, Native American, Asian American, and Pacific Islander. Approximately 215,000 youth under 20 years of age had diabetes (type 1 or type 2) in the United States in 2010. Among children with newly diagnosed diabetes, the prevalence of type 2 diabetes increased from less than 4 percent prior to 1990 to as high as 45 percent in certain racial/ethnic groups in recent years.

An estimated 79 million or 35 percent of United States adults who, based on fasting glucose or hemoglobin A1c (A1C) levels, are reported to have prediabetes are at high risk for developing type 2 diabetes, heart disease, and stroke. In adults aged 65 years or older, 50 percent have prediabetes. Lifestyle prevention strategies for people with prediabetes including weight loss and physical activity increases can prevent or delay the onset of type 2 diabetes and in some cases return blood glucose levels to normal (Chapter 1: Case 1; Chapter 9: Case 2).

Diagnosis of Diabetes Mellitus or Prediabetes

Prior to 2009, the diagnosis of diabetes was based on plasma glucose criteria, either the fasting plasma glucose (FPG) or the 2-hour value in the 75-g oral glucose tolerance test (OGTT). Beginning in 2010, the American Diabetes Association (ADA) also recommended the use of the A1C test to diagnose diabetes. The A1C test has several advantages to FPG and the OGTT, including greater convenience (since fasting is not required), greater preanalytical glucose stability, and less day-to-day variations due to illness or stress. Any of the following diagnostic criteria for diabetes can be used:

A1C ≥6.5 percent;* or

FPG ≥126 mg/dL (7.0 mmol/L);* or

2-hour PG ≥200 mg/dL (11.1 mmol/L during an OGTT using a glucose load containing the equivalent of 75 g of anhydrous glucose dissolved in water;* or

In patients with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).*

*In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.

Hyperglycemia that does not meet diagnostic criteria for diabetes is categorized as either

impaired fasting glucose (IFG) or impaired glucose tolerance (IGT). Both IFG and IGT are categories of increased risk for diabetes (prediabetes): *

FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG); or

2-hour plasma glucose in the 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT); or

A1C 5.7 to 6.4 percent.

*For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately grater at higher ends of the range.

Testing for Prediabetes and Diabetes

Unfortunately, type 2 diabetes is frequently not diagnosed until complications appear. Therefore, testing to detect prediabetes and type 2 diabetes in asymptomatic adults is important. There is a long presymptomatic phase before the diagnosis of type 2 diabetes is usually made and effective interventions can be utilized to prevent progression from prediabetes to diabetes and to reduce the risk of complications. Testing should be considered in all adults at any age with a body mass index (BMI) ≥25 kg/m^2 and who have one or more of

the known risk factors for diabetes listed in Table 8-1. In those without risk factors, testing should begin no later than age 45. If tests are normal, testing should be repeated at 3-year intervals, with considerations of more frequent testing depending on initial results and risk status (e.g., those with prediabetes should be tested yearly).

Table 8-1 Risk Factors for Development of Diabetes

Source: Adapted from American Diabetes Association. Standards of medical care in diabetes–2014. *Diabetes Care* 2014;37(Suppl 1):S14–S80.

Physical inactivity
First-degree relative with diabetes
Member of a high-risk ethnic population (e.g., African-American, Latino, Native American, Asian American, or Pacific Islander)
Women who delivered a baby weight >9 lbs (4 kg) or were diagnosed with GDM
Hypertension (blood pressure ≥140/90 mm Hg or on therapy for hypertension)
High-density lipoprotein cholesterol (HDL-C) level ≤35 mg/dL (0.90 mmol/L) and/or triglyceride level ≥250 mg/dL (2.82 mmol/L)

Women with polycystic ovarian syndrome (PCOS)

A1C ≥5.7%, IGT, or IFG on previous testing

Other clinical conditions associated with insulin resistance (e.g., severe obesity and acanthosis nigricans)

History of cardiovascular disease

Children and adolescents who are overweight (BMI >85th percentile for age and sex, weight for height >85th percentile, or weight >120 percent of ideal for height) and who have two or more additional risk factors for diabetes (listed below) should also be tested at age 10 years or at onset of puberty, if puberty occurs at a younger age. If tests are normal, testing should be repeated every 3 years. Risk factors include:

Family history of type 2 diabetes in first- or second-degree relative.

Race/ethnicity (Native American, African–American, Latino, Asian–American, Pacific Islander).

Signs of insulin resistance or conditions associated with insulin resistance including acanthosis nigricans (gray-brown skin, pigmentations) hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight.

Maternal history of diabetes or GDM during the child's gestation.

Pathophysiology of Diabetes

Type 1 Diabetes

Type 1 diabetes accounts for 5 to 10 percent of all diagnosed cases of diabetes. The primary defect results from a cellular-mediated autoimmune destruction of pancreatic beta-cells leading to absolute insulin deficiency (insulinopenia), as well as hyperglycemia, polyuria, polydipsia, weight loss, dehydration, electrolyte disturbance, and ketoacidosis. The capacity of a healthy pancreas to secrete insulin is far in excess of what is needed normally; therefore, the clinical onset of diabetes may be preceded by an extensive asymptomatic period (months to years), during which beta cells are undergoing gradual destruction. Persons with type 1 diabetes are dependent on exogenous insulin to prevent ketoacidosis and death. Although it can occur at any age, most cases are diagnosed in people younger than age 30 years of age, with peak incidence between 10 to 12 years in girls and 12 to 14 years in boys.

Type 1 diabetes is a result of a genetic predisposition combined with the autoimmune destruction of the islet beta cells. At diagnosis, 85 to 90 percent of persons with type 1 diabetes have one or more circulating autoantibodies.

Antibodies identified as contributing to the destruction of beta cells are (1) islet cell autoantibodies (ICAs); (2) insulin autoantibodies (IAAs), which may occur in persons who have never received insulin therapy; (3) autoantibodies to glutamic acid decarboxylase (GAD_{65}), a protein on the surface of beta cells (GAD autoantibodies appear to provoke an attack by killer T lymphocytes, which may be what destroys the beta cells in diabetes); and (4) autoantibodies to the tyrosine phosphatases IA-2 and IA-2β. Type 1 diabetes also has strong HLA association, with linkage to the DGA and DQB genes, and is influenced by the DRB genes. These HLA-DR/DQ alleles can be either predisposing or protective.

Frequently, after diagnosis and the correction of hyperglycemia, metabolic acidosis, and ketoacidosis, endogenous insulin secretion recovers. During this "honeymoon phase," exogenous insulin requirements decrease dramatically. However, the need for exogenous insulin is inevitable, and within 8 to 10 years after clinical onset, beta-cell loss is complete and insulin deficiency is absolute. The rate of beta-cell destruction is quite variable, being rapid in some individuals, mainly infants and children, and slow in others, mainly adults.

Type 2 Diabetes

Type 2 diabetes accounts for 90 to 95 percent of all diagnosed cases of diabetes and is a progressive disease that is often present long before it is diagnosed. Although approximately 50 percent of men and 70 percent of women are obese at the time of diagnosis, type 2 diabetes also occurs in non-obese individuals, especially in older adults. An affected individual may or may not experience the classic symptoms of uncontrolled diabetes, and they are not prone to develop ketoacidosis. Insulin resistance begins and progresses for many years before the development of diabetes, but impaired beta cell insulin secretory function must be present before hyperglycemia manifests. By the time diabetes is diagnosed, the individual has lost as much as 50 percent of beta cell function.

In type 2 diabetes, the normal biphasic insulin response to glucose is altered, resulting in postprandial hyperglycemia. The inadequate first-phase insulin response is also unable to suppress pancreatic alpha cell glucagon secretion, resulting in glucagon hypersecretion, which leads to an increase in hepatic glucose production and fasting hyperglycemia. The other major metabolic abnormality is a decrease in the ability of insulin to act on target tissues: muscles, liver, and fat cells. Compounding the problem is glucotoxicity, a deleterious effect of hyperglycemia – on both

insulin sensitivity and insulin secretion; hence, the importance of achieving near-euglycemia in persons with type 2 diabetes.

Insulin resistance is also demonstrated in adipocytes, leading to lipolysis and an elevation in circulating free fatty acids. Increased free fatty acids cause a further decrease in insulin sensitivity at the cellular level, impair insulin secretion, and augment hepatic glucose production (lipotoxicity). All these defects (cellular, hepatic, and beta-cell) contribute to the development and progression of type 2 diabetes.

As type 2 diabetes progresses, insulin production progressively declines. Therefore, patients with diabetes typically require more medication(s) over time and eventually exogenous insulin will be required. This is not a "diet" or medication failure, but rather a failure of beta cell function.

Nutrition Therapy for the Prevention of Diabetes

The increase in diabetes worldwide has made prevention of type 2 diabetes a high priority. Individuals with prediabetes are at high risk for the development of diabetes and cardiovascular disease. Large randomized controlled trials in individuals with prediabetes have repeatedly shown that lifestyle interventions are effective

in all ethnic groups, different age-groups, and various social and cultural settings worldwide. Modest weight loss (5 to 7 percent of body weight) and moderate physical activity (equivalent to 30 minutes brisk walking on most days of the week) are reported to decrease the risk of developing diabetes by 29 to 67 percent and/or delaying the onset of type 2 diabetes for at least 10 years.

Several trials have tested how efficacious drugs (i.e., metformin, acarbose, orlistat, rosiglitazone) would be in the prevention of diabetes. Each decreased the incident of diabetes to various degrees. Based on cost and side effects, the ADArecommends that only metformin be used, in combination with lifestyle counseling in those with IGT, IFG, or an A1C of 5.7 to 6.4 percent, and especially for those with BMI >35 kg/m^2, aged <60 years, or women with prior GDM.

Based on the evidence, the following are lifestyle recommendations for the prevention of diabetes:

Structured programs that emphasize lifestyle changes including education, reduced fat and energy intake, regular physical activity, and regular participant contact can produce a long-term weight loss of 5 to 7 percent of starting weight and reduce the risk of developing diabetes and are therefore recommended.

Engaging in regular physical activity (150 min/week) will decrease risk of developing type 2 diabetes. Regular physical activity reduces insulin resistance, independent of weight loss, and while initial weight loss may be achieved through restriction of energy intake alone, it is unlikely that weight loss maintenance can be achieved without regular physical activity.

Consuming at least 14 g fiber/1000 kcal per day and foods containing whole grains (at least one-half of grain intake).

Limiting intake of sugar-sweetened beverages.

Replacing saturated fatty acids with monounsaturated fatty acids or polyunsaturated fatty acids for improved insulin resistance and decreased risk of type 2 diabetes.

Limiting alcohol to one to two alcoholic drinks per day is associated with a lower incidence of type 2 diabetes likely resulting from increased insulin sensitivity. However, the data do not support recommending alcohol use to people who do not currently drink and abstinence is recommended for people with risks related to alcohol consumption.

Encouraging a Mediterranean-style eating pattern.

Treatment of Diabetes

Diabetes is a chronic disease that requires lifetime changes in lifestyle. The management of diabetes includes appropriate medical nutrition therapy, regular physical activity, self-management education, and medications. An important goal is to provide the individual with the necessary tools to achieve the best possible control of glycemia, lipids, and blood pressure to prevent, delay, or arrest the microvascular and macrovascular complications of diabetes while minimizing hypoglycemia and promoting weight loss and preventing weight gain.

Optimal control of diabetes requires the restoration of normal carbohydrate, protein, and fat metabolism. Insulin is both anticatabolic and anabolic and facilitates cellular glucose transport. In general, the counterregulatory hormones – glucagon, growth hormone, cortisol, epinephrine, and norepinephrine – have the opposite effect of insulin. In addition, incretin hormones (glucagon-like peptide 1 [GLP-1] and glucose-dependent insulinotrophic polypepetide, also called gastric inhibitory peptide [GIP]) are released from the gastrointestinal tract after food ingestion causing an “anticipatory” increase in insulin in preparation for the glucose and amino acids to be absorbed from the food.

Monitoring of Metabolic Outcomes

Glycemic control can be assessed by self-monitoring of blood glucose (SMBG), interstitial glucose by continuous glucose monitoring (CGM), or A1C measurement. Persons with diabetes can use SMBG to determine the impact that food choices and physical activity have on blood glucose levels and to make adjustments in lifestyle and medications required to achieve glycemic goals. The ADA recommends that patients on multiple-dose insulin (MDI) or insulin pump therapy do SMBG prior to meals and snacks, occasionally postprandially, at bedtime, and prior to exercise, or when they suspect low blood glucose, after treating low blood glucose until they are normoglycemic, and prior to critical tasks such as driving. For persons on non-insulin therapy, SMBG should be done sufficiently to facilitate reaching glucose goals. The accuracy of SMBG is instrument- and user-dependent and monitoring techniques must be evaluated on a regular basis. Patients also should be taught how to use the data to adjust food intake, exercise, or medications to achieve glycemic goals.

CGM measures interstitial fluid glucose (which correlates with blood glucose) in a continuous and minimally invasive manner. Continuous glucose sensors have alarms for hypo- and

hyperglycemia and small studies have shown the use of CGM to decrease the average time patients spend in hypo- and hyperglycemic ranges. CGM used with an intensive insulin regimen or insulin pump can be a useful tool to lower A1C in selected adults (aged ≥25 years) with type 1 diabetes.

Complementing day-to-day testing are measurements of glycosylated hemoglobin (simplified as A1C) reflecting a weighted average of plasma glucose over the preceding 6 to 8 weeks, and thus reflecting long-term glycemic control. When hemoglobin and other proteins are exposed to glucose, the glucose becomes attached to the protein in a slow, non-enzymatic, and concentration-dependent manner. The A1C test should be done at least two times a year in patients who are meeting treatment goals and who have stable glycemic control. The A1C test should be done quarterly in patients whose therapy has changed or who are not meeting glycemic goals. Lowering A1C to around 7 percent or below has been shown to reduce microvascular complications of diabetes and if implemented soon after the diagnosis of diabetes is associated with long-term reduction in macrovascular disease. Therefore, the ADA recommends that a reasonable A1C goal for many non-pregnant adults is <7 percent. A lower A1C goal (such as <6.5 percent) might be reasonable for selected individual patients, if this can be achieved without significant

hypoglycemia or adverse effects of treatment. Conversely, a less stringent goal (such as <8 percent) may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, and advanced complications.

Lipid levels and blood pressure should also be monitored. In most adult patients with diabetes, a fasting lipid profile should be measured at least annually. Blood pressure should be measured at every routine visit. The ADA glycemic, lipid, and blood pressure goals are listed in Table 8-2.

Table 8-2 Clinical Goals for Diabetes Therapy

Source: Adapted from American Diabetes Association. Standards of medical care in diabetes–2014. *Diabetes Care* 2014;37(Suppl 1):S14–S80.

Recommendations for Many Non-Pregnant Adults with Diabetes	**Goal**
Glycemic	
A1C	<7.0%*
Preprandial capillary plasma glucose	70–130 mg/dL* (3.9–7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (<10.0 mmol/L)

Recommendations for Many Non-Pregnant Adults with Diabetes	Goal
Lipids	
LDL-C (without overt CVD)	<100 mg/dL (<2.6 mmol/L)
LDL-C (with overt CVD)	<70 mg/dL (<1.8 mmol/L
Triglycerides	<150 mg/dL (<1.7 mmol/L)
HDL-C	>40 mg/dL (>1.0 mmol/L) in men
	>50 mg/dL (>1.3 mmol/L) in women
Blood pressure	
Blood pressure	<140/80 mm Hg

*Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid condition, hypoglycemia unawareness.

† Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in persons with diabetes.

Medical Nutrition Therapy

A healthy eating pattern and regular physical activity are important goals of medical nutrition therapy for all individuals with prediabetes and diabetes. For individuals with diabetes, other goals of medical nutrition therapy (MNT) are to assist in:

attaining individualized glycemic, lipid, and blood pressure goals.

achieving and maintaining body weight goals.

delaying and preventing complications of diabetes.

Clinical trials and outcome studies support MNT as effective in improving metabolic outcomes, such as blood glucose, A1C, lipids, blood pressure, weight, and/or quality of life in persons with diabetes. The Academy of Nutrition and Dietetics Evidence-Based Nutrition Practice Guidelines (EBNPG) for diabetes documented decreases in A1C of 1 to 2 percent (range: −0.5 to −2.6 percent) with MNT depending on the type and duration of diabetes and at what time point in the disease process interventions are implemented. These outcomes are similar to those from glucose-lowering medications. The evidence suggests that MNT is most effective at initial diagnosis, but is effective at any time during the disease process. Many different types of nutrition interventions are effective. Central to

these interventions are multiple encounters to provide education and counseling initially and on a continued basis. These outcomes highlight the importance of the registered dietitian (RD) in determining the most effective nutrition intervention for each individual and coordinating care with a multidisciplinary team.

In studies done primarily in individuals without diabetes, cardioprotective MNT implemented by RDs resulted in a reduction of total cholesterol by 7 to 21 percent, LDL-cholesterol by 7 to 22 percent, and triglycerides 11 to 33 percent. In hypertensive patients who consume excessive sodium, reducing intake to approximately 2300 mg/day can lower systolic blood pressure by 2 to 8 mm Hg; implementing a DASH eating pattern can lower systolic blood pressure by 8 to 14 mm Hg (Chapter 6). It is important to remember that these results are achieved without any attendant risk of medication side-effects.

Results from nutrition interventions on glycemia, lipids, and blood pressure are generally known by 6 weeks to 3 months and an evaluation should be performed by the RD at this time. At 3 months, if patients have made the lifestyle changes they are able and willing to make, and if target goals have not been achieved, medication changes (or adjustments)

are usually needed and should be recommended to achieve target goals.

Achieving nutrition-related objectives requires a multidisciplinary team effort that includes dietitians, diabetes educators, physicians, nurse practitioners, and the person with diabetes who must be involved in problem solving. A system of care that provides ongoing support and education is essential.

Prioritizing Nutrition Strategies for Diabetes

Historically, nutrition advice has been given to patients with diabetes, such as “don't eat foods with sugar” or “go home and lose weight.” This advice has often been accompanied by a calorie-level “diet sheet” or a pamphlet or brochure with general guidelines. Patients often find such information difficult to understand and implement. To achieve positive outcomes, appropriate priorities should be set for each patient.

Type 1 Diabetes The first priority for persons requiring insulin therapy is to integrate an insulin regimen into the patient's lifestyle. After an initial food/meal plan is determined (with the patient's input), it should be reviewed with the health professional who is planning the insulin regimen. With the many insulin options now available, an insulin regimen can usually

be developed that will conform to the patient's preferred meal times and food choices. Flexible insulin regimens using basal (background) insulin and bolus (mealtime) insulin or insulin pumps give the patient freedom in timing and composition of meals and are the preferred mode of therapy to maximize blood glucose control and minimize complications.

The total amount of carbohydrate in the meal (and snacks, if desired) is the major determinant of the bolus rapid-acting insulin dose and post-prandial glucose response. After determining the amount of insulin required to cover the patient's usual meal carbohydrate, patients can be taught how to adjust bolus insulin doses based on the amount of carbohydrate they are planning to eat (insulin-to-carbohydrate ratio). For persons receiving fixed insulin regimens and not adjusting mealtime insulin doses, consistency of day-to-day carbohydrate amounts at meals is important.

Type 2 Diabetes Previously, nutrition advice focused on losing weight and avoiding sugars. Today, the focus of MNT for type 2 diabetes is to implement lifestyle strategies that will assist in improving glycemia, dyslipidemia, and blood pressure. Since many persons with type 2 diabetes are insulin resistant and overweight, MNT often begins with lifestyle strategies that reduce energy intake and increase energy

expenditure through physical activity. However, many individuals have already tried unsuccessfully to lose weight and it is important to note that other lifestyle strategies, even without weight loss, can improve glycemia. Effective nutrition interventions include reduced energy/fat intake, individualized MNT, portion control, healthy food choices, and carbohydrate counting. A consistent and important theme for individuals with type 2 diabetes is reduced energy intake, which may or may not lead to substantial weight loss, but consistently improves glycemic control.

Modest amounts of weight loss and regular physical activity have been proven to prevent the progression of prediabetes to type 2 diabetes. Weight loss, especially of intra-abdominal fat, reduces insulin resistance; however, as individuals move from being primarily insulin resistant to insulin deficiency, the role of weight loss becomes more controversial. At later stages of the disease when medications, including insulin, need to be combined with MNT, prevention of weight gain often becomes an issue, although glycemic control must take precedence over concern about weight. In weight loss studies in subjects with type 2 diabetes, weight loss seems to plateau at 6 months, and weight loss is more difficult to accomplish in people with diabetes.

Unfortunately, weight loss of 4.7 kg among patients with type 2 diabetes did not result in greater decreases in cardiovascular events compared to control, in spite of improved A1C, HDL, thyroid hormone, and blood pressure.

In addition, a recent systematic review of weight-loss interventions in overweight/obese adults with type 2 diabetes demonstrated no differences by types of intervention and only a non-significant impact on A1C. This may be because most of the trials failed to achieve a weight loss of 5 percent or greater from baseline. Thus, the majority of the trials could not achieve weight losses that seem to be necessary to produce beneficial metabolic outcomes. A weight loss of >6 kg (7 to 8.5 percent), regular physical activity, and frequent contact with RDs appears necessary for consistent beneficial metabolic outcomes. How to achieve this weight loss in randomized trials remains unclear.

Macronutrient Recommendations

Numerous studies have attempted to identify the optimal mix of macronutrients to guide eating patterns for people with diabetes. The ADA systematic review of macronutrients concluded that there is not one effective mix that applies broadly, and that the mix of carbohydrate, protein, and fat should be

adjusted to meet the metabolic goals and individual preferences of each individual.

Carbohydrate Because carbohydrate and adequacy of insulin determine post-prandial glucose response, it is addressed first. With the continued popularity of low-carbohydrate diets, it should be remembered that foods containing carbohydrates – fruits, vegetables, whole grains, legumes, and low fat-milk – are important components of a healthy diet and should be included in an eating plan for persons with diabetes. Furthermore, the majority of people with diabetes do not eat a high (or low) carbohydrate diet. Both people with type 1 and type 2 diabetes report eating moderate amounts of carbohydrate. Vegans or vegetarians are perhaps the primary people with diabetes who tend to eat a higher carbohydrate diet (~65 to 75 percent of total energy), which is reported to improve glycemic control as well as serum lipids and blood pressure.

Observational studies in persons with type 1 and type 2 diabetes report A1C benefits from a higher carbohydrate, lower-fat eating pattern. It is suggested, however, that the carbohydrate content may be less important than the total and saturated fat content. Higher fat, especially saturated fat, intake in numerous studies has been shown to contribute to an increase in insulin resistance. High-fat meals have been shown to interfere with insulin signaling,

whereas lower fat diets improve insulin sensitivity.

In clinical trials both high- or low-carbohydrate eating patterns lead to similar improvements in A1C and body weight. The total energy intake appears to be of more importance that the type or amount of carbohydrate. Therefore, it seems appropriate to recommend an eating pattern with moderate amounts of fruits, vegetables, whole grains, legumes, and low-fat dairy foods – all components of a healthy eating pattern.

The glycemic index (GI) measures the relative area under the glucose curve of 50 g of digestible carbohydrate compared with 50 g of either glucose or bread. It does not measure how rapidly blood glucose levels increase after eating carbohydrate-containing foods ("fast-acting" carbohydrates), which is a common misimpression given to the public. A major problem with the GI is the variability of responses to carbohydrate-containing foods among individuals. Short-term studies comparing high- versus low-GI diets report mixed effects on A1C levels. The Canadian Trial of Carbohydrate in Diabetes, a 1-year study comparing low or high GI diets, reported no significant difference in A1C or lipids by altering the GI or the amount of carbohydrate. An ADA systematic review concluded: "In general, there is little difference in glycemic control and cardiovascular disease risk factors

between low-GI and high-GI diets." Furthermore, as with carbohydrate, most individuals with diabetes seem to consume a moderate GI diet and it is unknown whether reducing the usual GI by a few units will result in improved long-term glycemic control.

All persons with diabetes can, however, benefit from basic information about carbohydrates: what foods contain carbohydrate (starches, fruit, starchy vegetables, milk, sweets and desserts; one average serving is equivalent to 15 g) and how many servings to select for meals (and snacks if desired). For all, monitoring total carbohydrate intake either by carbohydrate counting, food selection, or experience-based estimation is a key strategy in achieving glycemic control. The following are recommendations for carbohydrates:

In persons on MNT alone, glucose-lowering medications, or fixed insulin doses, meal (and snack) carbohydrate intake should be kept consistent on a day-to-day basis, as consistency has been shown to result in improved glycemic control. For persons with type 2 diabetes total energy intake is important and therefore careful attention to portion sizes is critical.

In persons with type 1 or type 2 diabetes who adjust their mealtime insulin or who are on insulin pump therapy, insulin doses should be adjusted to match carbohydrate intake (insulin-to-carbohydrate ratios).

Recommendations for fiber intake are similar to recommendations for the general public (DRI: 14 g/1000 kcal per day). Diets containing 44 to 50 g of fiber per day are reported to improve glycemic control; however, fiber intakes up to 24 g/day have not shown beneficial effects on glycemia. Diets high in total and soluble fiber, as part of cardioprotective nutrition therapy, have been shown to reduce total cholesterol by 2 to 3 percent and LDL-C up to 7 percent.

Whole-grain foods contain fiber, vitamins, minerals, phenolic compounds, and phytoestrogens lower serum lipids and blood pressure, improve glucose and insulin metabolism and endothelial function, and alleviate oxidative stress and inflammation in the general population. At least half of recommended grain intake should be whole grains.

If persons with diabetes choose to eat foods containing sucrose, the sucrose-containing foods should be substituted for other carbohydrate foods. Sucrose intakes of 10 to 35 percent of total energy intake do not have a negative effect on glycemic or lipid responses when substituted for isocaloric amounts of starch.

Non-nutritive sweeteners and sugar alcohols are safe when consumed within the accepted daily intake levels established by the Food and

Drug Administration. However, some of these products may contain energy and carbohydrate from other sources.

Eating a minimum of 5 servings of fruits and vegetables daily is recommended for both prevention and treatment of high blood pressure.

Protein Aside from sugars, protein is probably the most misunderstood nutrient with inaccurate advice frequently given to persons with diabetes. Although non-essential amino acids serve as substrates for gluconeogenesis, in subjects with controlled diabetes, this glucose does not enter the general circulation. Ingestion of protein results in acute insulin and glucagon responses with minimal, if any glucose or lipid response. Protein also does not slow the absorption of carbohydrate, but because it can increase acute insulin responses without increasing glucose concentrations, it should not be used to treat acute hypoglycemia or to prevent overnight hypoglycemia (e.g., by adding protein to bedtime snacks).

There is no evidence to suggest that usual intake of protein (15 to 20 percent of energy intake) be changed in persons who do not have renal disease. In persons with diabetic kidney disease (DKD), (either micro- or macroalbuminuria), lower protein diets (achieved average of 0.9 g/kg per day) versus usual protein diets (average 1.2 g/kg per day)

do not significantly improve the rate of decline of glomerular filtration rates (GFR). Therefore, the ADA 2013 nutrition recommendations concluded that reducing the amount of dietary protein below the usual intake is not recommended because it does not alter glycemic measures, CVD risk measures, or the course of GFT. Therefore, the focus of MNT for persons with DKD should be on assisting with control of blood glucose levels and hypertension (Chapter 9: Renal Disease).

Dietary Fat A long-term high fat and high saturated fat diet are associated with an increase in insulin resistance. Limiting intake of saturated fatty acids to less than 7 percent of total energy, consuming minimal *trans* fatty acids, and dietary cholesterol less than 200 mg/day are recommended.

The ADA also recommends two or more servings of fish per week (with the exception of commercially fried fish filets). Plant sterol and stanols esters have also been shown to lower total and LDL-C in persons with type 2 diabetes and can be substituted for other fats in the diet, such as margarine or cream cheese. However, the ADA does not recommend omega-3 supplements for primary or secondary prevention of CVD as randomized controlled trials do not provide evidence for their effectiveness.

Micronutrient Recommendations

Vitamins and Minerals There currently is no evidence of benefit from vitamin or mineral supplementation in persons with diabetes who do not have underlying deficiencies. Routine supplementation with antioxidants is not advised because of lack of evidence of effectiveness and concerns related to long-term safety. There is also insufficient evidence to support the use of chromium, magnesium, and vitamin D to improve glycemic control in persons with diabetes.

Sodium For both normotensive and hypertensive individuals, a reduction in sodium intake lowers blood pressure. The recommendation for the general public to reduce sodium to <2300 mg/day is also appropriate for persons with diabetes. For persons with both diabetes and hypertension, further reduction in sodium intake should be individualized.

Alcohol Recommendations for alcohol intake are similar to those for the general public. If individuals choose to drink, alcoholic beverage consumption should be limited to an average of up to 2 drinks per day for men and an average of up to 1 drink per day for women. One drink is defined a 12 ounces beer, 5 ounces wine, or 1.5 ounces of distilled spirits, each of which contains approximately 15 g of alcohol. For individuals using insulin or insulin

secretagogues, alcohol should be consumed with food to reduce the risk of hypoglycemia. Occasional use of alcoholic beverages should be considered an addition to the regular meal plan, and no food should be omitted.

Moderate amounts of alcohol, when ingested with food, have minimal acute or long-term effects on glucose and insulin concentrations in people with type 1 or type 2 diabetes. Moderate alcohol intake (1 to 2 drinks per day) is associated with a decreased risk of and mortality from cardiovascular disease (CVD). The type of alcohol-containing beverage does not make a difference. On the other hand, excessive amounts of alcohol (3 or more drinks per day), on a consistent basis, contribute to hyperglycemia, hypertension, cirrhosis, and other medical conditions.

Physical Activity

Physical activity should be an integral part of the treatment plan for persons with diabetes. Exercise helps improve insulin sensitivity, reduce cardiovascular risk factors, control weight, and improve well-being. People with diabetes can exercise safely. The exercise plan will vary depending on age, general health, and level of physical fitness. A minimum of 150 min/week of moderate intensity aerobic physical activity (50 to 70 percent of heart rate) is advised. In the absence of contraindications,

resistance training three times per week is encouraged. Persons taking insulin or insulin secretagogues should monitor their blood glucose and take appropriate precautions to avoid hypoglycemia; carbohydrate should be eaten if pre-exercise glucose levels are less than 100 mg/dL (5.6 mmol/L).

Bariatric Surgery

Performing bariatric surgery in persons with diabetes continues to be controversial, especially in persons with a BMI of 30 to 35 kg/m^2. The ADA recommendations state that bariatric surgery may be considered for adults with BMI >35 kg/m^2 and type 2 diabetes, especially if the diabetes or associated co-morbidities are difficult to control with lifestyle and pharmacological therapy. A meta-analysis of 136 weight-loss surgery studies, including 22,094 individuals BMI ≥40 revealed an overall type 2 diabetes remission rate of 84 percent after Roux-en-Y gastric bypass and 48 percent after adjustable gastric banding 48 percent. Patients challenged with prediabetes may benefit the most since most studies report close to 100 percent prevention of progression to diabetes (Chapter 1: Case 2). The role of bariatric surgery in patients with type 2 diabetes and a BMI of 30 to 35 kg/m^2 is under discussion In two recent reports, mildly to moderately obese persons with uncontrolled

diabetes who underwent bariatric surgery had better short-term glucose control and weight loss than persons who received medications and lifestyle advice. But the surgery had potential complications and it is unknown whether the benefits of the surgical interventions extend beyond 1 to 2 years. Therefore, long-term benefits, cost-effectiveness, and risk of bariatric surgery in persons with type 2 diabetes require additional investigation.

Medications

Glucose-Lowering Medications If metabolic goals are not being met in persons with type 2 diabetes, there are now seven classes of oral medications as well as injectable medications, including insulin, which can be combined with nutrition therapy. This provides numerous options for achieving euglycemia in persons with type 2 diabetes. Metformin is usually the first line-drug, but many people benefit from taking two or more of the medications because each addresses a different problem. Such combination therapy is so common that a number of combination pills are also available. However, because of the progressive nature of type 2 diabetes, many individuals will also require insulin therapy alone or in combination with other agents to achieve glycemic control. Classes of glucose-lowering medications are:

Amylin mimetics (pramlintide), which activate amylin receptors, there bydecreasing postmeal glucagon secretion and delaying gastric emptying;

Alpha-glucosidase inhibitors (acarbose, miglitol), which work in the small intestine to inhibit α-glucosidase enzyme that digests carbohydrates, thereby delaying intestinal carbohydrate digestion/absorption and lowering postprandial glycemia;

Biguanides (metformin), which suppress hepatic glucose production, lower insulin resistance, but do not stimulate insulin secretion;

DPP-4 inhibitors (sitagliptin, saxagliptin, linagliptin), which inhibit dipeptidyl peptidase-4 (DDP-4) enzyme that degrades glucose dependent insulinotropic polypeptide (GIP) and glucose-like polypeptide (GLP), whose actions are to increase insulin secretion in the presence of elevated plasma glucose and to reduce postmeal glucagon secretion;

GLP-1 receptor agonists (exenatide, exenatide extended release, liraglutide), which activate GLP-1 receptors, thereby enhancing insulin secretion in the presence of hyperglycemia, decreasing postmeal glucagon production, delaying gastric emptying, and may suppress appetite;

Insulins (human NPH, human Regular, lispro, aspart, glulisine, glargine, detemir, premixed [several types]), which increase glucose disposal and decrease hepatic glucose production;

Sodium-glucose transporter 2 (SGLT-2) inhibitors (canagliflozin, dapagliflozin) which cause glucose to be flushed out in the urine by blocking a transporter protein that returns glucose to the bloodstream after it is filtered through the kidneys;

Meglitinides (nateglinide and repaglinide), which acutely promote insulin secretion and are taken at the start of a meal;

Sulfonylureas (second-generation: glyburide/ glibenclamide, glipizide, glimepiride), whose actions are to promote insulin secretion by the beta cells of the pancreas over longer periods of time;

Thiazolidinediones (pioglitazone, rosiglitazone), which decrease insulin resistance in peripheral tissues and thus enhance the ability of muscle and adipose cells to take up glucose.

Insulin All persons with type 1 diabetes and many persons with type 2 diabetes who no longer produce adequate endogenous insulin need replacement of insulin that mimics normal insulin action. After eating, plasma glucose and insulin concentrations increase

rapidly, peak in 30 to 60 minutes and return to basal concentrations within 2 to 3 hours in non-diabetics. To mimic this, rapid-acting insulin, such as lispro, aspart, or glulisine, is given at mealtime; doses are adjusted based on the amount of carbohydrate in the meal.

Basal or background insulin, such as determir, glargine, or NPH, is required in the post-absorptive state to restrain endogenous glucose output primarily from the liver and to limit lipolysis and excess flux of free fatty acids to the liver. Glargine and detemir are insulin analogs of 24-hour duration with no peak action time. They can be injected any time during the day, as long as they are taken around the same time each day, and cannot be mixed with other insulins. NPH is also occasionally used as background insulin but usually has to be given twice a day. The type and timing of insulin regimens should be individualized based on eating and exercise habits and blood glucose concentrations. There are also premixed insulins that are usually used in persons with type 2 diabetes, often when insulin is initiated.

Many patients find insulin pens to be a convenient way to inject their insulin doses. Insulin pens are available containing regular, NPH, lispro, aspart, glulisine, or 70/30 or 7/25 premixed insulin.

Insulin pump therapy delivers insulin in two ways: in a steady, measured, and continuous

dose (the basal insulin), and as a surge (bolus) dose at mealtime. Insulin pumps can also deliver precise insulin doses for different times of day, which may be necessary to correct for situations such as the dawn phenomenon (increase in blood glucose level that occurs in the hours before and after waking). Pump therapy requires a committed and motivated person who is willing to do a minimum of four blood glucose tests per day, keep blood glucose and food records, and learn the technical features of pump usage.

Types of insulin and their action times are given in Table 8-3.

Table 8-3 Action Times of Human Insulin Preparations

Type of Insulin	Onset of Action	Peak Action	Effective Duration
Rapid-acting			
Lispro (Humalog)	<15 min	1–2 h	2–4 h
Aspart (Novolog)	<15 min	1–3 h	3–5 h
Glulisine (Apidra)	<15 min	0.5–1 h	3 h
Short-acting			
Regular	0.5–1 h	2–4 h	3–5 h
Intermediate-acting			
NPH	2–4 h	4–10 h	10–16 h
Long-acting			
Glargine (Lantus)	4–6 h	None	24 h
Detemir (Levemir)	3–4 h		5.7–24 h
Mixtures			
Humalog Mix (75/25)	<15 min	Dual	
Novolog Mix (70/30)	<15 min		10–16 h
Humalog Mix (50/50)	<15 min		
Humulin (70/30)	0.5–1 h		10–16 h
Novolin (70/30)	0.5–1 h		10–16 h

Source: Adapted from American Diabetes Association. Insulin. *Diabetes Forecast 2008 Resource Guide*. 2008;RG11–RG14.

Treatment of Hypoglycemia

Any carbohydrate-containing food will raise glucose levels, including glucose tablets, sucrose, juice, regular soda, or syrup. Glucose is the preferred treatment, and commercially available glucose tablets have the advantage of being premeasured to help prevent over-treatment. Treatment begins with 15 to 20 g of glucose and an initial response should be seen in approximately 10 to 20 minutes. Blood glucose should be evaluated again in approximately 60 minutes as additional treatment may be necessary. Adding protein has no benefit in treatment or in the prevention of subsequent hypoglycemia. Severe hypoglycemia (the individual is unable to ingest oral carbohydrate) requires administration of glucagon. For insulin users, prevention of hypoglycemia is a critical component of diabetes management.

Self-Management Education

For metabolic goals to be achieved there must be open communication and self-management education. With chronic illnesses such as diabetes, the role of healthcare providers shifts from providing direct medical care to facilitating self-management by individuals with diabetes and their families. Many healthcare providers choose to use a team approach with registered dietitians (as well as

other team members) in their medical center or clinic or delegate the educational and skill-building components by referring to a registered dietitian and/or a diabetes education center.

It is reported that individuals who hold two important beliefs are more likely to engage in effectively self-management behaviors than are those who do not hold these beliefs: (1) consider diabetes to be serious and (2) believe that their own actions make a difference. An individual's self-efficacy and self-confidence in making and maintaining a change are significant predictors of later adherence. A simple, but effective role that all healthcare providers can provide is to endorse and support lifestyle changes and to express confidence in the patient's ability to make change.

Case 1 Type 1 Diabetes Mellitus and Diabetic Ketoacidosis

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Objectives

Describe the role of exogenous insulin and medical nutrition therapy in the management of type 1 diabetes and in the prevention and/or treatment of acute and long-term diabetic complications.

Take an appropriate medical and lifestyle history of a person with type 1 diabetes.

Recognize the importance of individualizing rapid-acting insulin algorithm based on carbohydrate intake, physical activity, and blood glucose monitoring.

Evaluate and identify potential metabolic complications of diabetes mellitus based on nutritional and physical activity history, use of medications, and alcohol consumption.

MN is a 33-year-old Hispanic woman with type 1 diabetes, which was diagnosed at the age of 30. She reports feeling lightheaded in the late afternoon and notes that she feels better after eating. MN also reports difficulty sleeping. Her blood glucose monitor log indicated from before breakfast to before dinner blood glucose. Tests range from 70 mg/dL and 150 mg/dL. MN is 5′4″ (163 cm) tall and currently weighs 132 pounds (60 kg). Recent assessment of her

kidney function and an eye examination were normal.

Past Medical History

MN was diagnosed with type 1 diabetes 3 years ago after being brought to the emergency room by her mother in ketoacidosis. At the time of her diagnosis, MN recalls losing 9 pounds (4.1 kg) in 2 days after coming down with a cold and suffered from dizziness, fatigue, and frequent urination and experienced excess thirst and hunger.

Family History

MN's mother developed type 1 diabetes in her late 30s and had poorly controlled diabetes until a hospitalization for a myocardial infarction six months ago. Her mother also has hypertension and microalbuminuria. Her paternal grandfather developed diabetes in his late 60s and was treated with oral medication.

Social History

MN has a hectic schedule during the week. She works long hours at a law firm and attends classes two nights a week. MN tries to go to the gym before work, but is often too tired. MN does not smoke and drinks alcohol only socially on occasional weekends when she goes dancing with friends. She may have two or three frozen margaritas when she goes out dancing, but feels

weak shortly after drinking and reports that she "is just too tired to dance the way she used to."

MN's usual schedule and food intake

Biosynthetic human insulin (Humulin) given subcutaneously as 16 units NPH and 6 units regular before breakfast and 5 units NPH and 5 units regular before dinner. She takes no other medications.

A 2000 calorie food plan distributed among 3 meals and 3 snacks, which she received from the nutritionist at the hospital when she was first diagnosed 3 years ago. It consists of 50 percent carbohydrate, 20 percent protein, and 30 percent fat. MN has noted that "sticking to her diet" is one of the most difficult aspects of her diabetes self-care.

Monitoring and recording capillary glucose by means of a glucose monitor before breakfast and dinner. Her goal is to maintain her fasting capillary glucose level between 80 and 150 mg/dL, but it is above 150 mg/dL about 50 percent of the time. Her morning readings are usually elevated. Her glucose self-monitoring results are rarely below 60 mg/dL.

MN's Usual Intake

Breakfast (office 7:30 a.m.)	
Instant oatmeal	1 package
(flavored, apple-cinnamon)	
Coffee	12 ounces (360 mL)
Whole milk	2 Tbsp.
Sugar	2 packets
Orange juice	12 ounces (360 mL)
Lunch (fast food restaurant 1:00 p.m.)	
Hamburger	4 ounces (113 g)
Roll	1 each
Lettuce	1 leaf
Tomato	2 slices
Apple juice	12 ounces (360 mL)
Snack (vending machine 5:00 p.m.)	
Pretzels	1 ounces (28 g)
Cola	20 ounces (600 mL)
Dinner (home 8:00 p.m.)	
Chicken breast (baked)	6 ounces (170 g)
Rice	1 cup
Spicy black beans	1 cup
Olive oil	1 Tbsp.
Mixed salad	1 cup

Breakfast (office 7:30 a.m.)	
French dressing	2 Tbsp.
Iced tea (sweetened)	16 ounces (480 mL)
Snack (home 11:00 p.m.)	
Chocolate chip cookies	3 small
Whole milk	8 ounces (240 mL)

Total calories: 2863 kcal

Protein: 124 g (17% of total calories)

Total fat: 87 g (27% of total calories)

Saturated fat 27 g (8% of total calories)

Monounsaturated fat: 35 g (11% of total calories)

Cholesterol: 287 mg

Carbohydrate: 403 g (56% of total calories)

Dietary fiber: 25 g

Sodium: 2386 mg

Physical Examination

Vital Signs

Temperature: 101.3 °F (38.5 °C)

Heart rate: 120 BPM

Respiratory rate: 28 BPM

Blood pressure: 120/60 mm Hg

Height: 5′4″ (163 cm)

Weight: 132 lb (60 kg)

BMI: 22.7 kg/m^2

Exam

General appearance: Sick-looking woman with rapid respirations. Acetone was noted on her breath. By examination she was assessed to have lost at least 10 percent of her body weight

Eyes: Dry conjunctivae; normal fundoscopy

Throat: Erythematous, but tonsils were neither large nor pustular. Her buccal mucous membranes were dry

Neck: No thyromegaly

Heart: Normal S1 and S2, no murmurs, rubs, or gallops

Lungs: Clear to oscultation

Abdomen: Soft but diffusely tender; no hepatosplenomegaly

Extremities: Cool and mottled in the periphery with weak but equal pulses

Neurological: Lethargic but easily aroused; once aroused, she is able to provide a coherent history. She responded to verbal orders and was oriented to person, place, and time. The rest of her examination was normal

MN's Laboratory Test During Her Previous Hospitalization

Patient's Lab Values	Normal Values
White blood cells: 20,800/mm3	4500–11,000/mm^3
Segmented neutophils: 7.2×10^3/L	2.5–7.5 (10^3/L)
Hematocrit: 47%	36–46%
Glucose: 720 mg/dL	70–99 mg/dL
Sodium (Na): 128 mEq/L	133–143 mEq/L
Potassium (K): 4.5 mEq/L	3.5–5.3 mEq/L
Chloride (Cl): 95 mEq/L	98–108 mEq/L
Bicarbonate: 7 mEq/L	22–28 mEq/L
BUN: 35 mg/dL	7–18 mg/dL
Creatinine: 2.0 mg/dL	0.6–1.2 mg/dL
Calcium (Ca): 9.2 mg/dL	9.0–11.0 mg/dL
Phosphate (PO_4): 2.4 mg/dL	2.5–4.6 mg/dL
Acetone: 4+	Negative
Venous pH: 7.10	7.35–7.45
Triglyceride: 300 mg/dL	desirable <150 mg/dL
Cholesterol: 220 mg/dL	desirable <200 mg/dL

Patient's Lab Values	Normal Values
Hemoglobin A1C: 8.5%	4–6%
Urinary Lab Values	**Normal Values**
Specific gravity: 1.031	1.002–1.030
pH: 4.5	5–6
Glucose (Chem strip): 4+	negative
Ketone bodies(Chem strip): 4+	negative
Protein (Chem strip): negative	negative

Treatment and Course

New Insulin Regimen

To reduce her risk of hypoglycemia and to help improve her HbA1c, MN's intermediate acting (NPH) insulin was changed to 24 units of long-acting glargine to provide basal insulin. Depending on her carbohydrate intake, MN takes between 5 and 10 units of rapid-acting lispro before meals to give her more flexibility in her lifestyle. The glargine insulin provides basal insulin without peaks and is proven to decrease the incidence of both hypoglycemia and prebreakfast hyperglycemia caused by the Somogyi effect.

Case Questions

Explain how MN's symptoms and laboratory tests at the time of her diagnosis were related to a deficiency of insulin.

How are acute and long-term chronic (microvascular and macrovascular) complications associated with diabetes controlled?

How does the HbA1C level relate to the average blood glucose levels?

How would switching from multiple daily injections (MDI) to a continuous subcutaneous insulin infusion (CSII) affect glycemic control compared to working on dietary strategies?

Why is medical nutrition therapy (MNT) a vital component of managing patients with type 1 diabetes?

What are the goals of MNT in patients with type 1 diabetes?

How does Diabetes Self-Management Training (DSMT) differ from MNT?

What adjustments to her MNT are needed for her physical activity plan?

How should insulin be adjusted to the patient's carbohydrate intake?

How can acute complications (ketoacidosis and hypoglycemia) be prevented in this patient?

Answers to Questions: Case 1

Part 1: Diagnosis and Pathophysiology

1. Explain how MN's symptoms and laboratory tests at the time of her diagnosis were related to a deficiency of insulin.

Insulin-dependent tissues require insulin for glucose uptake and normal energy metabolism. Type 1 diabetes develops after approximately 80 to 90 percent of the beta cells of the pancreas have been destroyed (usually as the result of an autoimmune inflammatory reaction involving primary insulitis, cytotoxic T-lymphocytes, and secretion of interleukins and tumor necrosis factor alpha). The insulin secretory capacity of the pancreas normally exceeds the body's need. The decline of the islet cell mass, therefore, remains non-symptomatic for a long time, unless the body's insulin requirements increase, such as during infection or stress. When insulin secretory capacity becomes insufficient to regulate hepatic glucose output and glucose uptake by peripheral tissues, hyperglycemia occurs.

MN begins to excrete glucose in her urine when her plasma glucose has exceeded the

reabsorption capacity of her kidneys. The kidney threshold for glucose is about 180 to 220 mg/dL. Above this plasma glucose level, osmotic diuresis begins. As her kidneys begin to filter more glucose, urinary volume and water loss increase. Hyperglycemia results in polyuria (increased urinary volume and frequency) that in turn leads to hypovolemia (decreased volume of circulating plasma) and secondary polydipsia (increased thirst prompting fluid intake). Polyphagia (increased appetite) presents concurrently because insulin-dependent cells are in a "starved state," despite hyperglycemia.

In the absence of insulin, the body releases fatty acids from adipose tissue due to increased adenylate cyclase activation and decreased inhibition of hormone sensitive lipase. The liver produces ketone bodies (beta-hydroxybutyrate, acetoacetate, acetone) from the increased levels of acetyl CoA formed from the oxidation of free fatty acids. Ketone bodies accumulate in the blood (ketonemia) and are excreted in the urine (ketonuria). Ketonemia is a normal response to starvation; in starvation induced ketonemia, blood glucose is low-normal.

In diabetic ketoacidosis (DKA), blood glucose levels are elevated. The primary source of blood glucose in DKA is hepatic gluconeogenesis. Gluconeogenesis is a process whereby certain amino acids, pyruvate, lactate, and intermediates of the TCA (tricarboxylic acid)

cycle are converted to glucose. Gluconeogenesis is, directly stimulated by stress-induced hormones (cortisol, adrenaline, glucagon), in antagonism with insulin, increases lipolysis in adipose tissue, and raises free fatty acid levels in plasma. The increased levels of free fatty acids provide energy (ATP, NADH) and reducing equivalents for gluconeogenesis. Insulin primarily inhibits hepatic gluconeogenesis by its antilipolytic action in adipose tissue.

Ketone bodies are relatively weak acids that generate large numbers of hydrogen ions by dissociation, causing metabolic acidosis. The serum bicarbonate level – an indicator of the partial pressure of CO_2 – decreases as hyperventilation decreases CO_2 in alveolar air and in arterial blood, and as the excess hydrogen ions are buffered by bicarbonate and eliminated with urine. Acidosis means the accumulation of protons. These protons in the extracellular fluid are exchanged with intracellular potassium. The potassium and other electrolytes are lost in the urine. A patient in DKA may display hypokalemia, hyperkalemia, or normokalemia depending on the stage of the condition and fluxes of potassium. Regardless of plasma potassium concentration, total body potassium stores are significantly decreased.

With insulin deficiency, weight loss can occur as body fat and protein stores are reduced because of increased rates of lipolysis and proteolysis. MN's rapid weight loss (9 pounds in 2 days) is likely to occur in severe insulinopenia and hyperglycemia despite an increase in appetite and caloric intake. This weight loss is due to fluid loss and not from loss of muscle mass and adipose tissue.

2. How are acute (hyperglycemia and hypoglycemia) and chronic (macrovascular and microvacular) complications associated with diabetes controlled?

The acute complications of type 1 diabetes include hypoglycemia and hyperglycemia often resulting in ketoacidosis. Factors associated with increased risk of hypoglycemia include intensive therapy, better glycemic control, irregular schedule, and alcohol consumption (especially if combined with exercise or decreased carbohydrate intake). Counter-regulatory hormones responded to the stress of her illness resulting in a release of glucose from her liver. MN's pancreatic beta cells were unable to respond by producing insulin to facilitate tissue uptake of the excess glucose.

Chronic microvascular complications that affect smaller blood vessels in the eyes and kidneys and neurological functioning are closely related

to elevation of blood glucose. The Diabetes Control and Complications Trial (DCCT) demonstrated that intensive treatment of patients with type 1 diabetes dramatically reduces the risk of progression to retinopathy, nephropathy, and neuropathy by 50 to 75 percent. The DCCT intensified diabetes management by including self-monitoring of blood glucose at least 4 times a day and the use of multiple insulin injections or the use of a continuous insulin infusion pump to reduce hemoglobin A1C from approximately 9 to 7 percent. The DCCT intensive treatment was, however, associated with an increased risk of hypoglycemia and weight gain. Use of nutritional strategies, such as more regular meal times, use of snacks, and adjustments to match insulin dosage to carbohydrate intake were stressed as an essential component of behavior modification. Because weight gain will adversely affect glycemia, lipid levels, blood pressure, and general health, prevention of weight gain should be advised.

The duration of diabetes is an important component in the development of diabetic complications. The risk of complications increases with longer duration of diabetes and poorer metabolic control. Microvascular complications are related to the direct impact of high glucose levels, but elevated blood pressure contributes to excretion of protein and renal complications. Macrovascular complications

are associated with an abnormal plasma lipoprotein profile as well as with atherosclerosis, ischemic heart disease, and stroke. Diabetes, especially when accompanied by insulin resistance, is associated with increased triglycerides and cholesterol (very low density lipoprotein [VLDL] and low density lipoprotein [LDL]). The DCCT showed 25 percent less hypercholesterolemia with tight control.

Control of blood pressure and lipid levels is essential to prevent or ameliorate the macrovascular complications of diabetes. The improvement of glycemic control resulted in a borderline significant reduction in macrovascular complications during the 7 to 10 years of follow-up in the DCCT. This result is most likely due to the fact that the cohort was below the age of 40 years on study entry and too young.

Microalbuminuria is an indication of increased risk for both atherosclerosis and diabetic nephropathy, and the American Diabetes Association (ADA) recommends the use of angiotensin-converting enzyme (ACE) inhibitors as a means to slow down the progression of nephropathy.

3. How does the HbA1C level relate to the average blood glucose levels?

The correlation between HbA1C and average glucose level is very high ($r = 0.92$). The ADAhas recommended that clinical laboratories report the estimated average glucose (eAG) as well as A1C levels. Table 8-4 provides corresponding eAG in mg/dL and in mmol/L for various HbA1c levels.

Table 8-4 HbA1c and Corresponding Average Glucose Levels

HbA1c (%)	mg/dL	mmol/L
6	126	7.0
7	154	8.6
8	183	10.2
9	212	11.8
10	240	13.8
11	269	14.0
12	298	16.5

A calculator for converting HbA1C to eAG is available at http://professional.diabetes.org/eAG.

4. How would switching from multiple daily injections (MDI) to a continuous subcutaneous insulin infusion (CSII) affect glycemic control compared to working on dietary strategies?

The DCCT demonstrated that MDI with three to four injections per day and the CSII pump were both effective in improving glycemic control when the dosage of bolus insulin was matched to the amount of carbohydrate consumed. While the type of intensive insulin therapy was not related to glycemic control, predictors of better control included following a regular meal plan and adjusting food and/or insulin in response to hyperglycemia. Over-treating hypoglycemia and consuming extra snacks beyond the meal plan were associated with poorer control. Adjusting insulin dose for meal size and content and consistent consumption of an evening snack were associated with better glycemic control but to a lesser degree.

Part 2: Medical Nutrition Therapy

5. Why is medical nutrition therapy a vital component of managing patients with type 1 diabetes?

Medical nutrition therapy (MNT) is vital to achieving more stable glycemic control.

The goals of MNT are to match insulin regimens to the patient's usual schedule of meals, carbohydrate intake, physical activity, and energy needs. The timing and dosage of insulin therapy need to “mimic” how the beta cells of the pancreas normally secrete insulin in response to food intake. The Dose Adjustment for Normal Eating (DAFNE) trial determined

that patients with type 1 diabetes experienced a better quality of life by adjusting insulin for their normal eating pattern despite needing more injections.

Insulin needs to be provided for basal needs (long-acting such as insulin glargine, Lantus, or insulin determir Levemir). Long-acting insulin has a relatively flat action curve, resulting in a lower risk of hypoglycemia compared to intermediate acting insulin, and has a peak action that occurs between 4 to 8 hours after the insulin is injected. Preferred meal-time bolus insulins are rapid-acting insulins such as insulin lispro (Humalog), insulin aspart (Novolog), or insulin glulisine (Apidra). Regular insulins (Humulin R and Novolin R) are also available, but because of their peak times of action often require snacks to prevent hypoglycemia. Insulin pumps can also be programmed to provide basal and bolus insulin.

The amount of rapid-acting insulin is based on the carbohydrate content of meals. If the patient prefers snacks with more than 15 g of carbohydrate, rapid-acting insulin may also be needed before the snack. If the patient prefers snacks on a daily basis, regular insulin before meals may work better than a rapid-acting insulin, since this would cover those carbohydrates. Patients who have a fixed insulin dose and schedule must be consistent with both the amount of carbohydrate eaten

and the timing of meals and snacks. However, patients on flexible insulin regimens can adjust their bolus insulin and accommodate changes in the times and amounts of carbohydrate eaten. Adjustments in insulin and/or carbohydrate intake are also important for planning physical activity and in managing sick days. For planned physical activity, it may be necessary to decrease bolus insulin doses or to consume additional carbohydrates.

To reduce her long-term risk for cardiovascular disease, MN's diabetes goals include an LDL-cholesterol of less than 100 mg/dL, and a blood pressure goal of less than 130/85 mm Hg. To achieve this goal, cholesterol synthesis inhibitor drugs (”statins”) and hypertensive medications are often needed in addition to increased physical activity and a diet low in saturated fat, cholesterol, and sodium.

6. What are the goals of MNT in patients with type 1 diabetes?

The process of intensifying type 1 diabetes management to improve glycemic control involves several stages and individualization. At the time of diagnosis, the insulin dose can be calculated based on current body weight with approximately 0.5 to 0.6 units of insulin/kg per day with approximately half for basal needs and half as boluses for meals and snacks. During this initial stage, which usually includes three to

four office visits, diabetes management and MNT will focus on basic skills.

Nutrition counseling should emphasize tailoring insulin therapy to carbohydrate intake and eating times. Blood glucose monitoring data can be used to refine the dosage of basal insulin and meal-related insulin boluses. Patients need to master a basic understanding of the relationship between insulin action and lifestyle before moving on to more complex planning to achieve better glycemic control and a more flexible lifestyle.

7. How does Diabetes Self-Management Training (DSMT) differ from MNT?

DSMT and MNT are both professionally recognized clinical approaches to the management of diabetes and are defined by Medicare Part B and other diabetes regulations. DSMT is a broad and comprehensive self-management training program characterized by outpatient self-management, delivery by a qualified individual, and certification by a physician as part of a comprehensive plan to treat a patient with diabetes. DSMT typically involves a multidisciplinary healthcare team including a physician, registered nurse, pharmacist, and a registered dietitian. MNT is provided by a (licensed or certified as applicable) registered dietitian and nutrition professionals as defined by Medicare guidelines. Regardless of the

professional certification, all individuals involved in diabetes care must adhere to Medicare regulations and National Standards for Diabetes Self Management Education. (see http://professional.diabetes.org)

MNT is more specifically a part of the Nutrition Care Process that provides for individualized assessment, treatment, duration, and frequency of nutritional care pursuant to referral by a physician. The emphasis upon nutrition as a key component to diabetes care is characteristically greater in MNT than in the broader category of DSMT.

Guidelines for Coordinating Insulin Therapy and Food Carbohydrate

A. Make adjustments to reduce elevated glucose based on self-monitoring blood glucose.
Obtain self-monitoring blood glucose at 2 a.m. if patient encounters difficulty sleeping or evidence of hypoglycemia overnight (especially for intermediate acting insulin at dinner time).

B. Individualize adjustment of insulin for changes in carbohydrate.
Self-monitoring blood glucose four or more times per day provides useful information to help intensify therapy and improve glycemic control. Estimate bolus of insulin needed for usual meal intake while keeping

carbohydrate intake as consistent as possible to determine the ratio between carbohydrate intake and amount of insulin that is needed.
Adjustments are made for individual needs based on a diary, which documents the number of grams of carbohydrate consumed at each meal and blood glucose measurements before eating and 2 hour after the meal. If blood glucose levels are elevated (>140 mg/dL), more insulin is needed (e.g., 1 unit of rapid-acting insulin for every 12 g of carbohydrate). Fine-tune the ratio as needed. If hypoglycemia develops within 3 hours after the meal, the ratio of carbohydrate to insulin needs to be adjusted in the other direction (e.g., 1 unit of rapid-acting insulin for every 18 g of carbohydrate).

C. Try to evaluate the effects of one change for 3 days before making another change in carbohydrates or insulin therapy.
Patients learn to adjust insulin and/or carbohydrate intake based on blood glucose levels. This estimate can be based on the number of carbohydrate exchanges or servings from the food groups that contain approximately 15 g of carbohydrate per carbohydrate serving (milk and yogurt (1 cup); starches: rice (⅓ cup cooked), potatoes, pasta, starchy vegetables (½ cup); breads (1 slice or 1 ounce); cereals (¾ cup

dry), and fruit and fruit juices (½ cup or 1 small)). A more precise estimate can be made from a detailed listing of the carbohydrate content of foods.

Time	Food Intake	Carbohydrate Serving	Carbohydrate (grams)
Breakfast	12 ounces orange juice	3	45
	Instant oatmeal	2	30
	Coffee, milk and 2 packets sugar	1	15
Breakfast total			(90)
Lunch	Hamburger with roll Lettuce and tomato	2	30
	12 ounces apple juice	3	45
Lunch total			(75)
Snack 5 p.m.	Pretzels, 1 ounce	1.5	22
	Cola 20 ounces (regular)	5	75
Snack total			(97)
Dinner	Chicken		
	Rice 1 cup	3	45
	Spicy black beans 1 cup Green Salad	2	30
	16 ounce bottle of ice tea (sweetened)	3	45
Dinner total			(120)
Snack	Cookies, 2 small	1	15
	Milk 8 ounces	1	15
Snack total			(30)

Source: Judith Wylie-Rosett, PhD, RD, 2014. Used with permission.

MN eats approximately 90 g of carbohydrate at breakfast, 75 g at lunch, and 120 g at dinner. Her afternoon snack contains 97 g of carbohydrate and her night snack contains 30 g of carbohydrate. Trying to match her bolus insulin dose to cover the amount of the carbohydrate at meals and snacks may increase risk of hypoglycemia. Reducing her carbohydrate intake from beverages (fruit juices and sugar-containing beverages) may help in synchronizing carbohydrate and insulin intake. If nutritional needs are met, sugar can be incorporated into a diabetic meal plan

substituting for other carbohydrates on a gram for gram basis.

8. What adjustments to her MNT are needed for her physical activity plan?

Patients with type 1 diabetes need to develop an algorithm for adjusting insulin dose to accommodate frequent or typical activity considering the intensity and duration of the activity. Testing blood glucose before the exercise session, immediately after exercise, and again 45 minutes later can help estimate the blood glucose decrease for the specified activity. For example, half an hour of brisk walking (2 to 3 miles per hour) may reduce blood glucose by about 40 mg/dL Patients can use past experience to estimate the amount of carbohydrate that should be eaten to raise blood glucose by 40 mg/dL. If the blood glucose level is elevated right before exercising (e.g., 170 mg/dL), physical activity can help reduce blood glucose levels usually within one hour after exercising.

Patients with type 1 diabetes should be advised to monitor their blood glucose prior to and after exercise in order to detect and prevent hypoglycemia. Insulin dosage may need to be reduced when exercise is planned to prevent hypoglycemia. Additional carbohydrates may be needed for unplanned exercise depending on the glucose levels. If blood glucose is less than 100 mg/dL, about 15 g of carbohydrate is

needed for 30 minutes of walking or other low-to-moderate intensity activities; about 30 to 60 g of carbohydrate is needed for 1 hour of moderate to strenuous activity (monitor glucose accordingly).

If blood glucose is 100 to 200 mg/dL, no additional carbohydrate is usually needed for 30 minutes of walking or low-intensity activity; about 15 g of carbohydrate is needed for 1 hour of moderate activity. If glucose is 200 to 300 mg/dL, about 15 g of additional carbohydrate is needed for strenuous activity. If glucose is greater than 300 mg/dL, physical activity should wait until blood glucose is lower.

9. How should insulin be adjusted to the patient's carbohydrate intake?

Most patients need 1 unit of insulin for between 8 g and 16 g of carbohydrate, although some children may need 1 unit for 20 g of carbohydrate, and some obese patients may need 1 unit for every 5 g of carbohydrate. When information is limited, start by trying 1 unit of rapid-acting insulin for 15 g of carbohydrate for an average-size adult.

10. How can acute complications (ketoacidosis and hypoglycemia) be prevented in this patient?

Strategies to reduce the risk of hypoglycemic episodes include frequent blood glucose monitoring especially when eating and activity

patterns change. Caution is needed with regard to consuming alcoholic beverages. Individuals with type 1 diabetes should follow the guidelines for the general public with regard to the amount of alcohol they consume (a daily limit of no more than one 1 drink for women and 2 drinks for men). Food containing carbohydrate should be consumed with the alcoholic beverage.

An effective diabetes education program includes counseling on sick day management, which includes the use of short-acting insulin, monitoring of blood glucose and urinary ketones, and consumption of fluids containing sugar and salt (i.e., sports drinks that contain glucose and electrolytes). Patients should be taught to continue taking their insulin and to contact their physician early in their illness. Guidelines should be provided as to when to seek medical treatment including a weight loss of 5 percent or more of body weight, a persistent elevation in blood glucose concentration, respiration rate of greater than 35 BPM, or uncontrolled fever, nausea, or vomiting.

Case 2 Type 2 Diabetes Mellitus

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Objectives

Describe the differences between prediabetes and type 2 diabetes.

Identify the components of a healthy lifestyle for the prevention of type 2 diabetes.

Take an appropriate medical history, including family, social, diet and nutrition, physical activity, and weight histories, of a person with type 2 diabetes.

Provide effective medical nutrition therapy for patients with both prediabetes and type 2 diabetes.

MA, a 55-year-old Hispanic female, presents to her family physician with a 6-month history of fatigue and lethargy, mostly noticeable after meals and in the evening. She also periodically experiences transient hot flashes. She denies any recent change in weight or appetite, shortness of breath, skin or hair changes, change in urinary frequency, bowel irregularity, or memory impairment. She has noticed some increased irritability, both at home and at work, which she attributes to her fatigue.

Past Medical History

MA denies any personal history of diabetes, high blood pressure, high cholesterol, or heart disease. She has no history of previous hospitalizations or other illnesses.

Family History

MA has one sibling, a 49-year-old brother, who has no known medical problems. Both her parents have high blood pressure and are overweight.

Social History

MA is married with two children. She leads a sedentary lifestyle. She is a nursing supervisor who spends the majority of her workday in meetings. On the advice of a co-worker, MA has recently begun taking black cohosh for her hot flashes. She is taking no other medications or over-the-counter vitamins and/or supplements. MA rarely eats breakfast and buys sandwiches at work for lunch. Her dinner consists of store-bought frozen dinners, which are often accompanied by a dessert. She has never smoked cigarettes or used other tobacco products or any recreational drugs. She drinks alcohol on social occasions; on average about two glasses of wine twice per month. Her sex life is less active lately, which she attributes to her fatigue.

Review of Systems

General: Fatigue, lethargy for past 6 months

Endocrine: Negative for polyuria, polydipsia, or changes in appetite or weight

Genitourinary: Last remembered menstrual period was 1 year ago; she has no pain with intercourse

Neurological: Negative for headache, change in vision, numbness, or tingling in extremities

Physical Examination

Vital Signs (Initial Visit)

Temperature: 98.8 °F (37.1 °C)

Heart rate: 92 BPM

Respiration: 16 BPM

Blood pressure: 145/90 mm Hg

Height: 5′4″ (163 cm)

Current weight: 187 lb (85 kg)

BMI: 32 kg/m^2

Waist circumference: 37 inches (94 cm)

Weight history: MA describes a gradual weight gain since giving birth to her children, now ages 24 and 20

Exam

General: Obese female in no acute distress

(HEENT): Normal, visual acuity 20/20 bilaterally, normal funduscopic examination

Neck: No carotid bruits, thyromegaly, or lymphadenopathy

Lungs: Clear

Heart: Regular rate and rhythm, no murmurs

Abdomen: Obese, non-tender without organomegaly; no femoral bruits

Pelvic: Normal sized uterus, no adnexal masses or tenderness

Genitourinary: Normal introitus and labia, no lesions noted

Extremities: no cyanosis, clubbing, or edema

Pulses 2+ throughout

Neuro: normal neurologic exam.

Laboratory Data

Random capillary glucose: 210 mg/dL (normal: 70 to 99 mg/dL)

MA returned the following day for fasting blood work and was told to come back the following week to review and discuss the test results with her family physician:

MA's Laboratory Values: Second Visit	Normal Values
Plasma glucose: 135 mg/dL	70–99 mg/dL
Hemoglobin A1C: 8.5%	4–6 %
Cholesterol: 220 mg/dL	desirable <200 mg/dL
HDL-C: 48 mg/dL	desirable >50 mg/dL
LDL-C: 122 mg/dL	desirable <100 mg/dL
Triglycerides: 250 mg/dL	desirable <150 mg/dL
TSH: 2.5 μIU/mL	0.4–4.0 μIU/mL
Hemoglobin: 12.5 mg/dL	12.0–16.0 mg/dL

Based on her history and laboratory data, MA's problem list includes:

Type 2 diabetes mellitus

Class I obesity

Stage 1 hypertension

Dyslipidemia

Peri-menopausal hot flashes

MA was counseled to lose weight, begin a regular exercise program, and was given a prescription for metformin 500 mg to take

twice daily with meals. She was referred to a certified diabetes educator for nutrition and diabetes counseling, which included instruction on how to use a glucose-monitoring device. MA was also referred to a gynecologist to discuss the pros and cons of beginning hormone replacement therapy.

Three months later, MA returned to her family physician. She reported that her fatigue and hot flashes have improved and she has lost 10 pounds. Her blood pressure was 135/85 mm Hg and the rest of her physical examination was unchanged. Fasting lab data obtained 1 week prior to this visit was as follows:

MA's Laboratory Values: 3 Months Later	**Normal Values**
Plasma glucose: 115 mg/dL	70–99 mg/dL
Hemoglobin A1C: 7.7%	4–6 %
Cholesterol: 180 mg/dL	desirable <200 mg/dL
HDL-C: 51 mg/dL	desirable >50 mg/dL
LDL-C: 102 mg/dL	desirable <100 mg/dL
Triglycerides: 135 mg/dL	desirable <150 mg/dL

MA was started on the following medications:

Atorvastatin: 10 mg once daily

Enalapril: 2.5 mg once daily

Enteric coated aspirin: 325 mg once daily

Her metformin dose was maintained and combined with sitagliptin 50 mg twice daily to improve her glycemic control. On the advice of her gynecologist, MA has also started taking a combination pill of conjugated estrogen and medroxyprogesterone acetate (doses of 0.3 mg and 1.5 mg, respectively) 2 months ago to offset her menopausal hot flashes.

Case Questions

What medical conditions and risks do MA's symptoms and laboratory values represent?

Describe insulin resistance as it pertains to both prediabetes and type 2 diabetes mellitus.

What specific evidenced-based food/ nutrition recommendations would you offer MA given her current diagnosis?

What is the role of exercise in patients with prediabetes and type 2 diabetes?

What evidence exists regarding the prevention of type 2 diabetes for patients with prediabetes?

Answers to Questions: Case 2

Part 1: Assessment

1. What medical conditions and risks do MA's symptoms and laboratory values represent?

MA came to her family physician complaining of fatigue and lethargy and periodic hot flashes. This could represent many conditions. Physical and psychological causes should initially be considered. Taking a careful history and performing a pertinent physical examination and obtaining laboratory tests should reveal the underlying cause of MA's symptoms. The American Diabetes Association (ADA) recommends testing for type 2 diabetes in adults of any age who are overweight (BMI >25 kg/m^2) and who have one or more additional risk factors for diabetes. MA has several risk factors for diabetes: she is age over 45, obese, from Hispanic decent, has hypertension, and she does not exercise. She was diagnosed with diabetes based on her laboratory tests.

Acute changes in blood glucose levels have been associated with feelings of fatigue. Additionally, focus groups of patients with diabetes mention fatigue as a common symptom. MA's initial laboratory values indicate that her glycemic control is poor. The recommended hemoglobin A1c (A1C) goal for patients with diabetes is less

than 6.5 percent. MA's A1C is 8.5 percent, indicating her average blood glucose during the previous 3-month period was in the range of 210 to 220 mg/dL. The United Kingdom Prospective Diabetes Study (UKPDS) demonstrated that a 0.9 percent reduction in A1C in newly diagnosed patients with type 2 diabetes resulted in a 25 percent reduction in microvascular complications. This reduction was sustained over time in addition to risk reductions of 15 percent for myocardial infarction and 13 percent forall-cause mortality in the 10-year UKPDS post follow-up study. Since the A1C strongly predicts complications seen in diabetics, MA should have her A1C measured quarterly until she meets her glycemic goals and then at least twice a year thereafter.

Periodic hot flashes likely indicate the onset of menopause. Observationally, hormone replacement therapy had been shown to reduce the risk for cardiovascular disease in women during and after menopause. The Women's Health Initiative study determined that hormone replacement therapy should be undertaken with caution in post-menopausal women and only with the guidance of an experienced health professional.

Diabetes confers an increased risk of death from cardiovascular disease. Using poopled cohort atherosclerotic cardiovascular disease

(ASCVD) risk equations, MA's 10-year risk is 6 percent. Initial laboratory values and physical examination also show that MA meets all five ATP III criteria for the diagnosis of metabolic syndrome: hypertension (BP greater than 130/85 mm Hg), high triglycerides (greater than 150 mg/dL), low HDL-C (less than 50 mg/dL in women), diabetes (or insulin resistance and glucose intolerance in prediabetes), and abdominal obesity (indicated by a waist circumference >35 inches or 89 cm for women). MA's new diagnoses of stage 1 hypertension and type 2 diabetes mandate immediate therapeutic lifestyle changes and initiation of moderate intensive statin therapy as the standard of care according to the 2013 ACC/AHA guidelines on the treatment of blood cholesterol to reduce ASCVD risk in adults.

2. Describe insulin resistance as it pertains to both prediabetes and type 2 diabetes mellitus.

Insulin resistance is defined as diminished sensitivity of cells to the action of insulin. Insulin resistance is associated with type 2 diabetes, hypertension, dyslipidemia, central abdominal obesity, hyperinsulinemia, and other abnormalities. Insulin resistance is present in most individuals who develop diabetes many years before the development of diabetes and often heralds the onset of prediabetes. Prediabetes, also known as impaired glucose

tolerance or impaired fasting glucose, is the precursor to diabetes. As long as the pancreas produces adequate insulin, blood glucose levels remain normal. Impaired beta-cell function must be present before hyperglycemia develops. By the time diabetes develops, the individual has lost as much as 50 percent of beta-cell function. Treating insulin-resistant individuals may help to reverse prediabetes and delay or prevent the onset of type 2 diabetes mellitus.

The reasons for the development of insulin resistance are becoming better defined, and it is now apparent that genetics, diet, and the level of physical activity all play a vital role. Those with a personal history of impaired glucose tolerance, a first-degree relative with type 2 diabetes, and in women, a history of gestational diabetes or polycystic ovarian syndrome (PCOS) are at risk of developing insulin resistance. The condition is also associated with obesity, especially abdominal or central obesity.

Prediabetes and type 2 diabetes are characterized by both a progressive decrease in insulin production by the pancreas and the development of insulin resistance in skeletal muscle, adipose cells, and the liver. The effects of insulin resistance in muscle tissue are postprandial hyperglycemia and impaired glucose tolerance and in adipose cells an increase in circulating free fatty acids.

Medical nutrition therapy and regular physical activity can be very effective and may be sufficient treatment when insulin resistance is moderate or in the pre-diabetic stage when the pancreatic beta cells are still producing insulin. However, as the disease progresses, nutrition and pharmacological therapy may need to be combined to achieve the desired glucose and lipid outcomes, and to treat other co-morbidities such as hypertension and obesity.

As mentioned above, MA was successful at losing 10 pounds in the 3 months between medical visits, which helped to improve her lipid, glycemic, and blood pressure control. Not all patients are successful at weight loss. If or when failure to lose weight occurs, a patient's readiness for change should be assessed. Clinicians often find when patients focus on "what they can eat" rather than "what they cannot eat" they are more likely to lose weight. Motivational interviewing should be used to identify what a patient wants to learn, what he/she feels are areas of difficulty, what obstacles exist to achieving desired goals and outcomes, and to help identify problem-solving strategies to successfully implement and adhere to lifestyle changes. Involving a patient's spouse or partner in these discussions would also be helpful (see Chapter 1).

Part 2: Medical Nutrition Therapy

3. What specific evidenced-based food/ nutrition recommendations would you offer MA given her current diagnosis?

Randomized controlled trials have documented the effectiveness of medical nutrition therapy (MNT) for diabetes provided by registered dietitians. Continual, multiple encounters improve glycemic and other metabolic outcomes. Depending on the type and duration of the disease, MNT has been shown to decrease A1C by approximately 1 to 2 percent. The Academy of Nutrition and Dietetics has developed evidenced-based nutrition practice guidelines for the treatment of diabetes, which are similar to the ADA recommendations.

MA presents with type 2 diabetes, dyslipidemia, hypertension, and obesity. Her A1C goal is less than 6.5 percent. Recent scientific evidence supports treating patient with type 2 diabetes with a maximally tolerated statin regardless of LDL-C level because of the proven ASCVD event reduction benefits. MNT goals for patients with diabetes are to achieve and maintain normal or near normal glucose, blood pressure, and lipid levels to prevent or reduce the complications of diabetes and risk for CVD, and to address individual nutrition preferences and readiness to change. An analysis of a three-day food record can be undertaken to assess ways to modify or improve MA's eating

habits. Since MA is considered obese with a BMI of 32 kg/m^2, reducing her total calorie intake and increasing her activity level are important goals. Because her LDL-C is elevated, MA should be advised to reduce her saturated and *trans*-fat intake, to 5 to 6 percent of her total calorie intake per the 2013 AHA/ACC guidelines. This translates to a daily saturated fat intake of 8 to 10 g based on a 1500 kcal diet. Substituting foods containing phytosterols, at a maximum dose of 2 g per day, for other foods in her diet may be beneficial in reducing her LDL-C an additional 10 percent (see Chapter 6).

For individuals with diabetes, both the amount and source of carbohydrate contained in foods influence postprandial glucose levels and overall glycemic control. The total amount of carbohydrate depends on individual preference, weight management goals, and diabetes medication therapy. Carbohydrate counting is a common and effective strategy used for meal planning in patients with diabetes. One carbohydrate serving is equal to the amount of food providing 15 g of carbohydrate. Foods containing carbohydrate include fruit and fruit juice, milk and yogurt, starches, starchy vegetables (peas and corn), and baked desserts. A carbohydrate counting meal plan provides guidance and consistency by tracking either the number of grams of carbohydrate or carbohydrate servings per meal and snack.

Choosing carbohydrate foods according to their glycemic index (GI) is another strategy for meal planning. The GI classifies carbohydrate foods according to their effect on post-prandial glucose levels. Foods rich in fiber, such as apples, whole grain breads, beans, legumes, oats, and barley tend to have a low GI. Ebbeling, et al. published data supporting low-glycemic index diets' ability to enhance weight loss among obese young adults. Additionally, Jenkins and his colleagues reported that a low-glycemic index diet outperformed a high-fiber cereal diet in lowering A1C in a type 2 diabetic population. Other studies have reported no positive effects on A1C from low-glycemic index diets. It has been suggested that this inconsistency may be due to the definition of low versus high GI diets used as well as possible confounding dietary factors.

The recommendation for dietary fiber is no different for individuals with diabetes than for the general population. An adequate fiber intake for women (19 to 50 years) is 25 g/day and 38 g/day for men (14 to 50 years), which can be met with a diet rich in fruits, vegetables, and whole grain products. Clinical studies have suggested but not confirmed that increasing dietary fiber intakes above recommended levels (~50 g/day) would influence glycemic outcomes. The possible gastrointestinal side effects, limited food choices, and palatability

may make this an impractical recommendation to follow.

MA should be encouraged to consume 3 meals and 1 or 2 snacks per day. Her prior dietary routine of skipping breakfast hindered her blood glucose stability and thwarted efforts to increase her metabolism. Weight loss cannot occur or be maintained unless portion-controlled meals are consumed. The addition of a small, low-calorie snack may help to prevent overeating at mealtime. Based on this sample recommended diet, MA should continue to lose 1 to 2 pounds per week. The percent of total and saturated fat calories is within the current guidelines. Post-menopausal women need 1200 mg of calcium daily, according to recommendations of the National Osteoporosis Foundation. Increasing consumption of foods rich in calcium such as low-fat milk, yogurt, beans, and green leafy vegetables will help MA reach her daily calcium requirement. To be consistent with the Dietary Approaches to Stop Hypertension (DASH) recommendations, MA should avoid using the saltshaker at meals, watch her intake of pre-packaged soups, processed foods, salty snacks, and condiments, and increase her fruit and vegetable intake. MA can be allowed to use modest amounts of non-nutritive sweeteners (aspartame, sucralose) in her diet. Reduced calorie sweeteners include sugar alcohols (sorbitol, mannitol, and xylitol) and provide 2

calories per gram. Both are approved by the Food and Drug Administration; however, sugar alcohols may cause diarrhea if consumed in large quantities. Note that the dietary recommendations to assist MA in controlling her diabetes, blood pressure, and reducing her cardiovascular risk are all consistent.

A sample menu for MA is given here.

MA's Recommended Sample Diet

Breakfast (home)	
Banana	1 medium
Oatmeal, cooked	1 cup (234 g)
Non-fat milk	4 ounces (120 mL)
Tea, brewed	8 ounces (240 mL)
Snack (work)	
Fruit-flavored, non-fat yogurt	
(sweetened with sucralose)	4.4 ounces (125 g)

Breakfast (home)	
Tea, brewed	8 ounces (240 mL)
Lunch (home-made)	
Turkey breast meat	3 ounces (85 g)
Low-fat Swiss cheese	1 ounces (28 g)
Tossed green salad	2.5 cups
Low-calorie Italian salad dressing	3 Tbsp. (42 g)
Water	12 ounces (360 mL)
Dinner (Mexican restaurant)	
Chicken fajita (chicken breast, pepper, onions, salsa) (no cheese or sour cream)	1 each
Black bean soup	1 cup (240 mL)
Diet carbonated beverage	12 ounces (360 mL)
Snack (home)	

Breakfast (home)	
Dry roasted mixed nuts, unsalted	1.5 ounces (42 g)
Fresh apple	1 medium

Total calories: 1482 kcal

Protein: 76 g (20 % of total calories)

Total fat: 46 g (28% of total calories)

Saturated fat: 8 g (5% of total calories)

Monounsaturated fat: 21 g (13% of total calories)

Trans fat: 0.5 g

Cholesterol: 87 g

Carbohydrate: 194 g (52% of total calories)

Dietary fiber: 34 g

Calcium: 824 mg

Sodium: 2300 mg

4. What is the role of exercise in patients with prediabetes and type 2 diabetes?

A lifestyle that includes physical activity plays an important role in the prevention and management of patients with both prediabetes and type 2 diabetes. The American College of Sports Medicine (ASCM), The Centers for Disease Control and Prevention (CDC) and the

Surgeon General recommend 30 minutes per day of moderate intensity aerobic exercise. The definition of moderate intensity physical activity is 50 to 70 percent of one's maximal heart rate for age. Adults with diabetes should participate in a minimum of 150 minutes of aerobic exercise per week spread over 3 days and be encouraged to engage in resistance training two to three days per week unless contraindicated. However, before starting an exercise program the patient should consult with his/her physician.

Structured exercise programs of at least 8 weeks' duration have been shown to reduce A1C levels in patients with type 2 diabetes by an average of 0.6 percent independent of changes in BMI. In a recent study published by Gregg et al., an intensive lifestyle intervention increased the likelihood of partial remission of type 2 diabetes compared with diabetes support and education alone. Exercise reduces insulin resistance and lowers post-prandial glucose levels by increasing peripheral insulin uptake and increasing insulin sensitivity. Exercise may not contribute to a greater short-term weight reduction than diet alone, but it has been shown to be the single best predictor of long-term weight maintenance in overweight or obese people.

Additional benefits of exercise include decreasing the risk of CVD, improving one's

lipoprotein profile, and increased cardio-respiratory fitness. It is likely that the beneficial effects of exercise on the prevention of CVD are associated with improvements in the metabolic syndrome. In hypertensive patients with hyperinsulinemia, regular exercise has consistently produced reductions in blood pressure. Regular exercise has also been shown to reduce levels of triglyceride-rich VLDL particles. However, its effects on HDL-C levels have not been as favorable, probably due to the lack of intensive activity used in most studies. Physical activity performed regularly can also reduce stress and anxiety and promote feelings of well-being.

Since MA does not engage in a regular exercise program, asking her to walk at least 3 non-consecutive days a week to start (increasing up to 5 to 7 days) for 30 minutes a day is a reasonable initial exercise program. Ideally, MA should eventually incorporate some physical activity into each day. MA might start out with just 10 minutes a day during lunch, after work, or in the evening and work up to an optimum level gradually. Tailoring exercise to each patient's needs is very important to maximize adherence. Motivating patients to maintain a physically active lifestyle is not a simple task, but it is a worthwhile endeavor.

Given its many health benefits, all patients with diabetes or prediabetes should be physically

active and encouraged to begin a regular exercise program if they are sedentary.

5. What evidence exists regarding the prevention of type 2 diabetes for patients with prediabetes?

Worldwide, prediabetes and diabetes prevalence are steadily increasing, necessitating more intensive preventive measures. There is strong evidence to show that type 2 diabetes can be prevented or delayed. Therefore, individuals at high risk of developing diabetes (those individuals who are overweight or obese or who have a family history of diabetes) need to be aware of the benefits of modest weight loss and participation in regular physical activity.

For people with prediabetes, the benefits of therapeutic lifestyle modification have been demonstrated in several scientific studies. In the Finnish Diabetes Study, 522 patients with prediabetes and a mean BMI of 31 kg/m^2 were randomly assigned to a control group or a lifestyle intervention group and were given counseling on the following: weight reduction (5 percent or more), reduction of total and saturated fat (<30 percent of energy and <10 percent of energy, respectively), increased fiber (25 to 35 g/day), and increased physical activity (at least 30 minutes per day). After 4 years, the overall risk of diabetes was reduced by 58 percent in patients who participated in the

lifestyle intervention group compared to the control group.

In the Diabetes Prevention Program (DPP), 3234 subjects with impaired glucose tolerance and a mean BMI of 34 kg/m^2 were randomly assigned to one of three intervention groups, which included intensive lifestyle modification or a medicine treatment group, metformin or placebo. After an average follow-up of 2.8 years, the lifestyle group reduced the onset of diabetes by 58 percent while the metformin group reduced the onset of diabetes by 31 percent compared to placebo. The goals of the lifestyle intervention were at least a 7 percent weight reduction and a total of 150 minutes per week of physical activity. On average, 50 percent of the lifestyle group achieved this weight reduction goal, losing an average of 5.6 kg (~12 lb) and 74 percent maintained the required amount of physical activity.

Results from the Diabetes Prevention Program Outcomes trial, a long-term follow-up of the DPP, demonstrated that the reduction in risk of developing diabetes can be sustained over time. Eighty-eight percent of all eligible surviving DPP participants joined the DPPOS. After an average follow-up of 10 years, the lifestyle intervention and metformin groups reduced the risk of developing type 2 diabetes by 34 percent and 18 percent respectively compared to placebo.

Case 3 Polycystic Ovary Syndrome

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Objectives

Identify clinical features of polycystic ovarian syndrome (PCOS).

Describe the assessment of a patient with PCOS with regard to history taking, physical exam, and hormonal evaluation.

Describe the treatment of PCOS using diet, exercise, and medication.

Provide a nutrition and physical activity plan for a patient with PCOS.

MG is a 23-year-old female graduate student who presents to her primary care physician complaining of irregular menstrual cycles over the past 3 years. During this time she has also

noticed a steady increase in facial and body hair. She further reports that she has struggled with her weight and acne since her teenage years, and although she has tried several different diets and exercise programs, she has been unable to lose weight. Despite these cosmetic issues, MG says that her biggest concern regarding her condition is her future fertility. She reports no abdominal pain or tenderness, and complains of no further symptoms.

Past Medical History

MG experienced menarche at age 12, but experienced irregular periods until age 16, at which time her periods became regular. Subsequently they became irregular again at age 20, which represented the start of the present illness. Although she had previously not taken any medications, a recent visit to the University Student Health Clinic resulted in her being placed on oral contraceptives to regulate her cycle. Her past medical history is otherwise unremarkable. Aside from oral contraceptives, she does not take any medications or supplements.

Family History

Family history revealed that MG's father takes medication for his blood pressure. Her mother has type 2 diabetes mellitus. Additionally, an

aunt on her mother's side has struggled with infertility and amenorrhea.

Social History

MG does not smoke or use recreational drugs, and reported only occasional social alcohol use. She is in a long-term, monogamous relationship with her high-school boyfriend and they are currently living together. Although graduate school is stressful, she reports adjusting well and engages in many stress-relieving activities (walks in the park, dancing, and socializing with friends). Although not athletic, she does maintain a moderately active lifestyle.

Obstetric History

MG has never been pregnant.

Review of Systems

Skin: No complaints

HEENT: No complaints

Neurologic: No headaches, tremors, seizures or depression

Endocrine: Irregular menses, denies abnormal heat or cold intolerances

Cardiovascular: No complaints

Joints: No swelling, heat or redness

Physical Examination

Vital Signs

Temperature: 98.5 ^{o} F

Heart rate: 84 BPM

Blood pressure: 130/80 mm Hg

Height: 5′5″

Weight: 195 lb

BMI: 32.4 kg/m^2

Waist circumference: 37 inches

Exam

General: Marked truncal obesity on general appearance, with bulging at her flanks

Skin: Close inspection reveals sparse, dark hair growth in the peri-areolar area and on the abdomen and chin. Thickening of the skin was observed with brown pigmentation on the back of the neck

Neck: Non-palpable thyroid gland; no nodules are appreciated upon palpation

Cardiovascular: Regular rate and rhythm; positive S1/S2, with no S3/S4; no rubs or gallops

Pulmonary: Lungs clear to auscultation bilaterally

Abdominal: Obesity is appreciated; all four abdominal quadrants are non-tender to palpation, and rebound tenderness is absent. No hepatosplenomegaly is appreciated

Extremities: No edema

Pelvic exam: Unremarkable

Laboratory Values (Fasting)

Patient's Lab Values	**Normal Values**
Glucose: 112 mg/dl	70–105 mg/dL
2-hour postprandial glucose: 165 mg/dL	<140 mg/dL
Insulin: 17 µIU/mL	1.4–14 µIU/mL
Hemoglobin: A1C 6.0%	<5%
Total testosterone (T): 95 ng/dl	20–75 ng/dL
DHEA-sulfate: 5.1 mg/dL	0.6–3.3 mg/mL
Androstendione: 303 ng/dL	35–250 ng/dL
Sex-hormone binding globulin: 139 nmol/L	40–120 nmol/L
Prolactin: 19 ug/ml	<20 µg/L

TSH: 1.8 µ/mL	0.5–5.0 µIU/mL
hCG: <5 IU/L	<5 mIU/mL
LH: 16 µ/L	5–22 mU/mL
FSH: 6 µ/L	5–20 mU/mL
17-hydroxy-progesterone: 21 ng/mL	20–100 ng/dl
Progesterone: 1 ng/ml	<1 ng/mL
Estradiol: 16 pg/mL	14–27 pg/mL
24-hour urinary free cortisol: 40 µg	<90 µg
C-Reactive Protein: 0.8 mg/dL	<0.5 mg/dL

Imaging

Abdominal ultrasound revealed a "string of pearls" appearance in each ovary consistent with multiple antral follicles.

Diet and Physical Activity History

MG reports that she is not normally hungry in the morning and usually skips breakfast. She drinks a regular soda before her first class at 10:00 a.m. Lunch is typically a hoagie or hamburger, French fries or potato chips, and coke at the campus cafeteria. When she gets

home in the afternoon, she may snack on cookies or corn chips and salsa, and another soda until her boyfriend gets home. During the week, they cook dinner at home but usually eat out with friends on the weekends. When they cook, it is most often meat and potatoes, macaroni and cheese, or spaghetti with meat sauce, often with a vegetable side dish (broccoli, corn, or string beans). MG drinks water, juice, or sweetened iced tea with dinner. She often snacks on ice cream or cookies in the evening. They rarely eat any fresh fruit and only eat salads in restaurants.

MG does not have a regular exercise program. She drives to campus each day and walks a short distance to her classes. When she comes home in the afternoon, she is too busy studying and does not have time to go to the gym. Every other month or so, she and her boyfriend go out dancing, but she does not exert herself too much as she does not want to get sweaty out in public.

MG's Usual Intake

Snack (school 10:00 a.m.)	
Soda	12 ounces (360 mL)
Lunch (school cafeteria 12:30 p.m.)	
Hamburger	4 ounces (113 g)
Hamburger roll	1 each

Snack (school 10:00 a.m.)	
American cheese	1 slice (1 ounce)
French fries	Small (2.5 ounces)
Ketchup	4 Tbsp.
Soda	12 ounces (360 mL)
Snack (home 3:00 p.m.)	
Chocolate chip cookies	4 small
Soda	12 fluid ounces (360 mL)
Dinner (home 6:00 p.m.)	
Steak	4 ounces
Baked potato	1 large (299 g)
Butter	2 Tbsp.
Corn	½ cup (82 g)
Water	8 fluid ounces
Snack (home 10:00 p.m.)	
Chocolate ice cream	1 cup (110 g)

Total calories: 2752 kcal

Protein: 80 g (12% of calories)

Fat: 123 g (40% of calories)

Saturated fat: 54 g (18% of calories)

Monounsaturated fat: 44 g (14% of calories)

Cholesterol: 283 mg

Carbohydrate: 348 g (51% of calories)

Sugar: 177 g

Dietary fiber: 16 g

Sodium: 2638 mg

Case Questions

What is MG's likely diagnosis, and what clinical features aid in establishing this diagnosis?

What laboratory values are useful for establishing a diagnosis? Why?

What is the most likely pharmacotherapy that will be prescribed for MG? Why?

What is the appropriate and recommended dietary composition for patients diagnosed with PCOS?

What changes to MG's diet could help her control and manage PCOS?

What physical activity would you prescribe for this patient?

What is the prognosis for this patient to maintain a healthy body weight and to be able to achieve healthy pregnancies?

Answers to Case Questions: Case 3

Part 1: Medical Assessment and Diagnosis

1. What is MG's likely diagnosis, and what clinical features aid in establishing this diagnosis?

MG presents to her primary care physician complaining of irregular menses probably due to chronic anovulation. These findings can be caused by a number of medical issues, therefore, a full workup is useful to rule out other causes, including disorders of the neuroendocrine sex hormone axes (such as a pituitary tumor), as well as other primary issues of the ovary. In MG's case, her medical history and physical exam findings do not support these more serious diagnoses.

Further investigation reveals a history of being overweight and subsequent lab values suggest insulin resistance. Additionally, MG's lab values are consistent with hyperandrogenism (lab values will be discussed in more depth in question 2) and physical examination reveals hirsutism. The presence of acne and darkening of the skin (acanthosis nigricans) are also noted. These findings, in the context of menstrual irregularities, are pathognomonic for polycystic ovarian syndrome (PCOS).

A definitive diagnosis is supported by imaging, with the “string of pearls” appearance of the ovaries which is classically observed in patients with PCOS. The nomenclature “polycystic ovarian syndrome” is misleading, as each “pearl” does not represent a cyst, but actually an antral follicle. Note that the presence of these follicles alone is not sufficient to establish a diagnosis of PCOS, as many otherwise asymptomatic women will possess this finding as well (known as polycystic ovarian morphology).

2. What laboratory values are useful for establishing a diagnosis? Why?

MG's laboratory values are consistent with the clinical features of PCOS, namely insulin resistance and hyperandrogenism. MG's fasting glucose and insulin levels are elevated. Additionally, her 2-hour postprandial blood glucose is elevated. These findings are consistent with inadequate systemic response to insulin (insulin resistance). Finally, her hemoglobin A1C value is mildly elevated. This marker, commonly used in people with diabetics to monitor glycemic control, has recently been reported to be a useful marker in PCOS patients to stratify those at risk for insulin resistance (those with an A1C >5.7%). Additionally, CRP, a marker of inflammation commonly seen in metabolic disorders, is elevated in MG's case. All of these findings are

consistent with impaired insulin sensitivity and glycemic control commonly associated with PCOS.

Hormonally, MG exhibits hyperandrogenism. This status is determined using common markers for androgens (male hormones). Notably, her testosterone, androstenedione, and dehydroepiandrosterone sulphate (DHEAS) are elevated. The hyperandrogenism observed in PCOS is typically thought to be mainly driven by the ovary, but the adrenals play a role as well. Androstenedione and testosterone are the main androgens secreted by the ovary, whereas DHEAS is mainly produced by the adrenals. Sex hormone binding globulin (SHBG) is also used in aiding the diagnosis of PCOS. This serum protein acts to sequester sex hormones and is commonly elevated in women with PCOS. All of MG's tests are elevated, aiding in the diagnosis of PCOS. It is important to note that the female hormone axis need not be remarkably dysregulated in this disorder.

Additionally, clinicians should recognize that these serum lab values of hyperandrogenism and insulin resistance are not mere markers of disease. These factors are also intimately involved with the pathophysiology and etiology of the disease, and also can promote the underlying sequellae of PCOS, including diabetes. Therefore, it is important to know not

only the markers themselves, but the underlying mechanisms by which these factors can impact the health of the patient.

3. What is the most likely pharmacotherapy that will be prescribed for MG? Why?

Upon consultation with the patient, a decision on a clinical strategy is reached. The patient's earlier use of oral contraceptives (OCP) is to be continued to regulate her menses. Interestingly, recent evidence also shows that OCPs not only regulate the menstrual cycle, but also ameliorate hyperandrogenism in women with PCOS. These benefits make OCP a cornerstone in pharmacologic management of PCOS.

In addition to OCP, high-dose spironolactone is added to the regimen for its documented anti-androgenic effects in an effort to restore hormonal balance. To address the patient's glucose intolerance, metformin is prescribed to reduce insulin resistance which should also decrease her risk of diabetes, a common sequelae of PCOS. In concert with these medical interventions, the patient is counseled that weight loss and dietary modification may greatly improve her clinical outcome, and so she is deemed to be a candidate for medical nutrition therapy.

Part 2: Medical Nutrition Therapy and Lifestyle Intervention

4. What is the appropriate and recommended dietary composition for patients diagnosed with PCOS?

The appropriate dietary composition for patients diagnosed with PCOS includes a nutritionally complete diet that ultimately promotes weight loss. The Acceptable Macronutrient Distribution Ranges (AMDRs) published by the Institute on Medicine (IOM) for 97 to 98 percent of all females ages 19 to 30 years recommends 40 to 65 percent of total calories coming from carbohydrates, 20 to 35 percent from fat, and 10 to 35 percent from protein and dietary fiber intake of at least 25 g/day. Females with PCOS should aim for: reduced calories, lower carbohydrate (accomplished by reducing refined carbohydrate and increasing complex carbohydrate), higher protein, and lower fat (specifically reducing saturated fat and increasing monounsaturated fat).

Reducing caloric intake, irrespective of diet composition, should be the main focus to achieve weight loss in overweight women with PCOS. A reduced calorie diet with a deficit of 500 to 1000 calories per day is an effective option for weight loss in women with PCOS.

Carbohydrate content is important for patients diagnosed with PCOS due to the increased risk of diabetes in patients with PCOS. A lower-carbohydrate diet has been shown to decrease circulating testosterone levels, fasting insulin, and glucose levels, and increase insulin sensitivity in women with PCOS. Another study documented greater reductions in insulin resistance, improved menstrual regularity, and decreased free androgen index in subjects who lost weight on a low-calorie and low-carbohydrate diet. In each of these studies, the low-carbohydrate diets involved carbohydrate foods that were high in fiber and/ or low glycemic load.

At least one study found that a high-protein (30 percent of calories compared to 15 percent), low-glycemic-load diet led to a significant increase in insulin sensitivity and a decrease in high-sensitivity C reactive protein (hsCRP) concentration.

To address the dyslipidemia found in about 70 percent of women with PCOS, a monounsaturated fat-enriched diet will be beneficial to decrease triglycerides and low-density lipoprotein cholesterol (LDL-C) and increase high-density lipoprotein (HDL-C) cholesterol.

5. What changes to MG's diet could help her control and manage PCOS?

In order to gradually lose weight to better control and manage her PCOS, MG should focus on decreasing her total calories, particularly her consumption of sugar, refined carbohydrates, and saturated fat. She should focus on increasing fiber, lean protein, and monounsaturated fats in her diet.

MG's current calorie intake is high at 2752 kcal per day. The recommendation for the management of PCOS is to reduce total calorie intake by 500 to 1000 calories per day, resulting in a 1 to 2 pound weight loss per week. MG's revised diet for weight loss, totals (1929 kcal), which is a deficit of approximately 800 calories per day. If MG follows this lower calorie diet, this will lead to a gradual weight loss of about 1.5 pounds per week.

MG's current carbohydrate intake is high at 348 g (51 percent of calories). Not only is her diet high in carbohydrate, but it is high in sugar (177 g) and low in fiber (16 g). MG has been recommended to replace high carbohydrate foods and beverages with low carbohydrate tortilla wraps instead of bread and substituting zero calorie, zero carbohydrate flavored seltzer water, and unsweetened ice tea for high carbohydrate colas. By replacing these beverages MG will save 420 calories per day and reduce her sugar consumption by 117 grams. MG was advised to eat more fresh fruits, vegetables, whole wheat or whole grain breads

and pastas, and brown rice instead of simple carbohydrates such as white potatoes, pasta, cookies, and soda. Compared to refined carbohydrates, choosing complex carbohydrates will keep her feeling full until her next meal.

MG's current protein intake is low at 80 g (12 percent of calories). While MG needs more protein in her diet, she should be advised to consume more lean protein. First, MG's intake of high fat foods and refined carbohydrates seem to be replacing protein in her diet. MG snacks of sugary and fatty foods and beverages such as soda and cookies are high in calories and low in nutritional value. MG could incorporate protein into her snacks, such as yogurt, nuts, and seeds to increase the protein in her diet. In her revised diet plan, we almost doubled MG's protein intake was increased to 122 g (23 percent of calories). In addition, the high protein foods MG currently consumes include steak, hamburgers, meat sauce, and cheese, all which are high in calories and saturated fat. MG should focus on replacing these high calorie, high saturated fat protein foods with lean protein foods such as chicken, turkey, and fish, all of which are lower in calories and saturated fat.

The current recommendation from the American Heart Association is two servings of fish per week. In order to reduce her saturated

fat intake, MG should carefully select the meat and poultry she buys. MG enjoys red meat but should choose the leaner cuts, such as eye round or top round, sirloin, or tenderloin and should swap fried foods like French fries for baked potatoes or steamed vegetables. With a strong association between dyslipidemia and PCOS, MG needs to focus on reducing unhealthy saturated fat in her diet and replacing it monounsaturated fat. MG's revised diet, has a decreased fat intake of 72 g (34 percent of calories), decreased saturated fat intake to 14 g (6 percent of calories), and increased monounsaturated fat to 29 g (14 percent of calories). MG would benefit from a few counseling sessions with a registered dietitian who can explain the importance of eating breakfast, packing a lunch, how to shop for healthy foods, and can teach her how to incorporate more fruits and vegetables in her diet. A registered dietitian can also teach her how to shop for healthy foods.

Overall MG would benefit from eating more structured meals and a few snacks to keep her blood glucose levels stable, reduce insulin resistance, and prevent excessive hunger. Including breakfast as her first meal of the day will aid in controlling her blood glucose levels first thing in the morning. Studies have also shown that people who eat breakfast have lower body weight than people who skip breakfast. Eating breakfast also reduces hunger later in

the day, making it easier to avoid overeating which can contribute to weight gain. Eating breakfast also increases the body's insulin response, which would help MG further combat her insulin resistance.

MG should incorporate more low fat dairy foods into her diet. Currently, soda and other sugary snack foods are reducing her calcium and vitamin D. MG should choose non-fat or low-fat dairy products such as skim or 1 percent milk, light yogurt, reduced fat cheese, and sugar-free ice cream. Choosing these options will save MG calories and saturated fat. Finally, MG could pack her lunch and bring it to school to control portion sizes, reduce calories, and help her weight loss efforts.

Recommended Revised Diet for Weight Loss

Breakfast (home 7:00 a.m.)	
Whole wheat English muffin	1 each
Peanut butter	1 Tbsp.
1% lowfat milk	8 ounces
Snack (school 10:00 a.m.)	
Dry roasted, almonds no-salt added	¼ cup
Raisins	¼ cup

Breakfast (home 7:00 a.m.)	
Lunch (packed from home, eaten in school cafeteria 12:30 p.m.)	
Deli turkey, low sodium	3 ounces
Tortilla shell, low-carb, high-fib	1 each
Lettuce leaf	1 each
Tomato slice	1 each
Carrot sticks	½ cup
Celery sticks	½ cup
Reduced calorie ranch dressing	2 Tbsp.
Sugar-free jello	½ cup
Calorie-free, flavored seltzer water	12 ounces
Snack (home 3:00 p.m.)	
Fresh blueberries	½ cup
Light yogurt	6 ounces
Dinner (home 6:00 p.m.)	
Salmon, broiled	4 ounces
Quinoa, cooked	1 cup
Broccoli	Unlimited
Salad, lettuce with tomatoes and carrots	1.25 cups
Low-calorie raspberry vinaigrette	2 Tbsp.
Calorie-free, flavored seltzer water	12 fluid ounces

Breakfast (home 7:00 a.m.)	
Snack (home 8:00 p.m.)	
Sugar-free ice cream	1 cup

Total calories: 1929 kcal

Protein: 112 g (23% of calories)

Fat: 72 g (34% of calories)

Saturated fat: 14 g (6% of calories)

Monounsaturated fat: 29 g (14% of calories)

Cholesterol: 153 mg

Carbohydrate: 230 g (48% of calories)

Sugar: 95 g

Dietary fiber: 34 g

Sodium: 2300 mg

6. What physical activity would you prescribe for this patient?

When recommending physical activity to a patient, it is useful to describe activity using these four components:

Frequency Encourage daily activity. MG reported that she is too busy studying after school to exercise. During the week, encourage MG to take study breaks where she engages in short bouts of physical activity, such as taking three study breaks and exercising for 10 minutes each time. On weekends, encourage

MG to make time for longer bouts of exercise (45 to 60 minutes).

Intensity Encourage some moderate-intensity activity and some vigorous-intensity during the week with intensity increasing as she improves her cardiovascular conditioning. This can be monitored by teaching her to monitor her heart rate (max HR = 220 minus age).

Type Physical activity for MG could include activities that she enjoys such as dancing, biking, swimming, or sports such as volleyball or tennis.

Time (Duration) It is important to have a sustained period of aerobic exercise (45 to 60 minutes) for burning calories and contributing to weight loss. Shorter periods of activity (10 to 15 minutes) such as weight lifting or stair climbing are also recommended.

Logging In a systematic review which looked at 34 articles on various outcomes resulting from mobile phone application interventions, all four articles with a weight loss outcome cited significantly greater weight loss, body mass indexes, and waist circumference measurements in participants who logged their physical activity, compared to controls. MG should keep a physical activity log to keep her on track in accomplishing her weight loss goals. Keeping a physical activity log will also keep her

accountable and motivate her to continue her exercise program.

7. What is the prognosis for this patient to maintain a healthy body weight and be able to achieve healthy pregnancies?

Based on small studies of women with PCOS, there is clinical evidence that women who lose weight, maintain a healthy weight, and prevent the onset of diabetes can become fertile and have successful full-term pregnancies.

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9
Pulmonary Disease

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Objectives*

Define the nutritional deficits, requirements, and medical nutrition therapy in patients with chronic obstructive pulmonary disease and cystic fibrosis.

Examine available feeding options and their indications for mechanically ventilated patients and the risk associated with nutritional support.

Identify the association between obstructive sleep apnea syndrome and obesity, and

outline the nutritional recommendations for these patients.

Recognize the importance of incorporating nutrition into the history, review of systems, and physical examinations of patients with pulmonary diseases.

*Source: Objectives for the chapter and cases adapted from the *NIH Nutrition Curriculum Guide for Training Physicians*. (www.nhlbi.nih.gov/funding/training/naa)

Chronic Obstructive Pulmonary Disease (Chapter 9: Case 1)

Between 25 and 40 percent of patients with advanced chronic obstructive pulmonary disease (COPD) have some degree of nutritional depletion. Weight loss, with reductions in fat reserves and muscle mass, occurs in 30 percent of patients with COPD. Patients who lose 15 percent or more of their weight within a year are at risk for malnutrition, which is associated with a higher mortality even after adjusting for age, smoking habits, baseline BMI, and lung function. Mean survival of COPD patients with a low BMI is considerably shorter than those who are not underweight.

However, even patients at normal body weight may be undernourished. The prevalence of

malnutrition may be underestimated when BMI alone is used for assessment. Fat-free mass (FFM) index is a better marker of lean body mass compared to BMI because it is associated with prognostic indices such as six-minute walk distance, dyspnea, percentage of predicted FEV_1 and FEV_1/FVC ratio, airway obstruction, lung hyperinflation, and total lung capacity. Depletion of FFM with preservation of body weight occurs in 11 to 25 percent of COPD patients and is associated with impaired peripheral muscle strength. More severe COPD is associated with an increased risk of malnutrition, as weight loss leads to a reduction in the mass of the respiratory muscles and the diaphragm.

Patients with COPD benefit from nutritional assessment because the consequences of malnutrition include adverse effects on respiratory muscle mass and function that result in decreased respiratory muscle strength and exercise capacity. Furthermore, because malnutrition is also associated with decreased cell-mediated immunity, altered immunoglobulin production, and impaired cellular resistance of the tracheobronchial mucosa to bacterial infection, these patients are at increased risk for respiratory infections, especially pneumonia and bronchitis. Patients with advanced COPD are also at risk for osteoporosis. Low BMI and decreased

weight-bearing exercise capacity are independent predictors of osteoporosis.

Interestingly, an imbalance in oxidative status in the setting of malnutrition and low body weight may play a vital role in the pathogenesis and severity of COPD. The imbalances between the formation of reactive oxygen species and antioxidant capacity can cause cell damage, mucous hypersecretion, antiprotease inactivation, and increased pulmonary inflammation. Dietary intake of antioxidant nutrients, including vitamin C, vitamin E, β-carotene, and selenium, has been positively associated with increased lung function. In fact, studies suggest that foods high in antioxidants, including tea, fruits and vegetables and whole grains, may have protective or ameliorative effects on the development of COPD.

Mechanisms of Weight Loss in Patients with COPD

The causes of weight loss in patients with advanced COPD are multiple and still not fully understood. However, they can be separated into processes or conditions that result in poor nutritional intake, altered protein metabolism and a hypermetabolic state. Mechanisms of weight loss in patients with chronic obstructive pulmonary disease are shown in Figure 9-1.

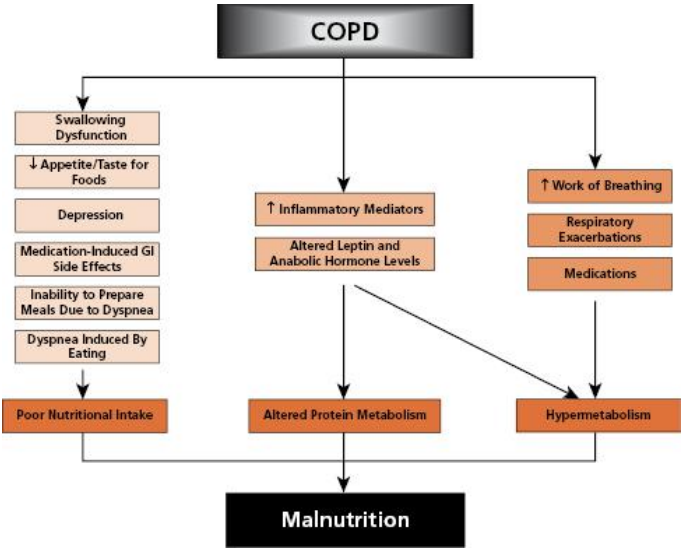

Figure 9-1 Mechanisms of Weight Loss in Patients with Chronic Obstructive Pulmonary Disease

Source: Horace M. DeLisser, MD. 2014. Used with permission.

Poor Nutritional Intake

Factors that may cause poor dietary intake in patients with COPD include:

Reduced appetite by up to 45 percent in cachectic patients.

Chronic sputum production and frequent coughing, which may alter the desire for and taste of food and may interfere with swallowing (deglutition).

Severe dyspnea and fatigue, which may result in an inability to prepare adequate meals.

Depression from the illness, which may result in anorexia.

Hyperinflation of the lungs, which causes flattening of the diaphragm and pressure on the abdominal cavity during eating, leading to early satiety and problems with swallowing.

Oxyhemoglobin desaturation during eating, which results in increased dyspnea.

Side effects of medications such as nausea, vomiting, diarrhea, dysgeusia, dry mouth, and gastric irritation. Medications may also increase the need for protein, calcium, vitamin A, and folic acid or result in altered serum levels of potassium, magnesium, vitamins, or cholesterol.

Hypermetabolism

Several causes of hypermetabolism result in increased energy requirements in patients with COPD. These include:

Increased Work of Breathing In patients with normal lung function, breathing expends 36 to 72 calories per day. Patients with COPD may have up to a tenfold increase in their daily energy expenditure from breathing. Both the increased resistive load and the reduced respiratory muscle efficiency experienced by these patients contribute to this increased daily

energy expenditure from breathing. This increased work of breathing results in an increased daily energy requirement. Patients will lose weight if they do not ingest additional calories to meet these increased needs. Alternatively, patients may reduce their activity in an effort to conserve energy.

Frequent, Recurrent Respiratory Infections Depending on the severity of the illness, respiratory infections may increase metabolic rate and, therefore, contribute to weight loss.

Miscellaneous Processes Other potential causes for hypermetabolism include disease-induced inflammatory mediators and the use of corticosteroids, β2-agonists, and/or theophylline.

Altered Protein Metabolism Recent studies suggest that elevated levels of the cytokines, especially TNF-α, contribute to weight loss, skeletal muscle loss, and increased resting energy requirement in patients with COPD. Low levels of serum leptin and testosterone have been found in patients with COPD, which are believed to cause increased protein catabolism. Increased levels of growth hormone in cachectic COPD patients may indicate growth hormone resistance. Reductions in phosphocreatine decrease lactate anaerobic metabolism, resulting in early onset lactic acidosis and exercise intolerance. Several

studies suggest that the metabolism of the amino acid leucine is abnormal in patients with severe COPD. In summary, protein degradation may increase when inflammatory mediators and stress hormones overwhelm processes that decrease protein turnover.

Medical Nutrition Therapy for COPD

Patients with COPD have difficulty meeting caloric requirements and frequently lose weight. Based on survival statistics, the goal for underweight patients is weight gain and the goal for overweight patients is weight maintenance. It is safe to assume that patients who are not ingesting their caloric requirements and present with weight loss may also suffer from vitamin and mineral deficiencies. Certain electrolytes (calcium, magnesium, potassium and phosphorus) are especially important because depletion may contribute to the impairment of respiratory muscle function. When severely undernourished COPD patients are rapidly re-fed with glucose infusions, careful attention must be paid to these electrolytes to avoid refeeding syndrome (Chapter 4: Case 2).

The goals of medical nutrition therapy for COPD patients are shown in Table 9-1.

Table 9-1 Medical Nutrition Therapy for Patients With COPD

Source: Jennifer Williams, MS, RD, CNSD. 2014. Used with permission.

Supply adequate calories, protein, vitamins and minerals to maintain desirable body weight (BMI 20–24 kg/m^2), energy level, and nutritional status.

Provide small, frequent meals with nutrient-dense foods, such as peanut butter and jelly sandwiches, and soft-textured, easily consumed foods such as omelets, yogurt, cottage cheese, and casseroles.

Add high-calorie, high-protein, liquid, or pudding nutritional supplements or milk shakes to the diet. Patients should sip these throughout the day instead of adding them to meals to avoid post-prandial dyspnea.

Recommend foods that require little preparation, such as frozen dinners heated in a microwave oven.

Follow *My Pyramid* recommendations.

Limit consumption of cured and red meat, high-fat dairy products, and refined carbohydrates.

Limit alcohol consumption to no more than two drinks (30 g alcohol) per day for men and one drink (15 g alcohol) per day for women.

Time the main meal when the patient's energy level is the highest.

Rest before mealtime to conserve energy.

Prescribe a daily multivitamin and mineral supplement.

Emerging areas of research include the use of anabolic steroids, growth hormones, and appetite stimulants for anabolism. The peptide ghrelin stimulates growth hormone secretion, food intake, and weight gain. Though appetite stimulants often result in an increase in adiposity, ghrelin improves body composition by decreasing muscle wasting via inhibition of production of anorectic proinflammatory cytokines. Appetite stimulants may cause hyperglycemia, which may be exacerbated by steroid medication.

Mechanical Ventilation

Rationale for Nutrition Support

Patients with respiratory failure requiring mechanical ventilation are unable to ingest food through the mouth because of the endotracheal or nasotracheal tube (unless the patient has a tracheostomy). Because many patients require mechanical ventilation for prolonged periods, nutrition support is necessary to prevent malnutrition.

Malnutrition associated with critical illness impairs cell-mediated immunity, alters

immunoglobulin production, and impairs cellular resistance to infection. Therefore, patients who have not been fed for 7 to 10 days are at increased risk of infection. In addition, malnutrition causes difficulty in weaning a patient from the ventilator, presumably due to respiratory muscle weakness. Conversely, ventilated patients with pre-existing malnutrition who are fed have improved respiratory muscle strength and function, which may facilitate weaning from the ventilator.

Immune-Modulating Enteral Feeding Formulas

Investigations have demonstrated that early enteral nutrition leads to decreased infections, reduced hospital length-of-stay, and even a reduction in mortality. It has also been noted that a high content of omega-6 polyunsaturated fatty acids (PUFAs) is unfavorable because of the potential to induce a pro-inflammatory state. This has led to the development of emulsions in which part of the omega-6 fatty acid component is replaced by less bioactive fatty acids, such as omega-3 derived from fish oils. Intravenous fish oil has been shown to blunt the physiological response to endotoxin in healthy subjects. Due to increased interest, immune modulating formulas were created and mainly include enteral formulas containing glutamine, arginine, omega-3 fish oils and anti-oxidants. Initially, omega-3 fish oils had

been found to improve outcomes in patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). Because of these findings, a grade A (highest) recommendation was provided by the American Society for Parenteral and Enteral Nutrition/ Society of Critical Care Medicine guidelines for the use of omega-3 fatty acids in patients with ARDS. Later trials aimed at defining the potential benefits of omega-3s and antioxidants for patients with ALI/ARDS showed less positive results. Further clarification is needed regarding the selection and dosage of antioxidant components for immunonutrition.

There has also been interest in the use of enteral nutrition support, enriched with glutamine. Glutamine enhances the immunological barrier in the GI tract via its trophism of enterocytes and colonocytes and serves as a substrate for glutathione, an antioxidant. Evidence of its potential benefit have come from studies showing a reduction in length of stays, both in the intensive care unit (ICU) and in the hospital, when patients received enteral nutrition support containing glutamine compared to those patients fed an enteral diet without glutamine.

Feeding Options

Most patients who require mechanical ventilation for more than several days should receive enteral nutrition via a naso-enteral

feeding tube as long as the GI tract is functioning (Chapter 12). Parenteral nutrition should be reserved for patients who are severely undernourished and/or do not have a functioning gut such as those with a bowel obstruction or an ileus (Chapter 13).

Minimizing Effects of Nutrition Support on CO_2 Production

The caloric and nutrient composition of the diet has a profound effect on gas exchange, especially CO_2 production. The respiratory quotient (RQ) is expressed as the ratio of CO_2 produced to oxygen consumed.

$$RQ = \frac{CO_2 \text{ produced}}{O_2 \text{ consumed}}$$

The RQ of carbohydrate is 1.0, while the RQ of fat is 0.7 and of a mixed meal is 0.83. Thus, CO_2 production is greater during carbohydrate metabolism than during fat metabolism. A diet high in carbohydrate therefore requires increased ventilation to eliminate the excess CO_2 and may complicate weaning from the ventilator. Consequently, high-fat, low-carbohydrate enteral feeding products have been formulated and recommended for feeding mechanically ventilated patients with severe COPD. These have not been proven effective, however, probably because excess CO_2 production associated with mixed or

high-carbohydrate diets is not clinically relevant unless caloric requirements are exceeded. Thus, it is essential to avoid overfeeding these patients because this can result in excessive CO_2 production, increased RQ, and difficulty in weaning from the ventilator. If indirect calorimetry is available to determine caloric expenditure, this should be recommended; otherwise 100 to 120 percent of predicted caloric expenditure should be used.

Cystic Fibrosis (Chapter 9: Case 3)

Cystic fibrosis (CF), a life-threatening genetic disorder, manifesting in child1ren and young adults, presents with profuse, abnormally thick exocrine gland secretions. These excessive secretions may obstruct pancreatic and bile ducts, intestines, and bronchioles, resulting in a variety of clinical problems, with chronic lung disease and pancreatic insufficiency being the most common. There is a clear association between worsening lung disease and malnutrition, but the degree of malnutrition seen in these patients varies considerably. Deficiencies of specific micronutrients may progress to clinically evident symptoms and signs if not recognized and treated. In addition, deficiencies of calories, protein, essential fatty acids, fat-soluble vitamins (A, K, E, and D), beta-carotene, zinc, iron, and sodium have been

reported for these patients. Bone disease, such as osteoporosis, is also being increasingly recognized.

Causes of Weight Loss and Malnutrition

The causes of weight loss and malnutrition in patients with CF are multifactorial. These include maldigestion and/or malabsorption (due to pancreatic insufficiency), inadequate oral caloric intake, increased caloric and nutrient needs, and the development of CF-related organ system disease, particularly pulmonary disease, liver disease, intestinal obstruction, and CF-related diabetes mellitus (CFRD).

Maldigestion and Malabsorption Most patients (80 to 85 percent) with CF have pancreatic insufficiency and as a result malabsorption of fats, proteins, carbohydrates, vitamins, and minerals, which, if untreated, leads to serious nutritional problems. Pancreatic enzyme supplements are administered with meals and snacks to assist with the absorption of nutrients. The amount and type of enzyme supplements depend on the degree of malabsorption and the fat content of the diet. Steatorrhea is considered a clinical indicator of fat malabsorption (Chapter 7: Case 2).

Increased Nutritional Needs Despite pancreatic enzyme supplementation, the energy

and protein needs of CF patients are significantly increased. This is due to loss of nutrients secondary to malabsorption and by higher than normal protein catabolism and energy expenditure due to frequent infections.

Increased Work of Breathing Patients with CF commonly suffer from chronic bronchitis, airway obstruction, and recurrent infections, which increase the work of breathing and result in higher energy expenditure. Muscle wasting and respiratory muscle dysfunction further exacerbates these effects.

Other Factors Gastro-esophageal reflux, abdominal pain, and psychosocial stress may also contribute to low caloric intake. Liver disease with decreased bile salt excretion also worsens malabsorption. CF-related diabetes mellitus with glucosuria also results in increased energy loss. Finally, patients who undergo significant intestinal resection may have decreased intestinal surface area for nutrient absorption.

Medical Nutrition Therapy for Cystic Fibrosis

Patients with CF are typically unable to meet their caloric and protein requirements or maintain their weight due to increased nutrient needs and losses, and inadequate caloric intake. CF is usually diagnosed in infancy or early childhood, and monitoring growth and

development in these patients is particularly important. Not uncommonly, CF patients remain at or fall below the fifth percentile in both weight-for-age and height-for-age on pediatric growth charts. The goals of nutrition therapy for CF patients:

Routine nutrition assessment, which includes height, weight, BMI, percent weight change, pediatric growth parameters, dietary history, physical examination, and evaluation of laboratory values.

Dietary counseling to provide adequate intake of calories, protein, vitamins, and minerals. This will include education about high-calorie, balanced meals with added salt, nutrient-dense snacks two to three times daily, and nutritional supplements.

Adequate pancreatic enzyme replacement therapy adjusted to avoid malabsorption.

Adequate vitamin and mineral supplements according to the *CF Foundation Guidelines*.

If patients continue to experience weight loss and fall below 85 percent of their ideal body weight, additional nutrition support may be necessary. Both enteral (using nasogastric or gastrostomy tubes) and parenteral feedings may be recommended, as clinically indicated.

Obstructive Sleep Apnea (Chapter 9: Case 2)

Obstructive sleep apnea (OSA) is defined as recurrent episodes of apnea during sleep caused by occlusion of the upper airway. Obesity is the primary risk factor for OSA and is present in up to two-thirds of all patients with OSA. OSA may be caused by an increased amount of fat surrounding the structures of the upper airway. Although not all obese patients have OSA, and occasional non-obese patients may have it, it is clear that weight loss in obese patients with OSA improves signs and symptoms. Symptoms of sleep apnea, such as snoring and excessive daytime sleepiness, should always be ascertained as part of the medical history in obese patients.

Two groups of inflammatory proteins are produced and released by adipose tissue: cytokines, such as TNF-α and adipokines, such as leptin. These cytokines may play a role in the development of insulin resistance and increased oxidative stress in obese patients.

Studies have suggested a role for the fat cell protein, leptin, in the pathogenesis of respiratory dysfunction in OSA. In fact, mutation in the leptin or leptin receptor gene has been found in some obese human subjects. Other investigations suggest that patients with OSA also have lower plasma levels of orexin, a

neuropeptide produced in the lateral hypothalamus, that increases appetite and alertness. It has been proposed that lower levels of orexin may result in decreased levels of alertness and may play a role in the pathogenesis of OSA.

In addition to weight loss, patients with OSA are most commonly treated with continuous positive airway pressure (CPAP) therapy. A CPAP machine is approximately the size of a toaster, and is connected to tubing that ends with a mask that must be worn snugly over the face. The machine blows air into the throat and splints the airway open during sleep. CPAP eliminates apneas and snoring.

Causes of Weight Gain and Obesity

Fatigue due to chronic sleep disruption, a common symptom of patients with OSA, may influence patients' eating behaviors. Often too tired and lacking in motivation to exercise, they tend to lead sedentary lifestyles. In addition, many patients with OSA report falling asleep often after eating, which further decreases their energy expenditure. Certain overweight patients with OSA may also be prone to binge eating as a result of depression about their illness and/or body image. Whatever the exact causes, a combination of decreased physical activity and increased caloric consumption contributes to weight gain in these patients.

Medical Nutrition Therapy for Obstructive Sleep Apnea

Weight Loss Because obesity contributes to the pathogenesis of OSA, weight loss is of primary importance in obese patients with OSA. Weight loss, even as small as 5 to 10 percent body weight, can dramatically improve breathing and sleep patterns. Patients would benefit from a referral to a registered dietitian for either individual or group nutritional counseling.

Increasing Activity Once patients begin to feel better and have more energy, they should be encouraged to begin a low-intensity exercise program, such as walking 15 minutes once or twice a day.

Lung Transplantation

Lung transplantation has become a viable alternative for some patients with severe pulmonary disease, including COPD, cystic fibrosis, and pulmonary hypertension. The nutritional implications for lung transplantation patients vary depending on whether they are waiting for or have received a transplant, and whether they are breathing spontaneously or mechanically ventilated following surgery. The following recommendations are listed accordingly.

Nutrition Assessment Prior to Lung Transplantation

Routine nutrition assessment prior to lung transplantation entails the following steps:

Assess nutritional status using BMI and the patient's weight history, and body composition measurement if equipment is available.

Assess albumin as a predictor of mortality. If protein status is depleted, supplement the diet with high-protein milkshakes and snacks.

Assess serum lipid levels.

Monitor the patient's satiety level and gastrointestinal symptoms, such as bloating and gas, which could interfere with adequate dietary intake.

Assess bone density with a DEXA scan pre- and post-lung transplantation.

Medical Nutrition Therapy Post-Lung Transplantation

Several of the drugs used for immunosuppression after lung transplantation have an impact on nutrition. Cyclosporine can cause hyperkalemia, and may also elevate serum cholesterol and triglyceride levels. These effects may require reducing dietary potassium, saturated fat, and cholesterol intake. Tacrolimus, often substituted for cyclosporine, causes hyperglycemia. The antimetabolite

azathioprine causes nausea, vomiting, and diarrhea. The similarly acting mycophenolate mofetil may produce diarrhea and dyspepsia. These problems may interfere with the provision of adequate intake and must be addressed.

Corticosteroids (e.g., prednisone) can cause hyperglycemia and increased appetite, which often leads to weight gain and potentially obesity. Patients taking corticosteroids may also experience fluid retention and osteoporosis.

Medical nutrition therapy immediately following lung transplantation is shown in Table 9-2.

Table 9-2 Medical Nutrition Therapy Following Lung Transplant

Source: Jennifer Williams, MS, RD, CNSD. 2014. Used with permission.

Adjust calorie intake to achieve desirable body weight.
Increase protein to promote repletion as clinically indicated and to assist with wound healing during the catabolic state following surgery.
Low-sodium and low-fat diet for prevention of fluid retention and hyperlipidemia association with steroid use.

Carbohydrate-controlled diet for those with steroid induced diabetes.

Daily multivitamin and mineral supplement.

Calcium and vitamin D supplementation for prevention of osteoporosis.

Case 1 Chronic Obstructive Pulmonary Disease

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Objectives

Assess the relevance of routine nutritional assessment parameters in a patient with pulmonary disease.

Explain the causes of weight loss in patients with COPD.

Outline the appropriate dietary interventions for a COPD patient with weight loss.

PD is a 53-year-old Caucasian woman diagnosed with chronic obstructive pulmonary disease (COPD) 8 years ago, who visits her physician complaining of shortness of breath (dyspnea). This has worsened progressively over the last 3 days since she caught a cold from her grandchildren. She explains that her level of dyspnea increases when she is sick or under increased stress, high humidity, extremely cold temperatures, or after a large meal. Currently, PD has two-pillow orthopnea and bilateral lower extremity edema. She reports an unintentional weight loss of 31 pounds (14 kg) within the last year. Pulmonary function tests from last year confirmed severe COPD with a forced expiratory volume (FEV1) of 36 percent predicted, a forced vital capacity (FVC) of 44 percent predicted, and a ratio of FEV1 to FVC of 39 percent. A recent chest X-ray revealed hyperinflation of lung fields, with diminished lung markings in the upper lung fields.

Past Medical History

PD has been treated for hypertension for 12 years and for hypercholesterolemia for the past

2 years. She has no previous history of diabetes mellitus, thyroid disease, or liver disease.

Medications

PD is currently taking verapamil, furosemide, potassium chloride, atorvastatin, prednisone, tiotropium bromide, alendronate, and albuterol. She does not take any vitamin/mineral or herbal supplements. PD has no known food allergies.

Family History

PD's mother died at age 70 of a heart attack. Her father also died of a heart attack at age 73.

Social History

PD lives with her husband in a two-story home. They have 4 children and 14 grandchildren. PD worked in a local department store as a salesperson until last year, when she retired because of her illness. She formerly attended church regularly with her husband, but lately has been too tired. Her husband has also recently taken over the food shopping. She reports the following substance use:

Alcohol intake: None

Tobacco: 1½ packs per day for 30 years; quit 5 years ago

Caffeine: One cup of coffee/day

Diet History

PD is on a low-fat, low-cholesterol, low-salt diet for elevated cholesterol and hypertension. PD provided the following 24-hour dietary recall that reflects her typical daily intake. She does not add salt to her food or use salt in cooking.

PD's 24-Hour Dietary Recall

Breakfast (home)	
Cream of wheat	1.5 cup cooked
White toast	1 slice
Jelly	2 Tbsp.
Coffee	1 cup
1% milk	4 ounces (120 mL)
Lunch (home)	
Low-fat yogurt	1 cup
Apple juice	6 ounces (180 mL)
Dinner (home)	
Baked chicken breast	4 ounces (114 g)
Baked potato	1 medium
Cooked carrots	½cup
Diet margarine	1 Tbsp.
Water	1 glass
Snack (home)	
Banana	1 medium

Total calories: 1262 kcal

Protein: 63 g (20% of calories)

Fat: 21 g (15% of calories)

Saturated fat: 7.0 g (5% of calories)

Monounsaturated fat: 5.0 g (4% of calories)

Cholesterol: 112 mg

Carbohydrate: 209 g (66% of calories)

Fiber: 11 g

Sodium: 1036 mg

Review of Systems

General: Weakness, fatigue, and weight loss

Mouth: Wears dentures (top and bottom; loose fitting)

GI: Poor appetite; no nausea, vomiting, or diarrhea; daily bowel movements

Extremities: No joint pain; has difficulty walking without a walker

Physical Examination

Vitals Signs

Temperature: 97 °F (36 °C)

Heart rate: 94 BPM

Respiration: 20 BPM

Blood pressure: 150/80 mm Hg

Anthropometric Data

Height: 5′6″ (168 cm)

Current weight: 134 lb (61 kg)

Estimated dry weight: 112 lb (51 kg)

[Dry weight is estimated by subtracting the weight of the fluid from the current weight. Fluid weight is estimated at 22 pounds (10 kg) since she has 2+ pitting edema on both ankles. Eleven pounds (5 kg) can be used to estimate fluid in patients with ascites and no peripheral edema]

Usual dry weight: 143 lb (65 kg)

BMI using estimated dry weight: 18 kg/m^2

Percent weight change using estimated dry weight (over 1 year): 22% decrease
[(65 – 51)/65]

Exam

General: Frail woman in no acute distress

Skin: Ecchymoses

HEENT: Normal non-palpable thyroid

Mouth: Loose-fitting dentures; no sores; symmetrical soft palate and uvula

Cardiac: Regular rate and rhythm; normal first and second heart sounds; jugular venous distention and hepatojugular reflux noted

Lung: Increased A–P diameter, decreased breath sounds throughout; diffuse mild expiratory wheezing with a prolonged expiratory phase

Abdomen: Non-distended, non-tender; no hepatosplenomegaly; normal bowel sounds

Extremities: 2+ pitting edema on both ankles

Rectal: Soft, heme-negative brown stool in vault

Neurologic: Alert; appropriate reactions; good memory; no evidence of sensory loss

Laboratory Data

Patient's Values	Normal Values
Albumin: 4.3 g/dL	3.5–5.8 g/dL
Hemoglobin: 10.8 g/dL	12.0–16.0 g/dL
Hematocrit: 35%	36–46%
Mean corpuscular volume: 78 fL	80–100 fL
Cholesterol: 265 mg/dL	desirable <200 mg/dL
LDL-C: 173 mg/dL	desirable <130 mg/dL
HDL-C: 42 mg/dL	desirable >40 mg/dL

Patient's Values	Normal Values
Triglycerides: 150 mg/dL	desirable <150 mg/dL
Arterial blood gases (ABG):	
pH: 7.37	7.35–7.45
pCO_2: 63 mm Hg	33–45 mm Hg
pO_2: 60 mm Hg	80–100 mm Hg
HCO_3: 35 mEq/L	24–28 mEq/L
SaO_2: 90%	95–100%

Case Questions

Does PD's percent weight change indicate a significant weight loss?

Estimate PD's caloric needs using the Mifflin–St. Jeor equation including a stress factor for COPD.

What factors have contributed to PD's weight loss?

Based on PD's history, what may account for her severe fatigue?

How does poor nutritional status compromise pulmonary function?

Discuss the impact of current medications on nutritional status.

What is the appropriate medical nutrition therapy for PD, including specific

recommendations to improve her nutritional and fluid status?

Answers to Questions: Case 1

Part 1: Nutrition Assessment

1. Does PD's percent weight change indicate a significant weight loss?

Progressive, unintentional weight loss of greater than 5 percent in 1-month or greater than 15 percent of body weight within a 1-year period is considered a severe weight loss, and represents a significant risk for malnutrition. PD had an unintentional weight loss of 22 percent over the past year, and her current BMI is less than 18.5 kg/m^2, both considered a risk for malnutrition.

2. Estimate PD's calorie needs using the Mifflin–St. Jeor equation including an activity factor for COPD.

The Mifflin–St. Jeor equation for women:

$$\text{BMR} = (9.99 \times \text{weight in kg}^*) + (6.25 \times \text{height in cm}) - (4.92 \times \text{age in years}) - 161$$
$$\text{BMR} = (9.99 \times 51) + (6.25 \times 168) - (4.92 \times 53) - 161 = 1138 \text{ kcal}$$

*Use estimated dry weight in this patient with bilateral pitting edema.

$$\text{Total Energy Expenditure (TEE)} = (\text{RMR}) \times 1.375 \text{ (lightly active)}$$
$$\text{TEE} = (1138 \times 1.375) = 1565 \text{ kcal/day}$$

When the TEE is compared to her current intake, which totals 1262, her calorie needs are about 300 greater than her actual intake. This could explain her continued weight loss.

3. What factors have contributed to PD's weight loss?

Because of reduced lung function, PD requires more energy to breathe. The normal daily intake of calories required to maintain her body weight is insufficient to meet the excessive demands of breathing for COPD patients. Elevated cytokines (e.g., TNF-alpha) and decreased levels of cell-derived protein (e.g., leptin and testosterone) exacerbated by frequent recurrent respiratory infections increase resting energy requirements and promote loss of weight and lean body mass.

PD's diet history reveals that her calorie intake meets only 80% of her nutritional requirements. Her low calorie intake is due in part to the low-fat, low-cholesterol diet originally prescribed to manage her hypertension and hypercholesterolemia. Patients with pulmonary disease may ingest even fewer calories because they are too tired to prepare food or to eat a meal. Such patients report dyspnea while chewing and swallowing food, preventing them from breathing

adequately and, thereby, increasing the amount of desaturation.

PD is currently retaining fluid, so her actual "dry" weight is 22 pounds (10 kg) lower than her reported weight. PD should be asked about recent lifestyle changes and possible depression, which could be contributing to her reduced appetite and unintentional weight loss. Also, her weight loss likely contributed to her ill-fitting dentures, which decreases her ability to chew meats and other foods.

4. Based on PD's history, what may account for her severe fatigue?

COPD can cause arterial hypercapnia, which limits exercise tolerance, which further contributes to loss of lean body mass. Similarly, arterial hypoxemia reduces the amount of oxygen available to tissues and other organs. PD has fluid overload, probably due to cor pulmonale (right ventricular failure). Patients with COPD typically have elevated hemoglobin and hematocrit levels due to chronic hypoxia. PD's hemoglobin and hematocrit are low, further reducing her body's ability to transport oxygen. Her low mean corpuscular volume (MCV) may reflect an iron deficiency or inadequate heme synthesis due to protein-calorie malnutrition. Again, recent lifestyle changes and possible depression may also contribute to her fatigue. PD's current calorie intake is inadequate, adding to her

fatigue. Liberalizing the monounsaturated and polyunsaturated fat content in PD's diet will provide additional calories without the potential to increase her lipids.

5. How does poor nutritional status compromise pulmonary function?

Poor nutritional status can compromise a patient with COPD by impeding pulmonary defense mechanisms and altering respiratory muscle structure and function. Limitations of pulmonary defense mechanisms include decreased surfactant production, decreased immunoglobulin levels, and impaired cellular resistance of the tracheobronchial mucosa to bacterial infection. Poor protein status, mineral deficiencies (calcium, magnesium, and phosphorus), and electrolyte (potassium) wasting can decrease the diaphragmatic muscle mass or function, reduce diaphragmatic strength and contractility, diminish the vital capacity, and depress ventilatory responses even to minimal exertion such as walking.

Part 2: Drug–Nutrient Interactions

6. Discuss the impact of current medications on nutritional status.

Interactions between medications and dietary intake can be complex. Patients with protein-calorie malnutrition have impaired drug metabolism. In this case, a patient with

COPD who has lost a significant amount of weight and who is consuming an inadequate amount of calories and protein can be expected to have significant alterations in her drug metabolism which increases the possibility of drug toxicity. The blood pressure lowering effects of verapamil have been shown not to be dependent upon dietary sodium intake, but verapamil absorption is lower with increased sodium intake. Corticosteroids increase hepatic glycogen storage to protect glucose sensitive tissues (heart and brain) resulting in gluconeogenesis and increased protein turnover. Prednisone can increase the hypokalemia produced by furosemide and thus the dose of potassium replacement should be monitored closely. With this in mind, the following considerations apply to the specific medications being used by this patient and should be kept in mind if problems arise.

Verapamil-SR

Slow-release forms need to be swallowed whole with food or milk. Other formulations can be ingested without regard to food.

Verapamil may cause constipation, dizziness, elevated liver enzymes, bradycardia, and hypotension.

Patients are advised to avoid alcohol. A diet low in sodium with limited caffeine may also be recommended.

Furosemide

It is recommended to be taken on an empty stomach but may be taken with food or milk to reduce abdominal distress.

Furosemide can produce anorexia, increased thirst, or nausea and should be administered with caution to diabetic patients. Furosemide lowers serum potassium, magnesium, sodium, chloride, and calcium and raises glucose, blood urea nitrogen, and may transiently elevate cholesterol levels.

High intake of dietary sodium will make furosemide less effective. Supplementation of potassium, magnesium, and calcium may be recommended.

K-Lyte/Cl

K-Lyte should be taken with meals and 8 ounces of liquid.

Possible side effects include gastric irritation, nausea, and iatrogenic elevations in serum potassium and chloride levels.

Atorvastatin

Patients should avoid grapefruit juice and limit alcohol consumption.

Side effects include nausea, dyspepsia, abdominal pain, constipation, flatulence,

rhabdomyolysis, and increased liver function tests.

HMG CoA reductase inhibitors decrease coenzyme Q_{10} synthesis, which may cause fatigue in some patients. This may respond to CoQ_{10} supplements (50 to 100 mg/day).

Prednisone

Prednisone should be taken with meals to avoid gastrointestinal intolerance.

Side effects include esophagitis, nausea, dyspepsia, increased appetite, weight gain, negative nitrogen balance, osteoporosis, fluid retention, hypertension, bruising, and slow wound healing. Hypercholesterolemia and reductions in serum zinc, vitamin A, and vitamin C levels can result from prednisone therapy. Prednisone may reduce absorption of calcium and phosphorous, and antagonizes the action of insulin, often resulting in hyperglycemia.

Avoid alcohol.

Supplement with potassium, calcium, phosphorus, folate, and vitamins A, C, and D.

Tiotropium Bromide

This inhaler may cause dry mouth, dyspepsia, abdominal pain, or constipation. Other side effects include possible glaucoma, and benign prosthetic hypertrophy.

Alendronate

Alendronate should be taken before meals with 6 to 8 ounces of water. Because of the risk of esophagitis, patients should avoid lying down for 30 minutes after taking their medication.

Albuterol (Nebulized or Inhaled)

Limit caffeine intake and take with food if gastrointestinal upset occurs.

Side effects include anorexia, dysgeusia, sore/dry throat, nausea, tremor, headache, dizziness, and increased blood glucose levels.

Part 3: Medical Nutrition Therapy

7. What is the appropriate medical nutrition therapy for PD, including specific recommendations to improve her nutrition and fluid status?

Providing adequate calories and protein for weight and skeletal muscle maintenance is a major goal of medical nutrition therapy. By liberalizing her monounsaturated fat intake, she will increase her calorie intake (see PD's recommended sample diet). The acute risks of weight loss and malnutrition at this time exceed the long-term risks associated with hypercholesterolemia, which can be pharmacologically managed, if needed, by increasing her dose of atorvastatin or waiting until prednisone can be discontinued and

rechecking her cholesterol level. Fluid balance is also an important consideration to prevent dehydration or hyponatremia. Consider referring both PD and her husband to a dietitian since her husband will be shopping and cooking and would benefit from nutritional guidance. Medical nutrition therapy should be aimed at maintaining PD's BMI between 20 and 25 kg/m^2 and an albumin level of 3.5 to 5.8 g/dL. Since she has microcytic anemia, she should be evaluated for iron deficiency. Medical nutrition therapy should also include the following:

Rest before mealtime.

Eat foods that are easy to chew, such as soft meats and casseroles.

Avoid eating in bed; sit upright when eating.

Drink Carnation Instant Breakfast, Boost, or Ensure; at least one can per day for additional calories, protein, vitamins, and minerals.

Include milk, which does not usually contribute to mucus/sputum production.

Use a microwave oven to prepare convenience foods and decrease cooking time.

Consume small, frequent meals consisting of nutrient-dense foods, such as peanut butter and jelly sandwiches.

Use additional margarine (tub or liquid) on bread, potatoes, and vegetables as a calorie supplement.

Consume the main meal at a time of the day when energy level is highest.

Avoid foods that cause gas or bloating, which makes breathing more difficult. Examples include cauliflower, broccoli, cabbage, Brussels sprouts, onions, beans, and melons.

Gradually increase intake of fiber-rich foods to enhance GI motility.

Limit fluid intake during meals. Instead, drink fluids between meals.

Avoid salty foods such as canned, smoked, or cured products to minimize fluid retention and bloating.

Take a multivitamin/mineral supplement and 500 mg/day calcium.

Patients on home oxygen should be advised to use oxygen when preparing and eating meals, and to avoid cooking on a gas stove. The microwave oven is a safer option.

Recommended Revised Diet for PD

Breakfast (home)	
Coffee	1 cup
Instant oatmeal	1 packet
2% milk	6 ounces (180 mL)

Breakfast (home)	
Raisins	¼ cup
Regular margarine	1 Tbsp.
Snack (home)	
Apple	1 medium
Lunch (home)	
Tuna salad	3 ounces (85 g)
Whole wheat bread	1 slice
Snack (home)	
2% milk	½ cup
Saltines (low sodium)	6 each
Peanut butter	1 Tbsp.
Jelly	2 Tbsp.
Dinner (home)	
Lean ground beef patty	4 ounces
Brown rice	½ cup
Tossed salad	1 cup
Olive oil	2 Tbsp.
Balsamic vinegar	1 Tbsp.
Snack (home)	
Low-fat yogurt	4 ounces
Orange	1 medium

Total calories: 1919 kcal

Protein: 76 g (16% of calories)

Fat: 89 g (42% of calories)

Saturated fat: 22 g (10% of calories)

Monounsaturated fat: 45 g (21% of calories)

Cholesterol: 143 mg

Carbohydrate: 213 g (44% of calories)

Fiber: 21 g

Sodium: 1346 mg

Case 2 Obstructive Sleep Apnea and Metabolic Syndrome

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Objectives

Understand how to effectively use a medical interpreter.

Recognize the importance of eliciting the patients' explanatory model.

Examine how socio-cultural and economic factors may influence the healthcare decisions of patients.

CC is a 34-year-old Mexican immigrant who works as a truck driver. He presents to his primary care physician complaining of daytime sleepiness, loud snoring, and fatigue. He is referred to the sleep clinic for an expedited sleep study, which confirms a diagnosis of severe sleep apnea. He is prescribed continuous positive airway pressure (CPAP) therapy and instructed to use CPAP during all periods of sleep in order to minimize his risk of falling asleep while driving. He is told that his usage of the CPAP machine will be monitored electronically. He is further informed that if he does not comply, and if he is still sleepy while driving, the physician is obligated to report him to the Department of Transportation for possible suspension of his commercial driver's license. He is advised to make sure he sleeps for 7.5 to 8 hours each night with the CPAP machine on, to lose weight, limit alcohol, and is

educated about safe driving habits. CC returns to the clinic one month later and his symptoms are minimally improved. The CPAP usage is checked and indicates that he used the device for at least four hours/night on only 20 percent of days during the recording period.

Past Medical History

CC has a history of hypertension. He reports that he has been taking three medications regularly to control blood pressure (lisinopril, amlodipine, metoprolol), but the readings have continued to remain high during recent visits to his primary care provider. He takes no vitamins, or herbal supplements. He admits to loud snoring at night and occasionally requiring naps during the day when he visits truck stops.

Family History

CC's family history is positive for overweight. His two brothers and one sister are overweight. His father has hypertension and had a myocardial infarction at the age of 63. His mother is obese, hypertensive, and has type 2 diabetes. Both parents and one brother snore heavily, but have not had testing to confirm sleep apnea.

Social History

CC is single and has never been married. He does not smoke. He averages two to three

bottles of beer daily. He eats three meals per day, mostly on the road, and admits to snacking during the day while driving. He states that he has no opportunity to exercise since he is driving a truck 6 days a week and frequently traveling.

Review of Systems

Skin: No history of rashes

HEENT: No visual complaints

Neurological: No headaches, tremors, seizures, or depression

Endocrine: Denies abnormal heat or cold intolerances

GI: Constipation

Cardiovascular: Normal rate and rhythm. No orthopnea or dyspnea

Joints: No swelling, heat, or redness

Physical Examination

Vital Signs

Temperature: 98.4 °F (36.9 °C)

Heart rate: 88 BPM

Blood pressure: 145/88 mm Hg

Height: 5′9″ (176 cm)

Current weight: 215 lb (98 kg)

BMI: 32 kg/m^2

Neck circumference: 18 inches

Waist circumference: 43 inches (109.2 cm)

General: Obese man in no acute distress

Exam

The conjunctivae are mildly injected. The nasal septum is midline, without nasal congestion, hypertrophy of the turbinates, or nasal polyps. The tongue is enlarged with lateral fenestrations. The airway is modified Mallampati class IV, and the uvula and palatal arch are not visible. There is 90 percent lateral narrowing and the anterio-posterior diameter of the pharynx is small. The tonsils are 1+ in size. Mild diffuse edema is evident in the soft tissues of the pharynx. Non-palpable thyroid. Acanthosis nigricans. Negative hirsutism or striae; no dorsal, cervical, or supraclavicular fat. His limbs are not edematous.

Laboratory Data

Patient's Fasting Values	**Normal Values**
Glucose: 116 mg/dL	70–99 mg/dL
Potassium: 3.8 mEq/L	3.5–5.0 mEq/L
Cholesterol: 216 mg/dL	desirable <200 mg/dL

Patient's Fasting Values	Normal Values
Triglycerides: 275 mg/dL	desirable <150 mg/dL
HDL-C: 32 mg/dL	desirable for male ≥40 mg/dL
Calculated LDL-C: 129 mg/dL	desirable <130 mg/dL

CC's Usual Intake

Breakfast (truck stop or motel)	
Coffee	24 ounces (720 mL)
Half and half cream	3 ounce (90 mL)
Sugar	4 packets
Conchas (Mexican Sweet Bread)	2 pieces
Orange juice	8 ounces (240 mL)
Lunch (fast food)	
Deluxe beef burrito	1 whole
Nachos with cheese	large
Cola soda	24 ounce large (720 mL)
Snack (truck stop)	
Oreo cookie snack-pack	6 cookies
Cola Soda	12 ounce (360 mL)

Dinner (home)	
Beef Enchiladas with cheese	2
Mexican rice	1 cup
Cheesecake	1 slice
Beer	12 ounces (360 mL)
Snack (home)	
Beer	12 ounces (360 mL)
Corn chips	6 ounces

Total calories: 4539 kcal

Protein: 88 g (8% of calories)

Fat: 164 g (32% of calories)

Saturated fat: 59 g (12% of calories)

Monounsaturated fat: 31 g (6% of calories)

Cholesterol: 393 mg

Carbohydrate: 632 g (55% of calories)

Fiber: 27 g

Sodium: 7436 mg

Case Questions

What are the risk factors for sleep apnea and why is it a concern among commercial drivers?

How is sleep apnea diagnosed and what are the potential adverse health effects?

How is sleep apnea treated?

In addition to OSA, what other medical conditions does CC present with?

How does CC's diagnosis of sleep apnea impact him professionally?

How should CC's low CPAP adherence be addressed?

How should the clinician go about determining whether CC understands his diagnosis of sleep apnea and its treatment?

How can communication be improved between CC and the healthcare team?

Now that communication issues have been discussed, what specific dietary recommendations would be appropriate and realistic for CC to implement?

How can CC increase his physical activity level?

Answers to Questions: Case 2

Part 1: Diagnosis and Treatment

1. What are the risk factors for sleep apnea and why is it a concern among commercial drivers?

Obstructive sleep apnea (OSA) is a medical condition characterized by intermittent airway closure during sleep. These airway closures lead to intermittent drops in oxyhemoglobin saturation, which triggers a surge in sympathetic activity and an arousal from sleep. The resulting sleep fragmentation can lead to daytime sleepiness and other neuro-cognitive deficits, while sympathetic hyperactivity and intermittent hypoxia have been linked to numerous cardiovascular sequela.

The three largest risk factors for sleep apnea include obesity, male gender, and middle-age. These are the typical characteristics of a commercial driver. Prevalence of sleep apnea ranges as high as 50 to 80 percent in commercial drivers, compared against rates of 2 percent for female and 4 percent for male employees in the general population. Additionally, daytime sleepiness experienced by sleep apnea sufferers puts them at risk for vehicular accidents, posing a huge public health burden. Risk of a vehicular crash for drivers with sleep apnea is 2- to 5-fold higher than those without. These crashes are also quite expensive; if a fatality is involved, federal data estimate that the cost of the crash exceeds $3 million.

2. How is sleep apnea diagnosed and what are the potential adverse health effects?

The diagnostic gold standard for sleep apnea is an in-laboratory polysomnography (PSG) or an overnight “sleep study”. PSG typically requires a technologist in attendance, who is available to check and correct faulty signals in real-time, so that data quality is maximized, and also to deliver treatment during the latter part of the night, if it is required. PSG provides an estimate of OSA severity by reporting the apnea–hypopnea index (AHI), a value that expresses the hourly number of breathing disturbances during sleep. AHI values of ≥15/hour are considered to indicate at least moderate apnea, and ≥30/hour to indicate severe apnea. PSG is relatively costly, requires technical expertise to perform and interpret, and is difficult to access. Because of these shortcomings, more recently, simpler, unattended sleep studies which can be self-assembled and performed in the home or in the berth of the vehicle have gained prominence. One major limitation of these studies, however, is that they typically do not measure sleep. Therefore, they may underestimate disease severity, if sleep time is over-estimated in conditions when the patient lies awake without moving. They also do not typically rate arousals from sleep, and are not able to diagnose conditions other than sleep anpea. Moreover, they may be associated with chain-of-custody issues, since the unattended nature of the studies leaves unclear who actually wore the device.

Several sets of guidelines are available regarding testing for sleep apnea for commercial drivers. These guidelines specify conditions under which truck drivers should be removed from service immediately due to potential crash risk, during which time diagnosis and treatment are offered. They also specify conditions under which an in-service evaluation would be appropriate. Occupational medicine providers, who conduct evaluations of commercial drivers for fitness for duty, should be well-versed in these guidelines.

A large prospective study found that persons with apnea experience increased risk of future development of hypertension. Among patients with refractory hypertension, defined as hypertension requiring at least 2 medications to control, the prevalence of sleep apnea is as high as 80 percent. Importantly, treatment of sleep apnea has been shown to improve hypertension in randomized clinical trials. Prospective data also links sleep apnea to increased incidence of myocardial infarction, stroke, coronary artery bypass grafting, coronary angioplasty, and to death from cardiovascular events. Cross-sectional data links sleep apnea with myocardial infarction, stroke, and insulin resistance.

3. How is sleep apnea treated?

The first-line treatment for sleep apnea is not a medication, but a device, which is worn during

sleep, called continuous positive airway pressure (CPAP). A CPAP machine is approximately the size of a toaster, and is connected to tubing that ends with a mask that must be worn snugly over the face. The machine blows air into the throat and splints the airway open during sleep. CPAP eliminates apneas and snoring, restores blood oxygen levels, reduces arousals, and consolidates sleep.

Randomized, controlled trials show that CPAP therapy reduces blood pressure and insulin resistance and improves neuro-cognitive function. These data hold true even after controlling for important confounding variables such as obesity. CPAP may also reduce highway crash risk, as assessed by performance in driving simulators.

The major problem with CPAP therapy is adherence; up to 50 percent of patients offered CPAP refuse it at the outset, and close to 25 percent abandon this treatment within 3 years. Improving adherence to therapy so that its benefits may be maximized for all affected patients remains an active area of investigation, and an elusive goal for many sleep medicine specialists. Currently, guidelines compiled by the Motor Carrier Safety Advisory Committee and the Medical Review Board of the Federal Motor Carrier Safety Administration indicate that minimum CPAP use should be at least 4 hours/night on at least 70 percent of days. CC

should be informed of this minimum requirement, and provided with supportive care to help meet this requirement. Such care includes appropriate selection and fitting of mask interfaces, and education regarding adverse effects of untreated apnea, benefits of therapy, and potential consequences on employment due to existing reporting guidelines for those who do not comply with therapy.

4. In addition to OSA, what other medical conditions does CC present with?

According to CC's physical examination and laboratory data, he also presents with refractory hypertension and metabolic syndrome. Laboratory tests reveal elevated triglycerides and blood sugar and low HDL-C, and physical examination shows an abnormally high waist circumference (43 inches). He therefore meets four of the five criteria for the diagnosis of metabolic syndrome. Metabolic syndrome has been identified as an independent risk factor for CVD by ATP III and increases the risk of developing type 2 diabetes (Chapter 1: Case 1). Additionally, his hypertension is considered "refractory," requiring more than three medications and still remaining uncontrolled. This condition has been associated with an 80 percent chance of having apnea. Additionally, a large study of interventions to improve diabetes

suggested that sleep apnea occurs in 80 percent of obese individuals with type 2 diabetes. Therefore, screening for sleep apnea is an important to consider in these subgroups.

The diagnosis of metabolic syndrome can serve also as a starting point for discussing lifestyle modification. Metabolic syndrome represents a cluster of metabolic abnormalities associated with abdominal obesity. Obesity frequently leads to insulin resistance, which in turn may lead to elevated BP, atherogenic dyslipidemia, and impaired fasting glucose levels. Clinicians should add waist circumference measurement to their clinical examination or assign clinical support staff to obtain this along with the patient's blood pressure prior to the clinician's evaluation. Waist circumference is an important marker of visceral fat, which is more prognostic of metabolic syndrome than body mass index (BMI). Waist circumferences should always be measured, since self-reported pant size will almost always be smaller than the patient's true girth. To get the correct waist measurement, wrap a tape measure around the smallest area below the rib cage and above the umbilicus. Accuracy is important, especially for patients at risk, because abdominal obesity is a crucial pathophysiologic link to other features of metabolic syndrome, particularly insulin resistance. A waist circumference of greater than 40 inches for men and greater than 35 inches for women defines significant abdominal

obesity. The International Federation of Diabetes has developed lower cut-off measurements for waist circumference specific to ethnicity (Chapter 6: Case 3).

5. How does CC's diagnosis of sleep apnea impact him professionally?

The association between sleep apnea and sleepiness should be highlighted in the population of commercial drivers. This is because sleepiness among commercial drivers impairs task performance and accounts for 31 to 41 percent of major crashes of commercial vehicles. Overall, large trucks are involved in nearly half-million traffic accidents each year. These accidents injure 130,000 victims each year, and incur huge costs. While we know little about the role of OSA in crashes in commercial vehicles, we do know that drivers of passenger cars who have OSA experience increased crash risk. A recent meta-analysis quantified at least a 2-fold increase in crash risk among sleep apnea sufferers.

Awareness of sleep apnea is rising among providers who evaluate commercial drivers for fitness-for-duty. These evaluations are required prior to obtaining a commercial driving license, and generally again every 2 years. Body mass index (BMI) has been offered as a useful screening tool, with thresholds as low as 30 kg/m^2 to as high as 35 kg/m^2 requiring

confirmatory sleep studies by various professional groups.

However, many commercial drivers have concerns about employment repercussions, lost revenue due to time taken off for testing and treatment, and out-of-pocket expenses for testing and treatment. These concerns may motivate CC to avoid discovery of any underlying sleep apnea, and require a thoughtful and culturally sensitive approach to encourage testing and treatment, particularly since the potential benefits to health, quality of life, and public safety are considerable.

Part 2: Enhancing Patient Communication

6. How should CC's low CPAP adherence be addressed?

Patients with severe sleep apnea, and particularly those who are very sleepy, who use the CPAP device as recommended, feel significantly better. They notice significant improvements in daytime sleepiness, and as a result, tend to use the CPAP more consistently. Additional, commonly-reported benefits include improvement in the frequency of nocturia, morning headaches, and improvements in short-term memory, concentration, mood and overall quality of life. It is therefore worrisome, given the severity of CC's apnea, that he is still not using the CPAP

device. This strongly suggests there are other factors that may be compromising his adherence.

It would be important to begin by ensuring that CC understands his disease and its treatment. Assuming he understands how to use the CPAP machine, the next step would be to ascertain the barriers he encountered when using this device. Given that his low adherence may potentially involve embarrassing, sensitive, and/or personal issues, it is important to continue this conversation with non-judgmental, open-ended questions.

To this end, it is essential to separate patient-related factors (social stigma of CPAP, stigma of diagnosis, health and cultural belief system that promotes or dissuades compliance) from machine-related factors (the CPAP machine is too noisy, the mask is leaking, the mask irritates the skin, the pressure is uncomfortable). Patients may worry about how the CPAP device will impact their social functioning, including their sexual behavior. Since 80 percent of patients with sleep apnea are obese, their self-esteem may also be low, which could affect their motivation to adhere to treatment. For this patient, since he is a truck driver, barriers that may have influenced his adherence include sleeping in his truck on a regular basis and being on the road most of the time. Some states with anti-idling laws may also

impede consistent nightly use of CPAP, which is typically plugged into the charger of the truck in order to provide sufficient electrical power to function overnight.

7. How should the clinician go about determining whether CC understands his diagnosis of sleep apnea and its treatment?

Ensuring that a patient understands his/her diagnosis is critical to promoting adherence to recommended or prescribed treatments. Patients enter the clinician's office with their own beliefs, concerns, and expectations about their illness and the medical encounter. This conceptualization of the illness experience can be described as the patient's explanatory model. This is the patient's understanding of the cause, severity, and prognosis of an illness; the expected treatment; and how the illness affects his or her life. In essence, it is the meaning of the illness for the patient. Patients' explanatory models of illness are to a large extent culturally determined.

Kleinman and associates, in their seminal paper referenced below, further discuss the importance of the explanatory model: “Eliciting the patient's (explanatory) model gives the clinician knowledge of the beliefs the patient holds about his/her illness, the personal and social meaning he/she attaches to their disorder, their expectations about what will

happen to them and what the health care professional will do, and their own therapeutic goals."

Comparison of the patient's model with the clinician's model enables the clinician to identify major discrepancies that may cause problems for clinical management. Such comparisons also help the clinician know which aspects of the explanatory model need clearer exposition to patients (and families), and what sort of patient education is most appropriate. And they clarify conflicts not related to different levels of knowledge but different values and interests. Part of the clinical process involves negotiations between these explanatory models, once they have been made explicit.

Eliciting the patient's explanatory model of illness through a set of targeted questions (shown in Table 9-3) is an important tool for facilitating cross-cultural communication, ensuring patient understanding, and identifying areas of conflict that will need to be negotiated. The wording and number of questions used will vary depending on the characteristics of the patient, the problem, and the setting.

Table 9-3 Questions to Elicit a Patient's Explanatory Model

Source: Adapted from Kleinman A, Eisenberg L, Good B. Culture, illness, and care: clinical

lessons from anthropologic and cross-cultural research. *Ann Intern Med*. 1978. 88:251–258.

What do you think has caused your problem?
Why do you think it started when it did?
What do you think your sickness does to you? How does it work?
How severe is your sickness? Will it have a short or long course?
What kind of treatment do you think you should receive?
What are the most important results you hope to receive from this treatment?
What are the chief problems your sickness has caused for you?
What do you fear most about your sickness?

8. How can communication be improved between CC and the health care team?

To improve communication between a Mexican immigrant, who may not speak English as a first language, and any member of the health care team, it would be helpful to invite a bilingual staff member, if available, to join the conversation. CC could also be asked if there is someone else who is more proficient in English to join him either on the phone or at the next visit. By saying: “CC, I am not sure I explained everything well enough for you to understand,”

the clinician is able to address any concerns without causing embarrassment for the patient or making him defensive.

Subsequently, the office staff needs to be informed so that they can prepare for CC's visit by ensuring that interpreter services will be available. Depending on available resources, this may involve the patient bringing someone or ensuring that bilingual staff is available for the visit, or arranging for a trained interpreter, either live or via telephone.

The following should be done to effectively use an interpreter, particularly when someone other than a trained medical interpreter is used:

Have a pre-interview discussion with the interpreter. (Tell the interpreter what you hope to accomplish with this interview and give a brief description of how the patient came to the current situation.)

Position the interpreter to the side and slightly behind the patient (Figure 9-2).

Look at the patient and not at the interpreter. (Experienced interpreters actually avoid eye contact with everyone in order to promote optimal interaction between the clinician and the parent and/or patient).

Speak in short sentences and avoid jargon and phrases that may not translate well from English into another language, such as “the ball is your court.” (It is important to note that

"interpretation" refers to the spoken word, while "translation" is about the written word.)

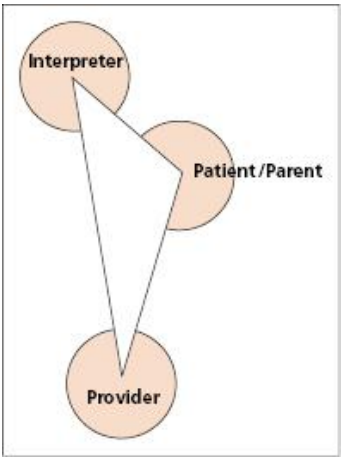

Figure 9-2 Proper Positioning for a Medical Interpreter

Source: Horace M. DeLisser, MD. 2014. Used with permission.

Part 3: Medical Nutrition Therapy

9. Now that communication issues have been discussed, what specific dietary recommendations would be appropriate and realistic for CC to implement?

CC's labs and physical examination revealed elevated triglycerides and blood sugar, low HDL-C, borderline hypertension, and an abnormally high waist circumference. He therefore meets all five of the criteria for the diagnosis of metabolic syndrome. He is also at

risk for diabetes and hypertension. CC's current diet is high in total fat, saturated fat, cholesterol, sodium, and sugar. He is also obese, with a BMI of 32 kg/m^2 and a waist circumference of 43 inches. At present, there is no single dietary recommended for all individuals with metabolic syndrome, therefore it is best to focus on the specific patient's metabolic alterations when offering nutrition counseling.

His current job is very stressful, he is on the road all the time, and says that he does not have time to exercise and has limited choices for healthy foods. These are all challenges for CC to improve his health. Because of his strong family history of obesity, diabetes, and hypertension, he is at risk of also developing these medical problems. It is important to help him understand that his current diet may make it more likely that he will develop those conditions. His goals should therefore include reducing this total calories, fat, saturated fat, sodium, sugar, cholesterol, and alcohol intake. As shown in his diet analysis, his current total caloric intake is 4539 kcal/day and his saturated fat intake represents 12 percent of his daily intake.

Nutritional goals could encourage CC to refuel his body just as he refuels his truck. Healthy eating practices will allow his body to perform at its best, provide extra energy, and increase

his alertness for long hours on the road. Tips for eating on the road are shown in Table 9-4.

Table 9-4 Tips for Truck Drivers While Eating on the Road

Source: Sharon D. Perkins, MES. 2014. Used with permission.

It's all about choice as well as portions.
Ask for nutritional information at the places you like to eat.
Ask “What do I like?” and “What do I need?” rather than “What do I want?”
Have a plan:
Walk in knowing what you will choose based on what you need.
Stick to your plan.
Request that food is prepared the way you want it … no gravy, broiled rather than fried, dressing on the side for you to control.
Look for steamed, baked, broiled, braised, poached, or grilled and skip the sautéed, pan-fried, or deep-fried items.
Look for health-focused entrees.
A box of crayons. Keep in mind that a colorful plate containing more veggies than meat should be a goal!

Forget the “clean plate” notion. At restaurants ask for a doggie bag and then refrigerate it for your next meal.

Avoid asking for *super-size* or *value size* items.

For sedentary patients with hypertriglyceridemia and insulin resistance (particularly those who are obese or have elevated waist circumference) a lower carbohydrate diet that limits sodas, juice drinks, refined grains such as sweetened cereals, baked goods, and desserts may be beneficial. The long-term effects of low-carbohydrate diets have not been adequately studied but short-term research shows that these diets lower triglycerides, raise HDL-C, and reduce body weight.

In addition, alcohol intake should always be quantified. Although alcohol has been shown to be cardioprotective in certain patients, it contributes a significant amount of calories and can raise triglyceride levels. For example, 6 ounces of red wine has approximately 120 calories, and 12 ounces of beer has 150 calories, equivalent to a 12-ounce can of regular soda. In addition, excessive alcohol consumption may cause hypertension, atrial arrhythmias, stroke, cirrhosis, pancreatitis, breast cancer, and accidents. Finally, alcohol also weakens the patient's resolve not to overeat and can thus contribute to many collateral calories. Limit

alcohol in patients with metabolic syndrome to 1 drink per day or a maximum of 7 drinks per week.

If CC follows the recommended diet shown here, he will have a reduction in calories, total fat, saturated fat, cholesterol, alcohol, sodium, and simple sugars. He will meet the recommendations for saturated fat of less than 7 percent, cholesterol of less than 200 mg per day, and fiber of 20 to 30 grams per day. He will also increase his fruit and vegetable consumption as recommended by the DASH diet (Table 6-6). Fish and nuts were included to increase MUFAs. Fruits and vegetables are ideal carbohydrate-rich foods, high in fiber and containing important phytonutrients such as antioxidant vitamins and flavonoids. This approach will also improve his constipation.

Two percent milk was suggested as a way to help CC reduce his consumption of half and half. After he becomes accustomed to the 2 percent, he can be encouraged to switch to 1 percent milk. Decaffeinated beverages were interspersed with caffeinated beverages to help lower his caffeine tolerance, prevent dehydration, and reduce truck stops. By lowering his caffeine tolerance, he will ensure that caffeine will be more effective when he does need it to stay awake.

A fast food meal was included because drivers avoid regular restaurants due to parking

options and time constraints. Truck stops and fast food restaurants do offer healthy options. He can improve his diet and "limited choices" by purchasing one of the electric coolers now available for trucks. This will enable him to pack healthy foods and maintain their freshness. Examples of healthy snacks for the road and tips for buffet style truck stops are shown in Table 9-5.

Table 9-5 Tips for Buffet-Style Truck Stops

Source: Sharon D. Perkins, MES. 2014. Used with permission.

First take a look at everything that's on the buffet.
Avoid the temptation to choose a little bit of everything.
Use medium-sized plates and use the serving utensils at a serving line to dictate the amount to take.
Concentrate on fresh vegetables at the salad bar and avoid pre-dressed salads.
Chose a colorful plate containing more vegetables than meat.
For an entree, select small portions of one or two main dishes and round out the meal with cooked vegetables.

Buffets often have a great selection of fresh fruits – try these for dessert.

Try a serving of fresh fruit and top it off with a little bit of soft-serve ice cream.

Drink water or tea without sugar.

Recommended Revised Diet for CC

Breakfast (truck stop or motel)	
Coffee	16 ounces (480 mL)
2% Low-fat milk	8 ounces (240 mL)
Sweetener	4 packets
Oatmeal	1 cup (with milk)
Banana	1 medium
Snack (on-board cooler)	
Apple	1 medium
Peanut butter	2 Tbsp.
Decaf iced tea (unsweetened)	12 ounces (360 mL)
Lunch (fast food and on-board cooler)	
Grilled steak soft taco	1 whole
Orange	1 medium
Iced tea (unsweetened)	24 ounces (720 mL)

Breakfast (truck stop or motel)	
Snack (on-board cooler)	
Fresh baby carrots	1 cup
Almonds	11
Decaf iced tea (unsweetened)	12 ounces (360 mL)
Dinner (home)	
Low-fat chicken enchilada	1
Onions and peppers	1 cup
Diced tomatoes	½ cup
Mexican rice	1 cup
Pinto beans	½ cup
Beer	12 ounces (360 mL)
Snack (home)	
Decaf iced tea (unsweetened)	12 ounces (360 mL)
Tortilla chips	1 ounce
Salsa	4 Tblsp.

Total calories: 2125 kcal

Protein: 93 g (17.5% of calories)

Fat: 37 g (15.7% of calories)

Saturated fat: 11 g (5% of calories)

Cholesterol: 85 mg

Carbohydrate: 350 g (66% of calories)

Dietary fiber: 37 g

Sodium: 2117 mg

10. How can CC increase his physical activity level?

Skeletal muscle is the most-insulin sensitive tissue in the body and therefore a primary target for impacting insulin resistance (IR). Physical training has been shown to reduce skeletal muscle lipid levels and IR regardless of BMI. Exercise has been shown to lower systolic blood pressure by an average of 4 to 9 mm Hg in patients with elevated blood pressure. The impact of exercise on insulin sensitivity is evident for 24 to 48 hours and disappears within 3 to 5 days. Thus, regular physical activity should be a part of any effort to reverse the effects of IR. In a meta-analysis of studies published on the impact of exercise in patients with type 2 diabtetes, Boule and colleagues concluded that exercise should be considered a desirable end-point and not just a means to achieve weight loss.

Exercise Prescription

A recent Institute of Medicine report recommends 1 hour of physical activity daily for health maintenance. The American Heart Association calls on health professionals to prescribe 30 minutes or more of brisk walking

on most or all days of the week. The greatest health benefits occur when sedentary individuals incorporate moderate-intensity exercise as part of their lifestyle. Low-intensity exercise can have a significant impact and may be easier for patients to comply with these regimens, since compliance declines as frequency increases. Encourage patients to find their own comfort level when it comes to physical activity. Help each patient find a level of activity that he or she can accomplish over the long-term. A combination of resistance and aerobic exercise is advisable, but any activity is better than none and patients who have been sedentary need to start with walking and increase duration and intensity gradually.

CC should exercise 30 to 60 minutes per day, on most days. Explain to him that exercise will make him healthier, reduce stress, help with sound sleep, help him look better and move easier. Exercise will help muscles and joints become stronger and a strong body is less susceptible to strains, sprains, and other injuries. Ways to exercise on the road are listed in Table 9-6.

Table 9-6 Tips for Exercising on the Road

Source: Sharon D. Perkins, MES. 2014. Used with permission.

Walk at rest stops and truck stops (around facility or on a walking path nearby).

Walk around truck or bus several times at each stop.

Walk when truck is being loaded/unloaded at the delivery site.

Park far from the building.

Take exercise equipment on the truck.

Ride a stationary bike at a truck stop fitness center.

Jump rope in the rest stop parking lot.

Pack low-weight dumbbells or cans to do arm curls.

Use resistant elastic bands for 5–10 minutes at rest stops.

Do crunches or push-ups in your cab (build up to this).

Tighten stomach muscles while driving, hold for 30 seconds, then release.

Case 3: Cystic Fibrosis

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Objective

Explain the nutritional abnormalities commonly observed in patients with cystic fibrosis.

Conduct a nutritional assessment of patients with cystic fibrosis.

Develop an appropriate nutritional care plan for patients with cystic fibrosis.

Recognize the importance of medical nutrition therapy in the long-term survival and well-being of patients with cystic fibrosis.

JF, a 21-year-old Caucasian female with cystic fibrosis (CF), presents to the pulmonary clinic with a 1-week history of increased cough, shortness of breath, and a 3-pound weight loss. She reports increased mucus production with a change in color from yellow to green. She has also been passing three to four foul-smelling, floating stools daily for the past several months.

Past Medical History

JF was diagnosed with CF at 5 years of age based upon recurrent upper respiratory tract infections, bulky, foul-smelling stools, and hepatomegaly. In addition, JF has scoliosis, diagnosed 2 years ago, and hearing loss due to frequent intravenous antibiotic therapy. She

has been hospitalized two times over the past year for acute exacerbations of CF. JF has no known food or drug allergies.

Medications

JF's current medication regimen includes Zenpep 10,000 (pancrealipase) – 6 capsules per meal and 3 capsules with snacks, azithromycin, albuterol and fluticasone via inhaler, hypertonic saline and dornase alfa via nebulizer, and omeprazole. She also receives chest physiotherapy via a therapy vest two times daily for 20 minutes each session in conjunction with her nebulized medications.

Diet History/Vitamin and Mineral Supplements

JF follows a high-calorie, high-protein, high-fat, extra-salt diet that includes three meals and three snacks daily. She also drinks two servings per day of Scandishake, a high-calorie, high-protein powder supplement that is mixed with whole milk, but she recently ran out of her supply at home. JF's current vitamin/mineral regimen includes Aquadek, a CF-specific multivitamin, 1 cap twice per day. Each Aquadek softgel contains vitamin A 18,167 IU, vitamin E 150 IU, vitamin D 120 IU, and vitamin K 700 μg in addition to multiple B vitamins and zinc. JF prepares her breakfast and lunch and her mother prepares dinner.

Social History

JF is a junior in college and lives at home with her parents. She denies smoking, alcohol, drug use, and sexual activity.

Review of Systems

Remainder of the review of systems was unremarkable except for poor appetite, shortness of breath, and increased frequency of bulky, foul-smelling stools.

Physical Examination

Vital Signs

Temperature: 101.4 °F (40 °C)

Heart rate: 110 BPM (tachycardia)

Respiration: 24 BPM (tachypnea)

Blood pressure: 134/74 mm Hg

Height: 5′2″ (157.5 cm)

Current weight: 88 lb (40 kg)

Usual weight: 91 lb (41 kg)

BMI: 16 kg/m^2

Exam

The patient's physical examination is normal except for the following observations:

General: Thin, ill-appearing female

Skin: Warm to the touch

HEENT: Right nasal polyp

Chest: New rales and rhonchi in right upper lung zone, no wheezing or dullness to percussion

Cardiac: Elevated rate, normal rhythm, no murmurs

Laboratory Data

Patient's Values	**Normal Values**
Albumin: 4.2 g/L	3.5–5.8 g/L
Hemoglobin: 13.4 g/dL	12.0–16.0 g/dL
25(OH) vitamin D: 18 ng/dL	>30 ng/dL
PIVKA II: 10 ng/mL	<6 ng/mL
Vitamin A (retinol): 0.3 mg/L	0.2–0.5 mg/L
Vitamin E (alpha-tocopherol): 5 mg/L	2–6 mg/L
Random glucose: 175 mg/dL	<200 mg/dL
Oral glucose tolerance test:	
fasting 89 mg/dL	fasting <100 mg/dL
1 hour 152 mg/dL	
2 hour 210 mg/dL	2-hour <200 mg/dL

Treatment

Because of her worsening symptoms, abnormal physical examination, and decreasing pulmonary function, JF is diagnosed with an acute pulmonary exacerbation of CF and admitted to the hospital. During her 2-week hospital admission, she received intravenous antibiotics, frequent respiratory treatments, and vigorous chest physiotherapy to help mobilize her secretions. A DEXA scan was ordered to determine her bone mineral density.

In addition, random blood glucose levels were consistently elevated in conjunction with an elevated 2-hour glucose on her oral glucose tolerance test suggesting CF-related diabetes. After consultation with endocrinology, an insulin regimen was initiated using a long-acting insulin daily in addition to a short-acting insulin matched to the carbohydrate content of her meals. Despite these therapies, JF's appetite remained poor, and she lost an additional 4 pounds (1.8 kg) during her hospital stay. Three-day calorie counts revealed that JF consumes approximately 1500 calories per day. A high-calorie, high-protein oral supplement was ordered to help her meet her calorie goals.

Follow-Up

JF was discharged to home when her weight reached 91 pounds (41 kg). She was advised to

continue monitoring her blood glucose levels until her post-hospitalization office visit.

Case Questions

What factors are most likely contributing to JF's weight loss?

What nutritional problems are patients with CF at risk for developing?

Is albumin a valid indicator of JF's nutritional status?

What is the significance of an elevated blood glucose level?

Are JF's current nutrition and vitamin therapies appropriate?

Is JF's current enzyme therapy appropriate?

What dietary recommendations would you give JF upon discharge?

What parameters should be used to monitor changes in JF's nutritional status after she is discharged from the hospital?

Answers to Questions: Case 3

Part 1: Nutrition Assessment

1. What factors are most likely contributing to JF's weight loss?

A negative calorie balance accounts for JF's weight loss, compounded by ongoing malabsorption and by increased energy needs due to fever and infections. JF's poor appetite may be due to her current lung infection and her antibiotic therapy. Decreased appetite in CF patients may also be due to esophagitis, cholelithiasis, salt depletion, and vitamin and mineral deficiencies leading to altered taste (dysgeusia). Psychosocial factors also commonly contribute to anorexia. JF's bulky, foul-smelling stools suggest fat malabsorption and an inadequate dose of pancreatic enzymes. In addition, JF has elevated serum glucose levels likely due to CF-related diabetes and worsened by her acute pulmonary exacerbation. Vitamin D deficiency may also play a role in depression which may result in decreased appetite.

2. What nutritional problems are patients with CF at risk for developing?

The importance of uncompromised nutritional status in the long-term survival and well-being of patients with CF is well documented. Pancreatic insufficiency occurs in about 90 percent of CF patients. Analysis of pancreatic secretions in those with pancreatic insufficiency reveals a marked decrease in the amount of water, bicarbonate, electrolytes, and enzymes (lipase, protease, and amylase). This results in inadequate digestion of food, producing

malabsorption and malnutrition with growth retardation and weight loss. Protein-energy malnutrition impairs immune responses, increases the risk for pulmonary infections, and leads to muscle wasting. A suboptimal BMI in patients with CF has been shown to play a direct role in decreased pulmonary function. Maintaining a good BMI optimizes pulmonary function in these patients.

Patients with CF are at risk for developing multiple fat-soluble vitamin deficiencies with their associated clinical manifestations. Vitamin K deficiency results in coagulopathy, a commonly encountered deficiency. Vitamin E deficiency can lead to hemolytic anemia in infants; and to neuropathy, ophthalmoplegia, ataxia, and diminished vibration sense and proprioception in older children and adults. Vitamin D deficiency causes rickets in young children and osteomalacia in adults and contributes to reduced bone mineral density. Vitamin A deficiency leads to night blindness, conjunctival xerosis, and epithelial keratinization.

Deficiencies of water-soluble vitamins are less common; however, vitamin B_{12} deficiency produces macrocytic anemia and neuropathy. Fat malabsorption, which occurs when CF patients are not receiving (or are not complying with) pancreatic enzyme replacement therapy, impairs the digestion of the glycoproteins

known as R binders, which are necessary for the transfer of vitamin B_{12} to intrinsic factor (IF). Salt depletion leads to lethargy, weakness, dehydration, and metabolic alkalosis. Essential fatty acid deficiency results in desquamation, thrombocytopenia, and poor wound healing.

Osteopenia is also commonly seen in CF patients, which may be due to malabsorption, decreased calcium intake, vitamin D deficiency, delayed puberty, reduced physical activity, medications (e.g., corticosteroids), and high circulating levels of inflammatory cytokins related to lung infections. A DEXA scan is recommended for all adults and children 8 years old and up who are at nutritional risk.

JF's DEXA scan indicates very low bone density. According to her 24-hour diet recall, JF's calcium intake was only 800 mg of elemental calcium. JF's estimated calcium needs are 2000 mg of elemental calcium per day. Therefore, JF was started on an oral calcium supplement to provide 500 mg, two times a day. Her serum 25(OH) vitamin D level was only 18 ng/mL. Currently, the goal is to achieve levels greater than or equal to 30 ng/mL. JF was started on 2000 IU/day of vitamin D_3 (cholecalciferol) to approximately double her current dose of vitamin D based on the Cystic Fibrosis Foundation consensus guidelines for treating vitamin D deficiency.

3. Is albumin a valid indicator of JF's nutritional status?

Serum albumin indicates visceral protein status. JF's albumin was normal, indicating good protein stores. Hypoalbuminemia reflects poor protein intake and/or increased protein losses, and suggests acute visceral protein depletion. Protein deficiency may develop in as little as 2 weeks. Most commonly, patients with CF are undernourished at the time of diagnosis and throughout their lives, but their albumin levels are normal until the end stages of their disease because the body preserves visceral protein in chronically ill patients. Therefore, the clinical diagnosis of malnutrition should be based on physical examination findings, such as temporal and interosseus muscle wasting, and information gathered in the medical and diet history. Similarly, anthropometric results, such as BMI, percent weight change, and diminished triceps skinfold thickness (TSF) and mid-arm muscle circumference (MAMC), reflect fat and muscle wasting due to chronically inadequate protein and energy intake (see Chapter 1).

Part 2: Medical Nutrition Therapy

4. What is the significance of an elevated blood glucose level?

Hyperglycemia is frequently seen during CF pulmonary exacerbations and with systemic steroid use which can lead to increased

morbidity and mortality in this population. Studies have shown that weight loss and declining pulmonary function can occur several years prior to the diagnosis of CF-related diabetes (CFRD). Glucose intolerance and CFRD often develops around 18 to 21 years of age in patients with CF. CFRD can be diagnosed by the following criteria: a fasting glucose level of greater than or equal to 126 mg/dL on two or more occasions; a random glucose level of greater than 200 mg/dL with symptoms of polydipsia or polyuria; a hemoglobin A1c greater than 6.5 percent on two occasions; or a 2-hour oral glucose tolerance test plasma glucose greater than 200 mg/dL. It is important to aggressively treat hyperglycemia during acute exacerbations and to closely monitor fasting and 2-hour post-prandial glucose levels for resolution of glucose intolerance as acute infections resolve.

5. Are JF's current nutrition and vitamin therapies appropriate?

Medical nutrition therapy A high-calorie, high-protein, and high-fat diet is indicated for patients with CF because of their increased resting energy expenditure and high potential for malabsorption. To optimize lung function, a BMI of at least the 50th percentile is ideal for children and adolescents from 2 to 20 years of age. For adults older than 20 years of age, women should have a BMI of at least 22 kg/m^2

and men should have a BMI of at least 23 kg/m^2 according to CF Foundation recommendations. If hyperglycemia or CF related diabetes is present, calories and carbohydrates should not be restricted. Extra salt is needed to replace the large amounts of sodium lost in perspiration. Six small meals per day are better tolerated than fewer, larger meals by patients with high caloric requirements. With the addition of oral high-calorie supplements JF was able to meet her caloric needs. Two Scandishakes (a high-calorie powder supplement to mix with milk) were added daily between meals, which provided JF with an additional 1200 calories per day.

Vitamin therapy Even with appropriate pancreatic enzyme therapy, fat malabsorption and associated fat-soluble vitamin deficiencies may still persist in patients with CF. A daily multivitamin supplement, enriched in fat-soluble vitamins A, D, E, and K that are in a water-miscible form to improve absorption, is indicated. Since vitamin K is produced by gut micro-organisms, antibiotic therapy significantly decreases gut bacteria and, as a result, diminishes vitamin K production. Therefore, vitamin K supplements are often given to patients with CF, especially those receiving chronic antibiotic therapy (at least 2.5 to 5 mg per week). Vitamin D deficiency is also common in patients with CF. Based on updated guidelines, vitamin D deficiency should be

treated by doubling the amount of vitamin D_3 (cholecalciferol) in their current supplements and re-checking the 25-hydroxy vitamin D level 3 months after supplementation is increased. Serum vitamin A, E, 25-hydroxy vitamin D, and PIVKA-II levels should be checked annually in all patients with CF and deficiencies should subsequently be treated.

6. Is JF's current enzyme therapy appropriate?

Malabsorption should be suspected in any patient with CF who reports an increased incidence of foul-smelling, floating stools and poor weight gain despite adequate caloric intake. Such patients require higher enzyme dosages to help them digest and absorb fat. Currently, JF is taking six capsules per meal and three capsules per snack of Zenpep 10,000 (10,000 units of lipase per capsule), which provides 1500 lipase units per kilogram per meal. Instead of increasing the number of enzyme capsules per meal, changing the prescription to Zenpep 20,000 (20,000 units of lipase per capsule) and altering the dosage to four capsules per meal and two capsules per snack will increase the total units of lipase the patient receives to 2000 lipase units per kilogram per meal. This will also minimize the number of capsules the patient must ingest with each meal and snack. The usual recommended meal dose of enzymes is 500 to 2500 units of

lipase per kilogram per meal. The use of gastric acid blocking medications can raise duodenal pH which enhances enzyme activity. As a result, H2 antagonists and proton pump inhibitors are often used in conjunction with pancreatic enzyme replacement therapy to optimize absorption. If symptoms of malabsorption persist after increasing the enzyme dose and adding an acid blocker, other causes of malabsorption should be explored.

7. What dietary recommendations would you give JF upon discharge?

Since patients with CF have such high calorie needs, it is very important *not* to limit calories or carbohydrates to control hyperglycemia. Instead, insulin therapy should be adjusted to optimize glucose control by matching the carbohydrate content of meals and snacks. If patients consume concentrated sweets, these should accompany a meal to reduce the glycemic response.

Upon discharge, JF should be instructed to increase her caloric intake with small, frequent, nutrient-dense meals and oral supplements to promote weight gain. Her insulin regimen may need to be adjusted based on her blood glucose levels, which she should continue to monitor at least once a day. She should be referred to an endocrinologist who can review her blood glucose log and assess improvement in glycemic

control with the resolution of her acute infection.

8. What parameters should be used to monitor changes in JF's nutritional status after she is discharged from the hospital?

Weight change Weight should be monitored three times a week during an inpatient admission and then checked at each outpatient appointment. Due to her worsening symptoms and poor appetite, JF's weight was 88 pounds (40 kg) when admitted to the hospital. Her BMI of 16 kg/m^2 suggests that she is undernourished. For adults with CF, the goal is for females to maintain a BMI above 22 kg/m^2 and males to maintain a BMI above 23 kg/m^2. Patients with CF have a high resting energy expenditure due to their increased work of breathing, inflammatory responses, and infections. They need on average 20 percent to sometimes up to 200 percent of the calorie needs of their same age peers. Calorie needs vary from patient to patient based on severity of disease, activity level, and degree of malabsorption.

Dietary intake/appetite JF's energy requirements are approximately 2560 calories per day to promote weight gain. This is based on her basal metabolic rate of 1084 calories per day multiplied by a factor of 1.9 for

malabsorption and moderate lung disease with 500 calories added for weight gain. Her daily intake in the hospital was approximately 1500 calories – a 1000 calorie per day deficit – which can lead to continued weight loss. Calorie intake should be increased to prevent further weight loss and promote weight gain. JF's intake should be assessed periodically to ensure that her calorie intake is adequate.

Laboratory Data Relevant laboratory tests to be monitored are fasting fat-soluble vitamin levels (PIVKA-II and vitamins A, D, and E) annually and iron studies if there is a concern for anemia. Albumin and pre-albumin levels can be affected by acute infection and therefore may not reliably detect a change in nutritional status. HgA1c may be useful in detecting a history of hyperglycemia, however, sometimes can be falsely low in patients with CF and therefore cannot rule out a diagnosis of CF-related diabetes. A 2-hour oral glucose tolerance test should be checked annually in all patients over the age of 10 years to screen for CF-related diabetes.

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10
Renal Disease

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Objectives*

Describe the specific medical nutrition therapy for acute kidney injury, chronic kidney disease, nephrotic syndrome, and nephrolithiasis.

Describe the goals of medical nutrition therapy for patients on hemodialysis and peritoneal dialysis.

Identify the impact of various forms of renal replacement therapy and renal transplant on a patient's nutritional status.

Explain the importance of regulating the intake of protein, calories, sodium, potassium, phosphorus, fluid, vitamins, and other minerals in patients with renal disease.

*Source: Objectives for chapter and cases adapted from the *NIH Nutrition Curriculum Guide for Training Physicians*. (www.nhlbi.nih.gov/funding/training/naa)

Acute Kidney Injury

Acute kidney injury (AKI) is the current name for acute renal failure. It is still characterized by a sudden decline in the glomerular filtration rate (GFR) of the kidney due to insults such as infection, exogenous nephrotoxins, trauma, dehydration, and shock resulting in ischemia, but is now staged with the hope that early intervention will result in better outcomes. (See Table 10-1). Patients with AKI are at high risk for malnutrition because of underlying illnesses, recent surgical procedures, or trauma, all of which place them in a catabolic, pro-oxidative, and proinflammatory state. In AKI precipitated by major trauma, critical illness, or sepsis, patients frequently undergo metabolic changes that accelerate degradation of protein and amino acids and result in the loss of lean body mass. The dramatic effects of this catabolic state include poor wound healing, increased infection, increased hospitalization, and higher mortality rates.

Table 10-1 Criteria for Stages of Acute Kidney Injury (AKI)

Source: Hark L, Ashton K, Deen D. *The Nurse Practitioner's Guide to Nutrition*, 2nd Edn. 2012: John Wiley & Sons, with permission.

Stage	Creatinine	Urine Output
1	Serum creatinine increased by 0.3 mg/dL or 1.5–2 times the baseline value	<0.5 ml/kg/h for >6 h
2	Serum creatinine increased 2–3 times the baseline value	<0.5 ml/kg/h for >12 h
3	Serum creatinine increased >3 times the baseline value or serum creatinine ≥4.0 mg/dL with an acute increase of 0.5 mg/dL	<0.3 ml/kg/h for 24 h or anuria (no urine ouput) for 12 h

Medical Nutrition Therapy for Acute Kidney Injury

Since malnutrition is so often seen in patients with AKI and is known to be an independent risk factor contributing to increased mortality, implementation of medical nutrition therapy is very important. Decisions on when to implement and how aggressive medical nutrition therapy should be depend on the patient's nutritional status and catabolic rate,

the phase of AKI, the amount of urine output, and clinical indications such as uremia or volume overload requiring dialysis or continuous renal replacement therapy (CRRT). Thus, medical nutrition therapy for the patient with AKI must be highly individualized and the goals are to:

preserve protein stores

hinder skin breakdown

prevent nutritional deficiencies until renal function returns, while maintaining fluid, electrolyte, and acid-base homeostasis.

Protein

Restricting protein intake to 0.8 g/kg per day may be indicated only for patients with AKI whose GFR falls to less than 10 mL/min and who are not catabolic or on any form of dialysis or CRRT. All forms of dialysis and CRRT contribute to protein losses. The protein intake of patients who are receiving hemodialysis (HD) should be at least 1.2 g/kg per day and patients receiving peritoneal dialysis (although infrequently used with AKI) are encouraged to ingest 1.2 to 1.3 g/kg of protein each day. Severely catabolic patients with AKI may have even higher protein needs and require CRRT or aggressive dialytic therapy to allow for sufficient protein intake.

Energy

Caloric requirements for patients with AKI vary depending on the degree of hypermetabolism. Usual recommendations are 35 kcal/kg per day, however, needs may actually be closer to only 20 to 30 kcal/kg per day, especially when total parenteral nutrition (TPN) is utilized. The most accurate determination of caloric requirements is by indirect calorimetry, but equipment to do so may be limited by cost and availability. Complications from slightly underfeeding are not as harmful as overfeeding patients with a high dextrose load, which can cause hyperglycemia, triglyceridemia, and CO_2 retention in patients with respiratory disease. Calories from the dextrose utilized in dialysate with peritoneal dialysis (PD), as well as in replacement fluids with CRRT, must be considered. Now, however, replacement fluids generally utilized with CRRT only have physiologic amounts of dextrose and use bicarbonate rather than lactate, thus do not contribute a significant source of calories. Also, PD is rarely utilized for patients with AKI.

Patients who have adequate gastrointestinal tract function but cannot tolerate food by mouth because of mechanical ventilation, altered mental status, anorexia, nausea, or poor adherence, should receive nourishment by enteral tube feeding (Chapter 12). Those with a dysfunctional GI tract require parenteral

nutrition (Chapter 13). Peripheral insulin resistance may cause hyperglycemia in catabolic patients with AKI, therefore blood glucose levels should be closely monitored. Insulin may be required, especially with the use of parenteral nutrition. Also, there may be alterations in lipid metabolism in patients with AKI. Lipids are not precluded in parenteral feedings, but triglyceride levels must also be monitored closely.

Vitamins and Minerals

Vitamin and mineral requirements for patients with AKI vary depending on the patient's nutritional status and whether they are receiving dialysis or CRRT. Serum electrolytes must be closely monitored in all patients with acute kidney injury (AKI). Initially, serum potassium and phosphate are likely to be elevated and serum sodium lowered in non-dialyzed patients who are oliguric (urine output <400 mL/day). Patients with acute intrinsic renal failure (usually defined as acute tubular necrosis – the major cause of AKI) may experience salt and water overload during the oliguric phase and salt and water depletion during the diuretic or recovery phase of the disease when urine output can exceed 2 to 3 liters per day. In the recovery phase, sodium, potassium, and fluid may need to be replaced to offset urinary losses. Oliguric or anuric patients receiving HD usually require a sodium

restriction of 2 to 3 g/day and a potassium restriction of 2 to 3 g/day. Those undergoing PD, frequent HD (more than three times per week), and some forms of CRRT generally have more liberal sodium and potassium requirements. Patients with AKI undergoing any form of dialysis or CRRT should receive supplemental water-soluble vitamins above the Recommended Dietary Allowances (RDA) to compensate for losses with these treatments. For those receiving total parenteral nutrition (TPN), the standard multivitamin dose should be feasible, especially when TPN is short-term.

Fluid

Daily fluid intake for oliguric patients should equal urine output plus approximately 500 mL to replace insensible losses; fluid needs increase if the patient has a fever. Most anuric patients can tolerate approximately 1000 mL/day with HD three times per week. These restrictions may be liberalized in patients receiving continuous or daily peritoneal dialysis, CRRT, or hemodialysis more frequently than three times per week.

Continuous Renal Replacement Therapy

Continuous arteriovenous hemofiltration (CAVH) utilizes catheters that are placed into a large artery and vein (often the femoral artery and vein). The arterial blood flows through a small filtering device with a large porous

membrane where plasma is filtered of water, minerals, and uremic toxins, and albumin and blood products return to the vascular space through the vein. This form of therapy removes large volumes of essentially albumin-free plasmanate, leaving water and electrolytes in a concentration equal to normal serum levels. It is often used for patients who are very volume overloaded and cannot tolerate standard HD due to very low blood pressure. Parenteral nutrition can be combined with CAVH to provide intravenous nutrition while controlling sodium and water balance and removing small amounts of metabolic waste products that accumulate in renal failure.

Continuous arteriovenous hemodiafiltration (CAVHD) combines HD and hemofiltration simultaneously and removes larger amounts of solutes as well as large volumes of fluid. CAVH and CAVHD use systemic arterial blood flows; other forms of CRRT including continuous venovenous hemofiltration (CVVH) and continuous venovenous hemodiafiltration (CVVHD) use a pumping machine that may result in less erratic blood flows and ultrafiltration rates.

Chronic Kidney Disease (Pre-Dialysis)

In 2002, the National Kidney Foundation (NKF) published clinical care guidelines for

those with chronic kidney disease (CKD). These guidelines help determine the stage of kidney disease based on kidney damage and/or level of glomerular filtration rate (GFR) as shown in Table 10-2. Stage 1 includes kidney damage (e.g. proteinuria) with normal GFR or a GFR of 90 or above. Stage 2 includes mild kidney damage and a GFR of 60 to 89. Stage 3 includes a moderate decrease in GFR to 30 to 59. In Stage 4 the GFR is 15 to 29 and in Stage 5 the GFR is less than 15. Medical nutrition therapy goals for patients with CKD Stages 1 to 4 prior to dialysis or renal transplantation are to retard the progression of CKD while providing adequate calories to maintain or achieve ideal body weight, and to prevent or alleviate the symptoms of uremia and restore biochemical, calcium/phosphorus, vitamin, and iron balance.

Table 10-2 Clinical Care Guidelines for Chronic Kidney Disease

Source: Hark L, Ashton K, Deen D. *The Nurse Practitioner's Guide to Nutrition*, 2nd Edn. 2012: John Wiley & Sons, with permission.

Stage of CKD	**Level of Kidney Damage**	**GFR (mL/min)**
1	Kidney damage (e.g., proteinuria)	Normal or ≥90
2	Mild kidney damage	60–89

Stage of CKD	Level of Kidney Damage	GFR (mL/min)
3	Moderate decrease in GFR	30–59
4	More severe decrease in GFR	15–29
5	Severe decrease in GFR	<15

Medical Nutrition Therapy for CKD

Protein

In CKD, as the GFR and excretion of nitrogenous wastes decline, it is necessary to control the level of protein intake while continuing to maintain a positive nitrogen balance. Protein restriction can minimize the symptoms of uremic toxicity by reducing the production of nitrogenous wastes in the blood. Some evidence also suggests that protein restriction early in the course of CKD due to glomerular damage may slow the progression of the disease and delay the need to initiate dialysis therapy. The generally accepted level of protein restriction for patients with CKD stages 1 to 3 is 0.75 g/kg per day, which is approximately what the DRIs recommend for normal, healthy adults. This is actually a restriction for most individuals, as the

American diet is generally much greater in protein content. For stages 4 and 5 (GFR <25 mL/minute), 0.6 g/kg per day (using an adjusted body weight if the patient is obese) is suggested, only if feasible to meet overall nutritional needs.

Approximately 50 percent of high biological value protein (HBV) is usually encouraged to ensure that essential amino acid requirements are met. The biological value of a dietary protein is determined by its constituent amino acids, with the highest value given to proteins that contain all essential amino acids, such as eggs, meats, and other animal proteins. It has also been shown, however, that carefully planned low-protein vegetarian diets containing soy and plant-based protein may reduce proteinuria, improve serum protein levels, and retard the progression of CKD as compared to animal proteins. Additional increased protein needs due to catabolism from use of glucocorticoid (steroid) therapy or recent surgery as well as acute illness with decreased oral intakes may contraindicate limiting dietary protein.

Energy

The recommendations for adequate energy intake for individuals with CKD not yet on dialysis are generally 35 kcal/kg per day to maintain body weight and allow for effective protein utilization. It has been recommended

that 30 kcal/kg per day be used for those older than 60 years of age due to a more sedentary lifestyle. Calories from complex and simple carbohydrates must be included in the diet to provide adequate energy to prevent weight loss. Low protein food products are available and can improve overall caloric intake while minimizing protein content, but the expense, taste, and availability must be considered.

Lipids

Additional fat, in the form of monounsaturated and polyunsaturated fats, may also be recommended to provide adequate calories for patients with CKD. Since dyslipidemia is prevalent in patients with CKD, lipid levels should be monitored, and an effort made to keep total cholesterol, LDL-C, HDL-C, and triglyceride levels within normal limits (Chapter 6). Pharmacologic therapy may be needed to manage lipid levels, as some studies utilizing statins have shown cardiovascular risk reduction for patients with CKD stages 2 to 3.

Sodium

As renal failure progresses to a GFR of about 10 percent of normal, renal sodium excretion subsequently falls. Sodium intake may have to be limited to prevent sodium retention, generalized edema, hypertension, and/or congestive heart failure, especially in the advanced stages of CKD when excretion

diminishes. *The NKF/KDOQI Clinical Practice Guidelines on Hypertension and Antihypertensives* recommend a sodium intake of less than 2.4 g/day unless a sodium wasting disease is present or medications causing sodium loss are prescribed.

Measuring urinary sodium in a 24-hour urine collection may be helpful in determining how much sodium is being excreted. Urinary sodium is reported in milliequivalents (mEq), making it necessary to convert from milligrams to milliequivalents to determine how many milliequivalents of sodium are associated with any given diet.

Conversion of milligrams of sodium to milliequivalents

To convert milligrams of sodium to milliequivalents, divide the number of milligrams by the molecular weight of sodium (23 mg Na = 1 mEq Na). For example, assuming that a low-sodium diet is limited to 2000 mg/day, it contains 87 mEq of sodium (Table 10-3).

Table 10-3 Foods With High Sodium Content

Source: Lisa Hark, PhD, RD. Adapted with permission.

Bacon
Barbecue sauce
Bouillon cubes*
Canned seafood*
Cheeses, processed
Chinese food
Cold cuts
Corned beef
Corn chips
Crackers*
Dried beef
“Fast Foods”
Frozen dinners (unless of a healthy variety).
Gravy, canned or packaged
Ham
Hotdogs
Meat tenderizers
Nuts, salted*
Olives
Packaged or prepared casserole dishes
Popcorn
Pickles
Potato chips, pretzels*
Relish

Salt pork
Sauerkraut
Sausages
Scrapple
Smoked meats or fish
Soy sauce
Steak sauce
Soups, canned* & dried mixes
Tomato juice*
Tomato sauce
Vegetable juice*
Worcestershire sauce

Some of the above foods may be acceptable if allowed in small servings.

*These items may be purchased “salt-free” or “low sodium” in many grocery stores. If following a low potassium diet, be sure to read labels as potassium chloride may substituted for sodium chloride; then these specific items should not be used.

Potassium

The kidney usually handles potassium efficiently until the GFR is significantly reduced (<10 mL/min). Thus, a dietary potassium restriction may be necessary only during the

latter stages of CKD. Exceptions include renal diseases such as diabetic nephropathy, in which aldosterone deficiency develops and potassium excretion declines. Use of an angiotensin-converting enzyme (ACE) inhibitor to control blood pressure in some individuals may also require a mild-to-moderate potassium restriction, even with good urine output. ACE inhibitors suppress the renin-angiotensin system, resulting in decreased aldosterone levels and subsequent elevations in serum potassium levels. Angiotensin receptor antagonists used to control hypertension can also cause hyperkalemia, though the likelihood is probably lower than with ACE inhibitors. When serum potassium levels are consistently greater than 5.0 mEq/L, a potassium-restricted diet of 2 to 3 g/day (51 to 77 mEq/day) should be initiated (Table 10-4).

Table 10-4 Foods With High and Low-To-Medium Potassium Content

Source: Lisa Hark, PhD, RD. Used with permission.

High-Potassium Vegetables	**High-Potassium Fruits and Juices**
Artichokes Beans (navy, lentil, kidney, pinto) Broccoli Brussels sprouts	Apricots Avocados Bananas Cantaloupes Dates

Carrots, raw French fries, Greens Lima beans Parsnips Potato, baked and chips Pumpkin Spinach Sweet potato Tomato Winter squash (butternut, acorn) Tomato juice Vegetable juices	Figs Honeydew melons Mangos Nectarines Oranges, orange juice Papayas Prunes Raisins Rhubarb Watermelon (if more than one cup chunks) Apricot nectar Prune juice
Other high-potassium foods	
Milk (more than 4 to 8 ounces/day) Chocolate Nuts Bran cereal	Salt substitutes (containing KCL) Molasses Potato chips
Low-to-medium potassium vegetables*	**Low-to-medium potassium fruits and juices***
Asparagus Beets Cabbage Carrots, cooked Cauliflower Celery Corn	Apples, apple juice Applesauce Blueberries Cherries Cranberries, cranberry juice Fruit cocktail

Cucumber Eggplant Green beans Green peppers Kale Lettuce Okra Onions Peas Potato (only when double-boiled) Radishes Wax beans Zucchini	Grapefruits, grapefruit juice (only 4 ounces/ day) Grapes, grape juice Lemons Limes Peaches, fresh (small) Pears, fresh (small), pear nectar Pineapples, pineapple juice (only 4 ounces/ day) Plums Raspberries (1 cup) Strawberries (1 cup) Tangerines

*Note that even low-to-medium potassium foods must be consumed in limited amounts daily.

Calcium, Phosphorus, Parathyroid Hormone, and Vitamin D

Mineral-Bone-Disorder (MBD) describes the clinical syndrome resulting from abnormal mineral bone metabolism which occurs with CKD. Renal osteodystrophy refers to only the complex bone lesions present in the majority of patients with CKD, and includes osteitis fibrosa and osteomalacia, which are associated with this disorder. Restriction of dietary phosphorus has been shown to prevent the development of

secondary hyperparathyroidism, which is frequently seen in patients with CKD. Also, in the past decade increased vascular and soft tissue calcifications have been seen in this population, believed to be related to calcium/phosphorus metabolism and treatment to maintain proper balance of these minerals. As a result, the *NKF/KDOQI Clinical Practice Guidelines for Bone Metabolism and Disease* recommend a phosphorus restriction of 800 to 1000 mg/day for individuals with CKD stages 3 and 4 when the serum phosphorus level is greater than 4.6 mg/dL (Table 10-5). With a protein-restricted diet, this is usually feasible, as animal protein-based foods are also high in phosphorus content. If dairy products are avoided in a vegetable-based low-protein diet utilizing soy products, this level of phosphorus restriction is also feasible.

Table 10-5 Phosphorus Content of Selected Foods

Source: Hark L, Ashton K, Deen D. *The Nurse Practitioner's Guide to Nutrition*, 2nd Edn. 2012: John Wiley & Sons, with permission.

Foods	**Portion Size**	**Phosphorus Content (mg)**
Dairy		
Cheese, cheddar	1 ounces	145

Foods	Portion Size	Phosphorus Content (mg)
Cheese, cream	1 Tbsp.	15
Frozen yogurt	½ cup	95–100
Half-and-half	½ cup	110
Ice cream	½ cup	70–100
Milk (whole, low-fat, skim)	8 ounces	220–230
Pudding (vanilla/ chocolate dry mix regular made with 2% milk)	½ cup	115–135
Pudding (chocolate dry mix instant made with 2% milk)	½ cup	350
Pudding, (vanilla/ chocolate/ tapioca/ rice-ready-to-eat)	½ cup	45–75
Yogurt (all kinds)	8 ounces	215–350
Protein foods		
Beef, cooked	3 ounces	150–200
Eggs, whole	1 large	95
Liver, Beef (panfried)	3 ounces	410
Peanut butter	1 Tbsp.	55
Sardines, Atlantic, canned in oil	3 ounces	415

Foods	Portion Size	Phosphorus Content (mg)
Tuna	3 ounces	140–265
Vegetables		
Baked beans and pork and beans	½ cup	95–150
Dried beans	½ cup	130
Chickpeas	½ cup	110–140
Lentils, boiled	½ cup	180
Soybeans, green boiled	½ cup	140
Soybeans, mature boiled	½ cup	210
Bread and cereals		
Barley, pearled cooked	1 cup	85
Bread, white	1 slice	25
Breads whole grain	1 slice	60
Cornbread (from mix)	1 piece	225
Raisin Bran	1 cup	225
Miscellaneous		
Chocolate	1 ounce	70
Nuts, mixed, dry	1 ounce	125
Peanuts, dry roasted	1 ounce	100

Foods	Portion Size	Phosphorus Content (mg)
Beverages		
Beer	12 ounces	50
Coffee, brewed	6 ounces	5
Colas	12 ounces	60

Note that inorganic phosphate contained in beverages and other food products are absorbed 100%, even if total phosphorus content does not seem high. Check labels for any ingredient containing the letters “phos” and avoid these products if following a low phosphorus diet.

A “phosphate binder”, which may be prescribed with meals, interferes with the absorption of phosphate in the small intestine while maintaining serum phosphate levels within normal range. Calcium acetate, sevelamer hydrochloride or sevelamer carbonate (non-absorbed phosphate-binding polymers without calcium or aluminum), and lanthanum carbonate have also been utilized (Table 10-6). These medications are used “off-label” for CKD patients not yet on HD. Sometimes, a combination of sevelamer and calcium acetate is used to provide phosphate binding without adding significant calcium. Serum calcium

levels may not decrease until the GFR is less than 30 mL/minute, thus initially eliminating any need for specific calcium supplementation until later stages of CKD. Since foods rich in calcium (primarily dairy products) are also high in phosphorus content and must be restricted; calcium carbonate and calcium acetate may be used between meals to increase serum calcium levels. The *K/DOQI Clinical Practice Guidelines for Bone Metabolism and Disease* recommends 1.5 to 2.0 g of calcium (including dietary and supplemental calcium) for CKD stages 3 and 4 and 1.5 to 1.8 g for stages 4 and 5 not yet on dialysis. Goals are to keep serum calcium levels within normal range.

Table 10-6 Selected Phosphate-Binding Medications

Medication	Dose	Ca^{2+} (mg) (elemental)	Al (mg)	Manufacturer
Calcium carbonate*				
Calcium carbonate, 1250 mg	1 tab	500	0	Roxane Labs
Oscal 500	1 tab	500	0	GlaxoSmithKline
Tums—Regular	1 tab	200	0	GlaxoSmithKline
Extra-strength	1 tab	300	0	GlaxoSmithKline
Ultra	1 tab	400	0	GlaxoSmithKline
500	1 tab	500	0	GlaxoSmithKline
Calcium acetate				
PhosLo	1 tab	169	0	Fresenius Medical Care_
Calphron	1 tab	169	0	Nephro-Tech,
Calcium Acetate	1 tab	169	0	Hillestad Pharmaceuticals
Phoslyra	5 ml	169	0	Fresenius Medical Care
Sevelamer HCL				
Renagel, 800 mg	1 tab	0	0	Sanofi Aventis
Renagel, 400 mg	1 tab	0	0	Sanofi Aventis
Sevelamer carbonate				
Renvela, 800 mg	1 tab	0	0	Sanofi Aventis
Renvela powder, 0.8 g	1 pkt	0	0	Sanofi Aventis
Renvela powder, 2.4 g	1 pkt	0	0	Sanofi Aventis
Lanthanum carbonate				
Fosrenol, 1000 mg	1 tab	0	0	Shire
750 mg	1 tab	0	0	Shire
500 mg	1 tab	0	0	Shire

*Calcium carbonate is now rarely used for phosphate-binding due to its calcium content relative to current suggested guidelines for calcium intake in CKD.
Source: Hark L, Ashton K, Deen D. *The Nurse Practitioner's Guide to Nutrition*, 2nd Edn. 2012: John Wiley & Sons, with permission.

Water Balance and Fluid Restriction

Fluid intake for individuals with CKD should be balanced by their ability to eliminate fluid. As long as urine output essentially equals the daily fluid intake, fluid balance is maintained. If edema becomes apparent, prescribing loop diuretics often increases sodium and water excretion sufficiently to maintain balance. In the latter stages of CKD, a fluid limit equal to the volume of urine output plus 500 mL/day for insensible fluid losses may be necessary to prevent edema and hyponatremia.

Vitamins and Iron

Protein and mineral restrictions to manage CKD usually result in a diet deficient in vitamins. Supplementation with folic acid (1 mg/day), pyridoxine (5 mg/day), the RDA for other B-complex vitamins, and ascorbic acid (60 to 100 mg/day) is often necessary. If the parathyroid hormone (PTH) level is above the goal range for the stage of CKD, a serum 25-hydroxyvitamin D level should be evaluated. If normal, it can be repeated on a quarterly basis; if less than 30~ng/mL, supplementation with vitamin D_2 (ergocalciferol) should be prescribed. Because of the kidney's inadequate conversion of vitamin D from 25-hydroxycholecalciferol [25(OH)D] to its active form, 1,25-dihydroxycholecalciferol [1,25(OH_2)D], supplementation of this active form or other analog of vitamin D is often required and individualized to keep serum PTH levels within goal range for the various stages of CKD. Vitamin A, on the other hand, may accumulate as CKD progresses and should not be supplemented. Vitamin preparations designed specifically for individuals with renal failure are available to meet patients' needs.

Most patients with CKD develop anemia primarily because of the kidney's decreased production of the hormone erythropoietin. This hormone stimulates the bone marrow to produce red blood cells. Many patients with

CKD begin treatment with erythropoietin stimulating agents (ESAs) in the form of epoetin alfa or darbepoetin alfa prior to initiating dialysis. To promote red blood cell production, iron supplementation is often necessary for patients receiving erythropoietin therapy, but varies depending on iron status.

Dialysis

The goals of medical nutrition therapy for patients on maintenance HD, both in-center and home hemodialysis (HHD), and maintenance PD, both continuous ambulatory peritoneal dialysis (CAPD) and continuous cycling peritoneal dialysis (CCPD), are to maintain:

protein equilibrium to prevent a negative nitrogen balance;

serum potassium and sodium concentrations within an acceptable range and maintain total body sodium as close to normal as possible;

fluid homeostasis by preventing fluid overload or volume depletion;

serum calcium, phosphorus, and PTH levels within an acceptable range to prevent renal osteodystrophy and metastatic calcification; and

adequate levels of vitamins and other minerals.

Medical Nutrition Therapy for Dialysis

Protein

Protein intake for patients undergoing maintenance dialysis must at least equal minimum dietary protein requirements but not worsen the uremic syndrome by causing retention of urea, electrolytes, and various minerals. The loss of amino acids, the catabolic stress of dialysis, and the level of protein intake in the pre-dialysis period may all contribute to poor protein status in the chronic dialysis patient. A protein allowance of 1.2 g/kg per day for in-center HD patients and 1.2 to 1.3 g/kg per day for HHD and PD patients will often minimize the accumulation of excessive nitrogenous wastes, maintain a positive nitrogen balance, and replace the amino acids lost during dialysis. During episodes of peritonitis, patients receiving PD have increased dietary protein needs due to greater losses of protein across an inflamed peritoneum. Many patients on both HD and PD periodically require supplemental commercial or homemade nutritional drinks, bars, or protein powders in order to achieve adequate protein intake.

Energy

The caloric intake for patients undergoing maintenance dialysis should be adequate to maintain or achieve ideal body weight. Unless the diet provides sufficient calories from carbohydrate and fat, endogenous protein is used for energy production, and the patient develops a negative nitrogen balance and loses significant muscle mass. With PD, calories gained from glucose absorbed from the dialysate must be considered when determining total caloric needs to prevent excess weight gain and obesity (Table 10-7). Patients on both HD and PD, however, may also require nutritional supplements to meet caloric as well as protein intake goals.

Table 10-7 Caloric Absorption from Peritoneal Dialysate

Source: Hark L, Ashton K, Deen D. *The Nurse Practitioner's Guide to Nutrition*, 2nd Edn. 2012: John Wiley & Sons, with permission.

Dextrose (%)	Dextrose (g/L)	Calories Available (3.4 g/L)
1.5	15	51
2.5	25	85
4.25	42.5	145

Approximately 60–76% of calories are estimated to be absorbed from longer dwell

times with CAPD and 40–50% with shorter dwell times with CCPD.

Lipids

As mentioned previously, lipid abnormalities are frequently prevalent in patients with kidney disease. Commonly, patients undergoing HD present with normal or high total cholesterol, LDL-C, and triglyceride levels. Patients on PD frequently have high total cholesterol, LDL-C, and triglyceride levels, and low HDL-C levels. Medical nutrition therapy is aimed at normalizing cholesterol and triglyceride levels without adversely affecting protein and overall caloric intakes in dialysis patients. Pharmacologic therapy for dyslipidemia is often initiated in order to avoid further restrictions to an already complex diet regime. In one study with HD patients however, it has been shown that statins do not decrease cardiac events.

Sodium and Fluid

Daily sodium recommendations are determined by the patient's blood pressure, weight, and level of kidney function. Excessive ingestion of sodium may promote excessive fluid intake and precipitate edema. The sodium and fluid allowances for maintenance dialysis patients depend largely on their interdialytic weight gains. For patients on HD, sodium intake is generally restricted to 2 to 3 g/day, with a fluid allowance of 1000 mL/day plus the amount of

urine output, if any. This will allow an acceptable fluid weight gain of approximately 1 pound per day. Sodium and water may be removed more easily with PD because it is performed daily or continuously, as well as HHD because it is usually done five to six times per week. A more liberal sodium and water intake is therefore possible for PD and HHD patients. It is, however, very important to encourage PD patients to limit sodium and fluid intake more strictly if they consistently use more concentrated dextrose solutions to remove excess fluid. The issue is that excessive use of such solutions can cause eventual damage to the peritoneum and thus decrease the ultrafiltration capacity of PD over time.

Potassium

Potassium intake must be individualized to maintain normal serum potassium levels. Patients on maintenance HD usually can maintain serum potassium levels between 3.5 and 5.5 mEq/L with diets containing 2 to 3 g/day (50 to 75 mEq/day). When serum potassium levels are persistently high, despite dietary counseling, the dialysate potassium content may be lowered or a sodium exchange resin added to the medication regime. When serum potassium levels are consistently low (hypokalemia), the dietary intake may be liberalized and/or dialysate potassium content increased. This is especially important for

patients receiving digoxin therapy, as hypokalemia can cause arrhythmias. Patients on maintenance PD usually maintain a normal serum potassium level without restricting potassium intake. If serum potassium levels fall below normal, dietary potassium is increased, and if unsuccessful, potassium supplements may be required. For those on HHD, the diet may be more liberal in potassium as well, depending upon frequency of and amount of dialysis performed (Table 10-4).

Calcium and Phosphorus

As renal function diminishes, phosphorus excretion decreases. With a GFR less than 25 mL/min, filtration is inadequate to excrete a normal dietary phosphorus load (1000 to 1800 mg). Dialysis therapy does remove phosphorus, but not efficiently enough to allow an unrestricted diet for those receiving three to four treatments per week. Nocturnal HHD, as well as in-center nocturnal dialysis, may remove more phosphorus due to longer treatment time (6–8 hours). The goal of medical nutrition therapy is to achieve and maintain a serum phosphate level of approximately 3.0 to 5.5 mg/dL, and even closer to the normal laboratory range. Phosphorus is widely distributed in foods, but is found primarily in muscle tissue (meats, poultry, and fish) and dairy products (Table 10-5). Therefore, reducing dietary phosphorus

intake often involves a concomitant reduction in total protein intake, but inorganic phosphates added as preservatives to products must be considered.

For patients undergoing conventional in-center HD and PD at home, in order to allow adequate protein intake, the usual phosphorus restriction is 1000 to 1200 mg/day. For those receiving nocturnal HD in-center or at home, the allowance may be greater. It is now also necessary to read labels of many beverages and convenience foods to determine if additives containing phosphate are present. Those foods or beverages that do contain such additives should be avoided as much as possible.

Controlling serum phosphorus by diet alone is usually not possible if the patient is consuming recommended protein levels (1.2 to 1.3 g/kg per day). Therefore, most patients on dialysis are prescribed phosphate binders, such as calcium acetate, sevelamer hydrochloride, sevelamer carbonate, or lanthanum carbonate, previously mentioned for pre-dialysis patients. All of these medications are prescribed with meals and snacks to promote phosphate-binding in the gut, which decreases phosphorus absorption. Calcium carbonate is not utilized for phosphate binding as frequently now that goals are to keep serum calcium levels lower. Medications other than calcium acetate may be better choices for phosphate-binding in efforts to avoid excessive

calcium intake and the potential for increased risk of soft tissue and cardiac/vascular calcifications. The *K/DOQI Clinical Practice Guidelines for Bone Metabolism in Disease* recommend keeping serum calcium levels between 8.4 and 9.5 mg/dL. Calcium-containing medications may be used for calcium supplementation as well as phosphate binding if needed for patients post parathyroidectomy.

Vitamins and Iron

Patients on both PD and HD generally receive supplementation of folic acid (1 mg/day), pyridoxine (10 mg/day), the RDA for other B-complex vitamins, and ascorbic acid (60 to 100 mg/day) due to probable existing dietary deficiencies of these vitamins and losses occurring during dialysis. Previously, there had been speculation that even higher doses of folic acid may be beneficial for patients with CKD, as this vitamin can reduce serum homocysteine levels, which are two to three times normal in this population. It has now been shown, however, that reducing homocysteine levels with folic acid in patients with end-stage-renal disease (ESRD) is not associated with decreased rates of cardiovascular events.

As mentioned above and in the pre-dialysis phase of CKD, dialysis patients also may require supplements containing the active form of vitamin D, administered either orally or

parenterally. This therapy is highly individualized. Intermittent or daily doses of oral calcitriol, doxercalciferol, or paracalcitol are generally utilized for PD and HHD patients to suppress high levels of PTH. Intravenous doses are generally used for HD patients and administered during the treatment. These may be used in conjunction with the calcimimetic medication, cinacalcet, to suppress elevated PTH levels. Cinacalcet should be taken with the heaviest meal for optimized gastric absorption, in addition to reducing gastrointestinal upset. This medication also controls serum calcium, which helps keep these levels in the ranges now suggested. Intravenous calcitriol is not generally used for suppression of PTH for HD patients any longer due to causing hypercalcemia. It may be utilized for patients who have had parathyroidectomies, however, to maintain normal serum calcium levels.

Iron supplementation for patients receiving either PD or HD is usually necessary if they are receiving erythropoietin stimulating agents for anemia. Periodic weekly or monthly doses of intravenous preparations of iron gluconate or iron sucrose are often given to HD patients to maintain a serum transferrin saturation greater than 20 percent and ferritin greater than 200 ng/mL. Iron dextran is rarely used now due to potential adverse reactions being more likely than with the other iron preparations mentioned. Oral iron, because it is poorly

absorbed and not always tolerated, is frequently given only to those with intravenous iron allergies. PD and HHD patients often benefit from coming to the dialysis facility periodically for intravenous iron when iron stores are decreased. When transferrin saturation is greater than 50 percent and/or ferritin levels are greater than 800 ng/mL, iron therapy is discontinued until repeat levels are obtained. Updates to the *NKF K/DOQI Clinical Practice Guidelines for Anemia* state that there is not sufficient evidence to supplement iron when the ferritin is above 500 ng/mL.

Renal Transplantation

The goal of medical nutrition therapy for patients who have undergone renal transplant surgery is to provide optimal nutrition without exacerbating the metabolic side effects of immunosuppressive drugs and other medical therapy. During acute tubular necrosis (ATN) and/or organ rejection, nutrient modifications may be necessary to prevent hyperkalemia, and to control hypertension and circulating blood volume. To be active on a transplant list, many transplant programs require a body mass index of <35 to 40 kg/m^2 to prevent risks of delayed healing and kidney function after surgery.

Medical Nutrition Therapy for Renal Transplant

Protein

Protein catabolism may occur in the post-operative period secondary to the stress of surgery and increased catabolic effects of high doses of steroids and other immunosuppressive medications. The recommended protein intake for these patients is 1.3 to 2.0 g/kg per day in efforts to reach net nitrogen balance. This level may be difficult to attain initially after surgery, but is a realistic goal considering the patient may have already been protein depleted prior to this surgery. A long-term protein intake of approximately 0.8 to 1 g/kg per day is suggested with successful transplantation. It has also been suggested that regular exercise may also help overcome some of the muscle wasting due to the catabolism of steroids.

Energy

Adequate calories are necessary in the post-operative period in order to utilize the protein ingested to promote wound healing and to withstand rejection, infection, and other complications. The recommended caloric intake for these patients is 30 to 35 kcal/kg per day, based on dry weight or usual body weight (UBW). Because increased appetite is a common side effect of steroid therapy, the

long-range goal is weight maintenance with controlled caloric intake, once a reasonable weight is achieved. It has been shown that early intensive nutritional counseling and follow-up are successful in preventing unwanted weight gain in the first year post-transplant. Regular exercise should also be encouraged to aid in weight maintenance.

Carbohydrate

Hyperglycemia may also occur as a consequence of high-dose steroids and other immunosuppressive drugs such as cyclosporine and tacrolimus. The patient may then require a carbohydrate-controlled diet and, at times, oral hypoglycemic agents or insulin therapy is prescribed. Need for such medications may subside with time, but a calorie-controlled diet should still be encouraged to prevent unwanted weight gain.

Lipids

Dyslipidemia frequently occurs after renal transplantation primarily due to immunosuppressive therapy as well as obesity. Consequently, total dietary fat may need to be limited, with emphasis on decreasing saturated fat and substituting monounsaturated and polyunsaturated fats in the long-term, chronic post-transplant period. Pharmacologic therapy has also been shown to correct dyslipidemia in this population, but should be used cautiously

in conjunction with immunosuppressive medications.

Sodium, Fluid, and Potassium

If steroid therapy results in sodium and fluid retention, reduced sodium intake is encouraged. In the absence of edema and hypertension, a more liberal sodium intake is acceptable. Generally, fluid is not restricted unless acute tubular necrosis (ATN) or rejection of the transplanted kidney is present. A higher incidence of hyperkalemia with the use of cyclosporine may indicate periodic potassium restriction, even in patients with a good functioning kidney. Rejection or ATN may also require potassium restriction. On the other hand, there is up to a 30 percent incidence of gastrointestinal distress including diarrhea with mycophenolate mofetil, one common anti-rejection drug. Thus hypokalemia could also result with this drug and potassium wasting diuretics.

Calcium and Phosphate

Generally, neither dietary phosphate restriction nor phosphate-binding medication is needed when the transplanted kidney is functioning well. In fact, hypophosphatemia due to increased phosphate excretion and bone uptake sometimes develops in the acute post-transplant period and may require a high-phosphorus diet and/or phosphate

supplementation. Calcium supplementation may be required in the chronic post-transplant period because steroid therapy interferes with calcium absorption.

Vitamins and Iron

Renal vitamin preparations may be continued temporarily for the post-transplant patient, especially if dietary restrictions are needed to treat ATN or rejection. Iron therapy may also continue if erythropoietin stimulating agents are necessary to treat anemia.

Herbal and Dietary Supplement Use in CKD

In recent years, complimentary and alternative medicine (CAM) has become very popular in industrialized countries. Patients with CKD prior to initiating dialysis, while undergoing dialysis, or after renal transplantation must be very cautious when considering the use of herbal remedies and dietary supplements. These products are not FDA regulated despite the fact that some of them are already known to be unsafe because they are carcinogenic, hepatotoxic, or nephrotoxic. There have been reported laboratory analyses of products lacking their stated ingredients or being contaminated with pesticides, poisonous plants, heavy metals, or conventional drugs. Also, for patients with CKD, herbal supplements may be

especially dangerous due to the unpredictable pharmacokinetics of these products. There is potential for drug-supplement interactions, due to the large number of medications required for most dialysis and transplant patients. One example is St. John's Wort, which interferes with the bioavailability of cyclosporine and tacrolimus, and has been reported to cause organ transplant rejection. Also, some herbal preparations such as ginseng, ecninacea, astragalus, and noni juice are promoted as immune system enhancers and may decrease the effect of anti-rejection therapy after transplantation. Green tea, dong quai, milk thistle, and ginger may also affect the immune system, thus herbal supplementation is generally contraindicated after kidney transplantation.

Although fish oils may have many positive effects for patients with CKD, they must be used with caution for patients taking anticoagulant or anti-platelet medications, as they can increase the risk of bleeding. Some bulk-forming laxatives, such as flaxseed, require large amounts of fluid intake, and therefore should be used with caution for CKD patients requiring fluid limitation. Also, noni juice should also be avoided by CKD patients requiring a potassium-restricted diet due to its high potassium content.

It is therefore very important to ask about the use of herbs and dietary supplements when taking a medication and diet history from all patients, especially those with CKD. Clinicians who care for these patients should be aware of CAM therapies and treatments and appropriately advise patients.

Nephrotic Syndrome

Nephrotic syndrome, a kidney disorder with many etiologies, is characterized by large quantities of protein (>3.5 g/day) in the urine. In all cases, this proteinuria is a consequence of damage to the glomerular basement membrane of the kidney, resulting in its increased permeability to protein. Patients often exhibit poor appetite, muscle wasting, and malnutrition (primarily due to protein deficiency) secondary to these large protein losses. Nephrotic syndrome is also characterized by edema or even anasarca, when it is associated with a decrease in serum albumin, resulting in decreased plasma oncotic pressure. Dyslipidemia, with elevations either in serum cholesterol and/or triglycerides, also occurs in nephrotic syndrome and correlates with the degree of proteinuria.

Medical Nutrition Therapy for Nephrotic Syndrome

Medical nutrition therapy for patients with nephrotic syndrome should aim to reduce proteinuria, prevent negative nitrogen balance, control dyslipidemia, and minimize edema.

Protein

A high-protein diet may exacerbate albumin excretion through the damaged glomerular membrane. A moderate protein restriction is recommended early in the diagnosis of nephrotic syndrome to reduce the amino acid load to the glomerulus, subsequently diminishing the quantity of albumin crossing the damaged glomerular membrane. The current recommended protein intake for patients on a moderate restriction is 0.8 to 1.0 g/kg per day. This amount may need to be adjusted based on nutritional status, clinical condition, and degree of proteinuria. Vegetarian diets utilizing soy protein rather than meat-based protein may also be beneficial for patients with nephrotic syndrome.

Energy

Adequate calories from non-protein sources are needed to utilize protein and promote weight maintenance or weight gain in patients with nephrotic syndrome. Small frequent meals may

be better tolerated if ascites is present; caloric needs for weight maintenance are estimated to be 35 kcal/kg per day. Because these patients are often edematous, usual or estimated dry weight should be used for this calculation.

Lipids

Dyslipidemia due to reduced lipoprotein clearance from the blood by lipoprotein lipase and a proteinuria-induced alteration in the structure of lipoproteins is common in patients with nephrotic syndrome. Elevated very-low-density lipoprotein (VLDL), intermediate-density lipoprotein, LDL-C, total cholesterol, and triglyceride levels, along with normal or decreased HDL-C levels, may warrant a dietary fat restriction to less than 30 percent of total calories with an equal balance among saturated, monounsaturated, and polyunsaturated fats. Dietary cholesterol should be limited to less than 200 mg/day. Pharmacologic therapy may be necessary if the patient's diet has no effect and the nephrotic syndrome is prolonged.

Sodium and Fluid

Controlling edema through sodium restriction and appropriate use of diuretics is essential in the management of nephrotic syndrome. Because edema is commonly associated with nephrotic syndrome, restricting sodium intake to 2 g/day or less may be necessary. The exact

level of restriction must be individualized based on the degree of edema. Fluid restriction is not generally recommended unless the patient is hyponatremic.

Potassium

Abnormal potassium levels may occur in patients with nephrotic syndrome depending on the diuretic prescribed to control their edema or if ACE inhibitors are used to control proteinuria. Monitoring serum potassium levels is essential to determine whether alterations require a low or high potassium diet.

Calcium and Vitamin D

Hypocalcemia frequently occurs in individuals with nephrotic syndrome if they are hypoalbuminemic. Serum calcium measurements include both free calcium and calcium bound to serum albumin. When attempting to determine if a calcium deficiency is present, it is therefore essential to use the following equation to correct the patient's serum calcium level to reflect the degree of hypoalbuminemia:

$$[(\text{Normal albumin} - \text{serum albumin})(\text{correction factor}) + \text{serum calcium}]$$

$$\text{Correction factor} = 0.8$$

$$\text{Normal albumin} = 4.0 \text{ mg/dL}$$

A concurrent vitamin D deficiency may lead to inadequate calcium absorption from the gastrointestinal tract in a number of these patients. As a result, if the serum calcium level, corrected for the degree of hypoalbuminemia, still falls below normal levels, a calcium deficiency is likely. Vitamin D supplementation is also recommended for these individuals.

Nephrolithiasis

The goals of medical nutrition therapy for patients with nephrolithiasis (kidney stones) are to eliminate the diet-related risk factors for stone formation and prevent the growth of existing stones. The influence of fluid and specific nutrients such as calcium, oxalate, protein, refined carbohydrates, and sodium on the risk factors for calcium stone formation are discussed in the following section.

Medical Nutrition Therapy for Nephrolithiasis

A higher protein diet, obesity, diabetes, and metabolic syndrome, are associated with an increase in the formation of kidney stones in recent years. It is beyond the scope of this chapter to discuss medications utilized for specific stones; the focus is primarily on dietary modifications which may help limit the formation of stones.

Fluid

First and most importantly, a high fluid intake is the essential component of diet therapy for patients with nephrolithiasis. An increase in urine volume to 2 liters per day or more is needed to maintain a dilute urine and reduce the concentration of stone-forming substances. Producing this volume of urine requires a fluid intake of approximately 2.5 to 3.5 liters per day. Observational studies have suggested that coffee, tea, beer, and wine may reduce the risk of stone formation while grapefruit juice and apple juice may increase the risk. It is usually recommended, however, that most fluids be derived from water. In warmer weather, the fluid intake needs to be increased to 120 ounces per day (three 8 ounce glasses every 4 hours).

Calcium

Hypercalciuria (usually idiopathic) is one of the common urinary abnormalities seen in patients who form calcium stones. Although much attention is directed toward the effect of dietary calcium on urinary calcium excretion, in reality most cases of calcium urolithiasis are not attributed to high dietary calcium intake. In fact, a very low-calcium diet has been shown to increase the absorption and subsequent excretion of oxalate, which promotes formation of calcium oxalate stones in susceptible individuals. Large studies have also shown that

the risk of becoming a stone former is much lower when dietary calcium intake is greater than 1000 mg per day compared to those with dietary calcium intakes less than 600 mg per day. Adequate calcium intake will also prevent long-term negative calcium balance.

Oxalate

Changes in oxalate excretion are more important than calcium excretion in altering the probability of developing calcium oxalate stones. Oxalate has a greater relative effect than calcium on urine supersaturation of calcium oxalate. The role of dietary oxalate in the formation of calcium oxalate stones is not clear, and the proportion of urinary oxalate that comes from the diet is controversial (estimated to range from 10 to 50 percent, but usually closer to 10 percent) (Table 10-8). The remainder of urinary oxalate is a product of endogenous metabolism.

Table 10-8 Foods With High-Oxalate Content*

Source: The Oxalate Content of Food: http://www.ohf.org.

Apricots, dried	Kiwi
Barley, raw (½cup)	Leeks
Beans	Lentil and potato soup
Chili	Miso

Black beans	Nuts, nut butters
White beans	Okra
Great northern beans	Poppy seeds
Navy beans	Potatoes, fried
Pink beans	Raspberries (black)
Beets	Red currants
Bran cereals,	Rhubarb
shredded wheat, cream of wheat	Sesame seeds
Buckwheat flour	Soy products
Carob powder	Sweet potatoes
Chocolate/cocoa	Tumeric, ground
Cornmeal, yellow (½ cup)	Tomato,
Dark leafy greens	canned paste
Spinach	Wheat bran, crude (2T.)
Collards	
Swiss chard	
Mustard	
Figs	
Granola	
Grits (white corn)	

*The oxalate content of foods is variable depending on climate, soil, portion of the plant

analyzed, as well as method used for measurement. This list is based on the “Very High” and “High” lists compiled from the website given here. This list should only be used as a guide, as some of the “Medium” oxalate-containing foods not listed may become high-oxalate foods if eaten in significant amounts.

Gastrointestinal disorders that cause malabsorption are the most common cause of enteric hyperoxaluria. Oxalate absorption tends to be excessive when malabsorbed fat forms soaps and binds calcium in the gut. Free oxalate is then easily absorbed in the intraluminal intestine. Small increases in urinary oxalate concentration greatly increase the potential for crystal formation. Hyperoxaluria has now been seen in an increasing number of patients who have undergone Roux-en-Y bariatric surgery for obesity (Chapter 1: Case 2). Control of dietary oxalate therefore may benefit those susceptible to oxalate stones, because large fluctuations in urinary oxalate are attributable to variations in diet. Oxalate in the urine can be decreased by reducing oxalate in the diet while maintaining enough calcium to achieve a proper balance between these two elements. Vitamin C supplements should be discouraged since ascorbic acid breaks down to oxalic acid and is excreted in the kidney.

Protein

Most studies have shown that animal proteins cause an unfavorable effect on stone formation because they increase calcium, phosphate, and uric acid excretion, while reducing citrate and urine pH. The increase in urinary phosphate and uric acid is due to the high purine and phosphorus content of animal proteins. The increase in urinary calcium and decrease in citrate and urine pH are due to their high content in sulfurated amino acids. Limiting intake of foods such as meat, fish, poultry, and eggs, to achieve a total protein intake of 60 to 70 g/day, may be helpful for patients with nephrolithiasis.

Sodium

A high-sodium intake increases calcium excretion by expanding extracellular fluid volume, increasing the GFR, and decreasing renal tubular calcium reabsorption. These alterations result in an increased quantity of calcium-containing crystals in the urine. A moderate reduction of high-sodium foods is recommended (2 to 4 g/day).

Carbohydrate

Refined carbohydrates are also known to be calciuric, but those high in fiber are anticalciuric. Thus, a diet lower in simple sugars and products made from refined flour,

but higher in complex carbohydrates made from whole grains, as well as fresh fruits and vegetables, is recommended.

Case 1 Chronic Renal Failure Advancing to Dialysis

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Objectives

Given the medical history, physical examination, and laboratory data, identify factors affecting the nutritional status of a patient with chronic kidney disease (CKD stage 5) initiating hemodialysis.

Describe the appropriate medical nutrition therapy for a patient with CKD on hemodialysis changing to peritoneal dialysis.

CD is a 28-year-old administrative hospital worker who presented to the emergency room complaining of headaches and shortness of breath. She was admitted to the hospital for evaluation when she was found to have a blood

pressure of 170/110 mm Hg and mild congestive heart failure (CHF) by chest X-ray. CD reports that over the past year, her weight has increased about 10 pounds (4.5 kg), although her dietary intake has remained unchanged or even lower due to desire for weight loss.

Past Medical History

CD has had no recent viral illness, sore throat, or upper respiratory infections but did report frequent sore throats treated with antibiotics as a child. She has never had rheumatologic symptoms, and has no knowledge of a family history of renal disease. She is currently not taking any medications, vitamins, minerals, or herbal supplements and has no known drug or food allergies.

Social History

CD has her own apartment and lives alone. She occasionally drinks alcohol, but denies tobacco and intravenous or oral drug use.

CD's 24-Hour Dietary Recall

Breakfast (home)	
Tea	8 ounces (240 mL)
Orange juice	8 ounces
Non-dairy creamer	2 Tbsp.

Breakfast (home)	
Bagel	Frozen, store bought, eating ½
Cream cheese	1 Tbsp. on whole bagel, eating ½
Skim milk	8 ounces
Lunch (grocery store)	
Salad with scoop of tuna or chicken salad	1 cup, eating ⅓
Iced tea (unsweetend)	16 ounces (480 mL)
Orange or grapes	1 medium orange
Dinner (home)	
Chicken breast, broiled	3.5 ounces (eating maybe almost ¾)
Broccoli, spinach	1/2 cup each
Margarine	1 tsp total for 2 vegetables
Salt	1 tsp total for vegetables and chicken consumed
Diet cola soda	16 ounces (480 mL)
Snack (movies)	
Salted nuts	2 small 1 ounce bags
Diet cola soda	16 ounces (480 mL)

Total calories: 1122 kcal

Protein: 68 g

Fat: 72 g

Carbohydrate: 118 g

Potassium: 2974 mg

Sodium: 1650 mg

Calcium: 819 mg

Phosphorus: 1095 mg

Review of Systems

General: Fatigue, weakness, shortness of breath

GI: Anorexia

Physical Examination

Vital Signs

Temperature: 97 °F (36 °C)

Heart rate: 96 BPM

Respiration: 24 BPM

Blood pressure: 170/110 mm Hg

Height: 5′4″ (162 cm)

Current weight: 130 lb (59 kg)

Usual weight: 120 lb (54.5 kg) 6 months ago (Use for estimated “dry” weight)

Exam

General: Well-developed female

Lungs: Decreased breath sounds with faint crackles at the right base

Cardiac: Regular rate and rhythm, systolic murmur at the apex, S_3 gallop

Abdomen: Soft, non-tender, no hepatomegaly

Extremities: 2+ peripheral edema on both legs, ring tight on finger

Skin: Warm to touch

Neurologic: Intact, mild asterixis

Initial Laboratory Data

Patient's Values	Normal Values
Sodium: 132 mEq/L	133–143 mEq/L
Potassium: 6.4 mEq/L	3.5–5.3 mEq/L
Chloride: 111 mEq/L	98–108 mEq/L
CO_2: 15 mEq/L	24–32 mEq/L
Calcium: 7.5 mg/dL	9–11 mg/dL
Adjusted calcium: 8.1 mg/dL	9–11 mg/dL
Phosphorus: 7.2 mg/dL	2.5–4.6 mg/dL
BUN: 90 mg/dL	7–18 mg/dL

Patient's Values	Normal Values
Creatinine: 8.0 mg/dL	0.6–1.2 mg/dL
Albumin: 3.2 g/dL	3.5–5.8 g/dL
Hemoglobin: 7.3 g/dL	13.5–17.5 g/dL
Hematocrit: 21.9%	41–53%
Transferrin saturation: 18%	20–50%
Ferritin: 142 ng/mL	20–300 ng/mL
Mean corpuscular volume: 70 fL	80–100 fL
White blood cells	
(WBC): 5.7×10^9/L	$4.5–11 \times 10^9$/L
Urinalysis: 3+ heme by dipstick, 1+ protein by dipstick	
Sediment: 15–20 red blood cells (RBC)/HPF, 3–5 WBC/HPF, 2–4 red blood cell casts and broad waxy casts/HPF	
Electrocardiogram: Normal sinus rhythm at 100, no ischemic changes	
Chest X-ray: Cardiomegaly, CHF	

Go to Questions 1–7

Dialysis Treatment Plans

CD received a temporary dialysis catheter and underwent two hemodialysis treatments in the hospital. During her hospitalization she was

educated on all dialysis modalities available and chose peritoneal dialysis (PD). She was discharged from the hospital with plans for a peritoneal dialysis catheter to be inserted the following week. She was educated on a "renal" diet by the hospital dietitian and medications were prescribed as well. She was to dialyze in the in-center dialysis facility close to the hospital.

Laboratory Data #2 (after 1 Week on HD)

Patient's Values	Normal Values
Sodium: 136 mEq/L	133–143 mEq/L
Potassium: 4.9 mEq/L	3.5–5.3 mEq/L
Chloride: 102 mEq/L	98–108 mEq/L
CO_2: 18 mEq/L	24–32 mEq/L
Calcium: 8.8 mg/dL	9–11 mg/dL (8.4–9.5)*
Corrected calcium: 9.4 mg/dL	9–11 mg/dL (8.4–9.5)*
Phosphorus: 6.0 mg/dL	2.5–4.6 mg/dL (3.5–5.5)*
BUN: 70 mg/dL	7–18 mg/dL
Creatinine: 6.2 mg/dL	0.6–1.2 mg/dL
Albumin: 3.3 g/dL	3.5–5.8 g/dL
Hemoglobin: 9.8 g/dL	13.5–17.5 g/dL (11–12 g/mL)*

Patient's Values	Normal Values
Hematocrit: 27%	41–53% (33–36%)*

*These are guidelines established for patients with chronic kidney disease (CKD) by the National Kidney Foundation Kidney Disease Outcomes Quality Initiatives (NKF K/DOQI) committees, but not currently utilized due to CMS requirements for lower doses of EPO.

Go to Questions 8 and 9

Follow-Up

CD did well on in-center HD for the first few weeks, until she began missing treatments due to work schedules and social activities and she cancelled her PD catheter insertion. She was subsequently readmitted to the hospital for nausea, vomiting, hyperkalemia, and congestive heart failure due to fluid overload. She admitted that she was not attending in-center HD as prescribed. CD was aggressively dialyzed during the hospitalization to remove fluid more rapidly with daily HD.

Laboratory Data #3 (Upon Admission to the Hospital after Non-Adherence to HD Schedule)

Patient Values	Normal Values
Sodium: 134 mEq/L	133–145 mEq/L

Patient Values	Normal Values
Potassium: 6.0 mEq/L	3.5–5.3 mEq/L
Chloride: 106 mEq/L	98–108 mEq/L
CO_2: 18 mEq/L	24–32 mEq/L
Calcium: 8.2 mg/dL	9–11 mg/dL (8.4–9.5 mg/dL)*
Phosphorus: 8.4 mg/dL	2.5–4.6 mg/dL (3.5–5.5 mg/dL)*
Albumin: 3.5 g/dL	3.5–5.8 g/dL (≥4.0 g/dL)*
Hemoglobin: 9.3 g/dL	13.5–17.5 g/L (11–12 g/dL)*
Hematocrit: 28%	41–53% (33–36%)*
Transferrin saturation: 23%	>20–50%*
Ferritin: 185 ng/dL	>200 ng/dL*

Go to Question 10

Case Questions

Based on CD's history, physical examination, and laboratory data, what is the most likely diagnosis?

What additional laboratory tests or studies help confirm this diagnosis?

What medications are indicated to manage her clinical condition at this time?

Based on CD's physical examination, should her current body weight be used to estimate her caloric and protein needs?

How can CD's caloric and protein requirements be estimated?

What dietary recommendations are indicated for her when undergoing hemodialysis based on her initial laboratory data values and what fluid and electrolyte management does CD require?

Using CD's lab values to estimate renal function and her vital signs and chest X-ray results to determine her hemodynamic status, what are the immediate and long-term treatment modalities you would recommend?

What modifications in phosphate-binding medication should be made once CD's phosphate level improves?

When CD's dialysis modality is hemodialysis, what dietary modifications are appropriate based on weight and laboratory data?

What dietary modifications are indicated once CD begins receiving CAPD?

Answers to Questions: Case 1

Part 1: Diagnosis and Medications

1. Based on CD's history, physical examination, and laboratory data, what is the most likely diagnosis?

CD has a history of recurrent streptococcal infections in childhood, which most likely increased her risk of developing acute post-streptococcal glomerulonephritis. Approximately 5 to 10 percent of patients with a history of streptococcal infections and acute glomerulonephritis (AGN) develop chronic glomerulonephritis (CGN) 15 to 20 years following the acute infections. CGN results in a markedly decreased GFR, which prevents sodium and water excretion and causes increased sodium and water retention. The result is volume-induced high blood pressure, and with significant sodium and water retention, eventually CHF. This renal disease is irreversible and not amenable to treatment with any form of drug therapy. It seems likely then that CGN is the diagnosis for this patient, and that she will require dialysis therapy.

2. What additional laboratory tests or studies help confirm this diagnosis?

Urinalysis Positive for blood and protein by dipstick which indicates renal glomerular damage. Red blood cell casts are highly

suggestive of glomerulonephritis and broad waxy casts suggest dilated renal tubules associated with CGN.

24-hour urine collection This procedure reveals the quantity of protein and creatinine excreted over 24 hours. If the amount of urinary creatinine can be measured in a 24-hour urine specimen, a creatinine clearance can be calculated.

Protein excretion 2.2 g/24 hours, normal value 0.1–0.2 g/24 hours.

Creatinine excretion 900 mg/24 hours, normal value 1.0–1.6 g/24 hours.

Creatinine clearance Estimation of creatinine clearance can be calculated using the Cockroff–Gault formula. This may be necessary if urine values are incomplete or not available. The calculation gives an adequate estimation of creatinine clearance as long as the serum creatinine value is stable over time.

Men: (140 − age)(weight in kg)/(72)(serum creatinine in mg/dL) = c.c.

Women: (140 − age)(weight in kg)/[(72)(serum creatinine in mg/dL)] × 0.85 = c.c.

CD's estimated creatinine clearance = (140 − 28)(54.5 kg)/(72)(7.0 mg/dL)
= 6104/504
= 12.1 mL/min(0.85) = 10.3

(normal creatinine clearance for a female = 87–107 mL/min)

Renal ultrasound Renal ultrasound reveals small kidneys bilaterally, which indicates irreversible renal disease (9 and 10 cm, right and left, respectively). Only a renal biopsy could actually confirm the diagnosis of CGN, but it is not done once small kidneys are identified since no treatment can reverse kidney damage. CD's significantly increased serum phosphate and decreased serum calcium levels suggest that the GFR is less than 30 mL/min, indicating significant renal dysfunction. Tests to eliminate other possible causes of CGN include.

Compliment levels CH_5O, C_3, and C_4 within normal limits, which makes the diagnosis of membranoproliferative disease, subacute bacterial endocarditis, and acute post-streptococcal glomerulonephritis highly unlikely.

24-hour protein collection Eliminates the diagnosis of nephrotic syndrome. CD's history and physical examination eliminate other causes of CGN such as Alport's syndrome.

3. What medications are indicated to manage her clinical condition at this time?

CD should be discharged on the following medications:

Diuretic (generally a loop diuretic) To control sodium and water balance (as long as she has urine output).

Phosphate binder Consider the use of a phosphate-binding polymer without calcium and aluminum, since CD's serum phosphorus level is significantly elevated.

Antihypertensive medication Use as necessary to achieve blood pressure less than 140/90 mm Hg. Her antihypertensive medication dosage will decrease as excess sodium and water are removed.

Renal multivitamin A supplement to correct dietary deficiencies seen in patients with CKD; only contains B vitamins and vitamin C, which are water soluble and believed to be removed during the dialysis process.

Epoetin alfa Use for anemia.

Iron sucrose Use IV to give during hemodialysis to boost transferrin saturation and support epoetin alfa in red blood cell production.

Part 2: Nutrition Assessment

4. Based on CD's physical examination, should her current body weight be used to estimate his caloric and protein needs?

This patient's total body water is elevated, as evidenced by 3+ peripheral edema of her legs and CHF; her current weight therefore does not reflect her “dry” weight. To estimate “dry”

weight, first ascertain the patient's usual weight. CD's usual body weight 6 months ago was 120 pounds (54.5 kg), and this is the value that should be used to estimate her protein and caloric requirements.

5. How can CD's caloric and protein requirements be estimated?

The normal estimated total daily caloric requirement is 35 kcal/kg. In CD's case, this amounts to (35 kcal)(54.5 kg) = 1900 kcal/day.

Daily protein recommendations for CKD stage 5 with hemodialysis are 1.2 g/kg per day. If significant proteinuria is present, the urinary protein losses may be added to the daily protein allowance. CD's 24-hour urine collection indicated a protein loss of 2.2 g, thus this was not factored into her protein requirements. Her daily protein intake therefore could be estimated as:

$$(1.2\ \text{g})(54.5\ \text{kg}) = 65.4\ \text{g/day}$$

Part 3: Medical Nutrition Therapy

6. What dietary recommendations are indicated for hemodialysis based on her initial laboratory data and what fluid and electrolyte management does CD require?

Protein CD's current meal plan, before any treatment intervention, contained 1122 calories

and 68 g of protein. To maintain a protein requirement of approximately 65 g/day while observing fluid and electrolyte restrictions, the following modifications are recommended:

Limit milk in coffee to 1 to 2 ounces (30 to 60 mL) per cup.

Substitute a plain hamburger on a bun, or an equivalent, such as 3 ounces of fresh roast beef, turkey, chicken, or rinsed water-packed tuna on two slices bread for a cheeseburger at lunchtime.

Encourage the amount of chicken at dinner to be 4 ounces (a large-sized chicken breast).

Omit all cheese and nuts because they are generally high in phosphorus and/or potassium and sodium, and substitute unsalted pretzels with one tablespoon of regular mustard as a night snack.

Electrolytes CD's total body water and sodium are elevated, as evidenced by 3+ peripheral edema and mild CHF on her chest X-ray. Therefore, a low-sodium diet (2.5 g/day) is indicated at this time. CD's potassium level is within the normal range; thus, no potassium restriction is needed at this time.

Her initial serum calcium and phosphorus levels of 7.5 and 10.2 mg/dL, respectively, are a result of decreased GI calcium absorption and increased phosphate retention. Lowering serum phosphorus levels by dietary restriction and

phosphate-binding medication will improve serum calcium initially without calcium supplementation between meals.

Restricting the daily allowance of dietary phosphorus to approximately 1000 mg is indicated. A phosphate-binding polymer was added in small doses in combination with calcium acetate to CD's medication regimen. The goal was to reduce serum phosphorus levels to less than or equal to 5.5 mg/dL and to normalize serum calcium levels.

Fluid Given that CD's 24-hour urine output was 700 mL in the hospital, a total fluid intake of 1200 mL/day or 40 ounces (700 mL plus 500 mL for insensible fluid losses) should be recommended. To stay within the fluid restriction of 1200 mL/day, limit morning coffee to 8 ounces (240 mL), the lunch beverage to 12 ounces (360 mL), the dinner beverage to 8 ounces (240 mL), and the snack beverage to 8 ounces (240 mL). Allowing for an additional 4 ounces (120 mL) of juice or water with medications is acceptable.

7. Using CD's lab values to estimate renal function and her vital signs and chest X-ray results to determine her hemodynamic status, what are the immediate and long-term treatment modalities you would recommend?

From these data, CD has a creatinine of 8.0 mg/dL, blood pressure of 200/120 mm Hg, and CHF. Therefore, CD underwent two acute hemodialysis treatments, which effectively removed sodium and water as well as the buildup of uremic products secondary to CGN. She chose PD instead of hemodialysis for her long-term treatment. PD will allow her to perform dialysis exchanges herself in her apartment and have more freedom so she can work during the day. A catheter (used to instill PD solution into the peritoneal cavity) was scheduled to be placed after she was discharged from the hospital. PD is usually started 2 weeks after a PD catheter is inserted to allow for adequate wound healing. She will initially do continuous ambulatory peritoneal dialysis (CAPD) training, as this modality requires less training time than PD done overnight by the automated cycler machine. This way she can get back to her job sooner, but will have to do at least one exchange at work. She will then plan to train for continuous cycling peritoneal dialysis (CCPD) when she can take a vacation.

Go to Dialysis Treatment Plans on Page 429

8. What modifications in phosphate-binding medication should be made once CD's phosphate level improves?

At this time, since CD's corrected calcium level is reasonable, no change would be made in phosphate-binding medications unless the sevelamer hydrochloride was not tolerated. Although this medication is expensive, the dietitian and social worker can work with the manufacturer of this medication or with the patient's insurance to make it feasible to obtain.

9. When CD's dialysis modality is hemodialysis, what dietary modifications are appropriate based on weight and laboratory data?

Pre-dialysis weight 58.2 kg (128 lb)

Estimated dry weight 54.5 kg (120 lb)

CD has the potential to gain fluid weight between hemodialysis treatments, because she receives them only three times per week (her predialysis weight is 3.5 kg greater than her dry weight). In addition, CD's urine output is diminished further because of her renal dysfunction. Thus, her fluid intake should be decreased to 1 liter per day, and she should be encouraged to maintain a sodium restriction of 2500 mg/day. The recommended daily protein allowance is now 1.2 g/kg for a total of 65 g. Because hemodialysis is intermittent, and CD reports that her urine output is minimal, she should be advised to limit her potassium intake to approximately 60 mEq/day. CD can accomplish this goal by eliminating fruits and

vegetables high in potassium such as bananas, orange juice, potatoes, and dark-green, leafy vegetables. Phosphorus restrictions for HD are similar to those for PD because no significant change is recommended in the protein content of CD's diet. However, because her phosphorus level is now rising again, CD is advised to avoid dairy products completely except for 4 ounces (120 mL) of milk per day.

Go to Follow-Up on Page 429 and 430

10. What dietary modifications are indicated once CD begins receiving CAPD?

The protein allowance should increase because CD's laboratory values at the start of CAPD exhibit a mildly depleted albumin level at 3.3 g/dL (normal 3.5 to 5.8 g/dL; most dialysis facility goals are ≥4.0 g/dL), and CAPD will remove significant amounts of protein. A protein intake of 1.3 g/kg per day (based on usual body weight (UBW) or “dry” weight) is 70 g/day. To reach that goal, the meat, fish, or poultry portions at lunch and dinner need to be increased to 4 ounces (113 g), and CD should be encouraged to eat a sandwich with at least 2 ounces (57 g) of meat as her nightly snack.

CD remains at least 8 pounds (3.5 kg) over her previous usual body weight of 120 pounds 54.5 kg). Current weight is 128 (58.2 kg): (132 pounds (60 kg) minus the 4 pounds (1.8 kg) of

PD fluid indwelling), she remains at least 8 pounds (3.6 kg) over her previous usual body weight of 120 pounds (54.5 kg). The same sodium (2.5 g/day) and fluid restrictions (1200 mL/day) are indicated until a regular schedule of PD exchanges can be performed. A potassium restriction is still necessary until CD is receiving a regular PD regimen with continuous removal of potassium with daily PD.

Phosphorus should still be restricted to maintain phosphate levels between 3.0 and 5.5 mg/dL, but the restriction can be liberalized somewhat to allow a greater protein intake (animal protein sources are the foods highest in phosphate). By continuing to limit milk to no more than 4 ounces per day, and limiting cheese to two times per week and eliminating cola and other sodas and beverages containing phosphoric acid, CD can achieve the new daily phosphorus allowance of 1000 to 1200 mg/day. An extra one or two Sevelamer HCL tablets may be prescribed with the night sandwich as well.

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Part IV
Fundamentals of Oncology and Nutrition Support

11
Cancer Prevention and Treatment

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Objectives

Discuss the role of dietary and lifestyle factors in the prevention of cancer.

Evaluate the impact of cancer on nutritional status of individuals with cancer.

Examine the nutrition-related side effects of cancer therapy.

Identify the role and benefits of medical nutrition therapy in the treatment of cancer.

Source: Objectives for chapter and cases adapted from the *NIH Nutrition Curriculum Guide for Training Physicians*. (www.nhlbi.nih.gov/funding/training/naa)

Introduction

Every year ten million people around the world develop cancer, and seven million die as result of the disease (12 percent of the nearly 56 million deaths from all causes worldwide). This year, cancer will impact one out of every three people before the age of 75. In North America alone, 600,000 people will die from cancer.

It is estimated that 50 percent of cancer incidence and 30 to 35 percent of cancer mortality in Americans is related to poor diet and excessive alcohol use. While genetics certainly play a role in predisposing one to cancer, lifestyle factors may have a significant influence on cancer risk as well.

Obesity and Cancer

Obesity is strongly associated with increased risk of many cancers including:

breast (among postmenopausal women)

colon

endometrium

esophagus

gallbladder

pancreas

kidney

Obesity is also a risk factor for cancer recurrence. The idea that excess weight may be linked to cancer risk is supported by evidence that calorie restriction protects against various types of tumors. The American Institute for Cancer Research (AICR) has published a report "Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective." The AICR reviewed over 7000 research studies, and conclusively established the link between obesity and cancer.

Several mechanisms have been proposed to explain how obesity affects cancer, but one important factor is the excess adipose tissue that causes alterations in hormone metabolism. One hypothesis is that high levels of insulin and insulin-related growth factors in obese people may promote tumor development. Insulin and insulin-like growth factor-1 (IGF1) stimulate cell proliferation, inhibit apoptosis, and promote angiogenesis. These cellular mechanisms potentially lead to uncontrolled cell growth and ultimately cancer.

Breast Cancer

Breast cancer is the most common cancer in women both in developed and developing countries, comprising 16 percent of all female cancers. Since 1970, scientists have suggested that there may be a link between excess body weight and breast cancer. According to the National Cancer Institute (NCI), weight gain during adulthood is the most consistent and strongest predictor of breast cancer risk. Now, newer studies show that this link depends on the menopausal stage of the woman. There is a strong relationship between obesity and increased breast cancer risk in postmenopausal women, but not in pre-menopausal women. Interestingly, research shows that among pre-menopausal women, a high BMI actually reduces the risk of breast cancer. However, postmenopausal women who gain a considerable amount of excess weight dramatically increase their risk of breast cancer. Cohort studies have shown that postmenopausal women whose BMI is in the top quartile increase their breast cancer risk by about 40 percent. Additionally, in the Women's Health Study (1999–2004), women with a BMI greater than 40 kg/m^2 had a 60 percent higher risk of dying from cancers of all causes than women with a normal BMI. This increased risk is not impacted by lifestyle factors or physical activity. Researchers hypothesize that breast cancer risk after menopause may be mediated

by the increase in endogenous estrogen production from excess adipose tissue.

Endometrial Cancer

A positive linear relationship exists between excess weight gain and risk for endometrial cancer, irrespective of menopausal status. Some studies suggest a linear increase risk of 200 to 400 percent for women with a BMI over 25 kg/m^2. Regardless of menopausal status, obese women are two to four times more likely to develop a uterine cancer than normal weight women.

Colon Cancer

Colon cancer also occurs more frequently in those who are obese compared to those who are of normal weight. Men with high BMI levels consistently show an increase risk of colon cancer; however, the evidence for women is not quite as strong. Weight gain in certain parts of the body may influence this risk. Specifically, abdominal fat seems to plays a role in the risk of colon cancer. Overweight men tend to collect fat in their abdomen, while in some women, fat is more likely to be distributed in the hips, thighs, and buttocks. Thus, it will be important for researchers to define the relationship between colon cancer and waist-to-hip ratio or waist circumference.

Nutrition and Cancer Prevention

Meat and Protein

It is difficult to isolate effects of protein alone, since increased protein diets are often high in fat and low in fiber. However, it is clear that increased meat intake is associated with increased risk of colon cancer and advanced prostate cancer. Specifically, according to the AICR, there is significant evidence that red meat intake from beef, pork, lamb, and processed meats such as bacon, sausage, hot dogs, salami, ham, sandwich meat, and pepperoni significantly increase the risk of colorectal cancer. Researchers recommend eating a maximum of 18 ounces of cooked red meat per week and avoiding processed meat completely. In fact, for every additional ounce of processed meat consumed per day, the risk of colorectal cancer increases dramatically. Processed meats have also been linked to a higher incidence of stomach cancer.

Swedish researchers found a statistically significant increased incidence of stomach cancer in those who consumed high amounts of processed meat in a cohort study of over 60,000 women. They hypothesized that this increase risk may be due to the nitrates and nitrosamines found in these processed meats. Nitrites and nitrates react with amino acids to form cancer-causing nitrosamines. These

compounds are used to provide a pink hue to cured meat without which the meat would turn brown during storage. Vegetables and fruit slow the conversion of nitrites to nitrosamines.

Other concerns with meat consumption involve cooking methods that use high temperatures such as frying, broiling, or barbequing. When meats such as beef, pork, poultry, and fish cook at high temperatures, the amino acids and creatine may form carcinogenic compounds called heterocyclic amines (HCAs). Researchers at the NCI have found 17 different HCAs formed from cooked meats that potentially cause cancer. A recent case-control study from the NCI found that people who regularly consumed beef medium-well or well-done increased their risk of stomach cancer by more than three times in comparison to those who consumed rare or medium-rare beef. Other NCI studies have shown that a high intake of well-done, fried, or barbecued meats is associated with an increased risk of developing colorectal, pancreatic, and breast cancer.

Carbohydrates, Fiber, and Whole Grains

The protective effects of eating whole grains to prevent cancer are not clearly established. However, many case-controlled studies have shown an association between high intakes of whole grains and low incidence of several types of cancer. A meta-analysis of 40 case-control studies that looked at 20 different types of

cancer found that those with high whole grain intake had a 34 percent lower overall cancer risk than those with low whole grain intake. While a decreased risk of gastrointestinal tract cancers is most commonly associated with whole grain intake, the lignans in whole grains (phytoestrogens) may affect hormone dependent cancers as well.

Fiber is known to provide many health benefits such as reduced risk of heart disease and diabetes and prevention of constipation. Studies continue to confirm the link between eating fiber and a reduction in breast cancer risk. A recent study found that diets rich in dietary fiber and, particularly, fiber from vegetables was associated with reductions in breast cancer risk, independent of menopausal status.

Both soluble and insoluble fiber reduce the risk of breast cancer, especially for women consuming upwards of 30 g/day. Evidence from several studies suggests that women who consumed 30 g of fiber per day had a significant risk reduction (32 percent) of breast cancer. Compare that to the women who were eating less than 25 grams a day, who only had a very minimal risk reduction (2 percent). It is thought that insoluble fiber assists with the excretion of excess free estrogens in the gut. This ensures that less estrogen is free and absorbed, and

consequently, the lower exposure to the hormone, the lower the risk of breast cancer.

Additionally, The European Prospective Investigation into Cancer and Nutrition (EPIC) project first demonstrated years ago that a high fiber diet was associated with a decreased risk of colon cancer. In 2012, they did a retrospective cohort study and found that total dietary fiber was inversely associated with colorectal cancer.

Fats

While total fat intake does not seem to alter cancer risk, diets high in animal fats are positively associated with colorectal and prostate cancer. Recently, omega-3 fatty acids from fish oils have received a lot of attention for their heart health and anti-inflammatory benefits. Omega-3 fatty acids, DHA and EPA, are converted into anti-inflammatory prostaglandins, which researchers believe may reduce tumor growth. Omega-3 fatty acids may be beneficial, omega-6 fatty acids may actually be harmful and promote prostate cancer. Omega-6 fatty acids cause the production of a family of eicosanoids including prostaglandins, which affect immunity and promote inflammation. The health impact of these various fatty acids is related to the ratio of omega-6: omega-3 fatty acids consumed. In the United States, 60 years ago, people consumed a dietary ratio of omega-6 to omega-3 that was

about 2 : 1. Today, the ratio is roughly 25 : 1. Over these 60 years, the incidence of prostate cancer in the United States has grown steadily. Scientists have demonstrated in cell culture that omega-6 fatty acids cause increased production of cytosolic phospholipase A2 (cPLA2), which causes the production of the enzyme Cyclooxygenase-2 (COX2). COX2 stimulates the release of prostaglandin E2 (PGE2) and promotes cell growth, a process that may ultimately lead to cancer.

Cancer Risk and Fat

High intake of total and saturated fat is associated with increased risk of breast, colon, lung, and prostate cancers.

High fat diets are associated with obesity, which is linked with cancer of the colon, rectum, esophagus, gall bladder, breast, endometrium, pancreas, and kidney.

Animal fat (from meat and dairy) was associated with increased risk of breast cancer in the Nurses Health study and others.

Higher omega-3 vs. omega-6 may reduce risk of breast cancer.

Low fat diet (<20 percent fat) may reduce risk of recurrence of breast cancer.

Phytochemicals

Phytochemicals are compounds found in plants that have the ability to protect the plant against disease and bacterial or fugal infections. Research shows that these compounds may play an important role in preventing tumor growth in humans. Over 4000 different types of plant phytochemicals have been identified. Two main classes of phytochemicals include, carotenoids and flavonoids, as shown in Table 11-1, but there are several other families of phytochemicals including other polyphenols, sulfur compounds, and saponins.

Table 11-1 Food Sources of Common Phytochemicals

Source: Darwin Deen, MD and Lisa Hark, PhD, RD, 2014. Used with permission.

Family	Examples	Foods
Carotenoids	Beta-carotene	Leafy green and yellow vegetables (broccoli, sweet potato, pumpkin, carrots)
	Lycopene	Tomatoes and tomato products, guava, pink grapefruit, watermelon
	Lutein	Spinach, kale, cabbage, Swiss chard, broccoli, Brussels sprouts, turnips, and collard greens
	Zeaxanthin	Carrots, peaches, green oranges, mango, corn, eggs, citrus fruits
	Beta-cryptoxanthin	Citrus, peaches, apricots peaches, apricots

Family	Examples	Foods
Flavonoids	Resveratrol	Red grapes, red wine
	Anthocyanidins	Blueberries, raspberries, Acai, eggplant, red grapes, blackcurrant
	Quercetins	Kale, apples
	Isoflavones	Soybeans, tofu, soymilk, soy products
	Catechin	Tea, wine
Sulfur compounds	Sulphoraphane	Broccoli
	Indoles	Cruciferous vegetables
	Ellagic acid	Strawberries, blueberries, raspberries
	Alliins (sulfur compounds)	Onions, garlic, scallions, leeks, chives
	Glucosinolates	Cruciferous vegetables-cabbage, broccoli, cauliflower

Flavonoids are found in grapes, apples, berries, green tea, and red wine, along with many other

foods. The chemical structure of these polyphenols makes them ideal for absorbing free radicals, and as effective antioxidants. Free radicals are unstable molecules produced by the cell that ultimately lead to cell damage and may cause cancer. Antioxidants interact with and stabilize free radicals and thus prevent them from causing harm to cells.

Berries

Blackberries, raspberries, strawberries, blueberries, cranberries, lingonberries, and deerberries (either winter green berry or partridge berry) all have a high content of flavonoids that absorb free radicals. Berries contain a unique phytochemical compound known as ellagic acid that may have the capacity to interfere with tumor genesis. Ellagic acid is a polyphenol antioxidant found in high concentrations in raspberries, pomegranates, and strawberries. In a recent study from the Hollings Cancer Institute, researchers demonstrated that ellagic acid can stop cancer cells from dividing for 48 hours. Ellagic acid can also cause apoptosis (cell death) within 72 hours in cultures of breast, pancreas, esophageal, skin, colon, and prostate cancer cell lines. Additionally, ellagic acid prevents the oxidation of the p53 gene that may lead to cancer. It is important to note that most studies investigating the properties of ellagic acid have been conducted in cell cultures and laboratory

animals. While human research with ellagic remains preliminary, there are several theories about the mechanism of action of this phytochemical. Ellagic acid may work by preventing the activation of carcinogenic substances in the body. Ellagic acid may also be a powerful inhibitor of tumor angiogenesis.

Raspberries and blueberries contain another class of polyphenol compounds called anthocyanidins, which are responsible for the blue and red colors of berries. Anthocyanidins are among the most potent antioxidants ever discovered. In isolated laboratory cancer cells, anthocyanidins stopped cells from synthesizing DNA and caused apoptosis. Anthocyanidins may also inhibit tumor angiogenesis. Other laboratory studies have shown that these phytochemicals inhibit the growth of lung, colon, and leukemia cancer cells while sparing healthy cells. This evidence puts berries at the top of the list of potential cancer-fighting foods (Table 11-2).

Table 11-2 Sources of Phytochemicals by Color

Color	Phytochemcial	Vegetables and Fruit
Red	Lycopene	Tomatoes, ketchup, watermelon, pink grapefruit

Color	Phytochemcial	Vegetables and Fruit
Red/ Purple	Anthocyanins, Ellagic acid (polyphenols)	Berries, grapes, red wine
Orange	α and β-cartotene	Carrots, sweet potatoes, cantaloupe, squash, apricots, pumpkin, mango
Orange/ Yellow	β-cryptoxanthin, flavinoids	Cantaloupe, peaches, oranges, papaya, nectarines
Yellow/ Green	Lutein, zeaxanthin	Spinach, avocado, honeydew, collard greens
Green	Sulforaphanes, indoles	Cabbage, broccoli, Brussels sprouts
White/ Green	Allyl sulphides	Onion, garlic, leeks, chives

Fruits and Vegetables

Vegetables Both the ACS and AICR recommend maintaining a diet rich in fruits and vegetables to reduce the risk of cancer. In particular, several cohort case studies suggest that fruits and vegetables may protect against cancers of the oropharynx, esophagus, stomach, colon, rectum, and lung. However, overall, the

results of studies linking cancer prevention to fruit and vegetable consumption have been inconclusive and inconsistent. Specifically, prospective cohort studies show a weak link between cancer risk reduction and fruit and vegetable intake. Despite weak data from prospective cohort studies concerning overall vegetable intake, there is significant evidence that high intakes of specific types of vegetables, such as cruciferous vegetables may reduce cancer risk. Cruciferous vegetables include cabbage, broccoli, Brussels sprouts, cauliflower, collard greens, kale, mustard, rutabaga, turnips, bok choy, Chinese cabbage, arugula, radishes, and several others. Such vegetables contain high concentrations of a group of sulfur compounds called glucosinolates. The breakdown of glucosinolates results in the release of indoles and isothiocyanates. This hydrolysis may be accomplished when these vegetables are chopped or chewed and come in contact with a plant enzyme called myrosinase. Indoles and isothiocynates may help prevent cancer by eliminating carcinogens, altering cell signaling pathways, or changing the metabolism and activity of certain hormones. For example, one study showed that consumption of 250 g/day of broccoli and 250 g/day of Brussels sprouts caused an increase in the urinary excretion of a possible carcinogen found in well-done meat. This suggests that such high intakes of cruciferous vegetable may decrease cancer risk by helping to eliminate

certain carcinogens found in food. Some studies have shown that cruciferous vegetables may also help prevent breast and prostate cancer, but currently the data remain inconsistent and indefinite.

Two other molecules have received attention for their potential cancer fighting properties: sulforaphane and indole-3-carbinol (I3C). Studies show that sulforaphane, an isothiocynate found in high concentrations in broccoli, has the ability to both cause excretion of toxic, cancer-causing substances from the body and cause cell death in tumor cells. Indole-3-carbinol is produced by the hydrolysis of glucosinolates but contains no sulfur atoms. Recent research has focused on I3C's ability to influence estrogen metabolism. I3C may play an important role in cancers that are dependent on estrogen such as breast, cervical, and uterine cancers. Several factors must be considered to maximize the indole and isothiocyanate content in these vegetables. Glucosinolates are extremely water-soluble and boiling cruciferous vegetables in water for more than 10 minutes may reduce the amount of glucosinolates by half. Steaming or stir-frying is a more effective way to maximize the amount of cancer-fighting compounds present in these vegetables. While NCI recommends consuming 5 to 9 servings of fruits and vegetables, there is currently no specific recommendation on cruciferous vegetable consumption.

Tomatoes Tomatoes have a high concentration of the carotenoid lycopene. Carotenoids are the molecules in fruits and vegetables that are responsible for their vibrant colors such as red, oranges, and yellows. Some carotenoids, such as beta-carotene, are precursors to vitamin A. Lycopene is not related to vitamin A, but it may be the carotenoid with the greatest cancer fighting potential. The association between lycopene and prostate cancer came from observations that countries where there is high tomato consumption such as Italy, Spain, and Mexico have much lower rates of prostate cancer compared to the United States or England. Several studies have shown that individuals who consume large amounts of tomatoes and tomato products have a reduced risk of developing prostate cancer. However, different tomato products contain variable concentrations of lycopene. For example, while tomato paste may contain 29.3 mg per 100 grams, canned tomatoes may contain only 9.7 mg per 100 grams. This variability makes it difficult to come to any definitive conclusions linking tomato products and prostate cancer prevention, but absorption is enhanced when eaten with fat.

Not all carotenoids demonstrate promising anticancer effects. Beta-carotene is a carotenoid found in many foods that are orange in color, including sweet potatoes, carrots, cantaloupe, squash, apricots, pumpkin, and mangos. In

1994, a cancer prevention study known as the Alpha-Tocopherol (Vitamin E)/Beta-Carotene Cancer Prevention Study (ATBC) found that lung cancer rates of male smokers actually increased with beta-carotene supplementation. A meta-analysis of randomized controlled trials, published in 2009, looked at the effect of beta-carotene supplementation on cancer incidence and showed that, specifically, the incidence of lung and stomach cancers were significantly increased in individuals who used beta-carotene supplements at 20 to 30 mg/day, in smokers and asbestos workers compared to the placebo group.

Overall, beta-carotene supplementation has not been shown to have any beneficial effect on cancer prevention and such supplements should not be recommended. Smokers should now be warned not to take beta-carotene supplements. Thus, current research suggests that any benefit from foods containing phytonutrients cannot automatically be related to their individual constituents.

Garlic Garlic is part of a larger group of vegetables known as the Allium family, which includes onions, scallions, leeks, and chives. Allium vegetables possess a sulfur-containing compound called alliin that is converted to allicin when raw garlic is crushed, chewed, or chopped by an enzyme known as allinase. Allicin then quickly converts to a number of

other compounds including diallyl sulfide (DAS), diallyl disulfide (DADS), and ajoene.

In the lab, DAS and DADS have shown promising effects on cancer prevention and progression through two main mechanisms: the ability to prevent the activation of carcinogenic substances and the potential to induce apoptosis in tumor cells. In laboratory studies, DAS inhibits cancer progression and onset in animals in which cancer was induced by carcinogenic substances. Garlic seems especially protective against cancers caused by nitrosamines, which are chemical compounds commonly found in preserved meat products such as salami, bacon, and sausage. In addition to garlic's action on carcinogenic substances, researchers believe that garlic may have the ability to directly attack and destroy tumor cells. Cancer is characterized by unregulated cell division, and organosulfur compounds such as DADS and ajoene have the ability to induce cell cycle arrest when added to cancer cells in cell culture. Additionally, DAS has the greatest ability to induce apoptosis in cancer cells grown in culture. According to AICR, DAS has actually killed leukemia cells in the laboratory, and ajoene has shown some similar effects. While more studies are needed before dietary recommendations can be made, garlic continues to hold a place in the list of foods that fight cancer.

Soy and Breast Cancer

Soybeans are legumes used to make tofu, soy milk, miso, tempeh, soy burgers, soy sauce, and soynut butter. Soy contains a class of phytochemicals called isoflavones. The main isoflavones in soybeans are genistein and daidzein. These compounds are similar in structure to human estrogen. Thus, isoflavones are often referred to as phytoestrogens. There is growing evidence for a beneficial action of isoflavones on various cancer-related biological pathways, such as cell-signaling, carcinogen activation, cell cycle regulation, angiogenesis, oxidative stress, and chronic inflammation. Researchers originally associated soy with reduced breast cancer risk after observations of diet differences in Eastern and Western cultural diets. The low rate of endometrial and breast cancer in Asia may be due to women's dietary habits and their high consumption of soy. Based on these initial observations, several studies have examined the influence of soy on breast cancer risk. The prevailing hypothesis is that phytoestrogens compete with estradiol for the binding sites on intracellular estrogen receptors. These phytoestrogens are acting as selective estrogen receptor modulators (SERMs). For example, genistein binds to estrogen receptors with a weaker affinity, which does not produce as strong of a cellular response but blocks estrogen from reaching the receptors – therefore potentially protecting

women from developing breast cancer. Several studies have shown that consumption of soy (55 g/day or more) reduces women's risk of developing breast cancer. Studies have found that pre-menopausal women may benefit from eating soy foods since their natural estrogen levels are high. However, another large study showed no correlation between soy intake and the risk of developing breast cancer. These contrasting effects may be due to the amount of isoflavone consumed in the studies or the timing of soy consumption (e.g., ingestion during adolescence). There may be a certain threshold needed for soy consumption before the protective effects are realized.

Another key factor that may influence the effect of soy on breast cancer risk is the age at which soy is introduced into the diet. Most studies have shown strong evidence for a decrease in breast cancer occurrence in women who consumed soy before puberty and during adolescence. AICR and the American Cancer Society (ACS) stress that data on soy and breast cancer are not conclusive. Additionally, many studies showing the positive impact of soy on breast cancer have been done exclusively in Asian women. Possible genetic differences in phytoestrogen metabolism make it difficult to extrapolate these results to non-Asian women. More information is needed before any dietary recommendations can be made. One exception to this rule may be for women who have

estrogen-receptor positive breast cancer or those taking anti-estrogen medications such as tamoxifen or aromatase inhibitors. According to AICR, patients taking such medication should limit or avoid soy intake until further studies are conducted.

Soy and Prostate Cancer

The role of soy phytoestrogens in prostate cancer is also controversial. While treating prostate cancer with estrogens inhibits cancer growth, estrogens have also been associated with the growth of both benign prostatic hyperplasia and prostate cancer. In a small study, Australian researchers found that men consuming a soy-enriched diet had a statistically significant drop of 12.7 percent in prostate-specific antigen (PSA) levels, compared to the control group whose PSA levels rose 40 percent. Additionally, researchers showed that by adding about 2 ounces of soy grits a day to the diets of men diagnosed with prostate cancer, they could cause quick and noticeable improvements in the subjects' PSA levels. PSA is commonly used to screen for prostate cancer and for tracking the disease once it has been diagnosed. Soy grits are soybeans that have been toasted and cracked into coarse pieces. During the late 1980s, researchers found that Japanese men in Hawaii who ate tofu at least 5 times per week had 65 percent less chance of developing prostate

cancer than those who ate tofu only once a week or less. In 1998, a study involving 12,395 men showed that men who drank a serving of soy milk at least once a day had a 70 percent less chance of developing prostate cancer than those who never drank soy milk. Soy has also been found to be potentially beneficial in treating prostate cancer and slowing its progression in many animal and *in vitro* studies. Lately, more human studies point to similar results. Despite these optimistic results, another study that followed 5855 Japanese American men for over 20 years found no association between tofu intake and prostate cancer risk. It is important to note the limitations of any cohort case study in which the data is based on dietary questionnaires and recall.

It has been speculated that the incidence of prostate cancer in Eastern Asia is lower than in Western societies because of high soy consumption in Asia. In a meta-analysis including five cohort and nine case-control studies, total consumption of soy foods and non-fermented soy foods were inversely associated with prostate cancer risk. However, in that meta-analysis, the inverse association between soy food consumption and prostate cancer risk was only seen in Asian men, whereas no association was seen among studies on men from Western societies. There are many possible explanations for this observation. For example, it could be that different types of soy

foods are consumed in Asian and Western countries, or that the amount soy food consumed in Western countries has failed to reach the threshold needed to produce an inverse association with prostate cancer.

Several mechanisms have been proposed for how isoflavones may impact prostate cancer. These include blocking androgen receptors, inhibiting tyrosine protein kinases and growth factor receptors, and preventing tumor angiogenesis. Still, researchers are not clear whether the benefits of soy seem to have on men's health are due to the soy protein, the isoflavones, daidzein, and genistein, or a combination. What is clear is that there are far more prostate cancers in the West compared to the East, and this may be attributable, in part, to the differences in diet and lifestyle.

Vitamins and Cancer Prevention

The ATBC Cancer Prevention Study found that 50 mg/day of alpha-tocopherol, a form of vitamin E, had no effect on lung cancer incidence. They also found that 20 mg of beta-carotene, a precursor of vitamin A, actually increased lung cancer incidence in smokers by 18 percent. Despite these disappointing vitamin supplementation studies, research shows that vitamin D may actually possess cancer-fighting properties. “Vitamin D” refers to both vitamin D_3 (also known as

cholecalciferol), which is created by skin cells called keratinocytes after exposure to UVB light, and vitamin D_2 (or ergocalciferol). Vitamin D2 comes from a plant sterol and is slightly different structurally from vitamin D_3. Neither compound is biologically active in the body. First, these compounds must be modified by hydroxylase enzymes and converted to 25-hydroxyvitamin D (25(OH)D) and then 1,25-dihydroxyvitamin D ($1,25(OH)_2$ D). Sunlight is the main source of vitamin D, but it is also found in foods such as salmon, tuna, mackerel, sardines, and cod liver oil. Milk is irradiated to increase its vitamin D content. Other fortified foods include cereal, orange juice, soymilk, and margarine. People who live in the northern climates in the United Statesand Europe do not receive as much sunlight and are more prone to vitamin D deficiencies.

In Canada and the northern United States, population rates of cancers of the bladder, breast, colon, ovary, and rectum are twice what they are in southern regions. Race also plays a role because higher levels of melanin in dark skin prevent UV penetration and thus vitamin D synthesis. In fact, white skin synthesizes vitamin D six times faster than dark skin. Those with more skin pigmentation are at an increased risk of vitamin D deficiency. Recently, researchers reviewed 63 observational studies that examined the protective effects of vitamin

D against various types of cancer including breast, ovarian, prostate, and colon cancers. The majority of these studies did show that vitamin D protects against cancer. This review suggests that taking 1000 international units (IU) (or 25 μg) of vitamin D_3 per day could lower one's risk of colon cancer by 50 percent, and by 30 percent for breast and ovarian cancer.

In laboratory studies, mice were induced with cancer and then treated with a synthetic compound that mimicked $1,25(OH)_2$ D. The compound reduced tumor growth in mice by about 80 percent. Researchers found that $1,25(OH)_2$ D seems to turn on certain genes that are responsible for causing cells with damaged DNA to stop growing. Thus, $1,25(OH)_2$ D may inhibit the uncontrolled growth of tumor cells. Clinical interventions will ultimately provide the best evidence to determine vitamin D's role in cancer prevention, but until those studies have been completed, an adequate dose of vitamin D has not been determined.

Minerals

Selenium is an essential micronutrient for all people. Selenium is thought to help control cell damage that may lead to cancer because it boosts the body's antioxidant capacity. Most people do not obtain the recommended dose of

200 μg/day from their typical diet. Selenium has been shown in multiple studies to be an effective tool in warding off various types of cancer, including breast, esophageal, stomach, prostate, liver, and bladder cancers. Selenium may also act in other ways to stop early cancer cells in their development. Specifically, when selenium is used in conjunction with vitamin C, vitamin E, and beta-carotene, it works to block free radical formation. Several promising studies have shown potential benefits of selenium in the prevention of prostate cancer. One epidemiological study suggested that men with high blood levels of selenium were about half as likely to develop advanced prostate cancer as the men with lower blood selenium. Selenium is found in nuts, cereals, meat, fish, and eggs. Vegetables such as garlic, onions, broccoli, asparagus, and tomatoes can also be good sources of selenium. While selenium may be an important mineral for preventing cancer, it may also be helpful for those suffering from cancer. Some believe that the use of selenium during chemotherapy in combination with vitamin A and vitamin E can reduce the toxicity of chemotherapy drugs.

Alcohol and Wine

Alcohol consumption is linked to an increased risk of cancer of the mouth, throat, larynx, esophagus, breast, and liver. According to ACS, alcohol users experience oral cancers six times

more often than non-alcohol users. Alcohol is also the primary cause of liver cancer. By altering the liver's ability to eliminate toxins and carcinogenic substances, alcohol may also affect many other cancers in addition to liver cancer. For example, findings from the Women's Health Study (1999 to 2004) suggest that moderate alcohol consumption increases the risk of breast cancer. The higher the alcohol consumption, the greater the risk of breast cancer. Additionally, recent studies have also shown strong correlations between high-alcohol and low-folate intake and increased cancer risk.

While alcohol may have detrimental consequences for human health, specific compounds in certain wines may actually have the potential to help fight cancer. Resveratrol, a cancer-fighting polyphenol found in nature, is produced by some plants when under attack from bacteria and fungi. This antibacterial chemical is found in the skin of grapes and therefore is a small component of red wine. Red wine is a unique alcohol. The distinctive properties of red wine are due to the long process of grape fermentation, which allows certain polyphenols to be extracted from the grape's skin and allows the wine to absorb resveratrol. Despite this fact, resveratrol remains a minor component in wine (1 to 7 mg/L). In 1996, researchers showed that resveratrol was able to inhibit initiation, promotion, and progression of cancer. In laboratory studies,

resveratrol triggered cell death in leukemic and colon cancer cells. Studies also show it slows the growth of cancer cells in the liver, stomach, and breast. Laboratory studies of isolated cell cultures have revealed several possible mechanisms of action for resveratrol. These mechanisms include modulation of the transcription factor NF-kB, inhibition of the cytochrome P450 isoenzyme CYP1A1, and expression and activity of COX enzymes.

In other laboratory studies with isolated cancer cells, resveratrol caused apoptosis specifically by inducing Fas/Fas ligand mediated apoptosis, p53, cyclins, and cdk (cyclin-dependent kinases). In addition, resveratrol has also proven to be a potent antioxidant and may possess angiogenic properties. Despite resveratrol's potential anticancer benefits, laboratory studies show that it may not be sufficient to explain what is known as the French Paradox, which is the observation that there is a relatively low incidence of coronary heart disease in regions of southern France and other areas where wine consumption is high. The French Paradox is the observation that many studies have shown that when humans ingest resveratrol, most of the compound seems to be rapidly metabolized and excreted. In 2004, a study investigating human metabolism of resveratrol found that when humans were given 25 mg doses, resveratrol was quickly metabolized and only trace amounts were found

in human plasma. Studies associating red wine consumption and cancer in humans are in their preliminary stages. As has been noted, consumption of large amounts of alcoholic beverages may actually increase the risk of some cancers. Advise those who drink alcohol to do so in moderation – less than one drink per day for women and two drinks per day for men.

Artificial Sweeteners

The role of artificial sweeteners on cancer risk has been widely debated since the 1970s, when animal studies linked saccharin to bladder cancer in rats. Later it was shown that the carcinogenic effect of saccharin seemed to be species specific.

However, in 1977, a case-control study of 480 men and 152 women in Canada found a positive association between the use of artificial sweeteners, particularly saccharin, and risk of bladder cancer. This ultimately led to the ban of saccharin in Canada. Additionally, later, in 2008, a case-control study concluded that regular use of artificial sweeteners for 10 years or more was positively associated with urinary tract tumors. While some animal studies and a few epidemiologic studies have found some associations between artificial sweeteners and cancer risk in humans, most human studies have failed to support this association. Furthermore, a recent study published in 2009

analyzed a series of case-control studies conducted in Italy between 1991 and 2004 investigating gastric, pancreatic and endometrial cancers in Italy and showed no additional risk of cancer with low-calorie sweetener consumption in the Italian population.

Food Processing and Preparation

The processing and preparation techniques used on foods can influence quality and may have protective, causative, or neutral effects on the risk of cancer. According to AICR, current evidence suggests that salt and salt-preserved foods are potential causes of stomach cancer, and that foods contaminated with aflatoxins are a cause of liver cancer. Although salt is necessary for human health, the total amount consumed is a critical factor and needs to be monitored. The *United States Dietary Guidelines* limit sodium to less than 2300 mg per day. This goal can be achieved by avoiding salt-preserved, salted, or salty foods, limiting consumption of foods processed with added salt, and use of preservation methods that do not require salt. Limiting consumption of foods that have been improperly processed, stored, or prepared is critical in order to avoid microbial contamination and adverse outcomes.

Physical Activity Recommendations

Being physically active is a key component of a healthy lifestyle and recommended for the prevention of many chronic diseases, including cancer. Sedentary lifestyles associated with weight gain, overweight, and obesity increase the risk of certain cancers. Regular physical activity is an important component of cancer prevention. AICR recommends that all individuals incorporate moderate levels of physical activity, equivalent to brisk walking, for at least 30 minutes every day. As fitness levels improve, individuals should aim for 60 minutes or more of moderate, or 30 minutes or more of vigorous physical activity every day.

According to the American Cancer Society (www.cancer.org), prevention guidelines related to diet and physical activity include:

Maintain a healthy weight throughout life

Balance calorie intake with physical activity

Avoid excessive weight gain throughout life

Achieve and maintain a healthy weight if currently overweight or obese

Adopt a physically active lifestyle

Adults: engage in at least 30 minutes of moderate to vigorous physical activity, on 5 or

more days of the week; 45 to 60 minutes of physical activity are preferable

Children and adolescents: engage in at least 60 minutes per day of moderate to vigorous physical activity at least 5 days per week

Eat a healthy diet, with an emphasis on plant sources

Choose foods and drinks in amounts that help achieve and maintain a healthy weight

Eat five or more servings of a variety of vegetables and fruits each day

Choose whole grains over processed (refined) grains

Limit intake of processed and red meats

If you drink alcoholic beverages, limit your intake

Drink no more than one drink per day for women or two per day for men

Nutrition in Cancer Treatment

Malnutrition in Cancer Patients

It has been well established that malnutrition in cancer patients is associated with poor prognoses, and that weight loss is an important predictor of mortality. Malnutrition is prevalent among patients with certain types of cancer, especially those with gastrointestinal,

pancreatic, head and neck, and lung cancers. From an epidemiological point of view, malnutrition affects over 80 percent of patients with upper gastrointestinal cancer and at least 60 percent of those with lung cancer. Malnutrition may result from the disease process, from the therapies used to treat the cancer, but usually, it is from a combination of the two.

In fact, at the time of diagnosis, approximately 50 to 75 percent of cancer patients are already malnourished. This increases the risk of morbidity and mortality. It is estimated that approximately 20 to 40 percent of cancer patients die from the effects of malnutrition and its complications, rather than from malignancy itself. Therefore, maintaining good nutritional status during cancer treatment is critical to increase the likelihood of successful completion of prescribed therapies by helping to lessen the associated toxicities that can often lead to breaks or discontinuation of chemotherapy and/or radiation therapy. Being adequately nourished during treatment can also greatly improve quality of life of the cancer patient.

The nutritional status of cancer patients is also influenced by the disease stage and treatment-associated side effects. Significant reductions in energy and protein intake are observed in some patients depending upon on the type and stage of cancer. Patients with stage

III/IV disease may have significant reductions from their usual energy and protein intakes. The majority of patients with advanced cancer experience some involuntary weight loss.

Reduced nutritional intake is almost always multifactorial. The 10 most common symptoms among advanced cancer patients are shown in Table 11-3, each of which can significantly impact nutritional status. Managing these symptoms is therefore crucial to improve the cancer patient's nutritional status, treatment outcomes, and quality of life.

Table 11-3 Common Side Effects of Anticancer Treatment

Source: Maureen Huhmann, DCN, RD, CSO and Theresa P. Yeo, PhD, MPH, AOCNP, 2014. Used with permission.

Pain	Infection
Fatigue	Stomatitis
Weakness	Dysphagia/Esophagitis
Anorexia	Nausea/vomiting
Weight loss	Gustatory changes
Lack of energy	Myalgias/arthralgias
Xerostomia	Dermatitis
Constipation	Hyperpigmentation
Dyspnea	Anxiety

Early satiety	Depression
Diarrhea/ Constipation	Insomnia and sleep disturbances
Early satiety	Anemia
Neutropenia	Bone marrow suppression
Organ Dysfunction	
Cardiac and pulmonary toxicities	
Neurotoxicity, particularly peripheral neuropathies and chemobrain	
Nephrotoxicity	
Hepatotoxicity	

Weight Loss

Up to two-thirds of patients with advanced cancer have some degree of weight loss. Studies have shown that of patients with cancer, 59 percent had decreased appetite, 67 percent had decreased food intake, and 54 percent were underweight. Patients with the highest weight loss were those with tumors of esophagus, stomach, and larynx. Patients with malignant solid tumors of the colon, lung, pancreas, gastrointestinal tract, or head and neck frequently experience weight loss, often starting in the pre-diagnosis phase. In fact, many pancreatic cancer patients will already have lost as much as 10 to 20 percent of their usual body weight at the time of diagnosis. This initial

weight loss is often exacerbated following the diagnosis of cancer, whether because of surgery, chemotherapy, or radiation therapy. As little as 5 percent weight loss prior to starting therapy have predicted a decreased response to therapy.

Cancer patients who experience weight loss have more dysgeusia, vomiting, xerostomia, dysphagia, anorexia, early satiety, and depression. Approximately half of all cancer patients lose some body weight, whereas the overall incidence of weight loss in cancer patients is 86 percent in the last 1 to 2 weeks of life. Multiple factors contribute to the weight loss experienced by cancer patients. Some additional factors not discussed previously include physiological changes associated with the development of the tumor itself, the host response to the tumor, and the side effects of cancer treatments (Table 11-4). If appropriate interventions are not implemented to prevent or slow the rate of weight loss often seen in cancer patients, prognosis is affected. In fact, a weight loss of greater than 2.75 percent per month has been shown to be an independent prognostic indicator of decreased survival in patients with cancer.

Table 11-4 Causes of Weight Loss in Cancer Patients

Source: Maureen Huhmann, DCN, RD, CSO and Theresa P. Yeo, PhD, MPH, AOCNP, 2014. Used with permission.

Metabolic Change	Side Effect
Physiologic abnormalities associated with the tumor	Malabsorption Obstruction Diarrhea Vomiting
Host response to the tumor	Anorexia Altered metabolism
Side effects of anti-cancer treatment	Mucositis Radiation enteritis Xerostomia Nausea, vomiting and diarrhea Alteration in sense of taste

Diagnosing Malnutrition in Cancer Patients

ASPEN guidelines recommend that nutritional screening and assessment of cancer patients should be performed early and often. One commonly used screening tool that has been validated in the cancer population is the

Patient-Generated Subjective Global Assessment (PG-SGA). Ongoing nutrition screening and assessment throughout the course of treatment are most effective in an interdisciplinary setting involving the whole healthcare team, including physicians, nurses, registered dietitians, and social workers.

Markers of nutrition status (serum albumin, prealbumin, anthropometric changes, body composition) may be affected by cancer, but may serve to also be helpful to assess the patient's nutritional status. One study found that of 185 colorectal cancer patients, low serum albumin levels were more useful than prealbumin in predicting short-term disease recurrence. In a retrospective review of patients with gastrointestinal malignancies, albumin levels below 3.2 g/dL were a better predictor of post-operative morbidity, complications, and mortality, while also being more cost-effective, than testing prealbumin. An acute phase response associated with the inflammatory effects of cancer may alter the levels of certain markers and this may limit their reliability.

Cancer Cachexia

Cancer cachexia is a complex, multifactorial syndrome that occurs in 50 to 80 percent of cancer patients. There is no agreement on an exact definition of cachexia. A systemic review of cancer cachexia proposed a new definition of cancer cachexia as:

> a multi-factorial syndrome defined by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment. The pathophysiology is characterized by a negative protein and energy balance driven by a variable combination of reduced food intake and abnormal metabolism.

A feature of cancer cachexia, which distinguishes it from simple weight loss due to inadequate energy intake or malabsorption, is its non-responsiveness to traditional treatment approaches. Randomized clinical trials with appetite stimulants (such as Megace and Marinol), 5-hydroxytryptamine antagonists (for example, Remeron), nutrient supplementation, and COX-2 inhibitors (a type of non-steroidal anti-inflammatory drug (NSAID) that targets an enzyme responsible for inflammation and pain) have all failed to demonstrate success in reversing the metabolic abnormalities seen in cancer cachexia. Studies have shown nutritional, pharmacological, or metabolic interventions are not effective in preventing the metabolic changes associated with cancer cachexia.

Cachexia is most prevalent among patients with gastrointestinal and lung cancers. With the exception of breast and prostate cancer,

patients with solid tumors are at greatest risk of developing cachexia. Cachexia has been identified as an independent predictor of shorter survival and increased risk of treatment failure and toxicity, thus contributing to the morbidity and mortality in the cancer patient. Cancer cachexia may account for almost one-quarter of all cancer deaths. Functional deficits associated with cachexia may be physical, immune, metabolic, or psychosocial. Cancer cachexia should be suspected when an involuntary weight loss of greater than 5 percent of pre-morbid weight is observed within 1 month, or 2 percent weight loss in individuals with BMI less than 20 kg/m^2. In addition to unintentional weight loss, other common manifestations of cancer cachexia are muscle wasting, anorexia, anemia, altered immune function, inflammation, and insulin resistance, which contribute to increased fatigue, and diminished quality of life.

Cancer cachexia is characterized by loss of muscle, with or without loss of fat mass, but is distinct from loss of muscle mass in starvation, depression, and malabsorption. Unlike patients in starvation states, patients experiencing cancer cachexia lose both adipose and skeletal muscle mass, while preserving visceral muscle mass. Loss of muscle mass can decrease immunity, make the body more prone to infections or skin breakdown, decrease the ability to heal, and increase mortality. Also

unlike starvation, the weight loss associated with cancer cachexia typically cannot be reversed with increased caloric intake alone. Weight loss is typically greater than would be expected for the current level of energy intake. Patients with cancer cachexia had an average calorie deficit of 250 to 400 kcal/day, and showed no improvement in weight loss with addition of a 1 kcal/mL supplement. However, using more calorically dense (1.5 kcal/mL), higher-protein supplements did help stabilize weight in some recent studies, but without any improvement in lean body mass.

Anorexia is also related to weight loss in a majority, but not in all, patients with cancer cachexia. Of patients with more than10 percent weight loss, 39 percent had no anorexia and 16 percent had normal food intake, while 12 percent of patients had anorexia with no weight loss. Anorexia correlated with weight loss in most, but not all studies. Often, an involuntary weight loss without any perceived change in appetite or dietary intake is what first leads a person to seek medical care, prior to their diagnosis of cancer.

Lung cancer patients, who lost 30 percent of their pre-illness body weight, experienced an 85 percent reduction in total body fat. With a 30 percent loss in weight, a 75 percent reduction in skeletal muscle protein was also seen, with non-muscle protein relatively unchanged. The

loss of lean body mass can lead to reduced organ function and weakness. A weight loss of greater than 15 percent in cancer patients typically causes impaired physiological function, with death occurring in up to 30 percent of patients.

Many of the changes in body composition and the severe weight loss of cancer cachexia are thought be the result of tumor-induced pathophysiological changes in normal metabolism. Some patients with advanced cancer become hypermetabolic, leading to increased energy requirements, altered insulin sensitivity, increased protein use, and increased cytokine synthesis. The increased metabolic rate combined with a reduced food intake can contribute to a severe, rapid weight loss in cancer patients. Inflammation measured by CRP seems a robust factor able to distinguish weight-losing from non-weight-losing cancer patients.

Glutamine is an amino acid used as a source of energy and nitrogen by rapidly dividing cells. For this reason, cancer patients, who require an increased amount of this amino acid, can be affected by deficiency, which may lead to changes in their immune status, the integrity of the intestinal mucous membrane and protein-energy metabolism, contributing to cancer cachexia. Supplementation with glutamine and arginine have had mixed results

per studies reviewed in the Academy of Nutrition and Dietetics Evidence-Based Library, and it is suggested that further studies be done.

Substrate Metabolism

Cancer patients experience an increased rate of body protein breakdown (by 50 to 70 percent) with a failure to maintain adequate protein synthesis. These individuals selectively break down protein from skeletal muscle mass to synthesize glucose while the non-muscle protein compartment is generally preserved. This imbalance in protein breakdown and synthesis results in an elevated state of protein catabolism. This decrease in muscle mass can explain why many cancer patients have reduced mobility, and therefore quality of life. Adipose tissue is also broken down to provide energy and is lost more rapidly than muscle mass in progressive cancer cachexia. This increased breakdown of body fat stores can result in elevated blood lipid and glycerol levels in cachectic patients. Cancer patients may also suffer from abnormal glucose metabolism. Glucose intolerance, hyperglycemia, and delayed glucose clearance are frequently observed in cancer patients. In addition, insulin resistance has also been observed in patients with gastrointestinal cancer.

Weight Gain

Although the development of advanced cancers is often associated with weight loss and cachexia, weight gain has been associated with certain types of cancer treatments. Weight gain has been reported in 50 to 96 percent of breast cancer patients receiving adjuvant cancer treatment. A significant number of these patients gain more than 20 pounds. Weight gain and being overweight have been associated with increased risk of cancer recurrence and mortality in breast cancer survivors. Weight gain has also been observed in prostate cancer patients who receive androgen deprivation therapy. The weight is gained in the form of sarcopenic obesity, or weight gain in the absence of lean tissue gain.

Obesity has been associated with advanced or fatal prostate cancer, but not overall incidence of prostate cancer. Obesity has also been associated with increased risk of recurrence in most, but not all, studies. In a retrospective cohort study, “weight gain from 5 years before prostatectomy to 1-year after was associated with a nearly 2-fold increased risk of prostate cancer recurrence.” This was a linear association, and remained significant even with different physical activity levels.

Weight gain may be related to increased food intake to manage symptoms, a decreased physical activity level, or a modification of

metabolic rate. Current interventions for weight gain in patients include calorie restriction and exercise training.

Nutrition-Related Side Effects of Cancer Treatment

Treatments for cancer may increase demands for nutrients and energy, while at the same time causing side effects that affect the intake or absorption of nutrients (Table 11-3). For example, the toxicity of chemotherapy and radiation treatments may lead to gastrointestinal symptoms that affect food intake, such as nausea, vomiting, and diarrhea. Nausea and vomiting are the two most common side effects of cancer treatment, occurring in 21 to 68 percent of advanced cancer patients. Nausea and vomiting can affect the amount and types of food eaten during treatment. Diarrhea can be a result of some chemotherapy regimens, and is common among cancer patients who are receiving radiation therapy to the pelvic area, such as patients with prostate, pancreatic, gastrointestinal, and gynecological cancers. Severe diarrhea can lead to weight loss, dehydration, and malnutrition.

Head and neck patients undergoing radiation therapy often experience dysphagastrointestinala and/or odynophagia in addition to some of the previously mentioned side effects. This may necessitate the temporary

placement of a feeding tube to help the patient maintain their nutritional status during treatment.

Chemotherapy is highly toxic to rapidly dividing cells such as those that line the gastrointestinal tract. Cancer patients may also develop treatment-induced oral or intestinal mucositis, which is an inflammation of the lining of the mouth and gastrointestinal tract and is a common side-effect of cancer chemotherapy and radiation therapy, particularly to the head and neck. Severe inflammation, lesions, ulceration, and bleeding can occur in the mouth, esophagus, and intestine. Patients can experience intense pain, cramping, nausea, and gastroenteritis. The severity and nature of the mucositis varies based on the patient's treatment regimen. Among patients with mucositis, food and fluid intake may be drastically limited and nutrient absorption may be reduced. Oral mucositis affects 100 percent of head and neck patients receiving radiation therapy, 70 to 80 percent of hematopoietic stem cell transplant recipients, 40 percent of patients receiving primary chemotherapy, and 10 percent of patients receiving adjunctive chemotherapy. The pain of oral mucositis affects their ability to eat, drink, speak, and sleep, and thus negatively influencing the patient's nutritional status, quality of life, and treatment regimen. Often, the sense of taste and smell is altered as well in patients

undergoing chemotherapy or radiation therapy. Xerostomia, either drug-induced or secondary to radiotherapy, can also lead to an altered perception of taste.

Similar to chemotherapy, radiation therapy is most toxic to cells with a high turnover rate. Radiation to any portion of the gastrointestinal tract can increase the risk of malnutrition. Greater than 70 percent of patients who receive radiation to the pelvic area experience acute inflammatory intestinal changes, including diarrhea, abdominal pain, and nausea, and vomiting. Treatment-related side effects of radiation to the head and neck, such as mucositis, xerostomia, taste change, and dysphagia tend to peak two-thirds of the way through treatment and, in some cases, can become permanent.

Patients with gastrointestinal cancer who experience weight loss, impaired functional performance, and poor nutritional status do not respond well to their cancer treatment. Individuals with poor nutritional status and weight loss before starting chemotherapy or radiation therapy often experience severe toxicity, poorer quality of life, and increased mortality than those who did not experience weight loss preceding chemotherapy.

The metabolic and nutritional abnormalities associated with cancer can cause severe fatigue and reduction in functional ability. Functional

capacity for all types of cancer patients is substantially influenced by deficits in current intake and recent weight loss. Better quality of life is observed in well-nourished cancer patients, compared to malnourished cancer patients. At the end of radiation therapy, increased nutritional intake was associated with improvement in quality of life among high-risk cancer patients.

Weight loss is the outcome parameter relied upon most in assessing the nutritional status of patients with cancer, with an involuntary loss greater than 10 percent in the past 6 months, or a BMI less than 18.5 kg/m^2 indicating malnutrition. However, keep in mind that weight may be unreliable in cancer patients experiencing fluid shifts and resultant edema.

Medical Nutrition Therapy for Cancer Patients

Medical nutrition therapy (MNT) can play a critical role in the management of cancer patients, from the initial phases of treatment and recovery through the long-term continuum of care, as shown in Table 11-5. Maintenance of nutritional status during cancer treatment is essential to increase the likelihood of successful completion of prescribed cancer therapies. Adequate and appropriate MNT therapy can help slow or minimize reduction in body

weight, reduce incidence and severity of cachexia and anorexia, reduce cancer treatment associated side-effects, improve quality of life, reduce risk of other medical conditions, and increase likelihood of survival.

Table 11-5 Goals of Medical Nutrition Therapy for Patients with Cancer

Source: Maureen Huhmann, DCN, RD, CSO and Theresa P. Yeo, PhD, MPH, AOCNP, 2014. Used with permission.

Reverse prior episodes of poor nutrition
Prevent further nutritional decline
Improve stamina and strength
Maintain weight
Support adequate calorie and nutrient intake
Prevent weight loss and promote weight gain
Prevent malnutrition, anorexia, and cachexia
Reverse malnutrition and weight loss that have already occurred
Improve body composition
Enhance immune function
Maximize tolerance to cancer therapies
Improve functional or performance status
Reduce fatigue

Improve physical functioning and quality of life

Disease and treatments have a major impact on nutritional status. By improving the nutritional status and preventing weight loss of the cancer patient, we can improve the prognosis, quality of life, and functional status by facilitating improved tolerance to treatment. Dietary counseling, recommended for patients at risk of malnutrition, should be introduced early. Administering oral nutritional supplements to malnourished patients has been shown to lead to a reduction in mortality, complications, and the length of the hospital stay. Multidisciplinary intervention with a combination of dietary and pharmaceutical interventions can assist with the management of these symptoms.

Managing Gastrointestinal Side Effects

Appropriate nutrition can play a role in helping control nausea and vomiting, thus possibly reducing the need for antiemetic medications. Fluids are most important to prevent dehydration. There are several ways to control or relieve nausea such as consuming clear, cool drinks, ice chips, gelatin, popsicles, water ices, or sorbet, eating and drinking slowly, and eating smaller, more frequent meals. Dry, easy-to-digest foods, such as crackers, toast, pretzels, cereal are often tolerated. Cold or

room-temperature foods may help decrease nausea that is exacerbated by food odors. Consider adding fresh ginger or ginger tea to the diet to help reduce treatment-related nausea.

Ways to relieve vomiting include gradually drinking small amounts of clear liquids, avoiding solid food until the vomiting episode has passed, resting and temporarily discontinuing all oral medication, which can irritate the stomach and make the vomiting worse. If vomiting and diarrhea last more than 24 hours, an oral rehydration solution should be used to replace electrolytes. Consumption of adequate fluids is critical to avoid dehydration associated with diarrhea. Additionally, consumption of soluble fiber can help control the frequency of diarrhea. The “BRATT” diet (Bananas, Rice (white), Applesauce, Toast (white), Tea (decaf)) may be recommended initially. There is not always a one-size-fits-all treatment of gastrointestinal side effects in the cancer patient; therefore, it is important as healthcare professionals to individualize symptom management. For example, there are many reasons why a patient may be experiencing diarrhea. Diarrhea in a patient post-Whipple with pancreatic cancer receiving concurrent chemotherapy and radiation may be a result of malabsorption secondary to pancreatic enzyme deficiency. It may also be due to dumping syndrome as a result of gastric

and upper gastrointestinal surgery. Finally, it may occur as a side effect of chemotherapy and radiation in patients with other types of cancer.

Nutrition-related interventions for common treatment side effects experienced by cancer patients are presented in Table 11-6.

Table 11-6 Key Dietary Interventions for Cancer Treatment Side Effects

Source: Maureen Huhmann, DCN, RD, CSO and Theresa P. Yeo, PhD, MPH, AOCNP, 2014. Used with permission.

Symptom	**Intervention**
Taste Changes	Rinse mouth with baking soda prior to eating Use plastic cutlery and dishes Eat cool or room temperature foods Tart foods, flavorful seasonings, and marinated foods
Xerostomia	Drink fluids with meals, moisten and/or puree foods Use oral moistening mouthwash/gel Try papaya juice *Avoid*: caffeine, alcohol, commercial mouthwashes

Symptom	Intervention
Stomatitis Mucositis	Eat bland, soft foods, easy to swallow foods Cook food (especially vegetables) until they are soft and tender Cut food into small pieces, or puree food in blender Mix food with broth, gravies, or sauces to make them easier to swallow Try capsaicin candy *Avoid:* Acidic, spicy, rough, and salty foods
Diarrhea	BRATT Diet (Bananas, Rice, Applesauce, Toast, Tea) Initially low fiber → slowly increase soluble fiber Temporary avoidance of milk products (with the exception of yogurt) Increase fluid intake (including juice and broth) Prophylactic use of probiotics to prevent radiation-induced diarrhea

Symptom	Intervention
	Avoid: High fat foods, caffeine, alcohol, tobacco, strong spices
Dumping Syndrome	Small, frequent meals (every 2 hours) Increase protein and fat content of meals Fluids between meals Limit simple carbohydrates
Constipation	Gradually increase fiber rich foods (whole grains, bran cereals, fruits and vegetables) Drink 8 to10 glasses of fluid daily Drink 4 to 8 oz of prune juice once or twice a day Increase physical activity Fiber supplement → Stool softener → Laxative
Nausea	Fluids between meals Cold foods may be better tolerated *Avoid:* Foods with strong odors, high fat foods, strong spices

Symptom	Intervention
Vomiting	NPO → Clear Liquid → Full Liquid → Soft Maintain fluid intake (including juice and broth)
Early Satiety	Limit excessive intake of fat and fiber Small, frequent meals (every 2 hours) Increase protein and carbohydrate content of meals Fluids between meals
Bloating and gas	Avoid gas forming foods: cabbage, onions, gum, beans, corn Eat low fat and reduced fat foods

Food Safety

Certain cancer treatments, such as chemotherapy, can weaken the immune system. When the immune system is weak, the risk of infection is greater for cancer patients. Blood tests are usually performed during cancer treatment to check if patient is neutropenic. When cancer patients are determined to be neutropenic, they should be careful to avoid eating unsafe foods that may contain high levels

of germs because, unlike healthy individuals, they may not be able to defend against common bacteria. Food should be handled safely. As per recommendations by the American Cancer Society:

Wash your hands before eating or preparing foods.

Wash vegetables and fruits well.

Keep foods at the right temperatures.

Use special care in handling raw meats, fish, poultry, and eggs, keeping them away from other foods.

Thoroughly clean all utensils, countertops, cutting boards, and sponges that have contact with raw meat.

Cook foods to proper temperatures. Meat, poultry, and seafood should be thoroughly cooked. Use a food thermometer to check the internal temperatures of meats before serving.

Avoid raw honey, milk, and fruit juice, and choose pasteurized versions instead.

Store foods in a refrigerator or freezer (below 40 °F) straight after buying them to limit the growth of germs.

When eating out, avoid salad bars; sushi; and raw or undercooked meat, fish (including shellfish), poultry, and eggs as these foods are more likely to contain harmful bacteria.

If concerned about the safety/purity of the well water in your home, ask the public health department to check it for bacteria.

Source: American Cancer Society, 2014. Used with permission.

Maintaining Energy and Protein Intake

Nutritional status has an important effect on a patient's quality of life, sense of well-being, ability to fight disease and withstand the rigors of anticancer treatments. Early and sustained nutritional support is one of the most valuable adjuncts to the optimal management of cancer. Healthcare professionals should help patients aim to prevent weight loss, reduce muscle wasting, and avoid nutrient deficiencies. Weight management, and weight gain if possible, should be considered primary goals for cancer patients. Preventing weight loss is simpler, safer, and less expensive than trying to regain lost weight. Sufficient calories and protein should be provided to meet the complete nutritional and energy needs of each patient and to minimize protein catabolism and the use of stored energy reserves as soon as possible in the nutritional management of cancer patients. In order to support protein synthesis and minimize the magnitude of the nitrogen deficit, sufficient calories and protein should be provided. Requirements for calories in most patients range from approximately 25 to 35 kcal/kg, and protein from 1.0 to 1.5 g/kg

per day. Carbohydrates should provide the primary source of energy, and fat should represent 25 to 30 percent of calories to provide essential fatty acids and meet energy demands, while providing adequate protein, vitamins, minerals, and trace elements. Since patients often experience early satiety, nutrient dense foods may be necessary. Small, frequent meals are usually better tolerated than larger meals.

For patients with inadequate food intake, oral nutritional supplements may be appropriate. Use of high-protein and energy-dense oral nutritional supplements contribute to increased energy and protein intake, improvements in nutritional status, body weight, and quality of life as well as reductions in incidence and severity of anorexia, diarrhea, and radiation toxicity and treatment.

Integrative Approaches

Many complementary, alternative, and integrative medicine practices prescribe high-dose intravenous vitamin C, or ascorbic acid infusions as a pro-oxidative therapy for cancer patients. Recent in vitro and in vivo studies show that intravenous, but not oral, ascorbic acid produce pharmacological plasma concentrations that result in the production of hydrogen peroxide that results in neoplastic cytotoxicity. However, in an 2010 article reviewing 33 years of trials of at least 1600 patients on vitamin C and cancer, with

conflicting results, Cabanillas concluded that, “we still don't know whether vitamin C has an clinically significant antitumor activity.” Undoubtedly, further clinical trials showing promising results will be needed in the future before conventional oncology professionals embrace this treatment.

The role of glucose and cancer has been in question, as may be evident by the number of times an oncology healthcare professional is asked by a patient, “Doesn't sugar feed cancer?” To quote the American Cancer Society's response to this question:

> No, sugar intake has not been shown to directly increase the risk of getting cancer or having it get worse (progress). Still, sugars and sugar-sweetened drinks add large amounts of calories to the diet and can cause weight gain, which we know can affect cancer outcomes. There are many kinds of sugars, including honey, raw sugar, brown sugar, corn syrup, and molasses. Many drinks, such as soft drinks and fruit-flavored beverages contain sugar. Most foods and drinks that are high in added sugar do not offer many nutrients and may replace more nutritious food choices. For this reason, limiting the intake of foods and drinks with added sugar is recommended.

According to Adekola et al., cancer cells are more susceptible to glucose deprivation than

are healthy cells. Some studies have shown that by inhibiting glucose transport results in cell death and can decrease cancer cell proliferation. Work is being done to discover new therapeutic agents that are specific to the cancer cell's metabolism without adversely affecting the host.

One area of interest in oncology is the possible benefits of the ketogenic diet for patients with brain tumors. The ketogenic diet, traditionally used to control seizures in children, is a high-fat, low-carbohydrate diet that lowers circulating glucose levels and increases ketone levels, thereby essentially “starving” the tumor cells of energy. The current literature is limited on information regarding the potential anti-neoplastic effect of a ketogenic diet. To date, no randomized controlled trials have been carried out using the ketogenic diet for tumor therapy.

However, in vitro and in vivo studies have been encouraging. It is well documented that brain tumor growth in mice depends largely on circulating levels of glucose. High levels of glucose have been shown to accelerate brain tumor growth and angiogenesis, and prevent apoptosis. By reducing the circulating levels of glucose and increasing levels of ketones, by either restricting carbohydrates, or just restricting total caloric intake, it is theorized that this can be reversed.

An Italian case study by Zuccoli et al. of a 65-year old woman with GBM (glioblastoma) in 2008–2009 was the first report of GBM treated with both standard therapy (craniotomy, chemotherapy, and radiation therapy) and a restricted ketogenic diet (600 kcal/day). After 2 months of treatment, her weight had decreased by 22 percent (from 141 to 110 pounds), and there was no evidence of tumor. Two and a half months after discontinuing the low-calorie ketogenic diet, an MRI showed tumor recurrence.

Unlike healthy brain cells, which have the ability to metabolize ketone bodies for energy when glucose levels are decreased, most brain tumor cells cannot. This dependence on glucose makes the tumor cells vulnerable to therapies targeting glucose metabolism. Clearly, further studies are needed to determine the effectiveness of the ketogenic diet, either calorie-restricted or not, as an adjuvant treatment for patients with GBM.

Other researchers have studied the potential protective effects, such as slowing tumor growth, of not only dietary restriction (defined as 20 to 40 percent restriction in calorie intake), but also of fasting in cancer patients. However, per Lee et al., the current clinical applications may be limited, as reducing calories causes weight loss, and because it was not clear from studies that dietary restriction

could not also inadvertently protect cancer cells from chemotherapy. Further clinical trials are underway at USC.

Case 1 Prevention of Colon Cancer

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Objectives

Review the epidemiology of colon cancer.

Recognize lifestyle risk factors for the development of colon cancer.

Outline appropriate dietary and lifestyle modifications to reduce a patient's risk for developing colon cancer.

AB is a 52-year-old Caucasian man who comes to his primary care provider's office to discuss his concerns about colon cancer. His 48-year-old sister was recently diagnosed with an early-stage colon cancer and was treated with surgical resection. His mother has also had many colon polyps removed during colonoscopies over the years. He is primarily concerned with reducing his risk of developing

a colon cancer but he has never had a colonoscopy.

Past Medical History

AB had an appendectomy as a teenager. He has no other medical problems.

Medications

Vitamin C supplement (500 mg/day) and a daily multivitamin.

Social History

AB is married and has two young children. He drinks 4-5 beers three times per week. He smokes half-a-pack of cigarettes each day. He has smoked for 30 years. He works as a computer analyst and has a sedentary lifestyle.

Diet History

AB describes himself as a carnivore. He enjoys steak, hamburgers, meat loaf, hot dogs, lamb chops, and veal for dinner about five times a week. Breakfast consists of cereal or doughnuts and lunch at work is usually two slices of pepperoni pizza and an iced tea. He also enjoys ice cream after dinner several times a week. He rarely eats fruits and vegetables.

Review of Systems

General: Occasional fatigue

Gastrointestinal: Normal

Musculoskeletal: Mild joint pain in knees with stair climbing

Physical Examination

Vital Signs

Temperature: 98.8 °C

Heart Rate: 76 BPM

Respiratory Rate: 16 BPM

Blood Pressure: 148/86 mm Hg

Height: 170 cm

Weight: 120 lb (54 kg)

BMI: 41 kg/m^2

Exam

There are no pertinent findings on physical examination except for abdominal obesity. Stool GUIAIC is negative.

Case Questions

Describe the epidemiology of colorectal cancer.

What risk factors does AB have for the development of colon cancer?

What nutritional factors in this patient's diet increase his risk for colon cancer?

Describe the benefits of fiber and identify the differences between soluble and insoluble fiber.

What dietary recommendations can you give to AB based on his current diet plan?

Are there medications or supplements that can further reduce his risk of CRC?

Answers to Questions: Case 1

Part 1: Prevalence and Risk Factors

1. Describe the epidemiology of colorectal cancer

Colorectal cancer (CRC) is the third most common malignancy in the United States and the third leading cause of cancer mortality in men and women. In 2013, there will be an estimated 102,480 cases of colon cancer and 40,340 cases of rectal cancer in the United States. The overall lifetime risk of developing CRC for men and women in the United States is 5.79 percent (1 in 17) and 5.37 percent (1 in 18), respectively. The median age at diagnosis is 71 years.

Epidemiological data has demonstrated a global variation of incidence in CRC with developed countries representing the areas of highest risk. Although the majority of CRC cases are present in industrialized countries, incidence rates are rapidly rising in less-developed nations, which

may be attributed to developing countries adopting a more “Western” diet and lifestyle.

Since 1985, the overall incidence of CRC has decreased by 2.5 percent annually, and mortality rates have decreased in both men and women. Such reductions in incidence and mortality have been linked to increased screening and improved treatment. Males have a higher mortality rate than women.

The overall survival rate of CRC in the United States is 63 percent; however, survival rates vary by race and stage at diagnosis. Caucasians have a significantly higher survival rate than people of other racial backgrounds. In addition, the 5-year survival rate of localized CRC is almost 90 percent, while that of locoregional cancer is 66.3 percent. Distant disease has the worst prognosis, with survival rates of 10.3 percent.

2. What risk factors does AB have for the development of colon cancer?

AB's age and gender both represent risk factors for CRC; 85 percent of CRC cases are diagnosed after the age of 45. There is a steady increase in colon cancer incidence with age with the greatest incidence in older adults. There is some increased incidence of CRC in men for all age categories, but this gender gap narrows in the oldest age groups. Race and ethnicity are additional risk factors but not for this patient.

African-American and Japanese men and women have higher colon cancer incidence rates, while Hispanics, Asian/Pacific Islanders and Native Americans have the lowest incidence rates.

Individuals with a family history of CRC also have an increased risk for developing the disease. While known familial CRC syndromes (Lynch and polyposis syndromes) represent less than 5 percent of familial cases, there are likely additional genetic risk factors that have not yet been identified.

AB's high meat diet also increases his CRC risk. It is estimated that diet plays a role in 80 percent of all CRC. A diet that is high in fiber, particularly from fruits and vegetables, decreases the risk while limiting intake of red meat and saturated fat reduces risk.

Additionally AB's weight and alcohol intake further increases his risk, as obesity is a significant risk factor for the development of CRC. Insulin may be involved in colon cancer pathogenesis due to its mitogenic properties. Obesity is associated with related insulin resistance, and hyperinsulinemia. Numerous studies have shown a 2.5-fold increase in CRC in individuals with increasing levels of plasma C-peptide. Increasing physical activity is associated with a decreased risk of CRC. Studies have shown that physically active individuals have a 20 to 30 percent lower risk of colon

cancer compared to sedentary individuals. Physical activity often confers some protection against CRC in individuals with a high BMI.

AB's alcohol intake increases his risk for developing CRC. There is a positive relationship between alcohol use and CRC, as well as a dose-dependent risk associated with regular alcohol intake. An elevated CRC risk is seen with an alcohol intake of at least 30 g/day (about three drinks), with the greatest risk seen in individuals consuming more than 45 g/day. In this group of alcohol users, the relative risk is 1.4 times greater than those who do not consume alcohol. The mechanism behind the association of alcohol use and CRC may be attributed to alcohol's ability to impede folic acid metabolism. Low folate intake may increase the risk of CRC in specific persons.

Finally, AB's tobacco use also increases his CRC risk. Tobacco smoking releases a variety of carcinogenic compounds such as polyaromatic hydrocarbons, heterocyclic amines, nitrosamines, and aromatic amines. These carcinogens can reach colonic mucosa via the circulatory system or through direct ingestion. Individuals who use tobacco have a 2-fold increased risk of colorectal adenoma, a precursor lesion to CRC. Additionally, current smokers have a higher risk of CRC mortality. However, past smokers who have quit for at least 31 years no longer had an increased risk. It

is therefore important to encourage smokers to quit as early as possible.

Part 2: Nutrition Assessment

3. What nutritional factors in this patient's diet increase his risk for colon cancer?

The lack of fiber and folate in AB's diet increase his risk for CRC. Fiber and folate are considered bioactive food components and play a role in the chemoprevention of CRC. Bioactive food components can influence cancer outcomes through their ability to act as inhibitors of angiogenesis and inducers of cell cycle arrest and apoptosis.

Folic acid is a water-soluble B vitamin found in fresh fruit and green leafy vegetables. Folate is involved in DNA methylation and synthesis. Folate deficiency impairs these processes causing DNA damage and genomic instability. This may contribute to the carcinogenesis of CRC, as low levels of folate are associated with an increased CRC risk. Conversely, high dietary folate intake is associated with a 30 to 40 percent reduction in CRC risk. However, some studies also show an association between high folate intake and increased CRC risk, while other studies show no association between folate and risk. These differences may be attributed to the stage of carcinogenesis. For example, folate may be protective against CRC

in normal tissue, but it may also enhance pre-existing cancerous lesions. The benefit of adding folic acid to the food supply is uncertain in individuals with a precancerous stage such as adenomatous polyposis. The relationship between folate and CRC is therefore a complex one that may depend on additional factors. In summary, folate deficiency enhances DNA repair defects and increases abnormal methylation, therefore folate may have preventative effects on an individual before a precancerous stage. It is still unclear whether higher doses are beneficial or harmful with respect to CRC.

Fiber is also chemoprotective, as increased fiber intake is associated with a reduced risk of CRC. However, conflicting and inconsistent studies exist regarding the association between fiber and CRC, and the role of fiber thus remains controversial.

AB consumes large amounts of red and processed meat, which increases his risk of CRC. Studies have shown that individuals in the highest quintile of red meat consumption have increased relative risks of 22 to 50 percent. Specific mechanisms responsible for this association remain unclear. Potential mechanisms include the impact of red meat consumption on the secretion of endogenous insulin, which is a mitogen; red meat causes increased bile and acid production, and changes

in gut microbial flora, which is also associated with increased risk of CRC. Finally, red meat is also a source of carcinogenic heterocyclic amines.

AB's barbequing cooking methods may also increase his risk of CRC. Cooking at high heat converts certain food compounds into mutagens such as heterocyclic amines and/or polycyclic aromatic hydrocarbons, which are associated with CRC. The production of these compounds is catalyzed at high temperatures and increased cooking times. In addition, research has demonstrated that the risk of CRC is increased among meat eaters who consume meat with a heavily browned surface or meat prepared at high temperatures.

In addition, AB's low intake of fish may represent further risk of CRC. Some studies have shown an inverse relationship between CRC and fish intake. In addition, the incidence and mortality from CRC is lower in populations with higher rates of fish consumption. A recent meta-analysis estimated that fish consumption may reduce the risk of CRC by as much as 12%.

Finally, inadequate dietary calcium may increase AB's CRC risk. Calcium has a significant but modest ability to reduce this risk. It binds to toxic secondary bile acids and ionized fatty acids. Calcium also directly reduces cell proliferation and stimulates differentiation in colonic mucosa, while

inducing apoptosis. Studies have shown that the greatest risk reduction is achieved by intakes of 700 to 800 mg/day.

4. Describe the benefits of fiber and identify the differences between soluble and insoluble fiber

Fiber has many chemoprotective effects on the colonic mucosa. Fiber dilutes or absorbs fecal carcinogens and potentially inhibits chemically induced carcinogenesis. It also reduces the exposure period of colonic epithelial cells to carcinogens by decreasing the contact time between intraluminal contents and the mucosa. Fiber has been shown to alter bile acid metabolism by binding secondary bile acids, which are potential carcinogens. Finally, fiber increases the production of short chain fatty acids (SCFA), which serve as an energy source for intestinal epithelial cells and are involved in the maintenance of colonic homeostasis. SCFA also aid in the inhibition of inflammation and carcinogenesis of colonic mucosa and reinforce components of the colonic defense barrier. They decrease oxidative stress and promote cancer cell growth arrest, differentiation, and apoptosis.

A high intake of vegetables or fiber is associated with a significant (40 to 50 percent) reduction in risk for colon cancer. Fiber can be categorized as soluble or insoluble, and each has different properties and effects on the

gastrointestinal system. Soluble fiber is completely fermented by intestinal flora. Examples include some hemicelluloses and pectins, gums, psyllium, fructans, and some resistant starches. Soluble fiber is found in foods such as legumes, oats, and barley. Oat bran consists of 50 percent soluble fiber. Ripe fruit is an excellent source of soluble fiber, and examples include berries, bananas, apples, and pears. Vegetables such as carrots, broccoli, artichokes, and onions are also good sources. Soluble fiber generally delays gastric emptying and increases intestinal transit time. It also decreases nutrient absorption. Soluble fiber has also been shown to lower serum cholesterol and increase short chain fatty acids production, which represent a major energy source for the colon lining.

Insoluble fiber is found in plant cell walls and examples include lignin, some hemicelluloses, and pectins. Foods that contain insoluble fiber include whole grain products, wheat and corn bran, nuts, seeds, some vegetables, and fruits. Vegetables and most grain products contain more insoluble than soluble fiber. In contrast to soluble fiber, insoluble fiber is poorly fermented and digested by humans. Insoluble fiber increases fecal bulk. Its ability to hold water is important in maintaining larger and softer stool, and therefore insoluble fiber is often used to treat constipation. Insoluble fiber decreases

intestinal transit times thus reducing the exposure of colonic mucosa to carcinogens.

Most experts recommend daily intake of both soluble and insoluble fiber (25 to 35 g of fiber each day).

5. What dietary recommendations can you give to AB based on his current diet plan?

AB needs to incorporate more fiber into his diet. He can accomplish this by consuming at least 2.5 cups of fruits and vegetables each day and eating more whole grains rather than refined grain products. Examples of whole grains include wheat, rice, oats, and barley. In addition, specific high fiber foods including beans, whole-grain breads, cereals, rice, and whole-wheat pasta should be added to diet. Because whole-grain foods contain other beneficial nutrients as well as fiber, it is recommended that individuals consume whole-grain foods rather than using fiber supplements.

AB also needs to make his protein choices more thoughtfully. He should begin to reduce his consumption of red meat and use fish and poultry as his primary sources of protein. These should be baked or poached rather than broiled, fried, or barbequed.

AB should also achieve a recommended daily calcium intake of up to 1200 mg/day, since he

is older than 50 years. Dairy products and leafy green vegetables are excellent sources of calcium. If AB chooses to derive his daily calcium from dairy products, he should select low-fat or non-fat choices to reduce his intake of saturated fat. Additionally, AB should ensure that he is consuming enough folate in his diet. Most people get enough folate in their diet, and the best sources of folate are vegetables, fruits, and enriched or whole-grain products. The recommended daily amount of folate is 400 μg/day.

Lifestyle modifications are also important recommendations for AB to consider. First, he needs to increase his physical activity. He should engage in at least 150 minutes of moderate intensity or 75 minutes of vigorous intensity activity each week. Next, AB should quit smoking and reduce his alcohol consumption. Alcohol recommendations consist of no more than 2 drinks per day for men and 1 drink per day for women. A drink of alcohol is defined as 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of 80-proof distilled spirits.

6. Are there any medications that can further reduce his risk of CRC?

Aspirin and NSAIDs may be preventative against CRC. The long-term use of aspirin seems to be protective, and studies have demonstrated a dose-dependent relationship.

Aspirin and NSAIDs inhibit both variants of the enzyme cyclooxygenase, COX-1 and COX-2, which are involved in the synthesis of prostaglandins. The inhibition of cyclooxygenase decreases the inflammatory response, decreases epithelial proliferation and angiogenesis, and increases apoptosis. The United States Preventative Services Task Force concluded that the harms of aspirin and NSAIDs outweigh the benefits for their use in CRC prevention in adults at an average risk for CRC. Such adverse effects of aspirin and NSAIDs include cardiovascular events, bleeding, and hemorrhagic stroke. However, specific populations may benefit from aspirin or NSAIDs. For example, studies have shown that daily aspirin and non-aspirin NSAID use by individuals with a family history of colon cancer reduced risk. In such cases, the benefits may outweigh the risks.

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12
Enteral Nutrition Support

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Objectives*

Describe the indications and contraindications for enteral nutrition.

Identify the appropriate enteral formula to meet individual patients' requirements.

Identify the most appropriate route for tube feeding based on a patient's clinical condition.

Determine the most appropriate administration method based on feeding route and the patient's clinical condition.

Select appropriate monitoring tools and methods to identify, treat, and prevent complications from tube feeding.

*Source: Objectives for chapter and cases adapted from the *NIH Nutrition Curriculum Guide for Training Physicians*.

(http://www.nhlbi.nih.gov/funding/training/naa)

Tube feeding, or enteral nutrition, is a method of providing nutrition support to patients with a functional gastrointestinal (GI) tract who are unable to ingest adequate nutrients by mouth. Tube feeding provides many physiologic, metabolic, safety, and cost advantages over parenteral nutrition and should be utilized when possible. Since there are many tube feeding formulas available on the market, understanding formula composition is important when selecting tube feeds for an individual patient. Assessment of the patient's nutrient requirements, GI anatomy and function, and length of time for nutrition support, and clinical condition should be evaluated prior to selecting feeding tube access and mode of administration. Once the decision is made to start tube feeds, monitoring is crucial to prevent complications.

Tube Feeding Indications

A nutrition assessment is a helpful tool in determining which patients may benefit from tube feeds. Hospitalized patients may require short-term tube feeding if they are unable to eat due to mental status changes, poor appetite, dysphagia, or mechanical ventilation. Tube

feeding in the home setting may be appropriate for patients with ongoing difficulty eating. Advances in tube feeding have made enteral nutrition possible in conditions such as acute pancreatitis, high-output enterocutaneous fistulae, and open abdomen. Tube feeding would not be initiated if a patient has diffuse peritonitis, intestinal obstruction, intractable vomiting or diarrhea, paralytic ileus, or GI ischemia. Although it is occasionally used in patients with short bowel syndrome and severe malabsorption, it should not be relied upon as the primary means of nutrition in sick or malnourished patients. In situations where a patient or caregiver is refusing tube feeds, it is important for a clinician to assist with providing goals of care. Discussing the burden of tube feeds versus its benefits can help guide the decision for whether tube feeds should be provided for palliative care and hospice patients. Guidelines established by the American Society of Parenteral and Enteral Nutrition (ASPEN) recommend initiating nutrition support when patients are expected to (or have) not received adequate oral intake for 7 to 14 days. However, patients who are malnourished or stressed may require earlier initiation of nutrition support.

Tube Feeding Advantages

The old adage “if the gut works, use it” continues to be supported by clinical and

experimental studies that compare enteral to parenteral nutrition. It is important to consider bowel length and the condition of the bowel when determining if the GI tract is functioning adequately. Tube feeding offers many potential advantages over parenteral nutrition, including lower rates of infectious and metabolic complications, decreased hospital length of stay, and reduced cost. Tube feeding is more physiologic than parenteral nutrition and promotes efficient utilization of substrates. Significant immune benefits when using tube feeds versus parenteral nutrition have also been reported in a variety of patient populations. Enteral stimulation plays an important role in the immune system. Gut-associated lymphoid tissue (GALT) produces antigens and helps prevent translocation of bacteria across the mucosal barrier. It has been proposed that the benefits of tube feeding are partially due to its ability to preserve gut integrity and GALT function. Studies in patients with burns, head injury, and trauma have shown decreased rates of infection in those receiving tube feeds compared to those given parenteral nutrition. Certain nutrients, such as fiber, intact proteins and peptides, and specialized fatty acids can be added to tube feeds but not parenteral nutrition. Tube feeds also stimulate the release of cholecystokinin, which maintains normal gallbladder function. For critical care patients, early post-operative tube feeding has been shown to reduce rates of infection, hospital

length of stay, and trend toward reduced anastomotic dehiscence when compared to patients receiving no nutrition support therapy. These factors make tube feeds the preferred method for providing nutrition support.

Formula Selection

There are four main categories of tube feeding formulas; standard or polymeric, elemental and semi-elemental, disease specific, and immune-enhancing. Standard formulas are isotonic and contain intact protein, complex carbohydrates, and a higher amount of LCT than MCT. These formulas are typically used for patients with adequate digestion and absorption ability. Elemental and semi-elemental formulas contain hydrolyzed protein, either as free amino acid or peptides, and have a higher tonicity than standard formulas due to the predigested protein source. Elemental and semi-elemental formulas are intended for patients with impaired digestion or absorption, such as those with Crohn's disease, pancreatic insufficiency, radiation enteritis, and short bowel syndrome. Disease-specific formulas were developed for patients with glucose intolerance and kidney, liver, and pulmonary disease. They have a varying amount of protein, carbohydrate, fat, and electrolytes based on the needs of the specific disease state. Immune-enhancing formulas have been shown to improve immune cell

function, modulate inflammation, and reduce infection in specific patient populations. They contain the addition of varying amounts of glutamine, arginine, nucleotides, omega-3 fatty acids, and antioxidants. Benefits of immune-enhancing formulas have been shown in the following patient population: critically ill patients on mechanical ventilation, major elective surgery, trauma, burns, and head and neck cancer (Table 12-1).

Table 12-1 Classification of Tube Feeding Formulas

Formula Type	Characteristics
Polymeric/ standard	Whole protein, polysaccharide, and mixture of fat sources
Nutrient dense	Polymeric with reduced water (60–70%)
High nitrogen	Over 20% of calories as protein
Elemental/ semi-elemental	Oligopeptides and free amino acids (elemental) in place of whole proteins, low-fat, and/or higher concentration of MCT*
Immune-enhancing	Added glutamine, arginine, omega-3, and antioxidants

Formula Type	Characteristics
Hepatic disease	Increased branch chain amino acids and reduced aromatic amino acids
Renal disease	Reduced protein, water, electrolytes and minerals. May contain few non-essential amino acids
Glucose intolerance	High-fat, low-carbohydrate, fiber
Pulmonary disease	High-fat, low-carbohydrate, omega-3 fatty acids, and antioxidants

*MCT = medium chain triglycerides.

There are many disease-specific formulas available on the market. Products designed for hepatic encephalopathy have a very specific branch chain to aromatic amino acid ratio. Use of these formulas should be limited to patients with advanced liver disease and hepatic encephalopathy who fail to respond to conventional therapy. Formulas designed for patients with renal failure restrict fluids, potassium, phosphorus, and magnesium to match the dietary restrictions of this population. These products should only be used in renal disease when dialysis is inadequate. Specialty formulas designed to improve glucose

control contain a lower concentration of carbohydrate and are supplemented with fiber. These formulas are beneficial for patients who have uncontrolled blood glucose levels when using a standard polymeric formula in addition to oral hypoglycemic medication or insulin. They should not be routinely used for all diabetic patients as they tend to be higher in fat and are more expensive. Formulas designed for respiratory insufficiency contain 40 to 50 percent of total calories as fat to minimize the production of carbon dioxide through carbohydrate metabolism. These formulas are also nutrient dense for fluid restriction in patients with pulmonary edema. Use of these formulas should be limited to patients that continue to have respiratory difficulty in spite of standard treatments. For patients with acute lung injury or ARDS, an enteral formula supplemented with eicosapentaenoic acid (EPA), gamma-linolenic acid (GLA), and antioxidants is available with the aim of down-regulating the inflammatory response. A recent meta-analysis, including three randomized controlled studies, revealed a significant reduction in the risk of mortality and improved outcomes in patients receiving tube feeds containing EPA and GLA.

Immune-enhancing formulas have been shown to be beneficial in lowering infection rates, reducing infectious complications, and shortening length of stay when used in certain

population groups. Glutamine is supplemented in formulas to promote immune function and improve bowel integrity. Under appropriate experimental conditions glutamine has been shown to be essential for cell proliferation, it can act as a respiratory fuel, and it can enhance the function of stimulated immune cells. Patients that seem to benefit most from glutamine-containing formulas are those with post-operative wound infections, cancer requiring surgery, massive blood infusions, trauma, and acutely ill immune-suppressed patients. Arginine has also been supplemented in some formulas to prevent muscle wasting and promote wound healing and immune function. The benefits of arginine have been best demonstrated in surgical patients. The benefit in critically ill patients is not clear.

Calorically dense formulas (1.5 to 2.0 kcal/mL) are available for patients requiring fluid restriction. These formulas provide less water and have a modestly higher viscosity and osmolality compared to standard formulas. Occasionally, nutrient-dense formulas are used to decrease infusion time or the daily volume of tube feeding. If this is done for a patient that is not fluid restricted then additional water may need to be given to avoid dehydration.

When selecting a tube feeding formula it is important to consider a patient's nutrient requirements, GI function, and overall clinical

condition. Standard polymeric formulas should be used unless there is a clear indication that a patient would benefit from a specialty formula. Standard formulas are less expensive than specialty products and should be the formula of choice for many patient populations.

Selecting the Feeding Route

When selecting a route for tube feeding, it is important to consider estimated length of need, GI anatomy and function, and clinical condition. Short-term therapy, defined as 4 to 6 weeks, is typically managed with a nasogastric or nasoenteric tube. Nasoenteric tubes most frequently terminate within the duodenum. These can be placed at the bedside blindly or with an electromagnetic tube placement device. Radiologic or endoscopic techniques can also be used when the aforementioned methods are not successful; the patient requires positioning of the tube from the stomach into the small bowel, or when initial jejunal placement is necessary. Placement generally imposes little risk to patients except when tubes are placed blindly they may be inadvertently placed into the lungs. This risk is greatest for patients with an altered mental status or gag reflex but can also occur in patients without these problems. Radiographic confirmation is therefore highly recommended when tubes are placed or repositioned blindly. An advantage of nasogastric and nasoenteric tubes versus percutaneous tubes, which are

discussed next, is that the tubes can be easily removed when tube feeding is no longer needed. Orogastric and oroenteric tubes are occasionally used for short-term therapy with the main indications being facial or nasal injury, nasal deformity that precludes nasal tube placement, and the presence of sinusitis.

Patients who require long-term tube feeding often prefer a percutaneous feeding tube that is less visible and more comfortable than a nasal or oral tube. Insertion options for percutaneous feeding tubes include endoscopic, radiologic, and surgical (laparoscopic or open) techniques. Recently, it has been suggested that the terms transoral or transabdominal access be used to further describe how the feeding tube is brought into position with either the endoscopic and radiologic techniques. All three techniques can be used to place a tube into the stomach that is generally referred to as a gastrostomy tube. When it is placed it may be referred to as a percutaneous endoscopic gastrostomy (PEG). Tubes that are placed into the stomach with a portion of the tube being advanced through the pylorus into the proximal small bowel are used to provide feeding into the small bowel and simultaneous decompression of the stomach. They can be placed using all three techniques and are referred to as gastrojejunostomy tubes. Percutaneous feeding tubes placed directly into the jejunum, or jejunostomy tubes, are most often placed using

an endoscopic or surgical approach as radiographic placement is technically challenging. These tubes are preferred when gastric decompression is not needed or when the end of a gastrojejunostomy tube cannot be maintained in the small bowel. Percutaneous feeding tube placement carries some risks that include bleeding, wound infection, bowel perforation, obstruction, and the risks of anesthesia. However, these risks are minimized when an experienced physician is performing the procedure and the patient's clinical and nutritional status is not severely compromised.

Feeding into the stomach is the most physiologic way to deliver tube feeding as it allows feeding to be administered intermittently. It also requires the least amount of equipment to administer feeding which makes this approach less costly and more convenient than feeding into the small bowel. Gastric feeding tubes are used in the majority of patients who receive home tube feeding. Small bowel feeding tubes, which are ideally placed past the ligament of Treitz, are used for patients with delayed gastric emptying or gastric outlet obstruction. Additional conditions where this approach might be favored include patients with tracheal aspiration, reflux esophagitis, previous gastric surgery, early post-operative feeding, and where gastric feeding is poorly tolerated. Feeding beyond the ligament of Treitz has been shown to minimize stimulation

of the exocrine pancreas and is currently considered the favored route for providing nutrition support to patients with severe acute pancreatitis. Although controversial, many clinicians feel that small bowel tube feeding may decrease the risk of aspiration and will therefore use this approach to minimize the risk of aspiration pneumonia.

Administering Tube Feeding

Tube feeding schedules should be designed around the patient's clinical condition, physical activity, and the feeding access. Tube feeding can be administered as a bolus, as a gravity drip, or continuously for an extended length of time. Bolus feedings are defined as formula delivered via a syringe over approximately 15 minutes. Gravity drip feedings, sometimes referred to as intermittent feedings, are delivered using tubing outfitted with a roller clamp to control the rate of infusion. Gravity drip feeds are typically infused over 30 to 45 minutes. These two feeding techniques should only be administered via a gastric feeding tube because of the stomach's ability to accommodate a large volume. In general, bolus feeding is preferred for patients with gastrostomy tubes in the home setting as it allows them to follow a meal pattern, requires a minimal amount of equipment, and allows the greatest degree of flexibility while managing other routines of daily living.

Small bowel tube feeding should be administered with a feeding pump to allow prolonged constant infusion to minimize feeding intolerance. Feeding by this method is typically done over 8 to 24 hours. Patients who are critically ill often have abnormal GI motility and may require feeding over 24 hours to receive their entire tube feeding prescription, while patients who are less ill and often more mobile are good candidates for tube feeding that is infused more quickly over a shorter length of time. While the continuous feeding method is always done for patients with jejunostomy feeding tubes, this technique may also be used for patients with gastrostomy tubes who do not tolerate bolus or intermittent feedings. In patients who are being transitioned to oral intake, tube feeding is sometimes administered continuously overnight to limit appetite suppression that can occur when eating and tube feeding is done simultaneously.

In order to allow for GI adaptation to tube feeding, continuous tube feeding is generally initiated at 10 to 30 mL/h. The feeding volume is then increased by increments of 10 to 20 mL/h every 6 to 12 hours, depending on tolerance. Intermittent or bolus feedings are usually initiated at 60 to 120 mL and then advanced as tolerated to the goal volume. Mild bloating and loose bowel movements are common when tube feeding is initiated. If the patient shows any signs of severe intolerance to

the feeding, such as diarrhea, elevated gastric residuals, or vomiting, the administration should not be sustained and may be discontinued temporarily while the patient undergoes appropriate clinical evaluation.

Monitoring

Once tube feeds are initiated, monitoring is important to ensure that adequate nutrients are provided and to help prevent complications or manage them soon after they arise. A combination of physical assessment, laboratory data, and assessing GI function are used when determining patients' tolerance to tube feeds.

Feedings received should be compared to prescribed calorie and protein goals. Adjustments in prescriptions should be made for changes in clinical status or activity. Calories and carbohydrate provided from tube feeding and other sources such as intravenous fluids should be routinely monitored and adjusted to avoid the complications due to overfeeding. In critically ill patients, especially those with underlying pulmonary disease or recent injury, excessive carbon dioxide production caused by overfeeding can cause difficulty in ventilator support and weaning. If a patient is not responding appropriately to the tube feeding prescription, indirect calorimetry can be used to better define energy needs. In order to monitor hydration, it is important to

evaluate fluid intake/output and daily weights, especially in hospitalized patients. A rapid change in weight may suggest an alteration in hydration and should prompt further investigation. It is often helpful to establish a target weight for patients who require tube feeding outside of the hospital to ensure that they are receiving an appropriate calorie prescription. In many instances, patients who have been ill and lost weight need to achieve their pre-illness weight to fully recover. In patients who are overweight or obese, it may be desirable to promote gradual weight reduction for its many health benefits. Weight loss can be achieved by targeting energy intake modestly below requirements while providing a sufficient amount of nitrogen to promote wound healing and hepatic protein production. The patient's strength and feeling of wellbeing is another important indicator of adequate nutrient delivery. Finally, continued need for nutrition support should be routinely reevaluated.

Evidence for GI intolerance includes diarrhea, constipation, vomiting, abdominal distention, pain, tenderness, and elevated gastric residual volume (GRV). Patients with these signs and symptoms may need to be assessed for other conditions such as medication side effects, paralytic ileus, structural abnormalities of the GI tract, and *Clostridium difficile* infection. If these conditions are excluded and symptoms persist, adjustment of the rate of tube feeding

delivery or use of an alternative formula may be considered to improve tolerance. GRV is checked every 4 to 8 hours for patients being fed continuously into the stomach or just prior to bolus and gravity drip administration. It is considered abnormal if the volume is greater than 500 mL. Tube feeding should be held while the patient is assessed and the use of a promotility agent can be considered if it occurs on more than a few occasions. A small bowel feeding tube may be indicated if GRV is found to be repeatedly elevated.

A basic metabolic panel, including blood glucose, should be obtained every 1 to 2 days for hospitalized patients, especially at the start of therapy. Patients at risk for refeeding syndrome should receive approximately half of their nutrient requirements for 3 to 5 days and have their serum potassium, magnesium, phosphorus, and calcium checked daily before they are advanced to full feeding. Patients with diabetes mellitus or stress-induced hyperglycemia should have their blood glucose checked 3 to 4 times daily or more often if they are being managed with an insulin drip by protocol. Abnormalities in these laboratory measures should be corrected, and if severe, may require temporary reduction or discontinuation of tube feeding.

Complications

As with all medical therapies, tube feeding is associated with risks. These risks can be divided into three categories: GI, metabolic, and mechanical. GI complications include nausea, vomiting, diarrhea, and constipation. Metabolic complications include dehydration, electrolyte abnormalities, and blood glucose abnormalities. Mechanical complications are most often related to feeding tube placement and maintenance, but also include aspiration pneumonia. This section will focus on some of the GI and mechanical complications as management of the metabolic complications has already been discussed.

The most commonly reported GI complication for tube feeding patients is diarrhea. The tube feeding formula rarely causes this. Likely causes of diarrhea include medications, *C. difficile* colitis, underlying or unrecognized GI disorders, and sometimes the rate of tube feeding delivery. If a patient develops diarrhea while receiving tube feeding, it is important to evaluate all the potential causes and treat them appropriately. Medications that may cause diarrhea include antibiotics and elixirs that contain sorbitol (Table 12-2). Antidiarrheal medications that prolong intestinal transit may be used to control diarrhea but should only be used after *C. difficile* is excluded to avoid toxic megacolon. Constipation is a common

complication for patients who have been on tube feeds for a long time. High doses of pain medications and immobility can also cause constipation. Fiber-containing formulas and adequate water are most useful in preventing constipation in this population.

Table 12-2 Examples of Medications Associated with Diarrhea

Source: Jill Murphree and Douglas Seidner. 2014. Used with permission.

Sorbitol-containing medications
Propranolol solution
Acetaminophen elixir
Cimetidine solution
Ranitidine syrup
Bactrim suspension
Furosemide solution
Antibiotics
Ampicillin
Amoxicillin
Clindamycin
Tetracycline
Cephalosporins
Others
Potassium oral solutions

Oral phosphate supplements
Magnesium-based antacids
Promotility agents
Solubilizers such as propylene glycol and polyethylene glycol

Dehydration can occur when patients do not receive adequate fluid via tube feeding, additional water flushes through the tube, or intravenous repletion. The average water requirement for an adult patient is 30–40 mL/kg. Patients on diuretic therapy and those with unusual losses from drains, stool output, or emesis are at risk for dehydration. Routine monitoring of clinical status including weight, blood pressure, heart rate, and laboratory measures will help to identify dehydratoin before it becomes critical.

Aspiration is another potential complication for patients on tube feeds. Proper precautions to prevent aspiration from occurring include: elevating the head of the bed to 30 degrees or greater while the feeding is administered, monitoring for high GRV, use of post-pyloric feeding tubes in high-risk patients, and adequate airway management (Table 12-3). Monitoring endotracheal aspirates for pH and glucose concentration in critically ill patients have been used in the past to detect subclinical tracheal aspiration to reduce the incidence of aspiration pneumonia; however, close

investigation of these techniques have found them to lack sufficient sensitivity or specificity to be of clinical value.

Table 12-3 Aspiration Precautions

Source: Jill Murphree and Douglas Seidner. 2014. Used with permission.

Elevate the head of the bed to at least 30–45°.
Monitor for aspiration contents in the lungs.
Direct observation.
Monitor gastric residuals (>500 mL warrants holding tube feeding and considering promotility agents)
Consider use of dual lumen tubes when gastric emptying is poor or aspiration risk is high (small bowel feeding with continuous gastric decompression).
Monitor feeding tube placement.
Radiography.
Auscultation of insufflated air.
Observation of fluid pulled from the feeding tube.
Check pH of fluid aspirated from the tube.
Monitor and maintain adequate airway cuff pressure.

Mechanical tube complications can include tube placement into the lungs, tube occlusion, tube migration, tube breakage or leakage, buried bumper syndrome, and nasopharyngeal or esophageal irritation. Tube placement into the lungs can lead to pneumothorax, pneumonia, or hydrothorax if the tube feeding is delivered into the lung or pleural cavity. Radiographic confirmation of tube position is necessary when a nasal or oral tube is placed blindly. Some authorities have suggested that blind placement should be abandoned. Patients may pull out nasal feeding tubes either intentionally or inadvertently. It is important to secure feeding tubes in place either with tape or the use of a bridle system when patients are confused or agitated. Percutaneously placed tubes can be displaced as well. If this occurs in a tube with a well-healed enterocutaneous tract, a new or temporary tube should be placed in the tract as soon as possible because the tract can close quickly. Tube replacement through a tract that is less than 4 weeks old must be done cautiously to avoid disruption of the tract and misplacement of the tube into the peritoneal cavity. If a percutaneously endoscopic gastrostomy (PEG) is dislodged soon after initial placement it must be managed as a gastric perforation as the PEG method usually does not include suture fixation of the stomach to the abdominal wall. Feeding tubes can become clogged when water flushes are

inadequate or medications are inappropriately administered in the feeding tube.

It is recommended that feeding tubes be flushed daily and at any time the feeding is stopped or a medication is administered. Medications should be in a liquid form whenever possible and the tube should be flushed with water after each separate medication administration (Table 12-4). Although many beverages and solution are used to flush feeding tubes to resolve occlusion, the only ones that have been proven to be effective are warm water, pancreatic enzymes with sodium bicarbonate, and commercially available products that have been specifically designed for this task. It is popular to use colas and cranberry juice to unclog occluded feeding tubes; however, the acidity of these beverages can result in coagulation of protein in feeding formulas and may make tube occlusion worse. Enteral misconnection, the inadvertent connection of an enteral administration feeding set to a parenteral access device, is a complication that often leads to serious patient harm or death. Most, but not all enteral and parenteral tubing connectors are physically incompatible to help avoid this problem. However, since there is no universal standard for these devices in this country the complication does occur, albeit rarely, and thus requires meticulous nursing care, especially in

patients who receive medications and nutrition support by various routes.

Table 12-4 Administering Medication Through a Feeding Tube

Source: Jill Murphree and Douglas Seidner. 2014. Used with permission.

Use liquid form of medication whenever possible
Consult pharmacy on availability of liquid medication and if tablets are crushable
If crushing a medication, crush finely and disperse in warm water if clinically appropriate
Flush the feeding tube before and after each medication
Consult pharmacy on the timing of medications in relationship to the feeding to avoid drug–nutrient reactions
Consult pharmacy before administering drugs through a small bowel feeding tube. Some medications require the acidic stomach pH for proper action
Medications should not be mixed with enteral formulas
Do not crush enteric coated, sustained released or timed-released tablets or capsules
Do not mix medications together

Conclusion

Tube feeding offers a method of nutrition support to patients who are unable to consume adequate nutrition but have a functional GI tract. There are many advantages to tube feeding over parenteral nutrition and therefore it should be used whenever feasible and clinically safe. There are a wide selection of formulas, tubes, and administration methods. Detailed assessment of the patient's clinical condition, nutrient requirements, and activity will direct selection of feeding route, formula, and administration method. Monitoring metabolic, mechanical, and GI tolerance to tube feeding will guide adjustments in tube feeding therapy. Following these principles, tube feeding can support patients successfully for as long as the therapy is indicated.

Case 1 Enteral Feeding and Esophageal Cancer

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Objectives

Understand how to assess the nutritional status of patients with esophageal cancer.

Review the nutrition-related metabolic abnormalities that can affect patients with cancer.

Identify appropriate dietary recommendations for patients with odynophagia due to radiation therapy.

Understand indicators enteral nutrition support and methods for metabolic monitoring of patients receiving.

Recognize the benefits of enteral nutrition support in a patient receiving radiation therapy to the head and neck.

EM is an 85-year-old white female inpatient at a university hospital. She presented with a 32 pound weight loss over the past 3 months due to dysphagia (difficulty swallowing) and loss of appetite and has recently been diagnosed with esophageal cancer. EM is now status-post esophagectomy with jejunostomy tube placement. Chemotherapy and radiation therapy are planned. During this hospitalization, a swallowing study was performed to rule out a post-operative leak and to assess whether it was safe for EM to resume

eating and drinking. After she passed the swallowing test, a liquid diet was initiated, and she was eventually advanced to a regular diet as tolerated. However, she continues to feel afraid to eat, and has been consuming mostly liquids. Although her appetite has been improving, she says she is still “afraid of the food getting stuck, and choking” as it had prior to her surgery.

Past Medical History

EM's PMH includes hyperlipidemia, emphysema, and GERD.

Medications

EM “does not like to take medications.” EM's current medications include only sucralfate and a multivitamin.

Social/Diet History

EM lives alone, is divorced, and has no children. She has a remote history of smoking and alcohol abuse (she quit smoking and decreased her alcohol intake 30 years ago). She continues to drink a glass of wine in the evening. EM smoked a pack of cigarettes per day for 35 years (35 pack-year history). EM's dysphagia worsened over the past 3 months, she had anorexia, and her oral intake became very poor. She basically stopped cooking due to fatigue, saying that she was “sleeping most of the day.” She declined the offer of

home-delivered meals after post-surgical discharge. She says that she has groceries delivered by her local grocery store. She reports limiting her intake mostly to water and smoothies over the past month. She declined to take an appetite stimulant.

Review of Systems

General: Severe fatigue, weight loss

Gastrointestinal: Poor appetite, dysphagia, odynophagia

Neurologic: No sensory loss

Musculoskeletal: No muscle or joint pain

Physical Examination

Vitals Signs

Temperature: 99.0 °F (37.2 °C)

Heart rate: 80 BPM

Respiratory rate: 18 BPM

Blood pressure: 120/80 mmHg

Height: 5′1½″ (156 cm)

Current weight: 93 lb (42 kg)

Usual body weight: 125 lb (57 kg)

BMI: 17 kg/m^2

Percent weight change: Loss of 32 pounds, or 26 percent change over 3 months: [(125 – 93)/125] × 100

Exam

General: Cachectic appearing female in no acute distress

Head/neck: Bilateral temporal wasting

Cardiac: Regular rate and rhythm; no rubs, gallops, or murmurs

Chest: Status-post esophagectomy with clean, dry, and intact wound site

Abdomen: Soft, non-tender, non-distended; bowel sounds present; jejunostomy; tube site clean and dry

Extremities: 2+ left ankle edema. Trace right ankle edema; general decrease in muscle mass

Neurologic: Alert and oriented to person, place, and time; no abnormalities noted

Laboratory Data

Patient's Values	Normal Values
Albumin: 3.2 g/dL	3.5–5.8 g/dL
Hemoglobin: 11.4 g/dL	13.5–17.5 g/dL
Hematocrit: 33.4%	40–52%
BUN: 5 mg/dL	10–20 mg/dL

Patient's Values	Normal Values
Creatinine: 0.5 mg/dL	0.8–1.3 mg/dL
Potassium: 3.5 mmol/L	3.5–5.3 mmol/L
Sodium: 133 mmol/L	133–143 mmol/L

Go to Questions 1–2

Follow-Up Description

EM was discharged from the hospital, having successfully advanced from liquids, to soft solids, to a regular oral diet during her admission. Working on her swallowing with the speech therapist helped lessen her fear of choking. Her jejunostomy tube was not removed because in 4 weeks she would be receiving chemotherapy and radiation therapy that could adversely affect her appetite and oral intake. EM was instructed to flush her jejunostomy tube daily with 60 cm^3 of water to keep it patent (open). Four weeks later, EM began receiving concurrent radiation and chemotherapy, and after 2 weeks of these treatments, she developed severe odynophagia (painful swallowing). As a result, her oral intake greatly diminished. Based on a 24-hour recall and usual intake over the past week, EM reported consuming only half a cup of flavored gelatin, 6 ounces of applesauce, and one yogurt and fruit smoothie daily, which totals about 400 calories per day with inadequate protein, vitamins, and minerals.

Go to Questions 3–8

Case Questions

What factors are helpful in diagnosing malnutrition in this patient?

What nutritional and nutrition-related metabolic abnormalities can affect patients with cancer?

What are the possible adverse effects of radiation therapy for esophageal cancer patients and how can they affect EM's nutritional status?

In general, what dietary recommendations alleviate odynophagia, as experienced by a patient receiving radiation therapy for esophageal cancer?

What alternative feeding options are available for EM?

How should an enteral formula be selected and what issues related to fluid balance should be considered?

What clinical and laboratory parameters should be monitored for patients who receive tube feeding?

EM asks how long enteral nutrition support is planned. What factors determine when EM's jejunostomy tube can be removed?

Answers to Questions: Case 1

Part 1: Diagnosis

1. What factors are helpful in diagnosing malnutrition in this patient?

Based on EM's medical history, she has had a decreased appetite and dysphagia for the past 3 months, with worsening dysphagia over the past 6 weeks. Her diet is inadequate in protein, calories, vitamins, and minerals, which has contributed to EM's severe, involuntary weight loss of 26 percent of her body weight over the past 3 months. In addition, her BMI is only 17 kg/m^2, indicating that she is currently underweight. A BMI less than 18.5 before the start of treatment relates to overall survival in patients with head and neck cancers. Symptoms, such as anorexia and dysphagia, which are present before diagnosis, have been shown to cause a decrease in dietary intake, weight, and functional capacity of patients. Additional evidence that supports a diagnosis of malnutrition includes her cachectic appearance and temporal wasting found on physical examination. Laboratory data shows a decreased albumin level of 3.2 g/dL. Although hypoalbuminemia is often used as a nutrition indicator in clinical practice, its lack of sensitivity and specificity for nutritional changes limit its clinical use as an indicator of functional nutritional status.

At the time of diagnosis, as many as 75 percent of cancer patients are malnourished, which ultimately increases their morbidity and mortality. It is estimated that about a third of all cancer patients die from the effects of malnutrition and its complications, rather than from the malignancy itself. For EM, placement of a J-Tube at the time of her esophagectomy will provide enteral access as she was at risk for eating challenges after surgery, and during adjuvant chemoradiation therapy.

2. What nutritional and nutrition-related metabolic abnormalities can affect patients with cancer?

Patients with cancer and those undergoing treatment can experience symptoms that decrease oral intake, such as anorexia, dysphagia, alterations in taste and smell, mouth sores, and obstruction of the GI tract, which can be caused by tumor growth. Weight loss is not only driven by a decrease in intake of nutrients, but also by an alteration in metabolism due to the release of cytokines, including tumor necrosis factor and interleukins. This increased metabolic rate combined with a reduced food intake, can contribute to a severe, rapid weight loss in cancer patients. Psychological factors, such as depression and anxiety, and a lack of social support may also contribute to decreased appetite and oral intake.

Tumor-induced pathophysiological changes in normal metabolism, changes in body composition, and severe weight loss seen in some cancer patients is known as cancer cachexia. Cachexia is most prevalent among patients with gastrointestinal cancers. In addition to unintentional weight loss, other common manifestations of cancer cachexia are muscle wasting, anorexia, anemia, altered immune function, inflammation, and insulin resistance, which can contribute to increased fatigue and diminished quality of life.

Go to Follow-up Description after Laboratory Data

Part 2: Medical Nutrition Therapy

3. What are the possible adverse effects of radiation therapy for esophageal cancer patients and how can they affect EM's nutritional status?

Patients with head and neck cancer are at particularly high risk of malnutrition during radiation therapy. Radiation therapy for esophageal cancer can cause odynophagia, nausea, vomiting, dysphagia, problems with digestion, malabsorption, enteritis, fatigue, and anorexia. Each of these effects can significantly diminish EM's oral intake and affect her nutritional status.

4. In general, what dietary recommendations alleviate odynophagia, as experienced by a patient receiving radiation therapy for esophageal cancer?

For odynophagia, the patient should be advised to avoid foods with extreme temperatures; cool or room temperature foods are often better tolerated. Patients should also avoid foods that are spicy, salty, tart, or acidic; raw fruits and vegetables; dry, coarse, or sharp food; as well as alcohol and tobacco. Small bites of soft, moist, blended foods such as casseroles, mashed potatoes, soups, scrambled eggs, and yogurt are well tolerated. Pureeing foods in a blender or food processor may be necessary. Gravies, sauces, and broths may be added to foods to moisten them for easier swallowing. Small, frequent meals, and liquid nutritional supplements are helpful to increase energy and nutrient intake. Drinking through a straw may be more comfortable.

5. What alternative feeding options are available for EM?

Because of severe odynophagia resulting from radiation therapy, EM is not consuming adequate energy and nutrients. Therefore, she may continue to lose weight and become more malnourished if she relies on oral intake alone to provide her with adequate nutrition. Since her radiation therapy is planned for several

more weeks and she has a functional GI tract, she is a candidate for enteral nutrition support using her jejunostomy as a (long-term feeding) tube. After determining her caloric and protein goals, an enteral formula that best meets these goals should be chosen to supplement her oral intake. She should be encouraged to continue to try to consume foods by mouth as tolerated. Studies have shown that survival was significantly better for head and neck patients with continued oral intake, suggesting that clinicians should emphasize at least some oral intake as tolerated throughout treatment. As her oral intake decreases during treatment, tube feeds can be increased accordingly, to meet her estimated nutritional needs for energy and protein. Academy of Nutrition and Dietetics Oncology Guidelines, states that enteral nutrition can maintain weight by providing energy and protein for patients with stage III or IV head and neck cancer receiving intensive radiation therapy. However, although starting enteral nutrition earlier and using it longer was associated with fewer malnourished patients and improved health-related quality of life in one study, routine use of enteral nutrition following esophagectomy has not been shown to increase tolerance to therapy or survival in patients with esophageal cancer.

6. How should an enteral formula be selected and what issues related to fluid balance should be considered?

There are a variety of enteral formulas available, each of which provides different concentrations of macro- and micronutrients to meet patients' requirements. The enteral formula for EM should be selected based on her estimated energy and protein needs for weight gain and nutrient repletion, the function of her GI tract and its ability to digest and absorb nutrients, and her current oral intake. In most cases, a standard polymeric enteral formula will be well tolerated. Patients with severe enteritis may require an elemental enteral formula. There is insufficient amount of evidence to recommend enteral formulas that contain omega-3 fatty acids or other immuno-enhancing nutrients in this patient population. Gastric feedings can be provided either as continuous, intermittent, or bolus feeds. However, jejunal feedings, such as in the case of EM, should be given continuously or cycled with a controlled volumetric rate using a pump. Patients at home should be considered for nocturnal cycled infusions, so that they can be free of the pump during the daytime hours and can focus on eating.

Fluid balance is important to consider, particularly when enteral nutrition is the sole source of fluid intake. It is important to monitor fluid status in all patients receiving tube feedings in order to prevent dehydration. Fluid loses from diarrhea, vomiting, ostomies, fistulas, and drains can increase fluid

requirements. Patients may require additional fluid if the enteral formula is enriched with fiber or high in protein. If the patient cannot or does not consume adequate fluids orally, and if the tube-feeding regimen does not supply enough water to meet patient's fluid requirements, additional fluid can be provided with water flushes through the feeding tube several times throughout the day.

7. What clinical and laboratory parameters should be monitored in patients receiving tube feeding?

It is very important to monitor patients for tube feeding tolerance, hydration, electrolytes, and nutritional status. Physical symptoms that should be monitored include incidence of nausea, vomiting, stool frequency, diarrhea, and abdominal pain. Physical examination should include assessing abdominal distention or tenderness and evidence of edema or dehydration. Weight changes should be noted. In addition, serum electrolytes (sodium, potassium, chloride, bicarbonate), calcium, magnesium, phosphorous, BUN, creatinine, and glucose should be monitored daily when the patient begins receiving enteral nutrition support. While serum proteins are often used as makers of nutritional status. Acute phase reactant proteins, such as albumin, prealbumin, transferrin, and retinol binding protein should not be used alone to assess nutritional status, as

they are decreased with inflammation. Other acute phase proteins such as C-reactive protein (CRP) are elevated in the presence of inflammation. In an article published in Journal of Parenteral and Enteral Nutrition, Davis reported that, “prealbumin may not be a sensitive marker for evaluating the adequacy of nutrition support in critically-ill patients with inflammation.” Used together, CRP and prealbumin may be more useful in showing trends; if CRP is within normal limits, prealbumin may be more reflective of nutritional status.

It is important to note that in the first few days of initiating tube feeding, malnourished patients such as EM may exhibit a refeeding syndrome in which extracellular to intracellular electrolyte shifts of potassium, phosphorous, and magnesium may occur, requiring prompt repletion. Initiating enteral nutrition at a low rate with gradual advancement based on tolerance and electrolyte levels can reduce the risk of refeeding syndrome.

Once the patient is metabolically stable, the frequency of monitoring can be decreased as appropriate. The adequacy of energy and nutrients in the tube feeding can be assessed by stabilization or increase in weight, depending on the patient's clinical goals.

8. EM asks how long enteral nutrition support is planned. What factors

determine when EM's jejunostomy tube can be removed?

After her radiation therapy is completed, as EM's odynophagia decreases and her oral intake improves, the tube feedings should be decreased. Upon follow-up 2 weeks after radiation therapy was completed, EM reports less odynophagia. She has been able to increase her oral intake. She followed up with a dietitian who offered suggestions and recipes for high-calorie, high-protein, soft, easy-to-swallow foods. She was therefore instructed to decrease her tube feeding regimen through the jejunostomy tube since her oral intake had greatly improved. The patient's weight began to increase with adequate nutritional intake.

Two weeks later, she was able to further increase her oral intake and began to drink two cans (480 cm^3) of an oral nutritional supplement daily for additional energy and nutrients. An 8-ounce can of this supplement (240 cm^3) provides about 13 g of protein and 350 total calories along with vitamins and minerals. Since her oral intake was deemed adequate to meet her nutritional needs, and she was able to maintain her weight without supplementing with tube feeding, her tube feeding regimen was discontinued. She was monitored for 4 weeks off tube feeding. Her oral intake remained excellent and she continued to gain weight. Since no further

radiation therapy was planned, the decision was made to remove the feeding tube.

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Nutritional Content of Tube Feeding Formula

The type and quantity of protein, carbohydrate, and fat varies among tube feeding formulas. The amount of protein contained in a tube feeding formula can range from 8 to 25 percent of total calories. Nitrogen can be supplied as whole protein, partially hydrolyzed protein (peptides), or fully hydrolyzed protein (free amino acids). Individual amino acids, such as glutamine and arginine, have recently been added to some specialized formulas along with whole protein in order to promote immune function and improve bowel integrity.

Carbohydrate is the primary energy source in standard enteral formulas. The amount of carbohydrate in a tube feeding formula can range from 27 to 70 percent of total calories. Carbohydrate sources come from large molecules such as glucose oligosaccharides, maltodextrin, and hydrolyzed cornstarch. Smaller molecules such as mono- and disaccharides may be used and require a smaller amount of pancreatic enzymes and intestinal mucosal disaccharides for adequate digestion. Most commercially made tube feeding formulas are lactose and gluten free but some supplements designed for oral intake and infant formulas may contain lactose.

Fat is included as a component in tube feeding formulas to provide a concentrated energy source and essential fatty acids. The amount of fat in a tube feeding formula can range from 10 to 55 percent of total calories. Formulas typically contain a combination of long-chain triglycerides (LCT) and medium-chain triglycerides (MCT). LCT is more calorically dense than MCT (9 kcal/g versus 8 kcal/g) and is the only source of essential omega-6 polyunsaturated fatty acids. Omega-3 polyunsaturated fatty acids have been added to some specialized tube feeding formulas for their anti-inflammatory properties. LCT fats require an intact digestive tract for maximal absorption. Sources of LCT are primarily soybean and corn oil; however, safflower, canola, and fish oils are also used. MCT is easier than LCT to process as they are more miscible in water, are more readily hydrolyzed by pancreatic enzymes, do not require chylomicron formation, are transported directly to the liver through portal circulation, and are rapidly metabolized as fuel when they reach the liver. Sources of MCT include palm kernel and coconut oil.

Some tube feeding formulas contain added fiber (4 to 20 g/L), usually as a mixture of both soluble and insoluble fibers. Fiber helps normalize bowel function by increasing stool bulk and by indirectly providing energy for colonocytes. Soluble fibers are metabolized by

the intestinal flora of the colon which produce the short-chain fatty acids acetate, proprionate, and butyrate. Butyrate is the primary fuel of the colonocyte and as a result can improve absorptive function of the colon and lead to restitution of injured and inflamed mucosa. Short chain fatty acids lower the intraluminal pH of the colon and promote the growth of intestinal flora which helps protect against pathogenic strains of bacteria. Dietary fibers that lead to a favorable change of the intestinal flora are referred to as prebiotics. Fructooligosaccharides (FOS) and inulin are the soluble fibers that are added to tube feeding products because of their prebiotic effects. Fiber does however increase the viscosity of formulas and can contribute to the clogging of feeding tubes. As a result, it is best to administer fiber-containing formulas through a larger tube (≥8 ft) to avoid tube clogging.

Vitamins, minerals, and trace elements are also included in standard tube feeding formulas. Most formulas meet the United States Dietary Reference Intake (DRI) for these nutrients in 1.0 to 1.5 liters of formula. A vitamin and mineral supplement is appropriate for patients receiving less than the necessary volume to meet the requirements. Antioxidant vitamins (vitamin C and E) have been added to formulas to support specific diseases associated with oxidative stress such as inflammatory bowel disease and acute respiratory distress syndrome

(ARDS). Tube feeding formulas also contain 70 to 85 percent water. In general, tube feeds are not meant to provide full hydration for a patient and additional fluid should be given as water flushes through the feeding tube or by the intravenous route.

13
Parenteral Nutrition Support

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Objectives*

Describe the indications and contraindications for parenteral nutrition support.

Determine the composition of parenteral nutrition formulas and how the macronutrient, micronutrient, and fluid requirements are calculated.

Describe appropriate methods for monitoring and management of the complications associated with parenteral nutrition support.

Describe indications for home parenteral nutrition support and the associated long-term complications.

*Source: Objectives for chapter and cases adapted from the *NIH Nutrition Curriculum Guide for Training Physicians*. (www.nhlbi.nih.gov/funding/training/naa)

Parenteral nutrition (PN) is a complex admixture of amino acids, dextrose, fat emulsions, water, electrolytes, vitamins, minerals, and trace elements. It is provided for patients whose gastrointestinal (GI) tract is not functional, accessible, or safe to use and is infused via peripheral or central veins. The exact route of administration will depend on the length of therapy, nutrition requirements, goal of nutrition therapy, availability of intravenous (IV) access, severity of illness, and fluid status.

Indications for PN

Enteral nutrition (EN) is always preferable over PN due to its expense and potential for serious complications. PN should be used only when enteral feedings are not possible in patients who require nutrition support. The following conditions may warrant the use of PN.

Paralytic ileus

Mesenteric ischemia

Small bowel obstruction

High output enterocutaneous fistula

Severe GI bleed

Lack of enteral access

GVHD of the gut

Short bowl symdrome

Radiation enteritis

According to the 2009 *American Society of Parenterl and Enteral Nutrition* (ASPEN) guidelines for the provision of Nutrition Support Therapy in the Critically Ill Adult, PN should be initiated 5 to 7 days pre-operatively if a patient is malnourished; PN should not be initiated until 5 to 7 days post-operatively if EN is not feasible; PN should not be initiated unless the anticipated duration is ≥7 days.

Components of PN

Amino Acids

The primary function of amino acids in PN solutions is to maintain or improve nitrogen balance and promote maintenance of lean body mass. Parenteral amino acids are provided in the form of crystalline amino acids and contain a mixture of essential and non-essential amino acids providing 4 calories per gram. The concentration of amino acids in these solutions ranges from 3 to 20 percent. Thus, a 10 percent solution of amino acids supplies 100 g of

protein per liter. In general, 15 to 20 percent of the total energy prescription should be supplied as protein; however, this may differ based on tolerance, clinical status and disease state.

Carbohydrates

Carbohydrates are provided as an energy substrate and are supplied as dextrose monohydrate in concentrations ranging from 2.5 to 70 percent. A 10 percent solution yields 100 g of carbohydrate per liter of solution. Dextrose monohydrate used in PN solutions yields 3.4 calories per gram. The use of carbohydrate ensures that protein is not catabolized for energy during conditions of normal metabolism. Higher dextrose concentrations, usually greater than 10 percent, are used when central access is available as thrombophlebitis may occur in a peripheral vein.

Metabolic stress is characterized by insulin resistance, hyperglycemia, and impaired glucose oxidation. When glucose oxidation rates are exceeded, fat synthesis will occur, which may generate excessive CO_2. This may contribute to CO_2 retention in patients with respiratory disease. In addition, exceeding glucose oxidation rates may also contribute to hepatic steatosis or fat deposition in the liver. Therefore, dextrose infusion should be limited to 7 mg/kg per minute in stable hospitalized

patients and greater than 4 mg/kg per minute in the critically ill. Consideration should be given to the dextrose content of other intravenous fluids, which may be infusing simultaneously.

Lipids

Intravenous fat emulsions (IVFE) supply lipids, which are a source of essential fatty acids (EFAs) and a concentrated source of calories. In addition, the use of IVFE may aid in blood glucose control in the hyperglycemic patient.

IVFE are available in 10 and 20 percent concentrations for infusion and 30 percent for compounding. They are composed of aqueous suspensions of soybean or safflower oil, with egg yolk phospholipid as the emulsifier. Patients who are allergic to eggs should not be given IVFE and can be given safflower or sunflower oil topically or enterally. Glycerol is added to make an isotonic solution. A 10 percent emulsion provides 1.1 kcal/mL; a 20 percent emulsion provides 2 kcal/mL; and 30 percent emulsion provides 3 kcal/mL. To prevent EFA deficiency (EFAD), 2 to 4 percent of total calories should be provided from linoleic acid and 0.25 to 0.5 percent of total calories as alpha-linolenic acid.

The high levels of linoleic acid in soy-based lipids produces pro-inflammatory and immunosuppressive effects, particularly at high

doses and at faster infusion rates. A maximum dose of 1 g of lipid per kg per day should be infused to avoid hepatic effects such a steatosis, cholestasis, and/or parenteral nutrition related liver disease (PNALD), which can be seen in long-term PN patients. Daily infusion of lipid should therefore be avoided in long-term PN-dependent patients. However, increasing attention is being brought to alternative sources of fat emulsion such as medium-chain triglycerides, olive oil, and fish oils. Lipid emulsions should not be given in hypertriglyceridemia-induced pancreatitis or when serum triglyceride values are greater than 400 mg/dL.

Fluid, Electrolytes, Vitamins, Minerals, and Trace elements

Once the macronutrient portion of the PN prescription has been established, the day-to-day management centers on fluid and electrolytes. Daily fluid requirements can be estimated from the sum of fluid losses including urine, GI and insensible losses, minus the fluid gains, such as other IV fluids and/or oral intake. Weighing the patient daily is the best means of assessing net gain or loss of fluid. Rapid weight gain or loss (more than 4 pounds (1.8 kg) in 1 week) generally represents fluid changes and not tissue synthesis. Vital signs, such as blood pressure and heart rate, and physical examination changes (e.g., edema,

ascites, and skin turgor) also offer evidence of fluid status. In general, young adults require 30 to 40 mL/kg per day and older adults require 20 to 30 mL/kg per day.

Electrolytes are routinely added to PN solutions in amounts sufficient to provide for daily needs (Table 13-1). Electrolyte requirements will vary depending on the patient's current electrolyte, renal, and fluid status, as well as their underlying disease process. If the patient has been receiving maintenance IV fluids prior to starting PN, it is helpful to note the electrolyte composition of these fluids and use this as a guide to prescribe the PN formula. Patients receiving PN may have higher intracellular electrolyte requirements than patients receiving standard IV fluids.

Table 13-1 Daily Electrolyte Requirements during Parenteral Nutrition in Adults

Source: National Advisory Group on Standards, and Practice Guidelines for Parenteral Nutrition, ASPEN: Safe practices for parenteral nutrition formulations. *J Parenter Enteral Nutr*. 2004; 28(suppl):S38–S70.

Electrolyte	**ParenteralEquivalent of RDA**	**Standard Intake**
Calcium	10 mEq	10–15 mEq
Phosphate	30 mmol	20–40 mmol
Magnesium	10 mEq	8–20 mEq

Electrolyte	ParenteralEquivalent of RDA	Standard Intake
Sodium	NA	1–2 mEq/ kg + replacement
Potassium	NA	1–2 mEq/ kg + replacement
Acetate	NA	As needed to maintain acid-base balance
Chloride	NA	As needed to maintain acid-base balance

NA: Not applicable

Sodium is a major extracellular cation and functions in the maintenance of osmotic pressure and in acid–base balance. The usual dose is 1 to 2 mEq/kg per day. Requirements may be increased when there are excess losses from urine, ostomies, or fistulas or decreased in renal, cardiac, or hepatic failure. See Table 13-2 for electrolyte content of the GI tract secretions.

Table 13-2 Volume and Average Electrolyte Content of Gastrointestinal Secretions

Source	Volume (ml/d)	Na	K	Cl	HCO3
Saliva	1500	10	26	10	30
Stomach	1500	60	10	130	0
Duodenum	100–2000	140	5	80	0
Ileum	3000	140	5	104	30
Colon	500–2000	60	30	40	0
Pancreas	100–800	140	5	75	115
Bile	50–800	145	5	100	35

Source: Langley G. Fluid, Electrolytes and Acid-Base Disorders. In: *The A.S.P.E.N. Nutrition Support Core Curriculum: A Case-Based Approach-the Adult Patient*. Gottschlich MM (editor). American Society for Parenteral and Enteral Nutrition.2007;104–128.

Potassium is the major cation of intracellular fluid. The normal dose is 1 mEq/kg per day. Hypokalemia may result from diuretics, amphotericin B, nasogastric suction, or vomiting. Other medications such as cyclosporine and tacrolimus may cause hyperkalemia. The PN solution should provide maintenance potassium requirements. Acute deficits of potassium should be corrected outside of the PN with an intravenous (IV) replacement dose.

Sodium and potassium may be added to PN solutions in the form of chloride or acetate salts. Chloride is a major extracellular anion and functions in the maintenance of osmotic pressure and acid–base balance. Acetate maybe added to PN solutions when clinically appropriate since it is converted to bicarbonate in the liver and functions as a systemic alkalinizer. Bicarbonate should never be added to PN solutions since it is not compatible with other additives and may form a precipitate.

Calcium is an extracellular cation that is essential for normal muscle contraction, nerve function, blood coagulation, and bone

mineralization. The usual dose is 10 to 15 mEq/day. Sixty percent of serum calcium is bound to protein, primarily albumin. Therefore, in the presence of a low serum albumin level, a low serum calcium level needs to be adjusted for hypoalbuminemia.

$$\text{Corrected total calcium (mg/dL)} = \text{measured total calcium (mg/dL)} + 0.8 \times [4.0 - \text{serum albumin (g/dL)}]$$

This equation provides an estimate of the adjusted calcium level in the presence of hypoalbuminemia. When in doubt and when the serum albumin is less than 2.8 g/dL, an ionized calcium level should be obtained. Along with calcium, phosphorus is the major component of bone hydroxyapatite and teeth. Phosphorus is the primary intracellular anion and functions in the metabolism of carbohydrate, fat, and protein. The usual dose is 20 to 40 mmol/day. The combination of calcium and phosphorus in PN formulas has the potential of forming a precipitate. Thus, the maximum calcium and phosphorus product should be <200 in a PN formula as per the formula below.

$$\text{Calcium-phosphorus product} = \text{mEq Ca/L} \times \text{mEq } PO_4\text{/L}$$

Magnesium functions in enzyme reactions such as glycolysis and in all reactions involving adenosine triphosphate (ATP). Magnesium is often depleted in patients with protein calorie

malnutrition and prolonged IV fluid therapy. The usual dose of magnesium sulfate is 8 to 20 mEq/day. Magnesium sulfate provides 8.12 mEq/g of magnesium.

Vitamins, minerals, and trace elements are essential for humans and should be added daily to the PN solution in order to prevent deficiencies. Since they are provided parenterally and therefore bypass the digestive and absorptive process, the amounts are lower than the Dietary Reference Intakes (DRI). Parenteral vitamins and trace elements are given as standard multiple-vitamin and trace element preparations. In the event that vitamin, mineral, or trace element deficiencies or unusual losses occur, they can sometimes be supplemented above the amount normally added to the PN solution. Tables 13-3 and 13-4 show the daily multivitamin and trace element requirements as well as the common commercially available products.

Table 13-3 Daily Trace Element Requirements

Source: A.S.P.E.N. Board of Directors and the Task Force for the revision of safe practices for parenteral nutrition. *J Parenter Enteral Nutr*. 2004; 28(suppl):S38–S70.

Trace Element	**ASPENRecommendations**	**GI Losses**
Chromium	10–15 µg	20 µg/day

Trace Element	ASPENRecommendations	GI Losses
Copper	0.3–0.5 mg	500 µg/day
Manganese	60–100 µg	
Selenium	20–60 µg	
Zinc	2.5–5.0 mg[a]	Additional zinc[b]

[a] Additional 2 mg/day in hypermetabolic states.

[b] Additional 12 mg/L of small bowel losses and 17 µg/kg of stool or ileostomy losses.

Table 13-4 Adult Parenteral Multivitamins: Guidelines and Products

Vitamin	NAG-AMA Guidelines	FDA Requirements	MVI-12	MVI-13
A (retinol)	3300 units (1 mg)	3300 units (1 mg)	3300 units (1 mg)	3300 units (1 mg)
D (ergocalciferol cholecalciferol)	200 units (5 µg)	200 units (5 µg)	200 units (5 µg)	200 units (5 µg)
E	10 units (10 mg)	10 units (10 mg)	10 units (10 mg)	10 units (10 mg)
B1 (thiamin)	3 mg	6 mg	3 mg	6 mg
B2 (riboflavin)	3.6 mg	3.6 mg	3.6 mg	3.6 mg
B3 (niacinamide)	40 mg	40 mg	40 mg	40 mg
B5 (dexpanthenol)	15 mg	15 mg	15 mg	15 mg
B6 (pyridoxine)	4 mg	6 mg	4 mg	6 mg
B12 (cyanocobalamin)	5 µg	5 µg	5 µg	5 µg
C	100 mg	200 mg	100 mg	200 mg
Biotin	60 µg	60 µg	60 µg	60 µg
Folic acid	400 µg	600 µg	400 µg	600 µg
K	150 µg	0		150 µg

Source: National Advisory Group; American Medical Association; U.S. Food and Drug Administration; MVI-12 and MVI-13, multivitamin injections.

Nutrition Requirements

Determining nutrient requirements is dependent on age, gender, weight, body composition, activity level, and clinical status. In the clinical setting, this can be determined via indirect calorimetry or equations; in the research setting via direct calorimetry. Direct calorimetry measures the release of heat, however, it is expensive and impractical in the hospital setting. Indirect calorimtery (IC) is considered the gold standard in the intensive care patient where most clinicians use a metabolic cart to estimate the resting metabolic rate (RMR), however it is not often used due to its expense and the need for clinical expertise. Equations for the healthy subject such as the Mifflin–St. Jeor are used to estimate energy expenditure. Those equations that are most often used in the critically ill patient include the Ireton–Jones or the Penn State equations as seen in Table 13-5. ASPEN recommends a range of 20 to 35 calories per kilogram of body weight for adults.

Table 13-5 Predictive Equations

Source: Data from Wooley JA, Frankenfield D. Energy. In: Gottschlich MM (Editor). *The A.S.P.E.N. Nutrition Support Core Curriculum: A Case-Based Approach-the Adult Patient*. 2007: The American Society for Parenteral and Enteral Nutrition, pp. 19–32.

Mifflin–St Jeor	Men: Energy expenditure = 5 + 10 (wt in kg) + 6. (ht in cm) – 5 (age) Women: Energy expenditure = –161 + 10 (wt in kg) + 6.25 (ht in cm) – 5 (age)
Ireton–Jones	**Spontaneous breathing** IJEE (s) = 629 – 11(A) + 25(W) – 609(O) **Ventilator-dependent** IJEE (v) = 1784 – 11(A) + 5(W) + 244(S) + 239(T) + 80 where IJEE = kcal/day; s = spontaneously breath v = ventilatory-dependent; A = age (years); W = actual body weight (kg), S = sex (male = 1, female = 0); T = diagnosis of trauma (present = 1 absent = 0); O = obesity greater than 30 percent above IBW from 1959 Metropolitan Life Insuranc Tables or BMI greater than 27 (present = 1, absent = 0).
Penn State (2003b) (<60 years)	RMR (kcal/day) = Mifflin (0.96) + V_E (31) + T_m(167) – 6212 V_E = minute ventilation T_m = maximum body temperature
Penn State 2010 (>60 years)	RMR (kcal/day) = Mifflin (0.71) + V_E (64) T_m(85) – 3085

Routes of Infusion

The components of a PN solution will determine the osmolarity and infusion route. PN can be administered as a total nutrient admixture (TNA) also known as a 3-in-1, which

includes all macronutrients and micronutrients or as a 2-in-1 solution which excludes the IVFE.

Peripheral parenteral nutrition

Peripheral PN (PPN) is usually reserved for patients requiring short-term nutrition support (up to 2 weeks) who are not markedly hypermetabolic or fluid-restricted and have adequate peripheral venous access. Osmolarity should be considered because infusion of a hypertonic solution through a peripheral vein may result in phlebitis. To prevent this, solutions should have less than 900 mosmol/L. Dextrose contributes 5 mosmol/g and amino acids contribute 10 mosmol/g and therefore, are limited, whereas electrolytes provide approximately 1 mosmol/g. PPN is usually lipid-based because not only are IVFE isotonic, they also provide extra calories. PPN usually cannot provide adequate calories and protein in patients who are volume restricted, but can be helpful for several days until GI function returns or central access is obtained. Other contraindications to PPN include significant malnutrition, large nutrient or electrolyte needs, and/or renal or liver compromise.

Central Parenteral Nutrition (CPN)

Central PN which is also known as total parenteral nutrition is indicated in patients requiring long-term therapy or a concentrated formula. The solution may be a 2-in-1 or a

3-in-1 and is infused via a central vein. IVFE can be mixed into the solution or administered separately. Stability of the PN formula becomes a concern with the addition of IVFE due to the presence of destabilizing cations such as magnesium and calcium. The IVFE manufacturer's guidelines should be followed to ensure stability of 3-in-1 formulas. Lipid-based solutions are indicated in situations where restricting carbohydrate load is desirable, such as patients with persistent hyperglycemia. There is no limit on osmolarity of CPN since the solution is rapidly diluted by the high flow rate of blood returning to the heart.

Proper selection of venous access depends on nutrient requirements and length of therapy. For short-term CPN a temporary percutaneous non-tunneled CVC may be used in the acute setting via the subclavian or jugular vein. A peripherally inserted central catheter (PICC) may also be used if CPN is needed for weeks and not long-term. A tunneled catheter such as a Hickman®, Broviac® or Groshong® or implanted port may also be used for long-term access. A chest X-ray should be obtained before using a new CVAD to ensure that the line was correctly placed. The tip of a CVAD should be located in either the middle or distal superior vena cava adjacent to the right atrium to reduce the risk of catheter-related deep venous thrombosis.

Administration

In most institutions, the PN prescription is ordered for a 24-hour period as it results in fewer metabolic complications such as electrolyte abnormalities or hyper/hypoglycemic events.

Medications

Due to the complex nature of PN solutions most medications should not be added as there is potential for instability and incompatibility. However, some medications such as histamine H2 receptor agonists, are used to decrease gastric secretions. Regular short-acting insulin can be added to the PN solution to control blood sugars. Other medications, such as octreotide, heparin, corticosteroids and metoclopramide can be added to the PN solution when needed.

Monitoring and Management of Complications

Non-Infectious Catheter Complications

Heparin-induced thrombocytopenia (HIT) is a severe immune-mediated adverse reaction that occurs by intravascular platelet aggregation that can develop into arterial and venous thrombus. Catheter occlusions can also occur and are classified as either a complete or incomplete

occlusion. In a complete occlusion, fluid cannot be instilled and blood cannot be aspirated out, whereas an incomplete occlusion, fluid can be infused yet blood cannot be aspirated. A venous thrombus can occur if the catheter tip is malpostitioned and can be diagnosed via duplex ultrasound or venogram. A tunneled catheter breakage must be repaired urgently to prevent air embolism, leakage of blood, and bacterial contamination. An air embolism is a rare yet potentially fatal complication where either during or after insertion, there is catheter breakage or a disconnection of caps. Catheter dislodgement can occur with any CVC and move out of central circulation in which case the catheter should be replaced. Pinch-off syndrome refers to the compression of the subclavian vein CVC between the clavicle and first rib resulting in an obstruction of fluid passage through the catheter. An indication of pinch off syndrome is if there is a relief of the obstruction when the patient's arm is elevated. The catheter should be removed to prevent shearing and distal embolization of the pinched off segment,

Septic (Infectious) Complications

During CPN infusion, if there is a sudden change in the patient's usual temperature, in combination with new onset shaking chills, leukocytosis, or unexplained hyperglycemia, the CVC should be viewed as the possible source of

infection. This is known as a catheter-related blood stream infection (CRBSI). CRBSI is a clinical definition, used when diagnosing and treating patients, that requires specific laboratory testing that more thoroughly identifies the catheter as the source of the infection. A central line–associated bloodstream infection (CLABSI) is a primary infection in a patient that had a central line within the 48-hour period before the development of the infection and is not a bloodstream-related infection at another site or seeded by a remote source.

In a temporary CVC, if there is no other obvious source of infection the line should be removed and re-sited. A long-term CVC may be treated *in situ* providing the patient's symptoms improve after antibiotic treatment is started. However, the catheter must be removed if yeast or *Staphylococcus* are cultured. The prevalence of CRBSI can be reduced with proper catheter insertion technique and strict adherence to catheter care protocols.

Metabolic Complications

Hyperglycemia is the most common adverse effect of PN and has been associated with increased morbidity and mortality in hospitalized patients. Close monitoring of blood sugars along with aggressive treatment reduces hyperglycemia and improves outcomes. Capillary blood glucose levels should be

monitored every 6 hours until adequately controlled. Blood sugars in hospitalized patients receiving nutrition support should be maintained between 140 and 180 mg/dL.

To decrease the risk of hyperglycemia the initial dextrose concentration should generally be less than 200 g/day. For patients with diabetes or stress-induced hyperglycemia, initial dextrose concentrations of 100 to 150 g are recommended. In most patients, the goal concentration can be achieved by the second day.

PN-associated hyperglycemia may be treated by insulin drip, short- or long-acting insulin administered subcutaneously, insulin added to the PN or a combination of these methods. In some instances, it may be necessary to reduce dextrose calories and replace with lipid calories to aid in blood glucose control.

Hypoglycemia, defined as a blood glucose concentration of less than 70 mg/dL, may occur if an excessive amount of insulin is added to the PN solution or after abrupt discontinuation of high-dextrose PN infusion. To avoid hypoglycemia, insulin should be added in increments to the PN solution and blood sugars monitored frequently until the appropriate dose is determined. To prevent rebound hypoglycemia, PN infusions should be tapered down over a period of 1 to 2 hours to allow for serum insulin adaptation.

Dehydration and fluid overload are potential complications when PN is the primary source of fluid. Fluid overload or edema may be seen in patients with renal failure, liver failure, congestive heart failure, and hypoalbuminemia. Excessive PN volume can significantly exacerbate fluid retention states. Under these circumstances, a concentrated PN solution may be used. Fluid status should be evaluated daily to determine if the patient is dehydrated or at risk for fluid overload. Monitor intake, output, and body weight records daily. The physical examination should note the presence of edema, rales, ascites, distended neck veins, and other signs of fluid retention.

Electrolyte imbalances may occur in severely stressed patients, both before and after PN begins. It is best to correct any existing electrolyte abnormalities before PN is initiated. Close monitoring of electrolytes, especially potassium, magnesium, and phosphorus during the first few days of PN, is important. Corrections for severe electrolyte imbalances must be made promptly with IV replacements to avoid serious complications such as seizures, arrhythmias, or even death.

Refeeding syndrome may occur when starting PN in a patient after a period of prolonged starvation resulting in fluid retention and hyperglycemia in addition to severe imbalances of serum phosphorus, potassium, and

magnesium. Once PN begins, increased cellular uptake of electrolytes may cause extremely low serum levels. This dramatic shift can lead to generalized fatigue, lethargy, muscle weakness, edema, cardiac dysfunction, and potentially death. The risk of refeeding syndrome can be minimized by initially providing the patient a low-dextrose PN solution for the first several days while closely monitoring phosphorus, potassium, magnesium, glucose, and fluid status (Chapter 4: Case 2).

Transition from PN to EN

EN remains the preferred route of nutrition; therefore, as gastrointestinal function returns, the patient should be transitioned to enteral nutrition by tube or oral nutrition. When oral intake approximates 50 percent of a patient's needs, PN can be discontinued.

Home PN

Occasionally, patients who are clinically and metabolically stable and who exhibit no complications with continuous 24-hour PN may benefit from cycled PN to increase mobility and ease of care. Generally, cycled PN is infused over a 12- to 20-hour period in an effort to prepare patients for discharge to home or a facility with PN. Home PN (HPN) is indicated in patients with prolonged GI tract failure and/or inability to meet nutritional requirements by

enteral intake. Therefore, HPN can be used post-operatively awaiting GI function return, pre-operatively in malnourished patients, or long-term in those with intestinal failure.

Long-Term Complications of HPN

Metabolic Bone Disease (MBD)

MBD is seen in patients receiving long-term PN and the etiology is unknown. Possible causes include inadequate calcium and phosphorus, excess amino acids and vitamin D, cyclic infusions, metabolic acidosis, copper deficiency, and aluminum contamination. Providing at least 10 to 15 mEq of calcium, 20 to 40 mmol of phosphorus, and 15 mEq of magnesium can help minimize these effects. Those patients who are at risk should undergo a dual X-ray absorptiometry (DEXA) scan for diagnosis. If diagnosed, there are many treatments available including vitamin D and calcium supplementation.

Liver Disease

Liver dysfunction is common in patients receiving long-term PN which can progress to PNALD. By definition, PNALD is extensive portal fibrosis or cirrhosis, bilirubin greater than 3.5 mg/dL for greater than 1 month, ascites, portal hypertension, hepatic encephalopathy, or factor V < 50 percent.

Although it is of unclear etiology, there are ways to decrease risk of liver function abnormalities in home PN patients including avoiding overfeeding, preventing EFAD, and cycling PN. However, it is important to note that abnormal liver functions may be also non-PN related.

Case 1 Colon Cancer and Post-Operative Care

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Objectives

Describe the appropriate parenteral nutrition recommendations for a patient with colon cancer.

Assess the nutritional status of a critically-ill patient.

Identify clinical and metabolic parameters used to monitor patients receiving parenteral nutrition.

Recognize the adverse effects of malnutrition and the associated benefits of providing appropriate nutrition support.

Recognize the benefits of parenteral nutrition in a malnourished, critically-ill, surgical patient.

AJ is a 73-year-old Mexican man who presents to the Emergency Department with 72-hours of abdominal pain of increasing severity. He describes his pain as radiating through his entire abdomen. He also reports nausea and vomiting of gastric contents at least five times during the past 3 days. AJ also reports liquid greenish stools on about eight occasions. He has been unable to tolerate his usual meals, taking in primarily broth and juice. He mentions that he has been losing weight for the last 6 months without any apparent cause.

Past Medical History

AJ had a stroke 2 years ago leaving him with weakness of his right leg. He currently takes Coumadin and digoxin. He denies drug or food allergies. He had an appendectomy 23 years ago.

Social History

AJ is currently retired from his job as an employee for a commercial organization. He

was a heavy alcohol consumer, drinking up to 1 liter of tequila daily until 10 years ago when on advice from his physician, he stopped drinking. AJ smoked 20 cigarettes every day for 40 years but quit about 10 years ago.

Review of Systems

The review of systems was unremarkable except for nausea, abdominal pain, and unintentional weight loss.

Physical Examination

Vital Signs

Temperature: 100 °F (38 °C)

Heart rate: 112 BPM

Respiration: 23 BPM

Blood pressure: 100/60 mm Hg

Height: 5′6″ (170 cm)

Current weight: 99 lb (45 kg)

BMI: 16 kg/m^2

Ideal weight: 142 lb (64.5 kg)

Usual weight: 132 lb (60 kg) 1 year ago
Percent weight change: 25% over 6 months
(132 – 99)/132

Exam

General: Thin male who appears in severe distress

Skin: Pale, cold and dry

HEENT: Anicteric

Cardiac: Regular rate and rhythm, no murmurs or extra sounds

Pulmonary: Decreased breath sounds bilaterally, with rales

Abdomen: Marked abdominal tenderness, particularly in the hypogastrium with guarding and rebound; distended; no bowel sounds

Extremities: No cyanosis or edema. Paresis of right leg

Neurologic: Awake, alert, non-focal, no asterixcis

Clinical studies: An abdominal X-ray shows severely distended loops of the small bowel in right upper quadrant and no air in the rectum. An abdominal ultrasound reveals distended loops of small intestine. No evidence of cholelithiasis (gallstones). Bile ducts and liver appear normal

Laboratory Data

Patient's Values	Normal Values
Sodium: 139 mEq/L	133–145 mEq/L

Patient's Values	Normal Values
Potassium: 5.8 mEq/L	3.5–5.3 mEq/L
Chloride: 110 mEq/L	97–107 mEq/L
CO_2: 27 mEq/L	24–32 mEq/L
BUN: 41 mEq/L	10–20 mEq/L
Creatinine: 2.5 mg/d	0.8–1.3 mg/dL
Glucose: 137 mg/dL	70–99 mg/dL
Albumin: 2.8 g/dL	3.5–5.8 g/dL
Prealbumin: 11 mg/dL	20–40 mg/dL
Calcium: 7.6 mg/dL	9–11 mg/dL
Adjusted calcium: 8.1 mg/dL	9–11 mg/dL
Magnesium: 1.7 mg/dL	1.8–2.9 mg/dL
Phosphorus: 2.7 mg/dL	2.5–4.6 mg/dL
Amylase: 48 U/dL	60–180 U/dL
Bilirubin: 0.57 mg/dL	0.2–1.2 mg/dL
AST: 36 U/L	0–40 U/L
ALT: 14 U/L	0–36 U/L
Hemoglobin: 7.9 g/dL	13.5–17.5 g/dL
Hematocrit: 29%	41–53%
White blood cells: 32 tho/µL	4.0–11.0 tho/µL
Prothrombin time: 27 seconds	<15 seconds

Patient's Values	Normal Values
Platelet count: 1,315,000/mm^3	150,000–450,000/ mm^3

Hospital Course and Therapy

Upon admission to the hospital, a nasogastric tube with suction was placed and his nausea and vomiting resolved. He was placed on NPO (nothing to eat or drink) restrictions. His nasogastric tube drained 800 to 1200 mL of feculent fluid the first day. At the same time, he was rehydrated with IV fluids consisting of $D_5$1/2 normal saline. However, 24 hours after admission he continued to experience abdominal pain and his nausea and vomiting recurred when the nasogastric tube was clamped.

The surgical team decided to take AJ to the operating room to perform an exploratory laparotomy. The findings of the procedure were an occlusive tumor mass of 3.9 cm located at the sigmoid colon, with necrosis of the entire colon proximal to the tumor. AJ had a total colectomy, with Hartmann's procedure and an ileostomy. The histopathological examination reported a well-differentiated adenocarcinoma of the colon, Dukes–Ashley B, with free surgical margins and acute necrotizing colitis proximal to obstructing neoplasm. AJ was transferred to the ICU after surgery. He required mechanical

ventilation for 5 days. After correction of his volume deficit, AJ's serum creatinine dropped to 1.2 mg/dL. There was no evidence of renal failure.

Case Questions

List AJ's likely medical problems demonstrated by his overall clinical picture.

What are the possible etiologies of AJ's bowel obstruction?

What additional evidence from AJ's physical examination could be used to assess his nutritional status prior to initiating parenteral nutrition?

Why is parenteral nutrition the most appropriate form of nutritional intervention at this point in AJ's clinical course?

Using the Harris–Benedict equation, calculate AJ's resting energy expenditure (REE); also calculate AJ's protein requirement, and maximum carbohydrate and lipid oxidation rates. How does one calculate how much dextrose and lipid should be ordered in the PN?

What laboratory data should be used to monitor AJ while he is on PN?

Once AJ's abdominal sepsis and septic complications resolve and his bowel sounds show increased activity, he can be advanced

to an oral diet. How should AJ's feeding begin and what recommendations are appropriate upon discharge?

Answers to Questions: Case 1

1. List AJ's likely medical problems demonstrated by his overall clinical picture.

Bowel obstruction as evidenced by distended loops of small intestine and a lack of air in the rectum on abdominal X-rays and feculent fluid obtained from the nasogastric tube.

Possible mesenteric thrombosis,considering his past medical history of stroke.

Severe electrolyte imbalance demonstrated by hyperkalemia, elevated BUN and creatinine.

Possible bilateral pneumonia

Unintentional weight loss and severe malnutrition.

2. What are the possible etiologies of AJ's bowel obstruction?

In a compilation of the various causes of intestinal obstruction (both small and large bowel), taken from 13 reported series comprising a total of 12,731 adult patients, hernia accounted for 40 percent of the causes of the obstruction; adhesions 29 percent, intussusceptions 12 percent, and cancer 10

percent. However, in elderly patients, the main cause of large intestinal obstruction is colon cancer (70 percent of the cases), followed by diverticulitis (5 percent), and volvulus (10 percent). The symptoms are often insidious, though in most cases acute obstruction is the direct reason for a surgical consultation. Diarrhea, with the passage of blood and mucus, may result from an ulceration of the bowel. The occurrence of diarrhea may lead patients to assert that their bowel is functioning, but the looseness is secondary to the irritation caused by constipation as in AJ's case.

3. What additional evidence from AJ's physical examination could be used to assess his nutritional status prior to initiating parenteral nutrition?

Evidence of malnutrition includes decreased food intake, significant unintentional weight loss, decreased albumin and prealbumin levels, and thin appearance. Albumin and preabumin should be interpreted with caution as low values may reflect hemodilution or the presence of an inflammatory response. As negative acute phase reactants, these hepatic proteins can be falsely depleted during situations that result in a systemic inflammatory response (acute or chronic), such as trauma, surgery, or infection. It is helpful to simultaneously evaluate other markers of inflammation, such as temperature, white blood cell count or C-reactive protein.

Malnutrition plays an important role in the rate of post-operative complications that impair immune response mechanisms. Synthesis and regeneration processes are often affected, reducing the ability to fight infection. The GI tract must be supported during critical illness to maintain or restore rapid cellular turnover rate and the metabolic and immunologic adaptation to severe stress. Disruption in the ecologic equilibrium of the GI tract often occurs during critical illness. This damaged equilibrium may cause bacterial translocation, sepsis, and the systemic inflammatory response syndrome (SIRS). Bacterial translocation occurs from the small intestine to the mesenteric lymph nodes, triggering a cascade of deleterious events that can lead to multi-organic dysfunction and death.

4. Why is parenteral nutrition the most appropriate form of nutritional intervention at this point in AJ's clinical course?

AJ has malnutrition, altered metabolism due to inflammation, abdominal sepsis, cancer, and impaired intestinal function. Therefore, PN should be initiated as a method for nutrition support to prevent further malnutrition. Alternatively, immunonutrition could be considered at the appropriate time for this patient. In a meta-analysis of 11 randomized controlled trials accounting of 1009 patients,

immunonutrition proved to be effective in reducing the risk of infectious complications and length-of-stay in “critically ill” patients and in patients with GI cancer, when compared to patients receiving standard nutritional support.

Currently, available immunomodulatory formulas contain mainly glutamine, arginine, omega-3 fatty acids and nucleotides, and have been shown to decrease the incidence of infection, hospital stay, and hospital costs. Patients who require surgery, especially of the gastrointestinal tract may obtain the greatest benefit of this specialized nutritional therapy

5. Using the Harris–Benedict equation, calculate AJ's resting energy expenditure (REE) and calculate AJ's protein goal and maximum carbohydrate and lipid oxidation rates. How much dextrose and lipid should be ordered in the PN?

$$\begin{aligned}\text{REE} &= 66 + 13.7\ (\text{weight in kg}) + 5\ (\text{height in cm}) - 6.8\ (\text{age}) \\ &= 66 + 13.7\ (45) + 5\ (170) - 6.8\ (73) = 1035\ \text{kcal/day}\end{aligned}$$

$$\text{Total daily calorie needs with activity factor for in-bed patient} = \text{REE} \times 1.45 = 1500\ \text{kcal/day}$$

$$\text{Protein goals} = \text{Current weight} \times 1.3\ \text{g/kg} = 45\ \text{kg} \times 1.3\ \text{g/kg} = 65\ \text{g/day}$$

(Protein restriction is based on patient's initial renal parameters; when renal function normalizes, protein goal can be increased to 1.5 g/kg per day.)

Glutamine, while non-essential, is the most abundant amino acid in the body. The major additive in immune nutriton, it could be considered as adjuvant therapy for this patient. During metabolic stress (sepsis, surgery, trauma, or burns), intramuscular glutamine is rapidly released and intracellular levels of glutamine decrease. Under these conditions glutamine becomes conditionally essential.

Glutamine is also a fuel for cell division, primarily enterocytes and lymphocytes, as well as epithelial cells of the intestine.

Glutamine also plays a role in maintaining the intestinal barrier and is the precursor of the endogenous antioxidant glutathione. It plays an important role in the transport of nitrogen into the body and serves as a substrate for the renal amoniagenesis, while inducing the expression of heat shock proteins and stimulating the synthesis of nucleotides.

Glutamine contributes to the formation of mucin, maintains the integrity of the intestinal surface by the synthesis of *N*-acetylglucosamine and *N*-acetyl-galactosamine and an important precursor of arginine to citruline through transport and decreases insulin resistance.

Oral administration of 0.3 g/kg per day of glutamine is enough to maintain the integrity of the gastrointestinal tract. An enteral formula enriched with glutamine (30.5 g/100 g protein) results in a significant decrease in the incidence

of pneumonia and sepsis in critical care and surgical patients, and decreased hospital length of stay, reducing and post-operative complications. Supplementation of glutamine to TPN of 0.4 g/kg per day decreased natural killer cells (NK) suppressesing inflammation in patients with SIRS, and reducing mortality in critically-ill surgical patients.

Maximum glucose oxidation rate is 5 to 7 mg/kg per minute in hospitalized patients but parenteral carbohydrate infusion should not exceed 4 mg/kg per minute in the critically ill. At 3.4 kcal/g of hydrated dextrose, the maximum dextrose infusion should not exceed 880 kcal/day. Maximum lipid oxidation rate is 2.5 g/kg per day and fat has 9 kcal/g. The caloric equivalent of this lipid load is 1000 kcal. Many nutrition support specialists advocate an upper limit of 1.0 g lipid per kg body weight, which for AJ would be 45 g (405 kcal/day). The majority of lipid emulsions currently available in the United States are soy bean oil based and have been shown to increased inflammation and stimulate the eicosanoid pathways leading to down regulation of cellular immunity. There could be some consideration to eliminate or severely limit IV fat for the first 2 weeks. Current research is investigating the use of other oils, such as olive oil, MCT, or fish oil for potential benefits. Surgery, as mentioned earlier, induces strong local and systemic inflammatory responses, manifested by high

concentrations of several acute phase proteins and inflammatory cytokines. Elevation of these substances is associated with an increased risk of infection, morbidity, and mortality. Omega-3 fatty acids found in fish oil have effective anti-inflammatory properties, these properties are mediated by multiple mechanisms including, altering the structure and function of the cell membrane, modulating of signaling pathways, suppressing of the transcription of pro-inflammatory factors like nuclear factor *kB (NF-kB)*, altering gene expression and modulating eicosanoid production. Fish oil has also been shown to reduce the production of arachidonic acid and increases levels of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Increasing the concentration of EPA within the phospholipids competes with arachidonic acid for binding sites of cyclooxygenase and 5-lipoxygenase reducing tissue inflammation, without compromising mononuclear cell function. These effects play an important role in the generalized suppression of inflammatory response and the immunosuppression and capillary leak after major surgery.

With a goal of 1500 kcal/day, a protein calorie contribution of 280 kcal/day (70 g amino acid × 4.0 kcal/g), a lipid intake of 1.0 g/kg body weight, and a dextrose calorie infusion of 660 kcal/day (3.0 mg/kg per minute) will be used to keep serum glucose maintained at less

than 150 mg/dL. The initial infusion can be lower than the calorie goal in order to assess the metabolic response to the PN especially in a chronically malnourished patient who is at risk for refeeding syndrome. Insulin may be necessary to control blood glucose levels. Insulin can be added directly to the PN bag based on a sliding scale if requirements remain stable.

6. What biochemical laboratory data should be used to monitor AJ while he is on PN?

Sodium, potassium, chloride, CO_2, BUN, creatinine, calcium, magnesium, and phosphorus should be measured three times per day with initiation of TPN and then daily in critically ill patients. Daily electrolyte replacement in PN solution is designed to replenish any losses noted in the previous day's labs. When these laboratory data become stable and normal, frequency of checking may be reduced.

Capillary blood sugar should be checked at least three times a day when initiating parenteral nutrition in order to appropriately adjust sliding scale insulin.

ALT, AST, ALP, and total bilirubin should be checked at initiation and then weekly in a critically ill patient.

Prealbumin or transferrin should be checked at baseline and then weekly.

Serum triglycerides should be checked at baseline and weekly.

A 24-hour urine collection s weekly for measurement of urine urea nitrogen. With this information, nitrogen balance can be calculated (nitrogen balance = nitrogen intake – nitrogen excretion), and the protein content of the PN can be adjusted as required. To calculate nitrogen excretion the recommended formula is:

$$\text{Nitrogen urinary excretion (g/dL)} = \text{urinary nitrogen} \times 1.25 + 4$$

7. Once AJ's sepsis and complications resolve and his bowel sounds show increased activity, he can be advanced to an oral diet. How should AJ's feeding begin and what recommendations are appropriate upon discharge?

Oral feedings should begin with a clear liquid diet and be gradually advanced as tolerated, eventually to solid food. PN should not be discontinued until AJ tolerates at least 50 percent of his requirements through the oral diet, however, PN should be weaned accordingly as oral intake increases in order to avoid overfeeding. Tube feeding should be considered if the patient has a functional GI tract but cannot consume adequate nutrition by

mouth. Evaluation of the patient's nutritional progress should be included in any follow-up visits to his physician. AJ should be instructed to follow a low-fiber diet following his discharge. Fluid and electrolytes are of most concern following a total colectomy. AJ may experience high ostomy output at first, and should be encouraged to drink adequate fluids to prevent dehydration. He may also need to increase his intake of foods or beverages that contain sodium. Consultation with a registered dietitian may be helpful for AJ prior to his discharge as he or she could provide additional tips such as how to avoid foods that may cause obstruction, or recommendations for foods that help thicken output or eliminate unwanted odor.

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Appendices

Developed by Susan Lupackino and Lisa Hark

Appendix A: Food sources of vitamin A

Appendix B: Food sources of vitamin D

Appendix C: Food sources of vitamin E

Appendix D: Food sources of vitamin K

Appendix E: Food sources of vitamin C

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Appendices A–P used www.nutritiondata.com

Appendix A Food sources of vitamin A.

Source: www.nutritiondata.com

Food, Standard Amount	**Serving Size**	**Vitamin A (µg RE)**
Margarine	1 Tbsp	
Liver (beef, veal, goose, and turkey)	3 oz	13,000–19,000
Liver (chicken, lamb)	3 oz	6000–10,000
Various ready-to-eat cereals, with added Vitamin A	1 oz	180–376
Instant cooked cereals, fortified	1 packet	285–376
Beets	1 cup	3.4
Apricots, dried	½ cup	80
Broccoli, fresh, cooked	1 cup	120.2
Herring, Atlantic	3 oz	219
Cantaloupe, raw	¼ medium melon	233
Chinese cabbage, cooked	1 cup	360
Red sweet pepper, cooked	1 cup	371

Food, Standard Amount	Serving Size	Vitamin A (µg RE)
Peppers, chili	1 cup	405
Mustard greens, cooked	1 cup	442
Milk, (all types) with added vitamin A	1 cup	478
Winter squash, cooked	1 cup	535
Turnip greens, cooked from frozen	1 cup	549
Collards, cooked from frozen	1 cup	771
Kale, cooked from frozen	1 cup	885
Spinach, cooked from frozen	1 cup	943
Mixed vegetables, canned	1 cup	949
Pumpkin, canned	½ cup	953
Carrots, raw	1 cup	1026
Sweet potato with peel, baked	1 medium	1096
Mango, raw	1 cup	1262
Carrot juice	¾ cup	1692

Food, Standard Amount	Serving Size	Vitamin A (µg RE)
Tomatoes and vegetable juice	1 cup	3770
Fish oil, cod liver	1 Tbsp	4051

Appendix B Food sources of vitamin D.

Source: www.nutritiondata.com

Food, Standard Amount	Serving Size	Vitamin D (IU)
Herring, Atlantic	3 oz	1384
Fish oil, cod liver	1 Tbsp	1350
Fish, sardines, salmon, codfish	3 oz	649–71.4
Catfish	3 oz	425
Oysters	3 oz	268.8
Egg, yolk, raw, fresh	1 large	260
Milk (all types)	1 cup	299–97.6
Milk, whole	1 cup	100
Margarine	1 Tbsp	60
Cereals ready-to-eat	1 cup	126–88
Butter, salted	1 Tbsp	7.8
Cheddar Cheese	1.5 oz	5.1

Appendix C Food sources of vitamin E.

Source: www.nutritiondata.com

Food, Standard Amount	Serving Size	Alpha Tocopherol (mg)
Fortified ready-to-eat cereals	1 cup	33.8–13.5
Sunflower seeds, dry roasted	1 oz	7.4
Almonds	1 oz	7.3
Sunflower oil	1 Tbsp	5.6
Tomato sauce	1 cup	5.0
Safflower oil	1 Tbsp	4.6
Spinach, frozen, cooked	1 cup	3.7
Swiss chard, cooked	1 cup	3.3
Mixed nuts, dry roasted	1 oz	3.1
Turnip greens, frozen, cooked	1 cup	2.7
Pine nuts	1 oz	2.6
Peanut butter	2 Tbsp	2.5
Canola oil	1 Tbsp	2.4
Wheat germ, toasted, plain	2 Tbsp	2.3
Peanuts	1 oz	2.2

Food, Standard Amount	Serving Size	Alpha Tocopherol (mg)
Avocado, raw	½ avocado	2.1
Carrot juice, canned	¾ cup	2.1
Corn oil and olive oil	1 Tbsp	1.9
Mustard greens, frozen, cooked	1 cup	1.7
Sardine, Atlantic, in oil, drained	3 oz	1.7
Radicchio	1 cup	0.9
Herring, Atlantic	3 oz	0.9
Margarine	1 Tbsp	0.8
Salad dressing (Italian)	1 Tbsp	0.7

Appendix D Food sources of vitamin K.

Source: www.nutritiondata.com

Phyloquinone per Food, Standard Amount	Serving Size	serving (µg)
Kale, frozen, cooked	1 cup	1062
Collard greens, frozen, cooked	1 cup	1060

Phyloquinone per Food, Standard Amount	Serving Size	serving (µg)
Spinach, frozen, cooked	1 cup	889
Turnip greens, frozen, cooked	1 cup	529
Mustard greens, frozen, cooked	1 cup	419
Parsley, raw	¼ cup	246
Brussels sprouts, fresh	1 cup	218
Broccoli, fresh	1 cup	110
Asparagus, fresh	1 cup	91
Okra, frozen, cooked	1 cup	88
Cabbage, fresh	1 cup	67.6
Green peas, frozen, cooked	1 cup	38.4
Cauliflower	1 cup	17.2
Celery, raw	1 medium stalk	17
Carrot, raw	1 cup	16.1
Grapes, red/green, seedless, raw	1 ½ cup	12
Plums, raw	2 medium	11
Pear, raw	1 medium	8.1

Phyloquinone per Food, Standard Amount	Serving Size	serving (µg)
Tomato juice, bottled	8 fluid oz	5.6
Tomato, red, raw	1 medium	4.4
Avocado, raw	⅓ medium	4.3
Apricot, raw	½ cup	2.5

Appendix E Food sources of vitamin C.

Source: www.nutritiondata.com

Food, Standard Amount	Serving Size	Vitamin C (mg)
Guava, raw	½ cup	188
Peppers (all types), raw	1 cup	155
Peppers (all types) cooked	1 cup	150
Broccoli, cooked	1 cup	101.2
Strawberries, raw	1 cup	100
Brussels sprouts, cooked	1 cup	96.8
Kohlrabi, cooked	1 cup	90
Broccoli, raw	1 cup	81.2
Peas, Snowpeas, Sugar snap peas, cooked	1 cup	76.6

Food, Standard Amount	Serving Size	Vitamin C (mg)
Kiwi fruit	1 medium	70
Orange, raw	1 medium	70
Orange juice	¾ cup	61–93
Peas, edible-podded, raw [Snowpeas, Sugar snap peas]	1 cup	58.8
Tangerines, (mandarin oranges), raw	1 cup	52.1
Green pepper, sweet, cooked	½ cup	51
Grapefruit juice	¾ cup	50–70
Vegetable juice cocktail	¾ cup	50
Cantaloupe	¼ medium	47
Papaya, raw	¼ medium	47
Tomato juice	¾ cup	33
Raspberries, raw	1 cup	32.2
Melons, honeydew, raw	1 cup	31.9
Sweet potato, cooked	1 medium	22.3

Appendix F Food sources of folate.

Source: www.nutritiondata.com

Food, Standard Amount	Serving Size	Folate (µg)
Ready-to-eat cereals	1 cup	1010
Chicken liver	3 oz	495
Beef liver	3 oz	243.6
Spinach, frozen, cooked	1 cup	230
Lentils, cooked	½ cup	180
Tomato	1 medium	75–97
Mustard and turnip greens, frozen, cooked	1 cup	170
Seaweed, kelp, raw	1 cup	144
Chickpeas, canned	½ cup	140
Okra, frozen, cooked	1 cup	134
Collard greens, frozen, cooked	1 cup	129
Asparagus, fresh, cooked	1 cup	121.2
Peas, green, boiled	1 cup	94.4
Brussels sprouts, raw	1 cup	93.6
Broccoli, fresh, cooked	1 cup	84.2
Lettuce, romaine	1 cup	63.9
Orange juice	1 cup	110
Cauliflower	1 cup	54.6

Food, Standard Amount	Serving Size	Folate (µg)
Potato, baked with skin	1 medium	40
Egg, boiled	1 large	24

Appendix G Food sources of calcium (dairy).

Source: www.nutritiondata.com

Food, Standard Amount	Serving Size	Calcium (mg)
Lactose-Free Calcium Fortified Milk	1 cup	500
Plain yogurt, non-fat	8 oz	452
Romano cheese	1.5 oz	452
Plain yogurt, low-fat	8 oz	415
Soy Milk, calcium fortified	1 cup	368
Fruit yogurt, low-fat	8 oz	345
Swiss cheese	1.5 oz	336
Ricotta cheese, part skim	½ cup	335
Pasteurized process Swiss cheese	1.5 oz	324
Provolone cheese	1.5 oz	321
Egg, yolk, raw, fresh	1 large	313
Mozzarella cheese, part-skim	1.5 oz	311

Food, Standard Amount	Serving Size	Calcium (mg)
Cheddar cheese	1.5 oz	307
Fat-free (skim) milk	1 cup	306
Muenster cheese	1.5 oz	305
1% low-fat milk	1 cup	290
Low-fat chocolate milk (1%)	1 cup	288
2% reduced fat milk	1 cup	285
Reduced fat chocolate milk (2%)	1 cup	285
Buttermilk, low-fat	1 cup	284
Chocolate milk	1 cup	280
Whole milk	1 cup	276
Yogurt, plain, whole milk	8 oz	275
Ricotta cheese, whole milk	½ cup	255
Pasteurized process American cheese food	1.5 oz	232
Blue cheese	1.5 oz	225
Mozzarella cheese, whole milk	1.5 oz	215
Feta cheese	1.5 oz	210

Appendix H Food sources of calcium (non-dairy).

Source: www.nutritiondata.com

Food, Standard Amount	Serving Size	Calcium (mg)
Soy beverage, calcium fortified	1 cup	368
Collard greens, frozen, cooked	1 cup	357
Sardines, Atlantic, in oil, drained	3 oz	325
Tofu, firm, prepared with nigari	½ cup	253
Spinach, frozen, cooked	1 cup	245
Turnip greens, frozen, cooked	1 cup	197
Pink salmon, canned, with bone	3 oz	181
Okra, frozen, cooked	1 cup	176
Molasses, blackstrap	1 Tbsp	172
Beet greens, fresh, cooked	1 cup	164
Pak-choi, Chinese cabbage, cooked from fresh	1 cup	158
Soybeans, green, cooked	½ cup	130
Ocean perch, Atlantic, cooked	3 oz	116
White beans, canned	½ cup	96

Food, Standard Amount	Serving Size	Calcium (mg)
Kale, frozen, cooked	1 cup	93.6
Clams, canned	3 oz	78
Nuts, almonds, oil roasted	1 oz	74.5
Rainbow trout, farmed, cooked	3 oz	73
Oatmeal, plain and flavored, instant, fortified	1 packet prepared	99–110

Appendix I Food sources of sodium.

Source: www.nutritiondata.com

Food, Standard Amount	Serving Size	Sodium (mg)
Salt (sodium chloride)	1 tsp	2325
Pickle relish, sweet	1 cup	1987
Soup, canned (all types)	1 cup	850–2500
Tomato sauce	1 cup	1284
Soy sauce made from soy (tamari)	1 Tbsp	1006
Sauerkraut, canned	1 cup	939
Chicken Pot pie, frozen entree	1 pie	841
Potato chips, regular and baked	1 bag (1 oz)	837

Food, Standard Amount	Serving Size	Sodium (mg)
Pretzels, hard, plain, salted	10 twists	814
Cheese American	1.5 oz	670
Tomato juice, canned, with salt added	1 cup	654
Vegetable juice cocktail, canned	1 cup	653
Pickles, kosher dill	1 medium	569
Beef frankfurter, hot dog	1 frank	461
Olives, canned or bottled, green	1 oz	440
Scrapple, pork	2 oz	369
Gravy, canned	¼ cup	352
Canned tuna	3 oz	320
Canned vegetables	1 cup	243
Lunch meats (turkey, ham, salami, pastrami)	3 slices	250–500
Barbeque Sauce	1 Tbsp	212
Noodles, Chinese, chow mein	1 cup	198
Cheese Pizza	1 slice	194
Beef sausage, fresh, cooked	1 oz	184

Food, Standard Amount	Serving Size	Sodium (mg)
Salad dressings	1 Tbsp	147
Peanuts, oil-roasted, with salt	1 oz	121
Frozen Dinner	1 dinner	360–768

Appendix J Food sources of potassium.

Source: www.nutritiondata.com

Food, Standard Amount	Serving Size	Potassium (mg)
Beet greens, cooked	1 cup	1309
Spinach, cooked	1 cup	839
Tomato sauce	1 cup	810
Sweet potato, baked	1 medium	694
Potato, baked, flesh	1 medium	610
White beans, canned	½ cup	595
Yogurt, plain, non-fat	8 oz	579
Tomato puree	½ cup	549
Clams, canned	3 oz	534
Yogurt, plain, low-fat	8 oz	531
Prune juice	¾ cup	530
Carrot juice	¾ cup	517

Food, Standard Amount	Serving Size	Potassium (mg)
Apricots, dried	½ cup	514
Blackstrap molasses	1 Tbsp.	498
Halibut, cooked	3 oz	490
Soybeans, green, cooked	½ cup	485
Tuna, yellow fin, cooked	3 oz	484
Lima beans, cooked	½ cup	484
Artichokes, (globe or French), raw	1 artichoke	474
Winter squash, cooked	1 cup	449
Soybeans, mature, cooked	½ cup	443
Rockfish, Pacific, cooked	3 oz	442
Cod, Pacific, cooked	3 oz	439
Bananas	1 medium	422
Tomato juice	¾ cup	417
Peaches, fresh	1 medium	398
Prunes, stewed	½ cup	398
Milk, non-fat	1 cup	382

Food, Standard Amount	Serving Size	Potassium (mg)
Pork chop, center loin, cooked	3 oz	382
Rainbow trout, farmed, cooked	3 oz	375
Pork loin, center rib (roasts), lean, roasted	3 oz	371
Buttermilk, cultured, low-fat	1 cup	370
Cantaloupe	¼ medium	368
1%–2% milk	1 cup	366
Honeydew melon	⅛ medium	365
Lentils, cooked	½ cup	365
Plantains, cooked	½ cup slices	358
Kidney beans, cooked	½ cup	358
Orange juice	¾ cup	355
Split peas, cooked	½ cup	355
Yogurt, plain, whole milk	8 oz container	352

Appendix K Food sources of magnesium.

Source: www.nutritiondata.com

Food, Standard Amount	Serving Size	Magnesium (mg)
Beet greens, cooked	1 cup	97.9
Okra, cooked from frozen	1 cup	93.8
Halibut, cooked	3 oz	91
Quinoa, dry	¼ cup	89
Almonds	1 oz	78
Soybeans, mature, cooked	½ cup	74
Nuts, (various types)	1 oz	70–107
White beans	½ cup	67
Pollock, walleye, cooked	3 oz	62
Black beans, cooked	½ cup	60
Oat bran, raw	¼ cup	55
Soybeans, green, cooked	½ cup	54
Tuna, yellow fin, cooked	3 oz	54
Lima beans, baby, cooked from frozen	½ cup	50
Navy beans, cooked	½ cup	48
Tofu, firm, prepared with nigari	½ cup	47
Soy beverage	1 cup	47

Food, Standard Amount	Serving Size	Magnesium (mg)
Cowpeas, cooked	½ cup	46
Hazelnuts	1 oz	46
Great northern beans, cooked	½ cup	44
Oat bran, cooked	½ cup	44
Buckwheat groats, roasted, cooked	½ cup	43
Brown rice, cooked	½ cup	42
Haddock, cooked	3 oz	42
Spinach, frozen, cooked	1 cup	157
Pumpkin and squash seed kernels, roasted	1 oz	151
Bran ready-to-eat cereal (100%)	1 oz	103

Appendix L Food sources of iron.

Source: www.nutritiondata.com

Food, Standard Amount	Serving Size	Iron (mg)
Spinach, frozen, cooked	1 cup	6.4
Liver (various types) cooked	3 oz	5.0–9.9

Food, Standard Amount	Serving Size	Iron (mg)
Fortified instant cooked cereals (various)	1 packet	5.0–8.1
Soybeans, mature, cooked	½ cup	4.4
Pumpkin and squash seed kernels, roasted	1 oz	4.2
White beans, canned	½ cup	3.9
Blackstrap molasses	1 Tbsp	3.5
Lentils, cooked	½ cup	3.3
Fortified ready-to-eat cereals (various)	1 cup	19–28
Clams, canned, drained	3 oz	23.8
Clams, canned	3 oz	23.8
Kidney beans, cooked	½ cup	2.6
Sardines, canned in oil, drained	3 oz	2.5
Chickpeas, cooked	½ cup	2.4
Duck, meat only, roasted	3 oz	2.3
Prune juice	¾ cup	2.3
Shrimp, canned	3 oz	2.3
Cowpeas, cooked	½ cup	2.2
Ground beef, 15% fat, cooked	3 oz	2.2
Tomato puree	½ cup	2.2

Food, Standard Amount	Serving Size	Iron (mg)
Lima beans, cooked	½ cup	2.2
Soybeans, green, cooked	½ cup	2.2
Navy beans, cooked	½ cup	2.1
Refried beans	½ cup	2.1
Tomato paste	¼ cup	2.0
Oysters, eastern, wild, cooked	3 oz	10.2
Beef, lean ground, raw	3 oz	1.5
Beef, sirloin steak or filet mignon, raw	3 oz	1.2
Lamb, shoulder, arm, raw	3 oz	1.1

Appendix M Food sources of omega-3 fatty acids.

Source: www.nutritiondata.com

Food, Standard Amount	Serving Size	Omega-3 FA (g)
Flaxseed oil	1 Tbsp	6.7
Salmon, Atlantic, wild, cooked	3.0 oz	2.198
Flaxseeds	1 Tbsp	2.63
Walnuts	1 oz	2.5
Soybeans, cooked	½ cup	2.1
Canola oil	1 Tbsp	1.4

Food, Standard Amount	Serving Size	Omega-3 FA (g)
Walnut oil	1 Tbsp	1.3
Sardine	3.0 oz	1.2
Tuna, white, canned in water	3.0 oz	0.81
Wheat germ oil	1 Tbsp	0.86

Appendix N Food sources of oxalic acid.

Source: www.nutritiondata.com

Food, Standard Amount	Serving Size	Oxalic acid (mg)
Spinach, frozen	1 cup	1230
Beans in tomato sauce	1 cup	1148
Beetroot, pickled	1 cup	1135
Chard, Swish, boiled	1 cup	1129
Spinach, boiled	1 cup	420
Okra, boiled	1 cup	234
Chard, Swiss, raw	1 cup	232
Tea, Indian, 6 minute infusion	1 cup	185
Potato, sweet, boiled, mashed	1 cup	184
Peanuts, roasted	2 oz	137
Cocoa, dry powder	¼ cup	134

Food, Standard Amount	Serving Size	Oxalic acid (mg)
Berries, green goose	1 cup	132
Crackers, soybean	2 oz	118
Pecans	2 oz	111
Leeks, raw, boiled	1 cup	110
Grits, white corn, cooked	1 cup	99
Collards, raw, boiled	1 cup	95
Chocolate, plain	2 oz	66
Raspberries, black	1 cup	65
Parsley, raw	1 cup	64
Grapes, concord	1 cup	40
Squash, summer	1 cup	40
Berries, black	1 cup	26
Celery	1 cup	24
Berries, blue	1 cup	22
Wheat germ	1 Tbsp	19
Raspberries, red	1 cup	18
Eggplant, boiled	1 cup	17
Dandelion greens, raw	1 cup	14
Pepper, green	1 cup	12
Escarole, raw	1 cup	9

Appendix O Food sources of dietary fiber.

Source: www.nutritiondata.com

Food, Standard Amount	Serving Size	Dietary Fiber (g)
Cereal, All-Bran	1 cup	25.8
Wheat bran	1 cup	24.6
Cereal, Fiber One	1 cup	23.8
White beans, great-northern, canned	1 cup	14.4
Kidney beans, red, cooked	1 cup	13.8
Navy beans, cooked	1 cup	13.0
Black beans, cooked	1 cup	12.2
Pinto beans, cooked	1 cup	11.8
Lentils, cooked	1 cup	10.4
White beans, great northern beans, cooked	1 cup	10.0
Lima beans, canned	1 cup	8.6
Chickpeas, cooked	1 cup	8.6
Peas, cooked	1 cup	8.6
Peas, green, cooked	1 cup	8.6
Okra, frozen, cooked	1 cup	8.2
Brussels sprouts, cooked	1 cup	7.6
Split peas, cooked	1 cup	6.2
Pear, fresh with skin	1 small	6.0

Food, Standard Amount	Serving Size	Dietary Fiber (g)
Cracker, Matzo	6 crackers	6.0
Bread, pumpernickel	2 slices	5.4
Spaghetti, whole-wheat, cooked	1 cup	5.4
Figs, dried	3 pieces	4.6
Carrots, cooked	1 cup	4.0
Applesauce, canned, unsweetened	1 cup	4.0
Prunes, dried, stewed	6 pieces	3.4
Raspberries, fresh	1 cup	3.3
Spinach, cooked	1 cup	3.2
Orange, fresh without skin	1 small	3.0
Carrots, canned	1 cup	3.0
Apple, fresh with skin	1 small	2.8

Appendix P Food sources of purine.

Source: www.nutritiondata.com

Food, Standard Amount	Purine (mg/100 g)
Sweetbreads	825
Anchovies	363
Brains	363

Food, Standard Amount	Purine (mg/100 g)
Sardines	295
Scallops	295
Liver, calf/beef	233
Mackerel	233
Kidney, beef	200
Game meats	200
Herring	200
Asparagus	50–150
Bread and cereals, whole grain	50–150
Cauliflower	50–150
Fish, fresh and saltwater	50–150
Legumes, beans/lentils/ peas	50–150
Meat-beef/lamb/pork/ veal	50–150
Mushrooms	50–150
Oatmeal	50–150
Peas, green	50–150
Poultry, chicken/duck/ turkey	50–150
Shellfish, crab/lobster/ oysters	50–150

Food, Standard Amount	Purine (mg/100 g)
Spinach	50–150
Wheat germ and bran	50–150

Review Questions

Chapter 1 Overview of Nutrition Assessment in Clinical Care

1. Body mass index (BMI) may overestimate an individual's body fat in which of the following scenarios?

a. Underweight individuals

b. Normal weight individuals

c. Extremely muscular individuals

d. Obese individuals

2. Which of the following tissues manifest an iron deficiency and is likely to appear abnormal on physical examination?

a. Skin

b. Nails

c. Mouth

d. All of the above

3. Waist circumference (WC) is recommended to only be measured in patients with a BMI less than which of the following because it does not provide additional information about risk?

a. $\leq 25\ kg/m^2$

b. ≤30 kg/m^2

c. ≤35 kg/m^2

d. ≤40 kg/m^2

4. Which of the following BMI values indicates a patient is at risk of malnutrition and needs further nutritional assessment?

a. <18.5 kg/m^2

b. <19.5 kg/m^2

c. <20.5 kg/m^2

d. <21.5 kg/m^2

5. When interpreting serum albumin in hospitalized patients, levels may be falsely elevated irrespective of nutritional status in which of the following conditions?

a. Liver disease

b. Dehydration

c. Diabetes

d. Stroke

6. DE is a 45-year-old man is seeing his primary care physician for an annual physical. His doctor suspects he has metabolic syndrome based on the following measurements and fasting laboratory data:

Blood pressure: 140/80 mm Hg Waist circumference: 38″

Triglycerides: 230 mg/dL HDL-C: 35 mg/dL Glucose: 120 mg/dL

How many of the metabolic syndrome criteria does he meet based on these results?

a. 1

b. 2

c. 3

d. 4

7. CR is a 49 year-old man who has recently been diagnosed with colon cancer. He has lost 15 lb over the past 3 months, which is a clinically significant weight loss. His usual weight is 170 lb and his current weight is 155 lb. Which of the following percent weight changes accurately reflects the patients' weight history?

a. 2.5% weight change

b. 5.5% weight change

c. 8.8% weight change

d. 10% weight change

8. BF is a 56-year-old obese woman who has successfully undergone bariatric surgery. She has been prescribed a multivitamin, B_{12}, calcium, vitamin D, and numerous other supplements. How long after her surgery

should be advised to continue to take these supplements?

a. 1 year

b. 2 years

c. 5 years

d. For the rest of her life

9. PR is a 54-year-old man who recently underwent gastric bypass surgery. He presents to his surgeon 6 months post-operatively complaining of headaches, fatigue, and being cold all the time. Which of the following deficiencies is most likely associated with these symptoms in patients who have undergone gastric bypass surgery?

a. Vitamin C

b. Riboflavin

c. Zinc

d. Iron

10. DD is a 3-year-old boy from Africa who is admitted to the hospital and diagnosed with kwashiorkor. Which of the following macronutrients is believed to be deficient in patients with kwashiorkor?

a. Protein

b. Carbohydrates

c. Fiber

d. Calories

11. Side effects associated with Roux-en-Y bariatric surgery frequently include dumping syndrome. Which of the following dietary recommendations are appropriate to reduce dumping syndrome post-bariatric surgery?

a. Eat 3 meals everyday

b. Take vitamin and mineral supplements with meals

c. Avoid drinking fluids for at least 30 minutes after meals

d. Add more dietary fiber

12. SD is a 50-year-old woman with a BMI of 28 kg/m^2. She has been referred for nutrition counseling by her primary care physician and asks how many calories she needs to reduce each day to lose 1 lb per week. Which of the following is the correct answer?

a. 250 kcal/day

b. 500 kcal/day

c. 750 kcal/day

d. 900 kcal/day

13. Nutrition issues can be integrated into all components of the clinical assessment, including the medical history, social history, review of systems, physical examination, laboratory data, and treatment plan. Which of

the following sections is the most appropriate time to discuss the patient's dietary intake, either using a 24-hour recall, food frequency questionnaire or usual intake method?

a. Medical history

b. Social history

c. Review of systems

d. Physical examination

Chapter 2 Vitamins, Minerals, and Dietary Supplements

1. EF is a 56-year-old male who was treated for Crohn's disease with a resection of his terminal ileum. He has not taken any vitamin supplements following this procedure. He presents to his primary care physician complaining of numbness and tingling in his hands and feet. Which of the following vitamin deficiency should be suspected?

a. Vitamin C

b. Vitamin D

c. Vitamin B_{12}

d. Vitamin K

2. CF is a 16-year-old teenager who comes to her pediatrician because she has been having headaches and blurred vision. She has started taking large doses of vitamins to help reduce

her acne. Mega doses of which of the following vitamins could contribute to headaches and blurred vision (above the tolerable upper limit recommendation)?

a. Vitamin A

b. Vitamin B_{12}

c. Vitamin E

d. Vitamin B_6

3. NS is a 6-year-old boy who has been diagnosed with lead poisoning. According to the CDC, children exposed to lead are at increased risk of which of the following conditions?

a. Brain damage

b. Otitis media

c. Alopecia

d. Strabismus

4. GM is a 35-year-old homeless man who presents to the Emergency Department with a red, swollen tongue, soreness of the lips and mouth, dermatitis, and diarrhea. Which of the following vitamin deficiencies should be suspected in this patient?

a. Vitamin C deficiency

b. Iron deficiency

c. Niacin deficiency

d. Folate deficiency

5. Which of the following minerals functions as an antioxidant as a component of enzymes that protect cells from the damaging effects of free radicals?

a. Phosphorous

b. Selenium

c. Potassium

d. Chromium

6. When taken alone, in doses ranging from 300 to 900 mg/day, St. John's Wort has been shown to be moderately effective in the treatment of which for the following conditions

a. Mild-to-moderate depressive symptoms

b. Type 2 diabetes

c. Hypertension

d. Osteoarthritis

7. LF is a 22-year-old female who complains of weakness, fatigue, and feeling cold. When asked about her diet, she admits that she switched to a vegan diet 6 months ago and has been avoiding meat, chicken, and fish. Based on this scenario, which of the following deficiency should be suspected in this patient?

a. Magnesium

b. Vitamin K

c. Iron

d. Selenium

8. Which of the following supplements are appropriate to prescribe to a 35-year-old woman with chronic constipation and no other medical conditions?

a. Magnesium

b. Iron

c. B-complex

d. Vitamin D

9. TL is a 74-year-old female with a medical history of osteoporosis and a hip fracture 2 years ago. She has been taking 1000 mg/day of calcium for at least 10 years and now requests information about vitamin D. She lives in an independent living facility in Boston. How much vitamin D_3 would be appropriate to prescribed to TL based on the RDA?

a. 200 IU/day

b. 300 IU/day

c. 500 IU/day

d. 800 IU/day

10. Which of the following laboratory measures is the best determinant of iron status in a normal 18-year-old female with regular menses and no chronic health problems?

a. Ferritin

b. Transferrin saturation

c. Prealbumin

d. Total iron-binding capacity

11. VF is a 43-year-old female with a history of hypertension who is managed with a diuretic and beta-blocker. She presents to her primary care physician complaining of weakness. She is diagnosed with hypokalemia. Which of the following foods should she be advised to increase?

a. Whole grain cereal

b. Orange juice

c. Yogurt

d. Eggs

12. HV is a 42-year-old male who recently broke his hip after falling off his bike during a race. He is currently taking warfarin to reduce his chance of blood clotting. The function of which of the following vitamins is inhibited by warfarin therapy?

a. Vitamin E

b. Vitamin A

c. Vitamin D

d. Vitamin K

Chapter 3 Nutrition in Pregnancy and Lactation

1. Nutritional requirements for certain macronutrients and micronutrients increase significantly during pregnancy. Which of the following nutrient requirements increases the most during pregnancy?

a. Protein

b. Fat

c. Carbohydrates

d. Fiber

2. EH is a 17-year-old teenager who comes to a prenatal clinic for the first time at 18 weeks gestation. She has gained only a few pounds since she became pregnant. Based on her pre-pregnancy BMI (21 kg/m^2) what is the total amount of weight she should gain during pregnancy according to the Institute of Medicine's recommendations?

a. 10–15 pounds

b. 15–25 pounds

c. 25–35 pounds

d. 35–40 pounds

3. MW is a 32-year-old pregnant woman who comes to see her obstetrician for a routine prenatal visit. She is complaining of fatigue and

her hemoglobin and hematocrit results indicate that she is anemic. Pregnant women are more likely to experience anemia in which of the following trimesters?

a. 1st trimester

b. 2nd trimester

c. 3rd trimester

d. There is no difference in the prevalence of anemia during pregnancy

4. RL is a 31-year-old obese woman who is 26 weeks in gestation. She is being screened for gestational diabetes by her obstetrician since she has a family history of type 2 diabetes. Which of the following results for a 1-hour, 50-g glucose load would be considered a positive diagnosis for gestational diabetes?

a. 100–110 mg/dL

b. 110–120 mg/dL

c. 120–130 mg/dL

d. 130–140 mg/dL

5. Which of the following population groups in the United States has the highest prevalence of neural tube defects?

a. Non-Hispanic white women

b. Non-Hispanic black women

c. Asian women

d. Hispanic women

6. Breast-fed infants may feed more often than formula-fed infants because breast milk empties from an infant's stomach slightly more rapidly than formula-fed infants. On average, what is the approximate time for breast milk to empty from an infant's stomach?

a. 1 hour

b. 1.5 hours

c. 2 hours

d. 3 hours

7. JG is a 22-year-old woman who recently delivered a healthy, full-term infant. She is breastfeeding her 3-month old and complains to her family doctor about sore nipples. Which of the following strategies could help JG prevent and treat sore nipples associated with breastfeeding?

a. Make sure the infant is tummy to tummy and latching on properly

b. Apply moisturizer to the breast after feeding

c. Clean the breasts with a washcloth and soap after breastfeeding

d. Apply heat to the nipple area after feeding

8. RT is a 25-year-old female who has recently found out that she is pregnant. She questions her obstetrician about which exercises are

appropriate during pregnancy. Which of the following exercises would **not** be considered safe during pregnancy?

a. Rebounding on a trampoline

b. Walking

c. Yoga

d. Swimming

9. JN is a 33-year-old female who has been successfully breastfeeding her infant since she gave birth 4 weeks ago but now has been diagnosed with mastitis and prescribed an antibiotic. Which of the following is the most appropriate recommendation for breastfeeding women with mastitis?

a. Avoid breastfeeding with the infected breast

b. Discontinue breastfeeding

c. Continue breastfeeding and nurse frequently

d. Switch to infant formula until the mastitis is resolved

10. According to the CDC, to reduce the risk of bearing a child with a neural tube defect, what is the minimum amount of folic acid a woman of childbearing age should consume on a daily basis prior to becoming pregnant?

a. 400 μg/day

b. 600 μg/day

c. 800 μg/day

d. 1000 μg/day

11. GH is a 24-year-old woman who has been breastfeeding for the past 3 months. She questions her pediatrician about whether she is able to provide enough nutrition for her infant. What parameters should be used to determine if breastfeeding is providing adequate nutrition for an infant or child?

a. Monitoring growth and development on the growth charts

b. Measuring the amount of milk being produced by the mother

c. Tracking the frequency that the infant feeds

d. Assessing the number of bowel movements of the infant

12. LM asks how quickly after delivery she can return to her pre-pregnancy weight while she is breastfeeding. Which of the following would be considered a safe weight loss while breastfeeding?

a. 1–2 pounds/week

b. 1–2 pounds/month

c. 6–8 pounds/month

d. Women should not lose weight during breastfeeding

13. JS is a 31-year-old woman who has just found out that she is pregnant and asks her obstetrician about drinking coffee during pregnancy. She is very concerned about recent reports describing the increased risk of miscarriage related to excess caffeine intake. Since she has had two previous miscarriages according to the March of Dimes, what is the current recommendation for limiting caffeine intake during pregnancy?

a. Less than 200 mg/day

b. Less than 300 mg/day

c. Less than 400 mg/day

d. Less than 500 mg/day

Chapter 4 Infants, Children, and Adolescents

1. Pasteurized cow's milk is an important source of calories, protein, and calcium for children, but should not be introduced until a child is how old?

a. 6 months

b. 9 months

c. 12 months

d. 18 months

2. Dry, scaly dermatitis, alopecia, and easily pluckable, dull hair may be signs of which of the following deficiencies?

a. Protein deficiency

b. Essential fatty acid deficiency

c. Vitamin and mineral deficiency

d. All of the above

3. BB is an 18-year-old female whose parents suspect she has an eating disorder. Her symptoms include esophagitis and electrolyte abnormalities, suggesting which of the following?

a. BB is vomiting in an effort to keep her weight down

b. BB has been taking mega doses of vitamins

c. BB is using laxatives in an effort to keep her weight down

d. BB has amenorrhea

4. BB's parents request that she be hospitalized immediately for observation and treatment. Which of the following criteria should be used to determine if BB needs to be managed in an in-patient hospital setting rather than on an out-patient basis?

a. BB is medically unstable

b. BB is 25 to 30 percent below her ideal weight

c. BB is emotionally unstable

d. All of the above

5. Body mass index (BMI) is an important growth assessment tool in children over the age of two. Which of the following is the correct way to determine height for use in calculating BMI?

a. Using the height stick on the scale

b. Without shoes using a wall-mounted stadiometer

c. Using a tape measure with the child lying on a hard surface

d. By weight-for-length

6. What is the AAP's recommendation for daily juice intake for children aged 12 months to 2 years of age?

a. Less than 8 ounces/day

b. AAP recommends no juice for 1–2 year old children

c. Less than 4 ounces/day

d. Juice is a good source of vitamins, and thus should not be limited in children

7. Children under the age of two should not follow a low-fat diet because normal fat intake is required to maintain the development of which of the following systems?

a. Central nervous system

b. Respiratory system

c. Musculoskeletal system

d. Digestive system

8. ST is an 11-year-old boy with hypercholesterolemia and a positive family history of heart disease (his father had a heart attack at age 40). What is the recommended initial medical nutrition therapy for children with hypercholesterolemia over the age of 2 years?

a. A very high fat diet, such as the Atkins diet, to support weight loss

b. A very low fat diet, with <10% calories as fat

c. A balanced diet with <30% calories as fat, and <7–10% calories as saturated fat

d. No dietary recommendations as age 11 is too young to restrict a child's diet

9. Head circumference indirectly measures brain growth in infants and children. Assessing head circumference is recommended for infants and children up to what age?

a. 6 months

b. 12 months

c. 2 years

d. 4 years

10. JK is a 16 year-old boy who has been diagnosed as obese according to his BMI which is greater than the 95th percentile. His mother is very worried about this, but JK doesn't seem too concerned. What is the recommended method and approach to address his obesity in the office-based setting?

a. Work individually with JK only

b. Work with both JK and his mother

c. Work with JK's mother only

d. Refer JK to a multidisciplinary weight management program right away

11. JT is an 8-year-old girl who comes to see her pediatrician for a well-childcare visit. Her height is 127 cm and her weight is 25 kg. Her BMI is at the 50th percentile. Which of the following weight classifications is correct for this child?

a. Normal weight

b. Underweight

c. Overweight

d. Obese

12. DR is an 18-year-old overweight teenager who is diagnosed with non-alcoholic fatty liver disease (NAFLD) by his family physician. Which of the following is the most appropriate therapy for DR at this time?

a. Immediate drug therapy

b. Weight loss

c. Referral to a surgeon for bariatric surgery

d. There is no treatment for this condition

13. TY is a 4-year-old child who presents to the hospital with wasting and apparent emaciation, yet serum albumin and protein values are normal. It is suspected, however, that protein status may be depleted. What is the most likely explanation for these normal serum values?

a. Inaccurate test procedure

b. Increased blood volume (hemodilution)

c. Protein malnutrition

d. Decreased blood volume (hemoconcentration)

14. According to the CDC and AAP, the maximum amount of time a child should spend engaging in sedentary activities, such as watching TV and playing computer and video games, on a daily basis is:

a. 30 minutes/day

b. 2 hours/day

c. 3 hours/day

d. Equal to the time they are playing actively each day

15. The “hallmark sign” of refeeding syndrome, an imbalance that may lead to cardiac, neuromuscular, hepatic, hematologic, and respiratory dysfunction, and ultimately organ failure, involves which of the following?

a. Phosphate, magnesium, calcium, potassium

b. Potassium, sodium iron, biotin

c. Magnesium, niacin, folate, zinc

d. Calcium, zinc, iron, pyridoxine

Chapter 5 Older Adults

1. When making dietary modifications in situations where calorie and protein intake are inadequate, it is appropriate to

a. Present large portions of food and allow the patient to select what they want

b. Remove traditional dietary restrictions related to specific disease processes

c. Drink calorically dense beverages with meals

d. All of the above

2. Activities of daily living (ADLs) reflect an individual's most basic capacity for self-care, and may be limited in approximately 10% of older adults. Which of the following are considered ADLs?

a. Preparing meals

b. Housework

c. Feeding

d. Managing money

3. A Dual Energy X-ray Absortionmetry (DEXA) scan is used to assess bone mineral density. Which of the following scores indicate osteoporosis?

a. >−2.5

b. −1 to −2.5

c. <−2.5

d. −2.0

4. Malnutrition in older adults is associated with which of the following factors?

a. Moderate alcohol intake

b. Problems with chewing and swallowing

c. Reduced gait

d. Glaucoma

5. What dietary supplement is appropriate to recommend for a person with intermediate to advanced age-related macular degeneration (AMD)?

a. Multivitamin and mineral supplement

b. Combination of vitamin A, D, E, and K

c. Combination of magnesium, potassium, phosphorous, and calcium

d. Combination of zinc, copper, vitamin E, and vitamin C

6. Dehydration in older adults has been linked to impaired cognition, kidney stones, and constipation. This population is less likely to experience signs and symptoms of dehydration because of which of the following physiological changes associated with aging?

a. Increased total body water

b. Decline in thirst perception

c. Reduced tolerance to fluid

d. Increased taste sensation

7. RF is an 83-year-old female who is living in an assisted living facility. Her recent blood tests results show a low serum vitamin B_{12} level even though her dietary intake of vitamin B_{12} is adequate. Which of the following mechanisms most likely explains the cause of RF's low vitamin B_{12} levels?

a. Decreased ability to absorb protein-bound vitamin B_{12}

b. Increased conversion of vitamin B_{12} to the inactive form

c. Increased HCL production

d. Decreased vitamin C intake which is required for vitamin B_{12} absorption

8. Nutritional frailty is defined as which of the following in older adults?

a. Albumin <3.5 mg/dL

b. Oral health problems which change appetite

c. Sarcopenia and rapid, unintentional weight loss

d. Complaints of food tasting bland

9. Body composition changes are a normal consequence of aging. Which of the following age-related physiological changes results in a reduced caloric need in older adults?

a. Lean body mass declines, fat mass increases

b. Bone mineral density increases

c. Vitamin and mineral absorption declines

d. Fat mass is reduced

10. BMI is used in older adults to assess nutritional status. Which of the following BMI cut-off points should be used as a red flag to signal the patient is underweight and further assessment is warranted?

a. BMI <16 kg/m^2

b. BMI <18.5 kg/m^2

c. BMI <22 kg/m^2

d. BMI <25 kg/m^2

11. Cachexia is the term used to describe the clinical wasting syndrome that results from the nutritional and metabolic abnormalities seen in cancer patients. Which of the following mechanisms play a role in the cachexia, malnutrition, and associated weight loss seen in cancer patients?

a. Decreased gluconeogenesis

b. Decreased mobilization of free fatty acids

c. Enhanced taste and smell perception

d. Altered cytokine levels

12. RH is a 49-year-old woman who has been complaining of mood changes, sleep disturbances, and hot flashes. She is most likely experiencing menopausal symptoms. Which of the following supplements could help to reduce her complains of hot flashes?

a. Valerian

b. Black cohosh

c. Garlic

d. Magnesium

13. LD is a 52 year-old-woman who has recently been prescribed bioidentical hormones to reduce her side effects of menopause. She is

experiencing constipation due to the progesterone cream. Which of the following supplements have been shown to be effective in treating constipation.

a. Vitamin C and magnesium

b. Vitamin D and calcium

c. Vitamin E and selenium

d. Vitamin B_6 and potassium

14. For people with intermediate to advanced age-related macular degeneration, how much can a high antioxidant supplement decrease the risk of disease progression?

a. 10%

b. 25%

c. 50%

d. 90%

Chapter 6 Cardiovascular Disease

1. Heart failure affects approximately 5 million adults in the United States and is characterized by decreased cardiac output, venous stasis, and sodium and fluid retention. Which of the following nutritional issues is also commonly associated with heart failure?

a. Increased muscle wasting and malnutrition

b. Decreased fat requirements

c. Increased protein stores

d. Decreased carbohydrate requirements

2. Omega-3 fatty acids (eicosapentanoic acid and docosahexenoic acid) are effective at reducing which of the following serum levels if they are abnormally elevated?

a. Lp(a)

b. LDL-cholesterol

c. Triglycerides

d. All of the above

3. JK is a 45-year-old male who comes to see his primary care clinician for a routine physical exam. He is 5′8″, weighs 210 pounds (BMI: 32 kg/m^2). His waist circumference is 41 inches and his fasting lab data showed: glucose: 109 mg/dL; triglycerides: 345 mg/dL; LDL-C: 130 mg/dL; total cholesterol: 220 mg/dL. Which of the following dietary interventions is most appropriate to suggest JK implement based on his labs?

a. Reduction in sodium intake

b. Reduction in fiber intake

c. Reduction in calories to promote weight loss

d. Reduction in monounsaturated fat intake

4. The National Cholesterol Education Program ATP III guidelines include the diagnostic criteria for metabolic syndrome. Which of the following HDL-C and waist circumference measurements can support the diagnosis of metabolic syndrome in MEN.

a. HDL <50 mg/dL and waist circumference >35 inches

b. HDL <40 mg/dL and waist circumference >40 inches

c. HDL <35 mg/dL and waist circumference >40 inches

d. HDL <35 mg/dL and waist circumference >35 inches

5. In addition to reducing dietary saturated fat and cholesterol, which of the following nutrition-related strategies has the greatest LDL-lowering effect?

a. Decreasing total fat intake

b. Increasing insoluble fiber intake

c. Decreasing trans fatty acid intake

d. Increasing omega-6 fatty acid intake

6. Alcohol may have cardioprotective effects by increasing HDL-C levels and reducing LDL-C oxidation via the antioxidant polyphenols. Which of the following are considered polyphenols?

a. Cynarin, alpha-linoleic acid

b. Genistein, green tea

c. Capsaicin

d. Catechin, quercetin, resveratrol

7. The Dietary Approaches to Stop Hypertension (DASH) trial has developed nutritional recommendations based on effectively reducing blood pressure. Which of the following daily combined number of fruit and vegetable servings are recommended in the DASH diet?

a. 2 to 4 servings of fruits and vegetables

b. 3 to 6 servings of fruits and vegetables

c. 6 to 7 servings of fruits and vegetables

d. 8 to 10 servings of fruits and vegetables

8. Including viscous or soluble fiber in the diet can decrease LDL-C levels when consumed on a regular basis by binding with and removing bile acids in the body. Which of the following amounts of soluble fiber is recommended to consume on a daily basis?

a. 1 to 2 grams per day

b. 3 to 4 grams per day

c. 5 to 10 grams per day

d. 20 to 25 grams per day

9. Epidemiologic studies suggest that eating fish is beneficial to reduce the risk of heart disease. According to the American Heart Association and the American Academy of Nutrition and Dietetics, how often should fish be consumed to reduce cardiovascular risk?

a. 1 time per week

b. 2 times per week

c. 1 time per month

d. 3 times per month

10. ST is a 62-year-old man with diabetes who presents to his primary care physician to discuss his lipid levels. He does not smoke but has a family history of heart disease. According to the new guidelines, what is the target LDL-C level?

a. <100 mg/dL

b. <130 mg/dL

c. <160 mg/dL

d. <190 mg/dL

11. Which of the following risk factors for metabolic syndrome has different criteria among various ethnic groups?

a. Hypertension

b. Fasting plasma glucose levels

c. Waist circumference measurement

d. HDL levels

12. SL is a 78-year-old woman who has been discharged from the hospital after being diagnosed with heart failure. What is the most appropriate medical nutrition therapy for a patient with heart failure?

a. Limit potassium intake to less than 2000 mg/day

b. Limit total fat intake to less than 30% of total calories

c. Limit sodium intake to 2000 mg/day

d. Limit cholesterol intake to less than 200 mg/day

Chapter 7 Gastrointestinal Disease

1. JF is a 28-year-old female with severe Crohn's disease who recently underwent an intestinal resection of her ileum. Which of the following is true regarding dietary management in this patient?

a. Fat malabsorption is unlikely to occur

b. Probiotic supplementation should be considered

c. Dietary modification should include reduced intake of foods high in oxalate

d. Omega-3 fatty acid supplementation should be used to help reduce the risk of disease reoccurrence following surgery

2. RP is a 68-year-old man with chronic liver disease and ascites. He has lost a significant amount of weight and demonstrates signs/ symptoms of protein-calorie malnutrition. Which of the following is correct regarding malnutrition and dietary management in patients with chronic liver disease?

a. Iatrogenic causes of malnutrition may include restricted diets, diuresis, and frequent paracentesis

b. Malabsorption may occur due to diminished bile acid production

c. Restricted protein intake should be limited to periods of acute encephalopathy only

d. All of the above

3. PV is a 63-year-old man recently diagnosed with peptic ulcer disease. Nutritional management of patients with peptic ulcer disease includes which of the following?

a. Counseling on avoidance of common trigger foods including coffee, tea, colas, and alcohol

b. Drinking only low fat milk

c. Eating less frequent, larger meals to reduce gastric acid production

d. Avoiding drinking liquids with meals

4. AL is a 45-year-old obese male with a BMI of 45 who presents for dietary counseling. AL admits to drinking one to two alcoholic drinks a week. Lab data through his primary physician showed elevations in multiple liver enzymes and a subsequent ultrasound was consistent with fatty liver disease. Which of the following should be a component of dietary counseling of this patient?

a. Rapid weight loss is indicated due to elevations in multiple liver enzymes

b. Regular dietary counseling and gradual weight loss programs should be encouraged

c. Protein restriction should occur, both to limit calories and risk of encephalopathy

d. Both b and c

5. Individuals who are lactose intolerant and choose to avoid products containing lactose may not meet daily calcium requirements. Which of the following is the best lactose-free source of calcium to recommend to patients who are lactose intolerant?

a. Fortified whole-wheat bread

b. Spinach

c. Soy or almond milk (enriched)

d. Ice cream

6. LH is a 55-year-old female who has recently been diagnosed with celiac disease. Which of the following nutrition-related statements is correct?

a. A gluten-free diet should be adhered to until symptoms resolve, then certain gluten-containing grains may be gradually reintroduced based on reoccurrence of symptoms

b. Vitamin/mineral supplements should be considered in patients with celiac disease

c. A gluten-free diet excludes all foods containing wheat but allows rye and barley

d. Oatmeal can be safely eaten on a gluten-free diet

7. MG is a 22-year-old man with cystic fibrosis. He is non-adherent with his pancreatic enzyme regime and subsequently suffers from fat malabsorption. He has a normal appetite and caloric intake; however, he has recently lost 20 lbs (9.1 kg) over the past 8 months. Which of the following nutritional advice is most appropriate at this time?

a. Consume a low fat diet

b. Add 2 to 3 Tbps of MCT oil per day

c. Incorporate an appetite stimulant

d. Consume a low fiber diet

8. Which of the following nutritional recommendations is correct for a patient experiencing abdominal pain and bloating related to irritable bowel syndrome (IBS)?

a. Diets high in lactose and fructose should be encouraged

b. Asparagus, broccoli, and cauliflower should be consumed due to their tendency to cause less gas

c. If symptoms are particularly bothersome, skipping the next meal should be considered as foods are a common trigger of IBS

d. Increased consumption of fiber, especially in constipation-predominant IBS

9. LT is a 24-year-old woman with unintentional weight loss of 30 pounds (13.6 kg) over the past 4 months despite a normal caloric intake. LT also complains of foul-smelling stools. After several days of work-up, she is diagnosed with Crohn's disease involving predominantly the small intestines at the level of the ileum. Which of the following is the most likely cause of her weight loss?

a. Anorexia related to abdominal pain

b. Colonic perforation

c. Excessive fiber intake

d. Vitamin deficiency

10. HN is a 68-year-old man with advanced liver disease. Recent labs show an elevated prothrombin time (PT). Which of the following condition is most likely to cause an elevation in PT levels in patients with advanced/end stage liver disease?

a. Vitamin K deficiency

b. Ascites

c. Reduced production of clotting factors

d. All of the above

11. EB is a 28-year-old obese woman, recently diagnosed with gastroesophageal reflux disease (GERD). She states that her symptoms are nocturnal, occurring mostly in the middle of the night. Which of the following recommendations may be most helpful in alleviating her symptoms?

a. Sleep with at least three pillows at night

b. Take an over-the-counter sleeping pill

c. Avoid eating at least two hours before bedtime

d. Drink warm tea before bed

12. Dietary management of adult patients with severe ascites should include which of the following?

a. Sodium restriction to less than 2000 mg/day

b. Protein restriction

c. Carbohydrate restriction to 20 to 30% of calories due to risk of hyperglycemia

d. Increase in free water to 50% above maintenance levels to avoid dehydration

Chapter 8 Endocrine Disease: Diabetes Mellitus

1. In addition to a random plasma glucose ≥200 mg/dL and classic symptoms of hyperglycemia or hyperglycemia crisis, which fasting glucose level supports a diagnosis of diabetes?

a. ≥110 mg/dL

b. ≥118 mg/dL

c. ≥126 mg/dL

d. ≥132 mg/dL

2. The hemoglobin A1C is used to assess whether an individual has prediabetes and an increased risk of developing diabetes. What A1C percentile range is considered prediabetes?

a. 4.5–5.0%

b. 5.1–5.6%

c. 5.7–6.4%

d. 6.5–7.0%

3. Which of the following time period best reflects when expected outcomes from medical nutrition therapy would be seen in patients with diabetes?

a. Within 1 week after initiation

b. Within 2 to 3 weeks after initiation

c. Within 4 to 5 weeks after initiation

d. Between 6 weeks and 3 months after initiation

4. Which of the following statements best summarizes the first priority of medical nutrition therapy in patients with type 2 diabetes?

a. Improve serum glucose and lipid levels

b. Improve physical activity level

c. Improve body image

d. Improve albumin levels

5. According to the American Diabetes Association, which of the following statements is correct regarding carbohydrate intake in patients with type 2 diabetes?

a. Low glycemic index diet will improve lipid levels

b. Increasing dietary fiber by 10 grams per day will reduce glucose levels

c. The total amount of carbohydrate ingested is more important than the source or type of carbohydrate

d. Basal insulin doses are based on the total amount of carbohydrates and protein in the planned eating pattern

6. Using the carbohydrate counting method for meal planning in patients with type 1 diabetes, which of the following amount equals one carbohydrate serving?

a. 5 grams of carbohydrate

b. 10 grams of carbohydrate

c. 15 grams of carbohydrate

d. 20 grams of carbohydrate

7. According to the National Cholesterol Education Program Adult Treatment Panel III guidelines and the American Diabetes Association, what is the target LDL cholesterol goal for adults with diabetes?

a. <100 mg/dL

b. <130 mg/dL

c. <160 mg/dL

d. <190 mg/dL

8. Nutritional recommendations from the American Diabetes Association, American Heart Association, and the Dietary Guidelines

for Americans agree on which of the following dietary guidelines for healthy eating?

a. Restrict carbohydrate intake

b. Increase protein intake

c. Limit saturated fat and avoid *trans* fats

d. Use only monounsaturated fats

9. Which of the following recommendations regarding alcohol consumption in persons with type 1 diabetes is most appropriate?

a. Alcohol should be consumed without food to avoid excess calories

b. Alcohol should only be consumed with food to prevent hypoglycemia

c. Sweet wines should be avoided because they raise blood glucose

d. Alcohol should not be consumed

10. Two major studies showed a 58% reduction in the onset of diabetes in a population of people with prediabetes. What percentage weight loss was necessary to achieve this risk reduction?

a. 7%

b. 12%

c. 20%

d. 28%

11. Which of the following conditions increases a patient's likelihood of developing insulin resistance?

a. History of impaired glucose tolerance

b. First-degree relative with type 2 diabetes

c. Central obesity

d. All of the above

12. Which of the following glucose-lowering medications is frequently used as first-line drug therapy in people with type 2 diabetes?

a. Alpha-glucosidase inhibitors (acarbose, miglitol)

b. Thiazolidinediones (pioglitazone)

c. Biguinides (metformin)

d. Sulfonylureas (glyburide/glibenclamide, glipizide, glimepiride)

13. Which of the following guidelines are appropriate for treating hypoglycemia in a patient taking insulin?

a. Treat with 15 grams of carbohydrate, wait 15 minutes and retest, treat again if blood sugar has not increase, retest in 1 hour

b. Treat with 30 grams of carbohydrates and retest in 2 hours

c. Treat with a 20-ounce regular soda and retest in 1 hour

d. Treat with a candy bar

14. What is the target range for the pre-meal plasma glucose levels for many non-pregnant adults with diabetes?

a. 70–130 mg/dL

b. 100–140 mg/dL

c. 150–180 mg/dL

d. 180–200 mg/dL

Chapter 9 Pulmonary Disease

1. DH is a 45-year-old woman with obstructive sleep apnea syndrome (OSAS). Medical nutrition therapy for patients with OSAS should focus on which of the following?

a. Protein repletion

b. Vitamin and mineral deficiencies

c. Weight reduction

d. Fluid retention

2. SW is a 78-year-old man with COPD and has recently lost 5 pounds since her last visit 6 months ago. What is the most likely cause of weight loss in this patient?

a. Increased metabolic rate due to work of breathing

b. Side effects from her medications

c. Increased respiratory muscle mass

d. Vitamin toxicity

3. Which of the following appetite stimulant has been helpful for patients with COPD by improving body composition and decreasing muscle wasting by inhibiting cytokine production?

a. Metformin

b. Garcinia cambogia

c. Ghrelin

d. Sibutramine

4. There are many potential side effects of COPD medications that may interfere with a patient's dietary intake. Which of the following are the most common side effects?

a. Diarrhea

b. Gastric irritation

c. Dry mouth and dysgeusia

d. All of the above

5. RG is a 59-year-old female who successfully undergoes a lung transplant. She is prescribed long-term steroid treatment. Which of the following side effects of steroid therapy may require consultation for nutritional services?

a. Hypoglycemia

b. Hyponatremia

c. Hypokalemia

d. Hyperglycemia

6. What is the primary reason why patients with cystic fibrosis require extra sodium intake?

a. To maintain body weight

b. To reduce blood pressure

c. To replace losses in perspiration

d. To reduce edema

7. Children diagnosed with cystic fibrosis who have had multiple infections and are taking long-term antibiotics are more likely to develop which of the following vitamin deficiencies?

a. Vitamin B_{12}

b. Vitamin K

c. Vitamin A

d. Thiamin

8. PW is receiving mechanical ventilation in the ICU and prescribed enteral nutrition support. Which of the following additions to enteral formula has been shown to enhance the immunological barrier in the GI tract via enterocytes and colonocytes?

a. Glutamine

b. Theonine

c. Omega-6 fatty acids

d. Magnesium

9. Patients receiving enteral feedings who are on mechanical ventilation need to be monitored carefully to avoid overfeeding because too many calories can result in which of the following?

a. Decreased RQ

b. Increased sputum production

c. Excessive CO_2 production

d. Decreased dyspnea

10. PW is an 18-year-old boy with cystic fibrosis. Which of the following factors contribute to the osteopenia seen in patients with cystic fibrosis?

a. Malabsorption

b. Vitamin D deficiency

c. Delayed puberty

d. All of the above

11. FR is a 39-year-old obese male who was recently diagnosed with obstructive sleep apnea syndrome (OSAS) and prediabetes. Recent research has shown that some patients with OSAS have lower plasma levels of which of the following neuropeptide?

a. Orexin

b. Amyloid beta

c. Alanine

d. Cannabanoid

12. RD is a 12-year-old girl with cystic fibrosis who is admitted to the hospital with weakness and lethargy. She has had increased foul-smelling stools and a recent loss of 6 pounds. What is the most likely cause of the patient's weight loss?

a. Heart failure

b. Malabsorption

c. Liver disease

d. Anemia

Chapter 10 Renal Disease

1. BC is a 22-year-old male with acute renal failure who is admitted to the hospital. A nutrition support service consultation is requested to determine the patient's calorie requirements. Which of the following calorie requirements should be used for individuals with acute renal failure?

a. 10–20 kcal/kg per day

b. 20–30 kcal/kg per day

c. 30–50 kcal/kg per day

d. 50–60 kcal/kg per day

2. OK is a 62-year-old woman with stage 4 chronic kidney disease. She will most likely need dialysis in the next 6 months. Medical nutrition therapy for patients with chronic kidney disease prior to initiating dialysis restricts protein for which of the following reasons?

a. An attempt to slow the progression of chronic kidney disease

b. To compensate for an increase in excretion of nitrogenous waste products

c. To better control hypertension

d. To reduce appetite

3. AE is a 48-year-old man who recently passed a kidney stone containing calcium oxalate. Which of the following recommendations for diet modification should be made?

a. Reduce calcium intake

b. Increase protein intake

c. Increase in daily fluid intake to 1500 cm^3/day

d. Increase fiber intake

4. WG is a 52-year-old woman who has recently undergone renal transplantation due to stage 5 chronic kidney disease most likely caused by diabetes and hypertension; she had been undergoing hemodialysis three times per

week for 4 years. Which of the following side effects related to some immunosuppressive agents would require dietary intervention?

a. Hyperlipidemia

b. Hypermagnesemia

c. Hypoglycemia

d. Hyperphosphatemia

5. Restricting dietary phosphate intake for individuals with chronic kidney disease stage 5 with dialysis to maintain proper calcium/ phosphorus balance may decrease severity of which of the following medical problems?

a. Secondary hyperparathyroidism

b. Vascular and soft tissue calcifications

c. Rheumatoid arthritis

d. All of the above

6. Patients in early stages of chronic kidney disease who are taking which of the following therapies to control blood pressure and possibly slow the progression of chronic kidney disease may be at risk for developing hyperkalemia?

a. Dietary salt substitutes

b. Angiotensin converting enzyme inhibitors

c. Calcium channel blockers

d. All of the above

7. GN is a 46-year-old woman receiving hemodialysis (HD) in an outpatient facility. She is 5′3″ (160 cm) and weighs 110 lbs (50 kg). Her lab data are BUN: 65 mg/dL; albumin: 3.7 g/dL; creatinine: 9.2 mg/dL. Considering GN is receiving HD three times per week, how much protein should she be consuming daily?

a. <50 grams protein/day

b. 60–65 grams protein/day

c. 75–90 grams protein/day

d. >90 grams protein/day

8. The kidney plays an essential role in the metabolism of which of the following metabolic conversions?

a. Beta carotene to vitamin A

b. Oxalic acid to ascorbic acid

c. Ferrous sulfate to ferric sulfate

d. 25(OH)D to $1,25(OH)_2D$

9. DT is a 48-year-old woman with nephrotic syndrome. In addition to reducing dietary fat intake, protein intake should also be limited to 0.8–1.0 g/kg per day. Which of the following mechanisms explains why moderate protein intake is advised for patients with nephrotic syndrome?

a. To reduce the amino acid load in the glomerulus

b. To increase albumin excretion

c. To reduce nitrogen balance

d. To increase hepatic protein synthesis

10. TD is a 62-year-old man with chronic kidney disease and normocytic, normochromic anemia. He is undergoing peritoneal dialysis with the automated cycler machine at home. He is adequately dialyzed and felt to be adherent to his dialysis regimen. Which of the following mechanisms best explains the associated anemia in this patient with chronic kidney disease?

a. Blood loss due to dialysis procedure

b. Vitamin B_{12} deficiency

c. Decreased erythropoietin production

d. Folate deficiency

11. When assessing the nutritional status of a patient with chronic kidney disease undergoing chronic hemodialysis, it is important to use the patient's estimated dry weight for all calculations. Which of the following is the best definition of “dry weight”?

a. The weight when the patient is dehydrated

b. The weight when the patient has not drunk any fluids in 12 hours

c. The weight after the patient has received dialysis

d. The weight of the patient when no apparent edema or hypertension is present

12. NW is a 46-year-old male with stage 4 chronic kidney disease. He weighs 200 lbs (90.9 kg), an ideal body weight for him, and he is not retaining fluid. A 24-hour urine collection indicated a loss of 2.1 grams of protein due to proteinuria, but not likely significant to add to his protein needs. What are his daily protein requirements?

a. 50.3 g/day

b. 56.5 g/day

c. 73 g/day

d. 121 g/day

13. AP is a 64-year-old woman with type 2 diabetes who visits her internist for a yearly physical. Her serum creatinine and BUN levels are significantly elevated and the physician suspects renal disease. Which of the following parameters are appropriate to consider when she completes her 24-hour urine collection?

a. Urinary red blood cells

b. Protein excretion

c. Creatinine excretion

d. All of the above

Chapter 11 Cancer Prevention and Treatment

1. According to research on the link between obesity and cancer risk, which of the following women have the highest risk of developing breast cancer?

a. Pre-menopausal woman with a BMI of 30 kg/m^2

b. Post-menopausal woman with a BMI of 30 kg/m^2

c. Pre-menopausal woman with a BMI of 22 kg/m^2

d. Post-menopausal woman with a BMI of 40 kg/m^2

2. According to the National Cancer Institute, what is the strongest and most consistent predictor of breast cancer risk?

a. Amount of physical activity

b. High intake of saturated fat

c. Weight gain during adulthood

d. History of heavy menstruation

3. TB is a 48-year-old physically inactive man with a family history of cancer. He recently quit smoking and is eating more healthy foods. He asks his physician what additional preventive

steps he can take to reduce his risk of cancer. Which of the following lifestyle changes should be recommended to TB to help reduce his risk of developing cancer?

a. Eat only organic foods

b. Begin a regular physical activity program for 30 minutes every day

c. Eliminate all dairy foods

d. Eliminate all sugar from his diet

4. According to the American Institute for Cancer Research, dietary recommendations to reduce the risk of colon cancer include which of the following statements about red meat intake?

a. A maximum of 18 ounces of cooked red meat per week with no processed meat consumption

b. Cook meats well done, preferably using BBQ grilling methods

c. A maximum of 12 ounces of cooked red meat and 4 ounces of processed meat per week

d. Red meat has not been linked to colon cancer

5. Flavonoids are a class of phytochemicals that act as an antioxidant and absorb free radicals, thus potentially protecting against certain types of cancer. Flavonoids are found in high concentrations in which of the following foods?

a. Dark green leafy vegetables

b. Cruciferous vegetables

c. Tomatoes and tomato products

d. Berries, grapes, green tea

6. MC is a 55-year-old female who questions her gynecologist about the pros and cons of eating more foods with soy. Consumption of foods made with soy *may* be protective against which type of cancer?

a. Breast cancer

b. Colon cancer

c. Stomach cancer

d. Uterine cancer

7. Several compounds in red wine have been shown to possess antioxidant and anti-angiogenic properties. Which of the following polyphenols is present in red wine?

a. Quecetin

b. Resveratrol

c. Lycopene

d. Glucosinolate

8. FS is an 86-year-old man who was admitted to the hospital with dehydration and pneumonia. At what point should cancer cachexia be suspected?

a. If he experienced an unintentional weight loss greater than 5% of his weight over the previous month

b. Immediately upon first impression of the patient

c. Complaining of home and joint pain

d. If nausea and fatigue are present

9. AW is a 71-year-old woman who is receiving daily radiation treatment for colon cancer. Which of the following side effects of radiation treatment is most likely to affect this patient's nutritional intake?

a. Insomnia

b. Radiation pneumonitis

c. Nausea and vomiting

d. Alopecia

10. KB is a 53-year-old female who is receiving weekly chemotherapy following surgery for breast cancer. Which of the following nutrition recommendations can help control her complaints of nausea after treatment?

a. Avoid eating within 4 hours

b. Eating smaller, more frequent meals

c. Eating larger meals in the middle of the day

d. Add more fiber to meals

11. Excessive alcohol consumption has been linked as the primary cause of liver cancer. Alcohol users also experience which of the following types of cancers six times more often than non-alcohol users?

a. Pancreatic cancer

b. Brain cancer

c. Colon cancer

d. Oral cancer

Chapter 12 Enteral Nutrition Support

1. In a critical care patient who has a functional GI tract but is unable to ingest adequate nutrients by mouth, when is tube feeding a useful therapy?

a. Three days after coronary bypass surgery in a well-nourished patient

b. A patient with Crohn's disease who has a small bowel obstruction

c. Seven days after a stroke in a patient with aspiration and dysphagia when swallowing

d. Following surgery for ischemic bowel with 50 cm of remaining small bowel

2. When is a percutaneous endoscopic gastrostomy (PEG) tube indicated for a patient requiring tube feeding?

a. Never

b. When tube feeding is expected to be for greater than 4 to 6 weeks

c. When a patient has gastroparesis and failed an oral diet

d. When a patient is being weaned from intubation

3. When a patient is ambulatory and transitioning to eat small amounts of food, what is the best method for administering supplemental tube feeding to maintain their appetite?

a. Nocturnal cycle over 8 to 12 hours

b. 24-hour continuous

c. Three bolus feedings daily

d. Tube feeding should not be administered to patients who can eat

4. When a patient receiving tube feeding and antibiotics develops diarrhea, which of the following tests is indicated before prescribing anti-diarrheal medications in order to avoid toxic megacolon?

a. Small bowel biopsy for celiac disease

b. Stool for *Clostridium difficile* toxin

c. Bacteria culture of formula

d. Blood test for parasites

5. What is the benefit of adding fiber to enteral formulas?

a. Helps normalize bowel function

b. Promotes the growth of intestinal flora

c. Provides prebiotic effects

d. All of the above

6. Which of the following antioxidants are added to some enteral formulas?

a. Copper and manganese

b. Vitamin B_{12} and folic acid

c. Vitamin C and vitamin E

d. Calcium and potassium

7. What is the preferred feeding tube placement in an ICU patient with severe, acute pancreatitis?

a. Nasogastric

b. Nasojejunal

c. Percutaneous endoscopic gastrostomy

d. Surgical gastrojejunostomy

8. Lack of enteral stimulation in the GI tract may contribute to which of the following complications?

a. Gut atrophy and higher infection risk

b. Vitamin K deficiency and bleeding

c. Hypoglycemia and higher infection risk

d. Suppressed thyroid function and muscle wasting

9. What enteral formula density is appropriate for a patient who requires a fluid restriction?

a. 0.5–0.8 kcal/mL

b. 0.8–1.0 kcal/mL

c. 1.0–1.2 kcal/mL

d. 1.5–2.0 kcal/mL

10. Enteral formulas supplemented with glutamine are designed to accomplish which of the following?

a. Decrease inflammation

b. Improve glucose control

c. Promote immune function and improve bowel integrity

d. Normalization of BUN and creatinine

11. How can the risk of aspiration be reduced in a patient receiving enteral tube feeding?

a. Feed into the stomach

b. Elevate head of bed to greater than 30 degrees

c. Feed at night only

d. Hold tube feeding for gastric residual >200

12. What is the most commonly reported GI complication for a patient receiving tube feeding?

a. Nausea/ vomiting

b. Constipation

c. Reflux

d. Diarrhea

13. AK is a 65-year-old man who is undergoing radiation therapy for thoracic tumor. He has odynophagia and needs a nutrition consultation for a special diet. Medical nutrition therapy for a patient with odynophagia includes which of the following recommendations?

a. Low-fat diet

b. Avoidance of cooked fruits and vegetables

c. Soft, blended foods

d. High carbohydrate diet

Chapter 13 Parenteral Nutrition Support

1. Parenteral nutrition is utilized in patients in which of the following clinical scenarios?

a. Diminished motor capacity makes eating difficult

b. Enteral nutrition is not possible

c. When the patient has dementia

d. When the patient has poor oral intake

2. Central parenteral nutrition is indicated in which of the following clinical scenarios?

a. Long-term parenteral nutrition support (longer than 7 days) is anticipated

b. In fluid restricted patients

c. A patient has a moderately-to-severely elevated metabolic rate

d. All of the above

3. When using peripheral parenteral nutrition solutions, what is the maximum allowable concentration to prevent vascular damage?

a. 600 mosmol per liter

b. 800 mosmol per liter

c. 900 mosmol per liter

d. 1000 mosmol per liter

4. According to the Enteral Nutrition Guidelines for the Provision of Nutrition Support Therapy in the Critically Ill Adult, if a patient is malnourished parenteral nutrition support should be initiated in which of the following scenarios?

a. 5–7 days pre-operatively

b. Parenteral Nutrition should not be initiated until 5–7 days post-operatively if EN is not feasible

c. Parenteral Nutrition should not be initiated unless the anticipated duration is ≥ 7 days.

d. All of the above

5. How much of the total energy prescription for parenteral nutrition should be supplied as protein?

a. 5 to 10 percent

b. 10 to15 percent

c. 15 to 20 percent

d. 20 to 25 percent

6. The dextrose infusion rate of parenteral nutrition should be limited to how many mg per kg per minute in a stable hospitalized patient>

a. 5 mg per kg per minute

b. 6 mg per kg per minute

c. 7 mg per kg per minute

d. 8 mg per kg per minute

7. Lipid emulsions should **NOT** be given to patients receiving parenteral nutrition in which of the following situations (may be more than one)

a. In patients with hypertriglyceridemia-induced pancreatitis

b. In patients have egg allergies

c. In patients with serum triglycerides greater than 400 mg per dL

d. All of the above

8. Which of the following is the best IV access for long-term parenteral nutrition support?

a. Tunneled cuffed catheter

b. Non-tunneled central venous catheter

c. Peripherally inserted central catheter

d. Tunneled non-cuffed catheter

9. Which of the following potential metabolic complications of PN should be monitored?

a. Hyperglycemia

b. Electrolyte imbalances

c. Dehydration and fluid overload

d. All of the above

10. In order to reduce the risk of developing refeeding syndrome in a severely malnourished patient, which of the following PN solutions would be appropriate to administer for the first few days while closely monitoring phosphorus, potassium, magnesium, glucose, and fluid status?

a. Provide a high protein and high calorie PN solution

b. Provide a high electrolyte PN solution

c. Provide a low-dextrose PN solution

d. Provide a low protein PN solution

11. A long-term complication of PN support includes which of the following conditions?

a. Metabolic bone disease

b. Multiple sclerosis

c. Hyperparathyroidism

d. Fibromyalgia

12. When is the most appropriate time a patient should discontinue PN when transitioning to oral feeding?

a. As soon as the patient is able to tolerate any oral feeding

b. When the patient tolerates 50 percent of daily nutrition requirements through the oral diet

c. When the patient tolerates 75 percent of daily nutrition requirements through the oral diet

d. When the patient tolerates 100 percent of daily nutrition requirements through the oral diet

Review Answers

Chapter 1 Overview of Nutrition Assessment in Clinical Care

1. c
2. d
3. c
4. a
5. b
6. d
7. c
8. d
9. d
10. a
11. c
12. b
13. b

Chapter 2 Vitamins, Minerals, and Dietary Supplements

1. c
2. a
3. a
4. c
5. b
6. a
7. c
8. a
9. d
10. a
11. b
12. d

Chapter 3 Nutrition in Pregnancy and Lactation

1. a
2. c
3. c

4. d
5. d
6. b
7. a
8. a
9. c
10. a
11. a
12. b
13. a

Chapter 4 Infants, Children, and Adolescents

1. c
2. d
3. a
4. d
5. b
6. c
7. a
8. c

9. c
10. b
11. a
12. b
13. d
14. b
15. a

Chapter 5 Older Adults

1. b
2. c
3. c
4. b
5. d
6. b
7. a
8. c
9. a
10. c
11. d
12. b

13. a

14. b

Chapter 6 Cardiovascular Disease

1. a

2. c

3. c

4. b

5. c

6. d

7. d

8. c

9. b

10. a

11. c

12. c

Chapter 7 Gastrointestinal Disease

1. c

2. d

3. a

4. b

5. c

6. b

7. b

8. d

9. a

10. d

11. c

12. a

Chapter 8 Endocrine Disease: Diabetes Mellitus

1. c

2. c

3. d

4. a

5. c

6. c

7. a

8. c
9. b
10. a
11. d
12. c
13. a
14. a

Chapter 9 Pulmonary Disease

1. c
2. a
3. c
4. d
5. d
6. c
7. b
8. a
9. c
10. d
11. a
12. b

Chapter 10 Renal Disease

1. b
2. a
3. c
4. a
5. b
6. b
7. b
8. d
9. a
10. c
11. d
12. c
13. d

Chapter 11 Cancer Prevention and Treatment

1. d
2. c
3. b

4. a
5. d
6. a
7. b
8. a
9. c
10. b
11. d

Chapter 12 Enteral Nutrition Support

1. d
2. b
3. a
4. b
5. d
6. c
7. b
8. a
9. d
10. c

11. b

12. d

13. c

Chapter 13 Parenteral Nutrition Support

1. b

2. d

3. c

4. d

5. c

6. c

7. d

8. a

9. d

10. c

11. a

12. b

REGISTRATION FORM FOR DIETITIANS AND DIETETIC TECHNICIANS
CONTINUING PROFESSIONAL EDUCATION: LEVEL III

MEDICAL NUTRITION AND DISEASE, 5th Edition
Edited by Lisa Hark, PhD, RD, Darwin Deen, MD, MS, and Gail Morrison, MD

This conventional self-study activity is pre-approved by the Academy of Nutrition and Dietetics, Commission on Dietetic Registration for **48 credits**. Follow the instructions:

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2. Grade yourself using the answers in *Medical Nutrition and Disease*, 5th Edition (pp. 552–554). Successful completion of this self-study activity requires that you attain at least 80% correct. If you do not attain this score, retest yourself. Please note, credits are awarded for completion of the entire book only, not for individual chapters.
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Additional questions to Dr. Lisa Hark, please call 610-659-1834 or email to hark@lisahark.com.
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Edited by Lisa Hark, PhD, RD, Darwin Deen, MD, MS, and Gail Morrison, MD

Provider's Name: Lisa Hark, PhD, RD (hark@lisahark.com)

Activity Type: Conventional Self-Study (Code: 720)

Activity Topic: (Code: CL0000) Clinical Nutrition

Pre-Approved for 48 CPE Units, Activity date: September 1, 2014 thru August 31, 2019

Learning Need: (Code: 5000) Medical Nutrition Therapy CPE Level: 3

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Registration Number _____

Date Completed _____

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Registration Number _____

Date Completed _____

Answer Sheet: Medical Nutrition & Disease 5th Edition

Answer Sheet for Registered Dietitians

Medical Nutrition and Disease: Chapters 1–13 Review Questions located on pages 523–551. Fill in the correct answers and grade yourself when finished. Expiration date: August 31, 2019 Complete the other side. No additional self-reporting form is needed. More than one dietitian may read the book and copy these forms. There are no fees. Credits are awarded for completion of the entire book only, not for individual chapters.

Chapter 1
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Correct_____/166

Answers to these questions are located in *Medical Nutrition & Disease, 5th Edition* on pages 552–554.

Completion of this independent learning activity requires that you attain at least 80% correct

(133 correct answers out of 166). If not, retest yourself and indicate the corrected score on the form.

Questions, please email Lisa Hark, PhD, RD at hark@lisahark.com

Index

Tolerable Upper Intake Levels

- boron
- calcium
- choline
- copper
- defined
- fluoride
- folic acid
- iodine
- iron
- magnesium
- molybdenum
- niacin
- nickel
- phosphorus
- selenium
- vanadium
- vitamin A
- vitamin B_6
- vitamin C
- vitamin D
- vitamin E
- zinc

supplements
Tolerable Upper Intake Levels
toxicity