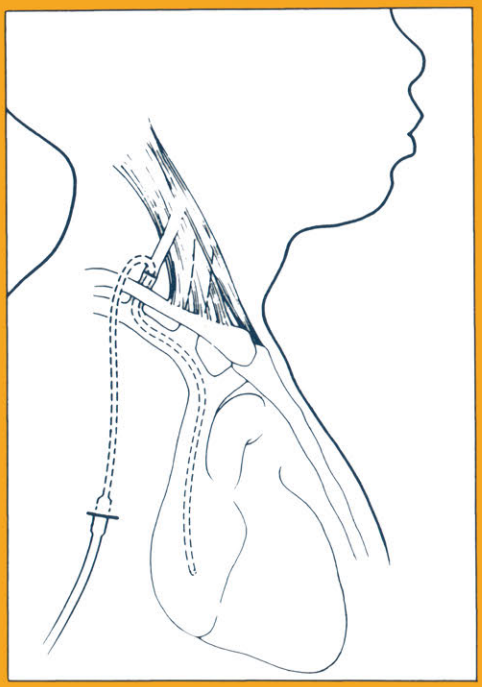
A Handbook of Parenteral Nutrition

Hospital and home applications



Edited by

H.A. Lee and G. Venkat Raman

SPRINGER-SCIENCE+BUSINESS MEDIA, B.V.

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To our wives Gilly and Kumkum

Contents

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Preface

Total parenteral nutrition (TPN) is now an everyday occurrence in most general hospitals. Over the last two decades this therapeutic modality has been made so simple that it is no longer the province of the specialized surgeon or physician. Indeed, as with the management of chronic renal failure so now with short bowel disease, home parenteral nutrition has become a reality, though this still requires a specialist team dedicated to its management.

Furthermore, as more patients will become suitable for home TPN treatment (either long term or short term) so better rationalization of (a) cost, (b) delivery systems and (c) patient training will be necessary. Lessons can be learnt from the somewhat diverse development of regular dialysis treatment in the early 1960s compared with the situation today. Here is a golden opportunity, with the UK National Registry, to rationalize on home TPN costs and to make sure the treatment is simplified and available to all those who may require this treatment.

This book is not designed to be an overall comprehensive review of parenteral nutrition. It is meant to set out simple guidelines and the requirements for effective TPN both in hospital and at home. It is aimed at doctors in training, interested physicians and surgeons, nurses, dietitians and pharmacists. The purpose is to stimulate interest and awareness, rather than to provide detailed 'small-print' information. For the person seeking greater knowledge, there are several excellent monographs on the subject.

The book sets out the historical background to the development of TPN, its use in hospital practice and its application (by self-care) in the home environment. This latter aspect, in particular, has been helped by the creation of the nurse specialist in nutritional support in many hospitals. In our own

district, in common with many others, the nutritional support team is multidisciplinary and provides advice on the biochemical, pharmaceutical, medical, nursing and psychosocial aspects of nutritional support (both enteral and parenteral), either in hospital or in the home.

It is the hope of the authors that this small volume will emphasize the relative simplicity of this treatment and broaden the indications for its application. We also hope that this book will help to influence respective sources of finance (the government in the case of this country), to provide adequate funding that is required for successful home TPN. There should be no question of any financial pressures being brought to bear upon the families of patients requiring TPN. It is the view of the editors that this therapeutic modality, particularly in the home environment, will increase and hopefully gain recognition from the government for central funding.

The editors would like to thank their contributors for their valuable contributions; without their cooperative assistance this volume would not have been complete, nor would it have the same degree of credibility. We are also grateful for the patient forbearance of our secretaries Mrs June Donovan, Mrs Susan Morris and Miss Heather Morton, who were instrumental in preparing the original manuscripts and the (many) subsequent re-editions. We are grateful to the nursing, dietetic and pharmacy staff, who have contributed so much to the formation and function of our Nutritional Support Team. We would like to thank Professor Miles Irving of Hope Hospital, Salford for providing free access to the information from the UK TPN Registry and Dr Alan Shenkin, Consultant Clinical Biochemist, of Glasgow Royal Infirmary for numerous trace element estimations and valuable clinical advice. Finally, we are indebted to all the patients who have undergone great suffering, with fortitude and courage, and taught us a great deal more than just medicine.

H.A. LEE
G. VENKAT RAMAN

1 *History of parenteral nutrition*

H.A. Lee

It is not the purpose of this chapter to review the early beginnings of total parenteral nutrition (TPN) but rather to discuss the evolution, particularly over the past 20 years, of this therapy. About 25 years ago it became apparent that TPN had value in the management of critically ill patients who were not being normally nourished because they either had gastrointestinal failure or could not tolerate the enteral preparations offered.

The earlier part of this century was spent in trying to evolve specific amino acid solutions that met the essential daily requirements of patients being fed intravenously. Simultaneously the search was on for intravenously administered energy components and the emphasis was on glucose; others were also trying to develop some form of lipid emulsion that could be given intravenously. By and large these problems were resolved in a general sense by the late 1950s when amino acid preparations (e.g. caseine hydrolysates, fibrin hydrolysates) became available as nitrogen sources along with glucose solutions of various concentrations, and fat emulsions. It must be remembered, however, that the early amino acid solutions were impure and contained many contaminants such as ammonia, and unknown quantities of trace elements. Furthermore, they contained varying amounts of electrolytes as well as nitrogen sources such as peptides about which there was little information as to their utilization. With respect to energy sources, the battle raged concerning glucose versus fructose versus xylitol, sorbitol or even the inclusion of maltoses and ethanol. By the early 1970s it was appreciated that the main energy sources should be glucose (varying concentrations) with or without a fat emulsion and the consensus view was

that the latter should be soya bean based. However, the problems did not cease there, because there were many controversies in the literature as to whether glucose alone should be used in certain situations, e.g. sepsis, or whether there was ever a case for combining glucose with fat. By the early 1980s there was clear cut evidence that the combination of fat and carbohydrate on an equienergetic basis with a suitable nitrogen source was the right way to approach total parenteral nutrition, be that on a short term basis or even long term. There were still the sceptics who claimed that to infuse fat during septic states was to exacerbate the negative metabolic equilibrium in these patients, although the work of recent authors has put this finally to ground.

Returning to the question of amino acid preparations, the 1970s saw the advent of crystalline amino acid solutions and though they were more expensive than the caseine hydrolysates (or other variations) nevertheless they were more physiological, chemically defined and well tolerated. Furthermore, the problem of other contaminants such as peptides, trace elements and vitamins was eliminated. Even to this present time, the question of the precise amounts of vitamins and trace elements to add to various TPN regimens is not resolved because these supplements are very difficult to measure and few laboratories have such facilities. Nevertheless, there are very few examples in adult practice of bona fide vitamin deficiency occurring as a result of TPN.

Returning to the question of trace elements (essential biological elements) much has been learned about these substances as a result of long term home parenteral nutrition (HPN). HPN has developed over the past 15 years and has grown from strength to strength. Indeed, it is true to say were it not for such patients being maintained on long term nutrition many of our current concepts about trace elements and vitamin requirements would not exist. As a result of such work, we are now better equipped to understand basic requirements for chromium, selenium, molybdenum, nickel, to name but a few. Considerable advances have also been made in terms of infant requirements of TPN.

Over the years, there has been much discussion as to whether or not hospitals could afford to administer parenteral nutrition (total or partial) to patients with clinical malnutrition. Much of this problem arose, of course, because many were

being treated with TPN when, in fact, they could have been treated with enteral nutrition (these products have improved enormously in the last decade). Nevertheless, if one considers that 5–15% of all acute hospital admissions require some form of aggressive nutritional support and one third of those require TPN then some idea of the size of the problem can be appreciated. Though TPN may be expensive, nevertheless one has to measure this against the cost of prolonged hospital stay and, indeed, increased morbidity and mortality. There is little doubt that appropriate administration of TPN can be life saving, totally cost effective and a tribute to modern advances in clinical medicine.

Over the past 10–15 years, the arguments have raged as to which patients would best benefit from giving TPN. It has to be said quite categorically that the only indication for TPN is total gastrointestinal failure, though of course, there may be partial indications when, although the gastrointestinal tract is partially available for nutrition, it cannot accommodate the total increased needs of a hypercatabolic patient – giving rise to partial or supplemental parenteral nutrition. In the past, far too much work on TPN has been done at the expense of enteral nutrition. Though I believe there is now rationalization, those patients really requiring TPN should be given it and there should be no excuse on the grounds of it being a specialized approach to metabolic and nutritional homeostasis. TPN is now available in all hospitals in the UK and many hospitals now have a Nutritional Support Team where advice can be obtained from interested clinicians, pharmacists, nurses and other ancillary staff.

One of the important breakthroughs in the last decade has been the advent of the 3 litre bag. Whereas, formerly, energy (glucose and fat) and amino acids had to be given through separate bottles, going into a triple line system, now all the ingredients can be given in a 3 litre bag without precipitation of particulate matter and without bacterial contamination. Furthermore, the bag can be prepared up to 7 days before use. Clearly, this approach has much to recommend itself to patients on hospital wards who are fairly stabilized and in whom it is known that normal gastrointestinal function will not return for a few weeks. However, in the intensive care situation, where day to day requirements may rapidly change, there are still those who would argue that the 3 litre bag could

be wasteful in terms of ingredients, accuracy and cost.

Also, over the past 20 years, there have been enormous advances in obtaining optimal angio access sites. Whereas formerly it was common practice to give intravenous (IV) feeding via peripheral veins it is now accepted that central lines (usually via the infra-clavicular route) are optimal for such nutritional approaches. Also it is generally agreed that such intravenous feeding lines should be dedicated to IV feeding requirements alone and other requirements such as cytotoxic drugs or antibiotics, be given by some other route. However, with the development of multi-lumen central catheters it is indeed now possible to give TPN via a central line and also other therapies such as cytotoxic agents or antibiotics. Over the last decade, much of the literature has been flouted by a confusion of terms concerning peripheral and central IV nutrition. Certain peripheral lines may be entered peripherally but end up centrally, and therefore, the difference between a central and peripheral line may be minimal. In peripheral hospitals with less expertise this type of catheter is an ideal way of providing TPN. Overall there has been some confusion about the approach of giving amino acids and 5% dextrose peripherally. Few patients so treated have been shown to achieve positive nitrogen balance. Nevertheless, it is gratifying to note that there are preparations available, comprising of crystalline amino acids, carbohydrate and fat that can be administered peripherally through a short cannula without inducing local thrombophlebitis. Although for many years peripheral TPN to the purist has been heresy, it is now possible and no doubt many more patients will benefit from the administration of TPN.

Over the last 10–15 years there has been a growing literature on the advent of home TPN and indeed in the UK there have been six annual reviews of this particular modality. There are a number of patients who have irreversible bowel disease, such as short bowel resection, radiation ileitis, pseudo obstruction of the bowel or, in infants, Hirschsprung's disease, where, but for intravenous nutrition, there would be no hope of survival. In the United Kingdom there is now a National Support Group for such infants. Overall in this country a few hundred patients have been treated at home on long term TPN. It must be noted that so far the question of home parenteral nutrition (HPN) has not received much attention. This has been regarded as somewhat avant garde and

therefore, appropriate funding has not been administered. There are many similarities between HPN and home dialysis. The latter has received widespread support; however, many families with small infants requiring home TPN have been frustrated in their attempts to obtain funding. It is worth remembering that whereas most chronic renal failure patients have no hope of regaining normal renal function, apart from successful transplantation, many HPN patients will, if they are given a period of bowel rest, reacquire their normal bowel function.

The questions of home parenteral nutrition abound. Should these be managed by the patients themselves, in other words, they make up their own bags, connect their own lines, etc., or, should they be dependent upon commercial enterprises? We in Portsmouth have been responsible for a so-called home DIY service, whereby patients are responsible for: (a) ordering on a monthly basis their own ingredients; (b) mixing them daily; and (c) administering them, without any morbidity or significant infective or metabolic problems. The difference between this approach and commercially supplied home TPN is of the order of £10 000 per patient per annum. Although the number of patients requiring this treatment is not large, i.e. 2 per million, nevertheless, it might be apparent that if more patients received this treatment then that differential of £10 000 per annum would be very substantial.

The current situation is that TPN is now available to many patients who have absolute gastrointestinal failure and who can be treated by comprehensive parenteral nutrition comprising energy, nitrogen, vitamins, electrolytes and trace elements. The cost of this treatment is now respectable in relation to the cost of in-patient stay. Furthermore, many patients with irreversible gastrointestinal failure can be managed on long term HPN. Whether or not in the future the prospect of bowel transplantation becomes reality is a matter for speculation and research. TPN is now a simple and rational approach to patient management and should be considered an integral part of the management of any acutely ill patient who happens to have concomitant intestinal failure, whatever the cause. With the advent of multidisciplinary teams it is no longer difficult to prescribe a comprehensive feeding regimen which increases the chances of patient survival. No longer can 'starvation in the midst of plenty' be allowed to occur in hospital practice

anywhere in the world. If that does really occur – in the presence of adequate finance, equipment and expertise – then it must reflect a measure of medical ignorance, if not carelessness.

Incidentally, it should be remembered that even though the cost of TPN is currently about £50 to £70 per day, the cost of an NHS bed is around £130 per day and if that patient's stay is prolonged because of the consequences of malnutrition, then clearly, the use of TPN is totally justified. Most importantly, home TPN allows the individual to work normally and have a near-normal home life style.

2 *General principles of parenteral nutrition*

G. Venkat Raman

With advances in the various aspects of clinical medicine the need and indications for parenteral nutrition are increasing progressively. This is due to a combination of availability of better medical and surgical facilities to treat conditions which were hitherto lethal; increasing age of patients so treated; and increasing awareness on the part of doctors, nurses and nutritionists, of the importance of providing adequate nutrition and of the fact that in potentially curable situations patients may actually die because of malnutrition. This is particularly true in conditions of high metabolic stress such as acute renal failure, burns and other major trauma (surgical or otherwise). In this age of 'hi-tech' medicine and bio-engineering it is only too easy to concentrate on intensive therapeutic modalities such as dialysis, cardiopulmonary monitoring and assisted ventilation and neglect the most fundamental aspect of patient management, namely provision of adequate food! It is worth bearing in mind that patients who are even moderately unwell are rarely capable of eating adequate amounts on their own. Thus it is essential for everyone involved in patient care to constantly address themselves to the question of whether or not each patient is receiving sufficient nutrition. The average human being has rather limited energy reserves and virtually no protein reserve. Thus in a situation of demand with inadequate supply the body rapidly uses up the energy reserves and then proceeds to break down protein for further energy, resulting in progressive loss of body cell mass.

If nutritional support is required then the next question that arises is: enteral or parenteral? The fundamental rule is to consider the enteral route first, as the optimum method, for

the following reasons:

1. it is easy to set into operation;
2. it is clinically safer;
3. requires less medical and nursing expertise;
4. more 'physiological';
5. much more satisfying to the patient; and
6. substantially less expensive.

Bowel loss or bowel failure is therefore an important prerequisite for parenteral nutrition. Parenteral feeding is often needed for finite periods of time to tide patients over illnesses. On the other hand it becomes obligatory and life supporting in conditions characterized by inadequacy or absence of bowel function, whatever the underlying cause. Here total parenteral nutrition (TPN) comes into its own and may be referred to as the 'artificial gut'. With the free availability of parenteral solutions and the equipment required it is no longer justifiable to deny patients nutritional support when required. The day has now arrived when the medical and allied professions are obliged to make, and act on, objective nutritional appraisal of each and every patient in a planned and rational way. Anything less may well be considered negligence.

2.1 INDICATIONS

Based on the above comments it is possible to draw guidelines with respect to indications but it will not be possible to cover every possible clinical situation. With increasing experience one learns to recognize the need for parenteral nutrition. Indeed, one has to be constantly aware of the danger of excessive and unwarranted use of this modality of treatment. The indications for parenteral nutrition may be classified as follows:

2.1.1 Conditions characterized by loss of bowel

1. Surgical resection. Large portions of bowel may have to be resected in cases of infarction caused by mesenteric arterial or venous thrombosis, malignant disease or inflammatory bowel disease.
2. Intractable bowel obstruction may be caused by multiple adhesions, pathological fibrosis, tuberculosis and carcinomatosis.

3. Enterocutaneous fistulae may occur secondary to previous surgery, inflammatory bowel disease or carcinoma.

These conditions generally require long term or even life-long parenteral nutrition due to the fact that they tend to result in permanent and critical loss of bowel. Such patients would then qualify for 'home parenteral nutrition' (HPN).

2.1.2 Conditions characterized by functional bowel failure

1. inflammatory bowel disease
2. recent abdominal surgery
3. pancreatic failure
4. cystic fibrosis
5. amyloidosis
6. Whipple's disease
7. malabsorption syndrome
8. malignancy of the small bowel
9. carcinoma of the oesophagus/stomach
10. severe bowel infections
11. intestinal motility disorders, e.g. pseudo-obstruction.

In this group many of the conditions are potentially reversible and may require parenteral nutrition for a limited period of time (weeks to months) in order to tide patients over periods of non-availability of adequate bowel function.

2.1.3 Conditions characterized by excessive nutritional demands with relative bowel incompetence

1. multiple trauma with or without surgery
2. severe septicaemia
3. burns
4. acute renal failure.

These conditions are potentially treatable and may often be associated with relative incompetence of intestinal mucosa, superimposed on a state of increased demand and may require short term parenteral nutrition (days to weeks). However it is important to remember that the serious nature of the disease in this group often results in high mortality. This often makes nutritional support mandatory in this setting.

2.1.4 Conditions characterized by injury or damage to the pharynx or oesophagus

1. facial burns
2. caustic burns due to acids, chemicals, etc.
3. severe enanthematous infections, usually viral
4. severe erythema multiforme (Stevens–Johnson syndrome).

These conditions are mostly reversible, provided the patient can be kept alive for the critical period by parenteral nutrition, usually a matter of days. Many of these cases can be managed by enteral nutrition.

2.1.5 Anorexia nervosa

On occasion the physician finds himself confronted by this distressing condition, which often raises contentious questions of ethical propriety of 'forced feeding' against the wishes of an individual. Whatever the philosophical arguments, there is little doubt that parenteral nutrition can achieve sufficient physical recovery to enable one to overcome life-threatening starvation and allow the opportunity to reassess the situation. It must be recognized that some of these patients in an advanced state of malnutrition, if untreated, may die a sudden death, usually the result of a cardiac dysrhythmia.

In spite of this long list, and the well-established principles of nutrition, all too often TPN is deferred until too late. There is a tendency to forget these considerations until the eleventh hour. Thus it is worth reiterating the need for vigilance and early nutritional support – and avoidance of hurried measures on a Friday afternoon when in fact things could have been commenced electively several days earlier!

2.2 METABOLIC RESPONSES TO STARVATION AND TRAUMA

The normal human being is characterized by a near-perfect balance between demand and supply of the various essential nutrients. In health the body is capable of considerable variation on the demand side of the equation in order to cope with wide variations in supply. Where the supply exceeds demand – a major problem of affluence, widely prevalent in the developed world – the body is generally unable to increase its catabolism adequately and the result is obesity. On the other

hand, when the primary problem is a lack of adequate supply, i.e. starvation, the body is capable of lowering its metabolic rate, now commensurate with the fall in energy supply. This mechanism is of enormous biological importance in keeping alive organisms in the face of food shortage, still a major problem in large areas of the developing world. The fall in metabolic rate ensures minimization of energy expenditure. Amino acid turnover and nitrogen loss are minimized in an effort to maintain positive nitrogen balance. The starved subject has an increased capacity to retain nitrogen compared to normal. Up to a point these measures are successful and one is able to survive on suboptimal intake of energy and protein for prolonged periods. In short term starvation breakdown of glycogen and gluconeogenesis (from pyruvate, lactate and glycerol) together yield adequate glucose for survival, the basal requirement being of the order of 2.3 g/kg body weight/day.

There is a critical point, beyond which however, in order to survive, the body has to break down endogenous substrates and muscle protein in order to provide the energy that is essential for vital organs. As starvation progresses the glycogen stores are rapidly depleted in the liver (a matter of hours) and then gluconeogenesis becomes the only source of glucose. Ultimately the glucose production may fall by as much as 50% and amino acids are conserved with maximal utilization of pyruvate, lactate and glycerol. Fatty acids and ketone bodies (acetoacetate and beta-hydroxybutyrate) liberated from fat metabolism inhibit glucose utilization by peripheral tissues and themselves become sources of energy for vital neural and cardiac tissues, a sequence of events often termed 'keto-adaptation'. Finally, amino acids are utilized to provide glucose, the final common pathway being transamination of pyruvate in peripheral tissues (in particular, skeletal muscle) giving rise to alanine which is transported to the liver for breakdown into pyruvate and aspartate. The former enters the tricarboxylic acid cycle to yield glucose while the latter contributes to the formation of urea. Alanine is the most important glucose precursor and while most of it is derived from the sources referred to above, a small fraction is derived from glutamine in the gut.

In spite of all that has been said, people have been known to survive total starvation for several weeks. This becomes all

the more remarkable when one considers that the total energy reserve in the average human being comprises approximately 20% of body weight as fat and less than 10% of body weight as protein (carbohydrate reserves are negligible). In a 70 kg man this would amount to a life sustaining energy supply for 30–40 days, assuming that there is no other concurrent illness or complicating factor. In a normal adult on a protein free diet there is an obligatory nitrogen loss of the order of 50 mg/kg body weight/day. The liver is by far the most important site of amino acid metabolism, with the notable exception of the branched chain amino acids (leucine, isoleucine and valine), which are predominantly metabolized in skeletal muscle.

In contrast to starvation – which is a much easier model to study and analyse – in states of clinical disease, trauma and infection the demand side of the equation is increased. This is further offset by the fact that the diseased patient is often incapable of supplying himself with adequate nutrition. As far back as 1942, Cuthbertson divided the post-traumatic phase into an early 'ebb' phase characterized by shutdown of all metabolic processes, followed by a later 'flow' phase (assuming the organism survived) characterized by hypercatabolism. If sufficiently severe this accelerated metabolic rate can lead to rapid consumption of the body's energy reserves and subsequent breakdown of muscle protein, leading to a negative nitrogen balance. Within a relatively short time this can lead to considerable loss of flesh, hypoproteinaemia, impaired immunological resistance, impaired wound healing and so on.

Thus it will be apparent that the requirements may vary considerably in clinical disease depending on which side of the supply–demand equation is primarily affected, and in which direction. Unfortunately, there is an 'obligatory' nitrogen loss with muscle wasting that is sometimes inevitable in severe trauma and illness. This makes the provision of nutritional support all the more imperative.

Though the exact control mechanisms which affect this hypercatabolic state are difficult to elucidate, it is well recognized that some of the circulating hormones play a major role in producing this effect – cortisol, catecholamines and glucagon. Their major antagonist with predominantly anabolic effects is insulin. Growth hormone is an anabolic agent, but nevertheless antagonizes insulin and tends to promote hyperglycaemia and

its role in states of trauma is not clear. Lipolysis of stored triglycerides in the adipose tissue results in liberation of free fatty acids and glycerol into the blood stream. The fatty acids represent direct energy substrates for tissues such as the myocardium, the remainder being converted in the liver to ketone bodies, acetoacetate and beta-hydroxybutyrate. The latter are then released into the circulation and act as energy substrates for different organs including nervous tissue. The glycerol released from adipose tissue is taken up by the liver where it is utilized by conversion to glucose. When the demands are excessive or external supply limited, the next step in providing energy comes from breakdown of the structural proteins of skeletal muscle into their basic amino acid units, which are then deaminated. The amino moiety combines with pyruvate to form alanine which is transported to the liver and metabolized as described earlier.

The supply of adequate exogenous energy in the form of glucose therefore is of paramount importance in mitigating, if not preventing, the series of events described above. In states of trauma and hypercatabolism though the excessive breakdown of endogenous tissues appears to some extent 'autonomous', there is little doubt that it can be significantly compensated for by the provision of adequate energy and nitrogen. It is easy to understand the necessity to provide extra nitrogen (or protein) in an attempt to combat the negative nitrogen balance that would otherwise result.

2.3 ASSESSMENT OF NUTRITIONAL STATUS

Having decided that a patient requires parenteral nutritional support, it is then important to be able to assess the current state of nutrition in order to plan the feeding regimen. For example, if support is started early in a patient before there has been any significant loss of reserves then it would be reasonable to administer 'maintenance' doses of the various constituents. On the other hand (as is often the case) if there has been significant utilization of the reserves of protein and energy, either because of the rampant nature of the disease or because of delay in starting support, then it would be necessary to administer larger doses of ingredients, in order to make up the deficit. There are several parameters that may be used to assess nutritional status and they will be discussed.

2.3.1 Clinical assessment

For all the technological and biochemical advances that medical science has made, there is no substitute for a sound clinical assessment, based on a thorough history and physical examination. Many physical signs provide important tell-tale clues. For example, oedema is usually cardiac, renal, hepatic or hypoproteinaemic in origin. Cardiac oedema is generally associated with a raised central venous pressure, enlarged liver and ascites, along with relevant cardiac or pulmonary signs. Renal oedema is characterized by proteinuria, detected by a simple bedside test. Hepatic oedema is often associated with other stigmata of liver failure such as splenomegaly, ascites, spider naevi, jaundice, history of alcohol excess and so on. The absence of any feature to suggest disease of the heart, kidneys or liver, then leaves the examiner with the likelihood of 'nutritional' oedema, the degree of which often reflects the degree (but not duration) of malnutrition. Indeed the essential ingredients of nutrition often announce their deficiency by means of physical signs which may be subtle. They will be dealt with later in this chapter. In general deficiencies tend to be multiple rather than single. The most common non-specific signs of malnutrition include pitting oedema (sometimes sacral if the patient has been confined to bed for any length of time), dry skin, hair loss, increased capillary fragility, pallor and muscle wasting. A careful dietary history is often of great relevance, particularly in the elderly and the socially isolated. Recognition of muscle wasting is very important and objective methods will be described later.

2.3.2 Body weight

This is an important simple measure of nutritional status. In the human being total body weight is composed of 55–60% water, 5% minerals and 35–40% organic materials; the organic material is composed of 40% as protein and 60% as fat, with only a tiny amount as carbohydrate. Weight can be related to the height and compared with the ideal body weight derived from standard charts. More than the absolute weight, it is important to get an idea of the actual weight loss that has occurred during the illness and this can be obtained either from history or from any previous weight record. After

excluding fluid depletion, weight loss due to flesh wasting is characterized by a protein content of 5–10% during the first week, which rises to 10–15% by the end of 3 weeks. Daily body weight measurement should be considered one of the vital signs in acutely ill patients; it is a highly neglected parameter of fundamental importance.

The degree of weight loss over time is an index of the ultimate outcome. The greater the ratio, the worse the prognosis. In general it is reasonable to resort to nutritional support (enteral or parenteral) if weight loss exceeds 10% of the pre-morbid body weight. If it exceeds 30% the prognosis must be considered very poor. Unfortunately the measured body weight can often mislead the unwary to false conclusions when there is any significant degree of oedema, which is often the case in these patients. As most of these ill patients are recumbent for the most part the oedema spreads itself diffusely and may not be obvious except to the discerning eye. Hence the importance of careful clinical assessment which must include examination of dependent areas, such as the sacrum. Though it is impossible to accurately estimate the quantity of oedema fluid it is possible to make approximations – the rule of thumb! The presence of even mild pitting is likely to represent about 2 l of free fluid; a deep pit may represent 4–5 l; generalized oedema with obvious pitting may represent as much as 10 l or more.

Lean body mass is a useful concept in representing the muscle mass and can be adequately measured by the creatinine/height index (CHI). This is calculated from the formula:

$$\text{CHI} = \frac{\text{AUC}}{\text{IUC}} \times 100$$

where

AUC = actual urinary creatinine excretion in 24 h
IUC = ideal urinary creatinine = 0.23 mmol kg^{-1} ideal weight (male)
= 0.18 mmol kg^{-1} ideal weight (female).

CHI when expressed as a percentage gives a rough measure of the current nitrogen status. A progressive deterioration in the index is good evidence for malnutrition. It is worth noting that

the absolute value of CHI takes no account of the patient's build and sequential values may be influenced by fluid shifts.

Body mass index (BMI) is another derived value which is a useful index of the fat reserves and a guide to the current nutritional status.

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

Thus one can get a good idea of the current state of nutrition of a patient by consideration of the pre-morbid, 'ideal' and current body weights, CHI and BMI in a composite way. Once again it is worth emphasizing the need to document serial changes while the patient is in hospital. The observed deterioration will often surprise the average clinician and can be a great eye-opener.

2.3.3 Skin-fold thickness (SFT)

This is a crude measure of the fat energy reserves. Using Harpenden skin callipers one can measure SFT at four standard sites (over the mid-portion of the triceps, corresponding part of the biceps, subscapular and suprailiac regions) and the mean value taken as representative. Though this may be ideal, in practice triceps SFT is adequate. The results can vary and some practice is required for reproducibility. For this reason it is recommended that the measurement be carried out thrice in succession at each site. A 'normal' value should be at least 40 mm, when the measurement at the four sites are added together, i.e. a mean value of at least 10 mm (normal range for males 10–14 mm; females 12–18 mm). It is important to stress that an absolute figure is meaningful only at the extremes; a serial change is more significant. The readings can be totally misleading in the presence of oedema; hence, in the presence of excessive oedema there is no point in trying to measure SFT. It is advisable to apply gentle pressure to the skin between the thumb and forefinger for 10 s before making the measurement, in order to dispel any interstitial oedema, which can be covert and result in distorted measurements.

2.3.4 Mid-arm muscle circumference

This is a crude measure of muscle mass and therefore of the existing protein reserves. The mid-arm circumference (MAC) is

measured with the arm hanging straight and limp, using a tape measure, at a point midway between the lateral epicondyle of the humerus and the acromion. The point should be marked with a skin marker for future measurements. The mid-arm muscle circumference (MAMC) is calculated by the formula:

$$\text{MAMC} = \text{MAC} - (3.14 \times \text{SF T})$$

Again an absolute figure is only helpful at the extremes, serial changes being more useful. The 'normal' ranges quoted vary as follows:

	Males	Females
MAC (cm)	23–30	22–28
MAMC (cm)	19–27	17–23

2.3.5 Serum albumin

This is probably still the most widely used biochemical index of nutritional status. In acute hypercatabolic illnesses serum albumin can plummet to remarkably low levels within a matter of days. While the absolute level probably does have a rough association with the extent of the disease and its outcome, in many chronic illnesses (such as nephrotic syndrome, inflammatory bowel disease and chronic liver disease) patients may survive with low serum albumin for protracted periods of months or even years. Therefore, it is very important to document the rate of decline of albumin, rather than depend on a single figure. Therefore while an absolute figure of 30 g l^{-1} is the limit below which it indicates nutritional deficiency, the rate of fall is a determinant of the nature of the illness and its outcome. In our opinion, enteral or parenteral nutritional support is indicated if the rate of fall of serum albumin exceeds 1 g l^{-1} day $^{-1}$. Due to its relatively long half-life (about 20 days) it is not the most sensitive indicator of early protein deficiency; nevertheless, it still remains the most reliable 'common' biochemical parameter of nutritional status.

2.3.6 24-h urinary urea excretion

This correlates very well with and is a good measure of nitrogen losses. It is easy to perform and available in most

hospitals. We consider this measurement most useful and recommend its use routinely. The unmeasured nitrogen losses (creatinine, uric acid and amino acids in the urine plus the losses in the faeces and other secretions) generally amount to about 25% of the urea nitrogen. This of course does not take into account the excessive losses that may be seen in conditions such as enterocutaneous fistulae or malabsorption states, when faecal estimations are required for accurate assessment. In renal failure appropriate correction has to be made for increase in the body's urea pool. Calculations are presented later in this chapter.

Catabolic rate is an important consideration in assessing the needs of the patient. Highly accurate measurements can be made using expensive and time-consuming methods involving oxygen consumption but this is generally neither available nor necessary. In practice urea generation is an excellent index of catabolism, owing to the fact that in states of injury and infection there is a predictable rate of gluconeogenesis from endogenous amino acids even in the presence of adequate energy supply. Thus one can categorize the degree of injury on the basis of 24-h urinary urea nitrogen excretion as follows: mild (5–10 g), moderate (10–15 g), severe (15–20 g) and extreme (> 20 g).

2.3.7 Serum short half-life proteins

Transferrin (half-life of 8 days), thyroxine binding pre-albumin (half-life of 2 days), retinol binding protein (half-life of 12 h) and complement component C3 are excellent indices of current nutritional status and low levels correlate with a state of negative nitrogen balance. Though they are more sensitive than albumin (half-life of 20 days) the measurements are difficult to perform and not generally available for routine use. Though their theoretical value is unquestionable, in practice one may be able to manage without the benefit of these estimations.

2.3.8 Lymphocyte count

This is sometimes a useful index of nutritional status in that low counts (in the absence of any other cause for lymphopenia)

may be an index of malnutrition and represents a state of impaired cell-mediated immune competence. The test is easily carried out and is available universally.

2.3.9 Skin anergy

Failure to produce a normal skin response to an injected antigen such as candida is a sign of impaired cell-mediated immunity, a result of nutritional deficiency. In practice this is rarely of use and the other parameters are more reliable.

2.3.10 Amino acid estimations

Serum amino acid profile and urinary 3-methyl histidine (3-MH) excretion are additional parameters, which are often of academic interest and rarely affect clinical management. Furthermore, their assay is time-consuming and expensive and not generally available. Nevertheless, in certain conditions such as hepatic failure and renal failure, these measurements may be of use in diagnosis and treatment. 3-methyl histidine is released from muscle during the process of breakdown but not re-utilized by the liver and hence its excretion in the urine reflects the degree of catabolism; 4.2 μmol of 3-MH is equivalent to 1 g of muscle protein.

2.3.11 Assay of trace element and vitamin status

These are only available at specialist centres and involve considerable cost and effort. Vitamins are provided in adequate quantities in standard nutritional regimens and therefore measurement of their status is likely to be merely of academic interest. On the other hand, there is still much that we do not know about trace elements and it is therefore worth making an attempt to measure their concentrations and attempt to correct any identifiable deficiency. We recommend routine measurement of all the currently available trace elements (copper, manganese, zinc, chromium, selenium) in any patient who requires medium to long term parenteral nutrition. These should be measured at weekly intervals for hospital patients and 2–3 monthly for home patients.

2.4 RECOGNIZING MALNUTRITION

Protein energy malnutrition (PEM) is well documented, well described and well recognized when it occurs in the rural setting of a developing nation. Though it is true that it is no longer a problem in the general population of the affluent world it is still a widespread and relatively common occurrence in hospitals, however well developed. Unfortunately there is very little appreciation of this real problem and for this reason malnutrition goes largely unrecognized in a system of medical care which is otherwise highly advanced and sophisticated. Nowhere is the adage 'what the mind does not know, the eye does not see' more true. Thus it is essential for the modern day doctor who deals with acutely ill patients to be familiar with the fundamental aspects of malnutrition, it's diagnosis and treatment.

PEM was originally categorized into kwashiorkor and marasmus. It is now recognized that these are not two distinct entities but rather form two ends of a spectrum of malnutrition. Kwashiorkor was thought to be the end result of protein deficiency, in the presence of a relatively acceptable energy supply, but it is now recognized that there are other contributory factors such as aflatoxins. Marasmus is the result of deprivation of both protein and energy. Typical examples of both extremes are commonly found amongst children of starving populations; intermediate forms ('marasmic kwashiorkor') are even more common. While it might sound incredible, these entities can be seen fairly regularly in hospital practice in the Western world! Marasmus in the child is relatively easy to recognize and is characterized by failure to thrive, weight loss, muscle wasting, loss of subcutaneous fat, irritability or apathy, a wizened and shrunken appearance, diarrhoea and disturbance in the various biochemical parameters referred to earlier; oedema is not prominent. The adult counterpart tends to be seen more often in those patients whose pre-morbid weight was either average of below average, i.e. in those with limited fat reserves. It is most likely to occur in those with chronic wasting diseases, the elderly, the alcoholic and the destitute. The clinical features include weight loss (low BMI), muscle wasting (low CHI), apathy, general weakness and loss of subcutaneous fat, with a 'skin and bone' appearance.

Kwashiorkor in the child is characterized by oedema, growth

retardation, muscle wasting, dry skin, brittle hair, protuberant belly, hepatomegaly, apathy and irritability. The degree of wasting may be masked by the oedema. This is particularly true for relatively well nourished adults, in whom the florid signs are generally absent, with the exception of oedema. Furthermore, in obese subjects with plenty of fat reserves to provide energy, an acute illness without adequate nutrition can result in a hypercatabolic state, leading rapidly to a state of negative nitrogen balance and an adult form of kwashiorkor. There may be no weight loss due to accumulation of hypoproteinaemic oedema, which may be interstitial and generalized, rather than the typical pitting ankle oedema. This situation may also arise in subjects who have been given prolonged peripheral dextrose infusions without any concomitant nitrogen source. Under these circumstances it is easy to be misled into making falsely high estimates of skinfold thickness and mid-arm circumference. Likewise, the BMI may be falsely high, but the CHI is always low (needs correction in the presence of renal failure) and is a reliable marker of protein malnutrition.

From the foregoing discussion it will be evident that obesity and malnutrition can coexist. Therefore in the acutely ill patient evidence of obesity should not lull the physician into complacency. It is worth reiterating that 'obesity' may be composed of a considerable amount of interstitial fluid. The second point worth bearing in mind is that the problem can arise far more quickly than is generally realized; for example multiple trauma or severe sepsis can produce a state of malnutrition in a matter of days in a previously fit person. Hence the need to step in with nutritional support sooner rather than later.

A number of systems currently exist for making assessments of the degree of 'illness'. The earlier systems have now largely been replaced by the one known as APACHE II (acute physiology and chronic health evaluation), which produces a point score based on twelve routine measurements, representing the degree of illness and the subsequent outcome. Though this sort of assessment of the current status may be of prognostic and therapeutic significance, it is not a guide to the nutritional requirements. Though accurate measurement of the deficit and the loss of the various nutrients (as described later in this chapter) would form the best index of a patient's requirements, a rough and simplified guide is presented in Table 2.1.

Table 2.1 Grading of malnutrition and determination of requirements

Grade	Monitored parameters				Malnutrition score (MS)	Recommended intake	
	Wt loss %	*CHI* %	*S. Albumin*	*Estimated N loss (g/kg BW)*		*N* ($g\ kg^{-1}$)*	*E* ($kcal\ kg^{-1}$)
1	0–5	> 95	> 36	< 0.1	1	0.1	30
2	6–10	90–95	31–36	0.1–0.15	2	0.15	35
3	11–15	85–90	26–30	0.15–0.2	3	0.2	35–40
4	15–25	75–85	21–25	0.2–0.3	4	0.3	40
5	> 25	< 75	< 20	> 0.3	5	0.3–0.5†	40–45†

Malnutrition score = sum of the ratings of the monitored parameters.
MS > 6 warrants nutritional support (enteral or parenteral).
MS > 12 often requires parenteral nutrition (partial or total).
*In renal failure N intake must not exceed 0.3 g kg^{-1} whatever the grade/score.
†This applies almost exclusively to severe burns.

2.5 IDENTIFYING PATIENTS AT RISK

Having gone through the parameters for nutritional assessment it is still worth identifying the high risk patient based on the clinical circumstances. The occurrence of one or more of the following criteria should alert the clinician to the possibility of, or the potential for, malnutrition:

1. critical loss of weight – either less than 80% of ideal weight-for-height or loss of 10% or more of the usual body weight within the previous month;
2. inability to feed normally for 7 days or more, due to illness or surgery;
3. known history of alcoholism;
4. elderly or socially isolated status;
5. excessive loss of nutrients in diseases such as malabsorption;
6. diseases characterized by excessive demands such as burns, severe infections, major trauma.

Such an approach can ensure early and effective treatment of susceptible patients. When one considers the potential reduction in morbidity and mortality there is a powerful argument for instituting early nutritional support, parenteral where appropriate, on the basis of the fundamental rule in medicine that prevention is better than cure. It is well worth bearing in mind that the relatively high cost of parenteral nutrition may be a mere fraction of the true cost of malnutrition – which can result in longer hospital stay, avoidable complications, protracted convalescence and death.

2.6 NUTRITIONAL REQUIREMENTS

In simple terms the patient receiving parenteral nutrition requires all the essential ingredients required in a normal diet, often in greater quantities. The food supplied should have adequate amounts of all the known essential ingredients and must be balanced in a qualitative sense. Currently available preparations contain most of the necessary ingredients and should be administered in varying proportions, tailored to the individual patient. It will be evident from the foregoing discussion that the requirements can vary widely, depending on the basic problem. A patient who is malnourished due to anorexia

nervosa would be on starvation metabolism and requires relatively 'normal' amounts of energy and protein, whereas one who has sustained multiple injuries would be hypercatabolic, requiring very much larger amounts of nutrients, of protein in particular.

2.6.1 Protein

For the normal adult an adequate protein intake is considered to be a minimum of 1 g per kg body weight, though in most western diets the intake is far higher. With respect to the patient requiring parenteral nutrition the requirement may vary from that of a normal individual (as in a patient recovering well after a limited surgical resection) to twice the recommended normal intake (as in a patient with extensive burns). For parenteral nutrition the protein requirement is conventionally prescribed in grams of nitrogen per day (1 g of nitrogen is equivalent to 6.25 g of protein).

The minimum obligatory nitrogen loss for a given adult in the basal state is about 50 mg per kg body weight per day. In practice nitrogen equilibrium is said to be achieved at 75 mg per kg per day. Endogenous urinary nitrogen excretion is related to the rate of resting energy expenditure (REE) and this is approximately 2 mg of urinary nitrogen per basal kilocalorie, while receiving normal nitrogen intake. It has been observed that ingestion of protein causes an increase in REE and this has been termed 'specific dynamic action'. This may be of relevance to injury and illness as it is known that after these events there is a parallel increase both in REE and nitrogen excretion, and it has therefore been suggested that the hypercatabolism in these conditions is a form of endogenous specific dynamic action resulting from tissue breakdown.

It is worth stressing that an estimation based on weight should take into account the weight loss that has already been sustained and all calculations must be based on either the premorbid weight or on a derived 'ideal' weight. The measured nitrogen losses represent the current status and may be taken to equate to the actual requirements only when measured early in the course of an illness; once significant loss of flesh has occurred then an appropriate correction must be applied to increase the intake. This may be made on the basis of the

percentage loss of body weight, body mass index or the creatinine height index, the last being the best index.

Nitrogen loss can be calculated in a number of ways. The most accurate method involves the collection of every sample of urine, stool, aspirate and other secretions over a 24-h period. The nitrogen content can then be estimated by the Kjeldahl method. This is expensive and labour intensive and only available in specialist centres. A relatively easy and accurate method consists of a 24-h urine collection which is analysed for urea. The daily nitrogen loss is then calculated from the urinary urea nitrogen; and the urinary non-urea nitrogen (contained in creatinine, creatine, uric acid and amino acids) which is approximately 2 g day^{-1} can be estimated by applying a correction factor of 6/5:

1. *Nitrogen (g) = 24 h urine urea (mmol) x 0.034
   = 24 h urine urea (g) x 0.56

This single figure is in itself adequate in most clinical circumstances. However, in complicated states such as renal disease, renal failure and gastrointestinal losses further corrections must be made as follows:

2. Correction for rise in body urea pool
   = Daily rise in blood urea (mmol l^{-1}) x body weight (kg) x 0.017
   = Daily rise in blood urea (g l^{-1}) x body weight (kg) x 0.028
3. Measured nitrogen loss in dialysate, ultrafiltrate, aspirate, wound drain, effluent, etc.
4. Nitrogen loss in proteinuria
   = 24 h urinary protein (g) x 0.16*
5. Nitrogen loss in faeces and sweat
   = 2 g (assumed) or amount actually measured
6. Extra nitrogen recommended on top to ensure positive balance = 2 g (empirical)

Nitrogen requirement (g per 24 h)
= A+B+C+D+E+F or A+B+C+D+4
= A+4 (renal function normal, no excessive GI loss)

*Gram molecular weight of urea = 60; 1 mmol = 60 mg
1 mmol of urea contains 28 mg of nitrogen.

In hypercatabolic states associated with acute renal failure and septicaemia we recommend some caution in calculating nitrogen requirements. This is because of the danger of excessive urea generation and its consequent osmotic and uraemic effects. In acute renal failure the nitrogen intake should not exceed 20–25 g day^{-1}. In septicaemia we recommend replacing the sum of A+B and no more (except in unusual circumstances). An experienced clinician can often successfully make an approximate assessment of the nitrogen requirements, based on the clinical characteristics of the disease and the patient.

For example a patient with complete bowel loss established on home TPN, will require only the basal recommended amounts, i.e. 0.15–0.2 g of nitrogen per kg body weight per day. The same would apply to a patient recovering well from limited abdominal surgery and who has not lost any significant weight. A patient with a significant degree of toxaemia, sepsis or trauma is likely to require 0.2–0.25 g of nitrogen per kg body weight per day.

On the other hand an acutely ill hypercatabolic patient with burns or acute renal failure may require 0.3 g of nitrogen per kg body weight per day, or more. Studies with continuous arteriovenous haemofiltration for acute renal failure in our unit have revealed that some patients may lose as much as 50 g of nitrogen per day! It is not known whether there is a critical limit for nitrogen administration, beyond which it cannot be utilized, though an upper limit of 20 g day^{-1} has been suggested.

Qualitatively the protein source must contain all the essential amino acids, namely iso-leucine, leucine, lysine, methionine, phenylalanine, tryptophan, threonine and valine. Histidine and arginine are considered semi-essential, particularly in children. Once adequate quantities of the essential amino acids are provided, the human body is capable of synthesizing the remaining 13 primary non-essential amino acids, namely alanine, asparagine, arginine, aspartic acid, citrulline, cystine, glutamine, glycine, glutamic acid, hydroxylysine, hydroxyproline, proline, serine and tyrosine. It is worth mentioning that the biologically active forms are the laevo-isomers. Though the non-essential amino acids can potentially be synthesized within the body, it is important to realize that in states of disease, stress and hypercatabolism the liver may not be capable of

adequate synthesis of these amino acids and therefore it will be obvious that the ideal intravenous source of amino acids should have a 'physiological' profile and incorporate all the amino acids mentioned above. We certainly do not recommend solutions which have predominant amounts of any one amino acid, such as glycine, though this is a matter of debate. The ratio of essential amino acids to the total amino acid content of the solution (ET ratio) varies widely depending on the preparation from 0.35 to 1. We recommend a value of 0.4 or 40% for this ratio. As mentioned earlier the branched chain amino acids (isoleucine, leucine and valine) are predominantly metabolized in skeletal muscle unlike the other amino acids which are metabolized in the liver. This fact has practical implications in situations where parenteral nutrition is required in a subject with liver failure.

There has been some evidence to suggest that peripheral infusion of isotonic amino acids may be adequate in maintaining positive nitrogen balance in certain post-surgical situations. We do not routinely recommend the use of this approach, which can only deliver modest amounts of nitrogen to the system, unless large volumes are used. This becomes all the more problematic when one tries to infuse adequate calories as well. Though it may be argued that post-surgical patients may be able to make do with limited amounts of nitrogen, it can equally well be argued that they could probably do with simple short term maintenance with isotonic dextrose!

We also do not recommend peripheral isotonic amino acids without dextrose as it is well known that this can result in inappropriate stimulation of glucagon release leading to an unacceptable increase in gluconeogenesis and ureagenesis. Nevertheless some authorities recommend peripheral feeding for certain situations; we would only recommend it in stable peri-operative situations in patients without evidence of compromised renal or cardiac function, requiring a maximum of 10 g of nitrogen and about 2000 kcal. Even so, this involves a large fluid load and an unusually high fat to carbohydrate calorie ratio.

The source of nitrogen is a matter of preference and familiarity. There are a number of acceptable and clinically proven amino acid solutions with varying amino acid profiles. We would advise our readers to become familiar with one or two ranges of products and learn to use them with success. In

our own practice we routinely use the Vamin range of amino acid solutions, and they have a well-proven record of safety and efficacy in the vast majority of clinical situations. Once again it is worth emphasizing the need to take into consideration the electrolyte content of the solutions and use electrolyte free preparations in appropriate conditions such as acute renal failure. We recommend solutions with a good profile of amino acids, in particular the essential amino acids. For peripheral infusion there is a preparation called Perifusin which contains 5 g N l^{-1}.

2.6.2 Energy

Energy supply is the fundamental requirement for all living tissues. In clinical nutrition it is now well established that an adequate supply of energy serves not merely to keep the organism alive, but also has a most important nitrogen sparing effect. Up to even recent times the only practical approach to catabolic states associated with illness or injury consisted of maintaining hydration with electrolytes and 5% dextrose in varying combinations. Inadequate though this might be, even that small amount of energy supply (2 l of 5% dextrose provide about 400 kcal) is capable of reducing the urinary nitrogen loss by half. While this may be acceptable in a relatively well patient undergoing elective surgery, it would be grossly inadequate in a patient who would be described as being acutely ill.

Basal energy requirement for resting energy expenditure (REE) for the average adult human being is of the order of 25 kcal per kg body weight per day, for a 70 kg man about 1750 kcal day^{-1} and for a 60 kg woman about 1500 kcal day^{-1}. In disease states additional energy must be supplied in order to cope with the increased demands as well as to recoup lost reserves; in hypercatabolic states REE can increase by up to 100%. Accurate measurement of metabolic rate or energy expenditure (by oxygen consumption and carbon dioxide generation) is essentially a research tool and is of no practical clinical value in assessing a patient's needs. While normal healthy volunteers can achieve positive nitrogen balance even when energy is restricted, ill patients require higher than normal energy to achieve the same positive nitrogen balance. In nutritional parlance energy intake refers to non-protein calories only. The ratio of (non-protein) energy to nitrogen (ENR) may

vary from 125 to 200. In general the lower the catabolic state, the higher should the ratio be; in a non-catabolic subject with a nitrogen loss of 7 g day^{-1} the energy supply could be around 1500 kcal, whereas in a hypercatabolic patient with a nitrogen loss of 20 g day^{-1} the energy supply ought to be around 2500 kcal. A rough and ready guide to requirements is presented in Table 2.1. Unfortunately, to this day there is an inadequate appreciation of a patient's energy needs in the eyes of the average clinician and this can often lead to florid examples of malnutrition in hospital practice. Energy may be obtained from a carbohydrate source, a fat source or from a combination of the two. From the earlier discussion it would be clear that an adequate energy supply is essential not only for vital cellular metabolism but also for its nitrogen sparing effect. There is no doubt that carbohydrate sources of energy are the first choice.

In normal physiology all consumed carbohydrate is absorbed in the form of glucose, fructose and galactose and the latter two are metabolized by the liver and converted to glucose, which is the endogenous natural substrate. A number of parenteral carbohydrate sources have been used for nutritional purposes, namely glucose, fructose, sorbitol, xylitol and ethanol. The ideal carbohydrate source should have the following characteristics:

easily utilized by all tissues
adequate caloric value
rapid metabolism without any adverse metabolic effects
should not react with synthetic materials used for infusion
non-irritant to veins
compatible with other parenteral nutrients
high renal threshold.

Glucose is the natural endogenous substrate which is probably the source closest to the ideal. However, patients in hypercatabolic states often have a tendency to accumulate glucose due to a metabolic block in the utilization pathways. This is a complex process and is closely related to the endogenous activity of insulin, which plays a critical role at different points in glucose metabolism, as discussed later. This impaired utilization is a major drawback with glucose. The second practical problem with the use of glucose is the necessity to use hyperosmolar solutions in order to provide sufficient calories

and this is incompatible with peripheral use as it will invariably result in phlebitis. Rarer complications with use of glucose include hyperosmolar non-ketotic coma and hypophosphataemia, the latter due to its ability to drive phosphate into the cells. For this reason it is very important to supplement adequate amounts of phosphate when glucose is being administered in large quantities. Finally, there are practical problems in combining glucose with amino acids in the manufacturing stage and therefore they can only be mixed in the hospital prior to administration, or be infused sequentially. There is general agreement today that the former is the preferred method.

Fructose became popular as an alternative to glucose on the grounds that insulin is not required for its metabolism. It has been recognized since that the argument is not valid because fructose is ultimately metabolized in the form of glucose; furthermore, it does not stimulate insulin secretion and is therefore metabolized rather slowly. Of an administered fructose load 70% gets converted to glucose and 30% to lactate. Therefore fructose infusion in practice is no different from a combined infusion of glucose and lactate. There is also a danger of lactate accumulation and lactic acidosis. Other potential problems include hyperuricaemia and hypophosphataemia. Sorbitol achieved limited popularity as it could be sterilized and manufactured in combination with amino acids, thereby removing the need for 'mixing' in hospital. However, it is metabolized completely to fructose in the liver and therefore has all the disadvantages mentioned above. It also has the disadvantage of a low renal threshold, which itself can lead to an osmotic diuresis.

Xylitol is converted in the liver to xylulose-5-phosphate which enters the pentose phosphate pathway and gets converted to glucose-6-phosphate. However, it has the potential problems of lactic acidosis, hyperuricaemia and impaired oxalate metabolism, which can lead to renal failure. Lastly ethanol has been considered a potential source but it has the disadvantage of producing impaired gluconeogenesis and lactate accumulation. From the foregoing discussion it will be evident that glucose on its own is by far and away the best carbohydrate source. We do not recommend the routine use of the other substrates for the various reasons discussed above.

A lot of experience has been gathered with the use of fat

emulsions as sources of energy and they are now established in clinical practice as being safe and effective. Their use as energy source has a few definite advantages over carbohydrates in that they:

1. have a much higher caloric value for comparable volumes
2. have a low osmolar load on the circulation and hence do not give rise to a diuresis
3. may be administered by the peripheral route
4. enable the administration of fat soluble vitamins and
5. ensure avoidance of essential fatty acid deficiency.

Intravenous fat emulsions are not all the same and there are considerable differences between solutions based on different oils. The older solutions based on cottonseed oil and linseed oil have now largely been superseded by that derived from soya bean oil and we shall confine all further comments and discussion to soyabean oil-based fat emulsions. There are a limited number of products available for clinical use and we routinely recommend the use of Intralipid. There is adequate evidence that this fat source is utilized in states of disease and trauma and augments the calorigenic effect of any concurrently administered carbohydrate, as well as having a nitrogen sparing effect. There is no convincing evidence that fat administration has any adverse metabolic effect. Fears about their adverse effect in certain conditions like pancreatitis and the adult respiratory distress syndrome have not been substantiated. The only real disadvantage of fat solutions is their relatively high cost.

Is a carbohydrate calorie identical to a fat calorie? Not quite. This has been a subject of much controversy and debate. Available evidence suggests that when energy supply is restricted or suboptimal, glucose is superior; when optimal the two are equivalent. In clinical practice administration of parenteral nutrition presupposes the provision of adequate calories and therefore routine use of lipids in addition to glucose is perfectly acceptable.

From the foregoing discussion it will be evident that energy is best provided through a combination of carbohydrate and fat sources, though there are some authorities who believe in the superiority of 'carbohydrate-only' energy sources. The latter have a definite disadvantage in that they tend to produce excessive carbon dioxide generation, which can result in

substantial delays in weaning patients off ventilators. So it is generally accepted that a dual energy source is ideal; the balance between carbohydrate and fat energy is a matter of debate. We routinely recommend the provision of about 60% of calories as carbohydrate and 40% as fat. Some authorities however recommend lower amounts of fat; some advocate no more than twice weekly administration of 0.5–1 l of a fat emulsion. The great advantage of incorporating a fat source is the ability to administer adequate calories in a relatively small volume of fluid and this is often of enormous importance in clinical management of patients with renal or cardiac problems, who can not tolerate large volumes of fluid. In rare circumstances the demand on economy of volume or the lack of access to the central circulation might force one to use rather more fat energy than carbohydrate energy, but as far as possible we recommend providing an absolute minimum of 30% as the latter.

(a) Energy requirements in different clinical situations

As a rule it is advisable to calculate the nitrogen requirements and then work out the energy requirement based on an estimation of the catabolic rate. In practice one can have rough guidelines for energy requirements in specific situations and here are a few examples where the requirement is expressed in relation to the REE:

Fever	+11–12% $°C^{-1}$
Elective surgery	+10%
Major surgery	+15–20%
Ambulatory convalescence	+20%
Multiple fractures/trauma	+20–30%
Severe infections	+20–50%
Acute renal failure	+30–60%
Major burns	+50–100%

The largest increases in REE are generally seen in young, well nourished, muscular males. It is important to recognize that wasting due to undernutrition will in itself reduce energy expenditure at rest in direct proportion. Therefore in a patient who has lost a significant amount of weight due to prior illness or starvation, any infection or trauma may result in an increased REE considered 'normal' when in reality it represents

a state of hypercatabolism. The reasons for increased energy expenditure in these clinical settings are: (i) an increased amount of work carried out by specific organs which demands an increased production of ATP (for example, increased work of breathing, left ventricle); (ii) impaired biochemical processes (futile cycles) which result in decreased availability of ATP; (iii) increased activity of neural and endocrine mechanisms for increased heat production for whatever reason.

(b) The role of insulin

Insulin is of fundamental importance in facilitating entry of glucose into the peripheral tissues such as skeletal muscle and adipose tissue for metabolism; it promotes phosphorylation of glucose within the cell to glucose-6-phosphate, an essential step in glycolysis; and it activates pyruvate dehydrogenase, a necessary step in the tricarboxylic acid cycle. It is the major anabolic hormone of the body and these effects are opposed by the catabolic 'diabetogenic' hormones – glucocorticoids, glucagon and catecholamines. In ill patients hepatic gluconeogenesis occurs concurrently, depending on the availability of substrates and promoted by the action of the diabetogenic hormones. In hypercatabolic situations it is well known that insulin secretion is relatively impaired in contrast to its opposing hormones which are much elevated, resulting in a net tendency to glucose production and impaired glucose utilization for the reasons mentioned above. This represents one of the major problems with the use of glucose as the sole energy source – persistent hyperglycaemia.

The situation may be aggravated by the fact that severe injury can lead to an impairment of insulin release, for reasons that are not well understood. Thus there is a state of insulin resistance as well as a relative deficiency. Whether or not to give insulin as a routine adjunct to parenteral nutrition is a matter of debate. We do not recommend the routine use of insulin as there has been no hard evidence to support its role. However, if there is persistent hyperglycaemia with blood glucose concentrations greater than 13 mmol l^{-1} (235 mg%) then we would recommend starting insulin in the form of an infusion, so as to maintain blood concentrations between 6 and 12 mmol l^{-1} (110–220 mg%). We recommend the use of a 'sliding scale' tailored to the blood glucose monitored every 4 h

by finger stabs. Where the levels are high or fluctuating widely (particularly if the patient is diabetic) hourly monitoring is advisable. The following starting dosage schedule is recommended:

< 6 mmol l^{-1}	0 u h^{-1}
6–9 mmol l^{-1}	½ u h^{-1}
9–12 mmol l^{-1}	1 u h^{-1}
12–15 mmol l^{-1}	2 u h^{-1}
15–22 mmol l^{-1}	4 u h^{-1}
> 22 mmol l^{-1}	6 u h^{-1}

Most clinicians would realize that this is a cautious approach compared to that in, say diabetic ketoacidosis, but it is very important to underline the dangers of over-treatment with insulin, which can lead to dangerous hypoglycaemia and this can go entirely unrecognized in the acutely ill patient, particularly if the patient is on ventilatory support; it may easily happen 'between feeds', particularly if there is a delay and the infusion rate is not turned down. If the patient continues to be hyperglycaemic on this regimen then it would be reasonable to increase the dosage as appropriate. In our experience in previously non-diabetic patients on TPN, only 20–30% develop persistent hyperglycaemia as defined above and require insulin treatment; by and large their insulin requirement has rarely exceeded 3 units h^{-1}.

On the other hand we have had at least one example of profound and severe hypoglycaemia occurring while the insulin infusion rate was a mere 1 unit h^{-1}. It is also worth mentioning the need for careful quality control on the bedside colorimetric estimations of blood glucose, in order to avoid serious overestimations. As in other clinical situations, when in doubt a venous sample should be sent to the laboratory for a formal estimation and if there is a doubt of hypoglycaemia, a bolus of 50 ml of 50% dextrose injected intravenously.

2.6.3 Minerals and trace elements

As far as the human being is concerned, essential biological element is a term applicable to no less than 27 elements found in nature. Some such as carbon, nitrogen and phosphorus contribute to the actual structure of the organism; hydrogen and oxygen form the basis for water which accounts for nearly

Table 2.2 Recommended daily intake for patients on total parenteral nutrition*

Trace element	*Daily recommended intake (per kg body weight)*		*Average adult requirements*	
Iron	0.25–1 μmol	(14–56 μg)	20 μmol	(1.1 mg)
Copper	0.25–1 μmol	(16–64 μg)	20 μmol	(1.3 mg)
Zinc†	0.75–3 μmol	(49–196 μg)	100 μmol	(6.5 mg)
Manganese	0.1–0.5 μmol	(5.5–27.5 μg)	10 μmol	(0.55 mg)
Fluorine	0.75–1.5 μmol	(14–28 mg)	50 μmol	(1 mg)
Iodine	0.01–0.02 μmol	(13–26 mg)	1 μmol	(1.3 mg)
Selenium	0.01–0.03 μmol	(0.08–0.24 μg)	0.5 μmol	(4 μg)
Molybdenum	0.003–0.01 μmol	(0.3–1 μg)	0.3 μmol	(30 μg)
Chromium	0.002–0.004 μmol	(0.1–0.2 μg)	0.2 μmol	(10 μg)

* Recommended intakes for parenteral nutrition are considerably lower than those recommended for oral intake. Nevertheless there is considerable variation in the amounts recommended, accounting for the range given.

The requirements for nickel, tin, vanadium and silicon have not been established so far. Cobalt is given in the form of vitamin B12.

† In acute hypercatabolic states, it is advisable to give additional amounts of zinc equivalent to 30% of the recommended value.

In conditions characterized by excessive loss of gastrointestinal fluid, additional allowances must be made for zinc (200 μmol or 13 mg/litre) and chromium (double the recommended value).

A micronutrient additive supplement (containing approximately the amounts shown above for an average adult) has been developed in the Glasgow Royal Infirmary, in conjunction with KabiVitrum, Stockholm.

two thirds of the body weight; and some macroelements such as sodium, potassium and magnesium, are essential for maintenance of the internal environment and electrochemical functions. The rest are referred to as trace elements and are present in small to minute concentrations in the blood. Nevertheless they play a vital role in forming part of several enzymes and transport proteins. The trace elements of recognized importance are listed in Table 2.2, along with the recommended daily parenteral doses (note that normal dietary allowances are much higher).

With advancing medical knowledge it is likely that more trace elements are discovered and the physiological role of many of them better understood. By and large TPN solutions contain known amounts of the macroelements and they are supplemented by measured amounts of certain trace elements such as iron, copper, zinc, manganese, iodine, fluorine and cobalt. The remaining trace elements, which were hitherto in the realms of medical ignorance, are beginning to announce

their importance and physiological roles. It is fortuitous – and fortunate – that they are present as 'contaminants' in adequate quantities in the water used to manufacture TPN solutions and this often serves to avoid deficiency states.

As they are unmeasured contaminants it is of course eminently possible that some of them might be present in quantities large enough to be toxic and may indeed be responsible for some of the unusual complications which seem peculiar to patients on TPN. This remains conjecture at this stage and will require continual evaluation. The following discussion includes elements with known physiological and medical importance, as well as those microelements of nebulous significance.

(a) Sodium

Sodium is the principal extracellular cation and has a multitude of vital functions, which include maintenance of osmotic pressure of body fluids, maintenance of adequate circulation, maintenance of acid–base balance and normal electrochemical transmission in nerve and muscle. Its extensive role has been well documented and cannot be discussed in any great detail here. Requirements can vary widely depending on the clinical situation and it is unrealistic to quote any standard figure. As a rule the requirements can be simply assessed by a combination of four parameters: (i) serum sodium concentration; (ii) quantitative urinary sodium excretion; (iii) clinical state of hydration; and (iv) the sodium content of other secretions, aspirates, etc. The average patient with normal renal function is likely to require between 100 and 300 mmol day^{-1}. In the presence of renal failure or cardiac failure there is obviously the need for sodium restriction. A number of commercially available TPN solutions incorporate a certain amount of sodium, a fact worth being aware of before prescribing. Any requirement in excess of that already present in the solution can be added to the TPN as sodium chloride. In general we recommend not exceeding a sodium concentration of 100 mmol l^{-1} in the TPN mixture.

(b) Potassium

This is the principal intracellular cation and exerts a vital influence on muscular activity, in particular in cardiac muscle.

It exerts a major influence on osmotic pressure and acid–base status within the cells. Again its physiological role is well established and will not be discussed in further detail. Requirements may also vary widely in different clinical situations. Unlike sodium which is predominantly extracellular, serum concentration is merely a rough guide to the actual potassium status of the patient. True hypokalaemia with a serum concentration less than 3 mmol l^{-1} probably reflects at least a 10% loss of total body potassium. On average, in the presence of normal renal function the daily potassium requirement is likely to be of the order of 50–100 mmol. The presence of hypokalaemia indicates greater needs (up to 200 mmol day^{-1}). Potassium supplementation can be dangerous in the presence of significant renal impairment and lethal hyperkalaemia may result, a fact worth remembering as many of the solutions have variable amounts of potassium incorporated and should therefore be used with caution in certain situations. It is worth mentioning that 3 mmol of potassium are retained per gram of nitrogen utilized. Appropriate increase in potassium supplementation is therefore advised, except in the hypercatabolic state when anabolic processes are restricted and there is a danger of hyperkalaemia.

(c) Calcium

This is a vital element, 99% of which contributes to the structure of the bony skeleton. The remainder is of fundamental importance in a number of vital physiological processes such as muscle contraction and blood clotting. However, in states of trauma and illness, characterized by a patient being bedbound, there is an automatic process of calcium resorption from the bone which increases the calcium levels in the blood, leading to hypercalciuria. The situation is further complicated by a highly efficient mechanism of tubular calcium reabsorption, which further tends to produce hypercalcaemia. For these reasons we do not recommend significant calcium repletion, apart from what is often contained in the routine additives. Excessive calcium administration carries with it a real danger of metastatic calcification, in particular nephrocalcinosis. On the other hand if the basic disease process is associated with calcium deficiency and hypocalcaemia (as in malabsorption states) then calcium supplementation is clearly indicated. If

large amounts are required then we recommend that the calcium should be given separately and not added to the TPN, as calcium (and other divalent cations) tend to make complex solutions unstable. The best guide to the calcium status is serum concentration.

(d) Phosphorus

This combines with calcium in contributing to the structure of bone to a great extent. In addition it is involved in a number of vital processes such as storage, release and transfer of energy (through adenosine triphosphate), glucose metabolism, a number of enzymatic reactions in conjunction with vitamins and regulation of acid–base balance. It also forms a vital part of the cell wall structure, in the form of phospholipids. Deficiency of this element may be produced by malabsorption, vitamin D deficiency, or excessive urinary loss. The major clinical long term manifestation of this is osteomalacia. The use of phosphate-free solutions for TPN has been shown to produce acute hypophosphataemia. This is due to the fact that hypertonic glucose solutions tend to cause a shift of phosphate into the cells and consequently this problem is not seen when phosphate-containing dextrose solutions are infused. Acute hypophosphataemia results in paraesthesiae, convulsions and coma. Many of the commercially available TPN solutions incorporate adequate amounts of phosphate. Phosphorus requirements increase with increasing degrees of carbohydrate metabolism, particularly when insulin is used in large amounts. The phosphate status can be assessed by a combination of serum inorganic phosphate and urinary phosphate excretion. The latter is a very sensitive index, the amount excreted dropping rapidly at the first sign of deficiency. In general the average daily requirement is likely to be of the order of 25–50 mmol day^{-1}.

(e) Magnesium

This is essential in a number of enzymatic reactions involved in oxidative phosphorylation and it also makes a major contribution to the structure of the skeleton. Though it is a macroelement, it is often forgotten in spite of its vital role, probably because it is not routinely measured. It has a profound

influence on neural activity and deficiency can result in muscle twitching, convulsions and coma, which often go undiagnosed. Unexplained and persistent hypokalaemia may be caused by hypomagnesaemia. We recommend routine measurement of serum concentration, which is a good index of the status. By and large the standard additives contain sufficient magnesium. The average daily requirement is of the order of 5–15 mmol day^{-1}. Diarrhoea tends to aggravate deficiency of this element. We strongly advise our readers to bear in mind the possibility of disturbance of this element in the presence of unusual or unexplained neurological features and establish a 'baseline' measurement at the start of nutritional support.

(f) Chlorine

This is closely associated with sodium and is the major extracellular anion. It participates in all the vital processes associated with sodium. Because it couples with sodium and potassium, chloride requirements are not specified separately. However, in special situations such as hyperchloraemic acidosis one has to be careful to avoid infusing large amounts of chloride which would aggravate the acidosis. In this situation bicarbonate becomes the preferred anion. Serum concentration is a good index of current status and measurement is advised, if not routinely, in the presence of significant or unexplained metabolic acidosis.

(g) Sulphur

This element forms a part of the molecular structure of a very large number of vital biological constituents such as certain amino acids (methionine, cystine), vitamins (thiamine, pantothenic acid), hormones (insulin, corticotrophin), enzymes and bile acids. However, very little information is available on measured intake and output of this element and it is not therefore considered separately on its own during parenteral nutrition. A deficiency state has not been reported, probably due to the fact that it is ubiquitous and present in adequate amounts in administered nutrients.

Having considered the macroelements, we can now turn our attention to the trace elements. The currently recognized ones are listed in Table 2.2, along with the daily (parenteral)

requirements, if known. Routine assays of the elements or their indices are expensive and not widely available. Hence it would be logical to provide the optimal amounts of each (if known) routinely during parenteral nutrition. Commercially available additives are listed in the Appendix. In addition, preparations of single elements are available for extra supplementation. While deficiency of these elements is obviously the subject of intense research and study it may be worth remembering their potential for toxicity; many of them are not added as such and are present as 'contaminants' during manufacture. In addition to the essential trace elements there is the possibility of toxicity due to other elements, such as arsenic, mercury, cadmium, lead and aluminium.

(h) Copper

This forms an essential component of a number of vital enzymes including cytochrome oxidase and is necessary for absorption of iron and its incorporation into the haem moiety of haemoglobin. Copper deficiency has been clearly documented in malnutrition, particularly in the presence of excessive diarrhoea. It is much more likely to occur in infants and children, due to the large hepatic reserves in the adult. Nevertheless with prolonged TPN deficiency may occur unless the element is supplied. Copper is carried as part of the transport protein caeruloplasmin. However, caeruloplasmin is one of the acute phase reactants, which rises in response to any injury or infection and therefore a low normal concentration might actually mask real deficiency. The clinical features of copper deficiency include microcytic hypochromic anaemia, bone marrow depression presenting as neutropenia, osteoporosis and delayed bone maturation in children. Diagnosis is supported by the finding of low serum copper and caeruloplasmin levels.

(i) Zinc

This forms an essential part of several metallo-enzymes and the insulin molecule and is vital for protein anabolism. Its deficiency has now been well documented and it is now recognized that zinc requirements rise significantly in hypercatabolic states and in conditions of excessive loss through the gastrointestinal

tract. In these conditions therefore it would be logical to increase the zinc content of TPN fluids. Deficiency of this element manifests clinically by impaired wound healing, rash around the mouth and genitalia, hair loss, depression and a syndrome (usually seen in infants) known as acrodermatitis enteropathica, characterized by alopecia, eczema, diarrhoea and growth retardation. The abnormalities are promptly reversed by the administration of zinc. Plasma zinc concentration is at present the best index of current status.

(j) Chromium

This is an element whose clinical significance was relatively unknown until recently. Its physiological role is unclear but deficiency has been reported in subjects on long term TPN. The clinical manifestations which included peripheral neuropathy, glucose intolerance and weight loss, were reversed by chromium administration. This is consistent with the finding, in experimental animals, of impaired glucose metabolism caused by chromium deficiency. A so-called 'glucose tolerance factor' has been identified as containing trivalent chromium. Chromium appears in present TPN solutions as a contaminant, and therefore one has to consider the possibility of toxicity due to excessive administration. We have observed one patient on home TPN who had persistently high plasma concentrations of chromium and died of hepatic failure. Plasma concentration seems to be the only available measure of chromium status.

(k) Selenium

This is an essential element which forms part of the glutathione peroxidase system. In conjunction with vitamin E it is an important antioxidant. Together they play an important role in the body's ability to mop-up free radicals and superoxides produced by inflammatory processes, which are capable of producing significant tissue damage. The physiological role of this element has been gradually elucidated over the years. Endemic deficiency in China resulted in 'Keshan disease', characterized by a progressive and often fatal cardiomyopathy. Since then it has been recognized that selenium deficiency can occur in patients on TPN. The clinical features include in addition to cardiomyopathy, skeletal myopathy, platelet

dysfunction, haemolysis and neuropathy. Plasma selenium concentration and glutathione peroxidase activity are good indices of current status.

(l) Molybdenum

This is a component of three important enzymes: aldehyde oxidase, sulphite oxidase and xanthine oxidase; the latter two enzymes and plasma molybdenum concentration are indices of current status. Deficiency of this element was first defined in a patient on long term TPN. Deficiency is manifested by headaches, night blindness, lethargy, disorientation and finally coma. Again this is an element which is present as a contaminant in TPN solutions and therefore there is the potential for toxicity; it has been suggested that molybdenum excess can result in a gout-like syndrome.

(m) Manganese

This element is a constituent of pyruvate carboxylase and is involved in mucopolysaccharide metabolism, normal reproduction and extrapyramidal pathways. Deficiency in animals is known to produce growth impairment and hypogonadism. In humans it has been known to produce anorexia, weight loss and dermatitis. Plasma or serum concentrations are thought to be adequate indices of current status. There is no evidence so far to suggest that this element might prove toxic in clinical conditions of health or disease, though excessive exposure has been associated with psychosis and Parkinsonism.

(n) Cobalt

This forms an integral part of cyanocobalamin (vitamin B12) and its deficiency may result in pernicious anaemia or subacute combined degeneration of the cord. However, this is not a clinical problem these days due to the routine inclusion of adequate amounts of vitamin B12 in parenteral nutrition. Free cobalt is difficult to measure and its status is easily measured by cyanocobalamin.

(o) Iron

This is a vital element of well-known importance in oxygen transport through the agency of haemoglobin. Though its deficiency is one of the biggest public health problems in large areas of the developing world (anaemia), it is not seen during TPN owing to its routine inclusion in standard regimens. However, situations of increased demand (childhood, pregnancy) must be borne in mind. Blood haemoglobin concentration, serum iron and ferritin are indices of current status.

(p) Iodine

This is an essential component of the thyroid hormones and its deficiency gives rise to a diffuse goitre and if uncorrected, myxoedema. It is not seen during TPN due to the trace amounts provided in additives.

(q) Fluorine

This element is important for normal constitution of teeth and bones. Deficiency is associated with dental caries. It is not essential and is not included in parenteral nutrition, particularly as excess administration can cause toxicity (dental and skeletal fluorosis). Trace amounts are included in some additives.

The other essential elements listed and their physiological actions are poorly understood. Therefore specific deficiency syndromes are not known to occur in the human being at the present time. The current trickle of information may well turn into a flood of knowledge. Vanadium has been shown to be an inhibitor of the sodium pump and this raises very interesting possibilities with regard to its potential role in clinical states of hypertension and oedema. Silicon is essential for normal development of cartilage and connective tissue in animals. The role of tin, nickel and other elements is unknown at the present time. There is little doubt that with advances in clinical research there is likely to be delineation of physiological roles and associated clinical problems.

2.6.4 Vitamins

It is uncommon to see overt vitamin deficiency in patients requiring nutritional support, but that is all the more reason for keeping a look out, particularly in the elderly. In geriatric patients, and in those from poor social circumstances, there is a definite possibility of longstanding self neglect and vitamin deficiencies might make themselves apparent. This becomes even more likely if the main source of energy supply has been alcohol rather than food! Routine plasma assays of vitamins or indices of their activity are not practical as they are difficult assays and only available at specialist centres. It is standard practice therefore to incorporate vitamins into the daily feeding regimen. It is worth noting that the fat soluble vitamins (A, D, E, K) need to be administered through the vehicle of a fat emulsion. In general the requirements for most vitamins rise significantly in acute illness, possibly several fold. The presence of adequate stores often means that patients may be able to get by for a matter of a few days without any problems. But once a week has gone by without normal intake, one has to be aware that vitamin deficiencies can manifest themselves in a number of subtle ways. For this reason we recommend routine treatment with a cocktail of all the known vitamins along with TPN, particularly if the patient has required nutritional support for a period greater than a week. Daily requirements are given in Table 2.3.

Vitamin A (a collective term for retinol, retinal and retinoic acid) is essential for integrity of epithelial cells, stability of membranes, maintenance of visual purple and normal growth. Deficiency is clinically manifested by dryness (xerosis) of skin and conjunctivae, follicular hyperkeratosis, Bitot's spots and night blindness. The clinical syndrome is easily recognizable and reversed by therapeutic administration. The diagnosis is essentially clinical.

Vitamin D (which represents cholecalciferol and ergocalciferol) is essential for calcium metabolism and bone maturation. Deficiency is manifested by osteomalacia in the adult and rickets in children. Diagnosis of deficiency may be supported by appropriate radiological changes. It is not seen during optimal TPN, which should incorporate adequate amounts of the vitamin.

Vitamin E (tocopherol) acts as an anti-oxidant in minimizing

Table 2.3 Vitamin requirements in parenteral nutrition

Vitamin	*Daily recommended intake (per kg body weight)*	*Av. adult requirements*
Thiamine (mg)	0.02	1.2–1.5
Riboflavin (mg)	0.03	1.8–2.2
Niacin (mg)	0.2	12–15
Pyridoxine (mg)	0.03	1.8–2.2
Vitamin B12 (ug)	0.05	3–4
Folate (ug)	5	300–400
Pantothenate (mg)	0.25	15–20
Biotin (ug)	0.5	30–40
Ascorbate (mg)	0.75	45–60
Vitamin A (ug)	10	600–750
Cholecalciferol (ug)	0.05	3–4
Vitamin E (mg)	0.15	9–12
Vitamin K (ug)	1	60–80

tissue damage caused by free radicals. Not much more is known about this vitamin. Deficiency is rare and may produce anaemia, but has not been reported during TPN.

Vitamin K (collectively referred to as naphthoquinones) contributes to normal blood clotting by leading to prothrombin synthesis by the liver. Deficiency may occur as a conditioned defect in patients with liver disease or chronic alcoholism. Deficiency manifests itself by prolongation of prothrombin time; it should not be seen during TPN due to routine provision. It is worth noting that all the above deficiencies are more likely to occur if the primary underlying illness has been one of malabsorption.

Vitamin C (ascorbic acid) is water soluble and it is essential for the integrity of connective tissue, particularly collagen synthesis. Deficiency is manifested by scurvy, petechial bleeding, peri-follicular haemorrhage, spongy bleeding gums and bleeding into joints. It is not uncommon in the elderly and the neglected. TPN should routinely contain adequate amounts of this vitamin.

The vitamin B-complex consists of a number of important water-soluble vitamins, which will be discussed briefly.

Thiamine is a component of the vital coenzyme thiamine pyrophosphate involved in oxidative decarboxylation. Alcoholism and chronic self neglect are major factors in the evolution

of thiamine deficiency in the Western world and it is a lot more prevalent than generally realized. Deficiency results in beriberi, manifested by general malaise, loss of muscle power, peripheral neuropathy, leading on to resistant oedema and intractable heart failure (sometimes wrongly labelled 'idiopathic congestive cardiomyopathy'). The diagnosis is essentially clinical and may be critical; prompt treatment may be life-saving.

Riboflavin acts as a prosthetic group in flavoproteins involved in the cytochrome system and tissue respiration. Deficiency presents with angular stomatitis, cheilosis, a smooth magenta tongue, corneal vascularization and angular blepharitis. The features are characteristic and must be recognized. They are promptly reversed by replenishment.

Nicotinamide is essential (in the form of the coenzymes NAD and NADP) for hydrogen transport within all living cells. Deficiency leads to pellagra (diarrhoea, dermatosis, depression, dementia and death).

Cyanocobalamin is essential for normal erythropoiesis and its deficiency gives rise to the well-known entities of pernicious anaemia, mild haemolysis, peripheral neuropathy and subacute combined degeneration of the cord. It tends to occur in food faddists, vegans, the self neglected, and in those with gastric problems such as gastric atrophy, carcinoma, etc. Folic acid is also necessary for normal erythropoeisis and its deficiency leads to megaloblastic anaemia. It is usually seen in elderly subjects with a poor nutritional intake, particularly that of green vegetables. The remaining B vitamins are less important and their deficiencies are very rare and poorly documented. Pyridoxine deficiency gives rise to glossitis, peripheral neuropathy and microcytic anaemia. Pantothenic acid deficiency leads to sleep disturbances, paraesthesiae, personality changes and impaired coordination. Biotin deficiency can lead to dermatitis.

2.7 NUTRITIONAL SUPPORT IN SPECIFIC SITUATIONS

2.7.1 Peri-operative nutritional support

There is evidence to suggest that pre-operative nutritional support in malnourished patients improves outlook and survival after major surgery. As a rough rule any patient

requiring major surgery would qualify for nutritional support if there has been weight loss of greater than 10%, or if the serum albumin is less than 30 g l^{-1}; a lymphocyte count of less than 1.2×10^9 l^{-1} is a less reliable criterion. In this situation nutritional support is as much prophylactic as therapeutic. Patient assessment tends to be fairly straightforward and the requirements can be calculated simply. There is no justification however, for recommending routine pre-operative parenteral nutritional support in patients who are not malnourished and in those undergoing relatively minor surgery.

Post-operative nutritional support is indicated far more frequently, particularly in patients who have undergone gastrointestinal or head and neck surgery, in whom the bowel is functionally incompetent. This is particularly true in cases who develop complications such as enterocutaneous fistulae. As a rule, any patient who has been deprived of nutrition by the normal enteral route for a period of 7 days would be eligible to start parenteral nutrition (often earlier in less well nourished subjects). Again assessment of the patient generally poses no major problems and the nutritional requirements are likely to be straightforward. The exception to this rule occurs in certain clinical situations such as fistulae and enterostomy, where large volumes of bowel secretions may be lost to the exterior and require replacement of extra amounts of the appropriate electrolytes – sodium, potassium, bicarbonate and zinc and magnesium in particular.

In situations where very large amounts of bowel surface have been resected due to infarction (of whatever aetiology) then it goes without saying that the patients can only survive on long term home parenteral nutrition.

2.7.2 Nutritional support in renal failure

Acute renal failure is usually of multi-factorial aetiology, and is characterized by a very high incidence of malnutrition, which sets in very rapidly, depending on the catabolic rate. Until recently, all therapeutic modalities were aimed at treating the primary disease and mitigation of the uraemic state by dialysis, with very little attention paid to the importance of maintaining adequate nutrition. Over the last decade the importance of nutritional support in this condition has been established with certainty. The calculation of nitrogen losses are somewhat

complicated by the renal failure (*vide supra*). Furthermore dialytic procedures tend to wash out large amounts of nitrogen, the measurement of which can be particularly tedious. With peritoneal dialysis and continuous haemofiltration it is possible to obtain complete collections of the dialysate or the haemofiltrate, whereas with conventional haemodialysis there is the need to have special equipment for repeated and accurate sampling. More often than not these patients do have failure of the bowel for one reason or another and require parenteral nutrition.

Studies in our unit have shown surprisingly large nitrogen losses – as much as 50 g day $^{-1}$. While there is no doubt that replacement of the nitrogen is essential, there is the question of the liver's maximal ability to synthesize protein beyond which, overloading the system with exogenous nitrogen is not only pointless but may actually be deleterious, leading to excessive urea generation. This critical level might vary from subject to subject but studies in our unit suggest that it is somewhere between 20 and 25 g of nitrogen per day. For practical purposes we would recommend the provision of nitrogen according to calculated losses, but no more than 20 g day^{-1}.

In particular it is worth noting that peritoneal dialysis results in the loss of a certain amount of albumin (approximately 20 g/40 l of fluid exchanged) as well as amino acids (approximately 15 g/40 l). While whole protein loss is unavoidable the amino acid loss can be minimized by addition of an amino acid solution to the influx of dialysis fluid with each cycle. Haemodialysis for 4 h a day results in amino acid losses of 8–12 g, but no loss of whole protein. Continuous haemofiltration which is a more recent form of treatment is characterized by amino acid losses of 20–30 g day^{-1}. Nevertheless this latest form of treatment has the considerable advantage of allowing free infusion of large volumes of fluid and therefore there is no restriction in the volumes required for TPN. It is very important to realize that the provision of nitrogen as prescribed is conditional on the availability of facilities for adequate dialysis. Where this is not the case, as in the underdeveloped areas of the world, increasing protein intake can be dangerous and there is a case for following the time-honoured teaching of protein restriction. We advocate the use of the 3 litre bag containing appropriate quantities of amino acids, glucose and fat. The energy to nitrogen ratio may vary from 125 (in hypercatabolic patients) to

200 (in mildly catabolic patients). Again it is worth emphasizing that many of the commercial preparations incorporate certain amounts of potassium and great caution must be taken in infusing them freely because of the dangers of hyperkalaemia. If that is a problem it is unquestionably safer to use potassium free solutions.

2.7.3 Nutritional support in oncology

Parenteral nutrition has a major potential role in the treatment of patients with various forms of malignant disease. By the very nature of the illness a high proportion of the patients will be malnourished, a state which is often aggravated by chemotherapy or radiotherapy. There have been some fears based on animal work that nutritional support may enhance tumour growth, but there is no evidence for such an effect in human cancer and there is considerable evidence to the contrary. TPN may be required for periods of weeks when a patient's bowel may be incompetent for all practical purposes, the result of toxic chemotherapy or radiotherapy.

2.7.4 Nutritional support in gastroenterology

Acute inflammatory bowel disease, usually Crohn's disease of the small bowel, may result in rapid deterioration in a patient's nutritional status within a matter of a few weeks. By and large enteral nutrition utilizing low residue elemental diets is successful in maintaining an adequate state of nutrition. Sometimes however, complications such as enteric fistula formation can make this inadequate, if not impossible, necessitating TPN. In this situation it is then the only means of sustenance and therefore life supporting. It is often a rewarding exercise because of the nature of the inflammatory bowel disease, which is characterized by remissions and relapses. Thus tiding over a difficult period with TPN can become critical. The nutritional requirements are relatively easy to calculate and adequate allowance must be made for any excessive gastrointestinal loss. In this and other forms of malabsorption, large amounts of protein may be lost through the gut, a fact not often appreciated by clinicians. This is one situation where measurement of nitrogen and protein loss in the urine without considering faecal losses can lead to a gross underestimation of

the true nitrogen loss; the real picture will only emerge if faecal estimations are made.

In chronic liver disease there is often a state of malnutrition due to a combination of hepatic dysfunction and a state of malabsorption occasioned by obstruction to flow of bile. Nutritional support can be of considerable value particularly if a patient is expected to undergo surgery, such as portacaval anastomosis. Modest amounts of nitrogen along with a relatively high caloric intake is indicated. There is evidence to show that provision of larger amounts of nitrogen may precipitate encephalopathy. Plasma amino acid profile in patients with chronic liver disease and encephalopathy show elevated blood concentrations of the aromatic amino acids (phenylalanine and tyrosine) with markedly diminished concentrations of the branched chain amino acids (isoleucine, leucine and valine). As these amino acids share a group specific transport system, the result is an excessive uptake of the aromatic amino acids by the brain and this is thought to lead to a disturbance in the synthesis of the various neurotransmitters with resulting encephalopathy. In support of these facts, treatment with an amino acid solution which incorporates high concentrations of the branched chain amino acids and low concentrations of the aromatic amino acids, has been shown to improve the clinical condition of these patients and establish positive nitrogen balance.

2.7.5 Nutritional support in burns

Severe burns are characterized by the largest ever documented increases in basal metabolic rate or energy expenditure (increases of up to 80%). This enormous increase in the rate of tissue breakdown will almost certainly result in death, unless vigorous nutritional support is provided. TPN is indicated in those patients with impaired bowel function, those not capable of maintaining a nasogastric tube because of facial burns or those whose requirements are so high that enteral nutrition may not suffice. The usual principles of nutritional assessment may not be applicable and the actual requirements are likely to be in excess of the estimates from urinary nitrogen, etc. Based on the patient's characteristics, a formula has been developed by Sutherland.

2.7.6 The team approach

In general nutritional support is likely to be indicated in patients with a wide variety of illnesses and therefore can fall into any one of the many medical disciplines. However, there is little doubt that certain specialties have a much higher incidence of the need for parenteral nutritional support, due to their very nature. These specialties include nephrology, gastroenterology, oncology, intensive care, burns and gastrointestinal surgery. For this reason expertise in nutritional support has brought together clinicians and nurses from diverse sub-specialties. In addition, parenteral nutrition involves pharmacists, dietitians, and other allied personnel. Optimal results are therefore likely to be achieved when there is a concerted action, making full use of all the available expertise for the benefit of the patient. It is now widely accepted that this is best achieved through the agency of a 'nutritional support team' of committed professionals from the categories mentioned above. A strong laboratory link is very important from the standpoint of infection control. The clinicians involved should ideally be of consultant status as well as doctors in training, and preferably from different specialties.

3 *Vascular access*

G. Venkat Raman

Access to the central vascular system is being employed increasingly in modern management and is required in a wide variety of clinical disciplines such as intensive care, surgery, medicine, nephrology, oncology and so on. The indications for its use are ever expanding. Arteriovenous shunts and fistulae are conventionally used for haemodialysis and obviously serve as an excellent means of access for nutrition, when required. However, they are rarely, if ever, used in the vast majority of medical and surgical patients without renal failure who require nutritional support. This discussion will therefore concentrate on central venous access for purposes of nutrition. As discussed in previous chapters peripheral feeding is only applicable in a few selected situations (e.g. elective surgery) and access may be obtained in the normal way.

The object of the exercise is to place a vascular catheter in one of the great veins, with its tip in the superior vena cava (SVC) or the right atrium. There are a number of ways of achieving this end. It is worth mentioning that access to the inferior vena cava is generally avoided, as the site of entry (femoral vein) is geographically prone to infection. Access to the SVC is obtained through either the subclavian vein (SCV) or the internal jugular vein (IJV). Pre-operative placement of a catheter in the IJV is favoured by anaesthetists and is only acceptable for short term use, as it has the disadvantage of an awkward position and difficulty in anchoring. The subclavian route is the preferred method in most hands and must be recommended as the optimal portal of entry. An alternative method which is considerably safer involves the insertion of a long catheter through a peripheral vein (usually the antecubital vein), with advancement of the tip of the catheter up the vein into the central system. The catheters in use are made of

synthetic material, such as teflon (PTFE), polyurethane and siliconized rubber. In general the more rigid the material, the easier it is to insert. The techniques will obviously vary depending on the catheter and the material. It is essential to remember that central venous catheterization must be carried out as a meticulous surgical procedure. There can be no excuse for neglecting surgical principles down to the last detail, in view of the potential dangers of infection. It is important to explain the procedure to the patient and obtain not only consent, but also his or her confidence and cooperation. A small dose of pre-medication (diazepam 5 mg or pethidine 50 mg) can often be of considerable help, both to the patient and the doctor. Patience and a relaxed attitude will go a long way in making the procedure not only easy, but also less stressful. Commonly used catheters are listed at the end of the book.

3.1 TECHNIQUES OF INSERTION

3.1.1 Catheter-over-the-needle

This is the simplest method and involves the same manoeuvre as the insertion of a peripheral cannula, familiar to most medical students and newly qualified doctors. After inserting the needle through the skin, entry into the appropriate vessel is indicated by a flashback of blood, at which point the needle is held steady with one hand, while the cannula is advanced into the vein with the other. The simplicity of the method is offset by the fact that the catheter has to be fairly rigid and hence there is the possibility that its tip might erode through the wall of the central vein. Secondly, if only half the lumen of the needle is in the vein, there would still be a flashback but the tip of the catheter itself would still be outside the vein and any attempt to advance it is likely to result in the tip impinging against the wall of the vein, causing damage and local bleeding. Thirdly, if the tip of the needle has gone through the vein altogether (counterpuncture) then the catheter could easily be advanced outside the vessel into the surrounding tissues. For these reasons this technique is not very popular. Nevertheless, it can be used in the short term on subclavian, jugular and femoral veins.

3.1.2 Catheter-through-the-needle/cannula

This procedure involves the introduction of a needle, usually with a surrounding cannula, into the appropriate vein. The cannula is advanced into the vein and the needle removed. The correct position within the vein can be confirmed by the free flow of blood; furthermore, accidental entry into an adjacent artery will be easy to recognize! The vascular catheter is now passed into the vessel through the cannula and when advanced far enough (by prior measurement) the cannula is withdrawn outside the skin and either anchored to the skin or withdrawn completely, depending on the design of the catheter used. There are now available a number of catheters with detachable hubs whereby it is possible to remove the cannula altogether before attaching the hub. This also facilitates tunnelling procedures. The advantage of this method is the ability to introduce soft catheters for long term use, which are much safer. The limiting factor is the relatively smaller size of catheter which can be introduced through a needle or a cannula.

3.1.3 Seldinger technique

This is by far the most popular and safest method. It involves entry into an appropriate vein by means of a needle, with or without an external cannula, followed by introduction of a supple soft tipped guide wire through the needle/cannula and advancement into the vein. Once it is well advanced into the vessel, the needle/cannula is removed. The vascular catheter is then threaded over the guide wire into the vessel and gently pushed in with one hand, while the wire is held steady and gradually withdrawn with the other. In order to go over the guide wire and through the tissues this type of catheter needs to be somewhat rigid. Even so, catheters made of polyurethane are sufficiently supple and atraumatic. These catheters tend to be relatively short (up to 20 cm) and are ideal for short term use (up to 4 weeks or so), rather than for long term use.

3.1.4 Surgical insertion

This method is generally resorted to for insertion of relatively large bore soft siliconized rubber tubes for long term or home

parenteral nutrition. The common portals of entry are the external jugular vein, the internal jugular vein and the cephalic vein. The appropriate vein is dissected and opened, followed by insertion of the catheter under direct vision, to a measured distance. The external portion of the catheter is generally tunnelled under the skin to an exit point at a distant site. It is well worth emphasizing the need to create the tunnel first if the catheter has a moulded hub which is not detachable! This method is obviously labour-intensive and sometimes requires general anaesthesia. On the other hand it is safe and can be used to insert large bore long term feeding catheters. An important advance has been the introduction of implantable devices which are entirely subcutaneous. They are widely used for long term chemotherapy and may achieve a similar popularity in parenteral nutrition.

Detailed descriptions of the surface anatomy and approach to the individual veins can be found elsewhere. In cases where all the usual sites have been lost through repeated use or surgery, then as a last resort an arteriovenous fistula may be constructed for long term use. 'Medical' insertion of a catheter into the subclavian vein will now be described in some detail, as it is the safest and most widely used method. Central to the method described is a 14 or 16 gauge needle with an outer cannula. The following description will apply to the first three techniques described above. For long term feeding there are now cleverly designed catheters which combine the techniques, as described later. Except in emergency situations, it is worth ensuring that the patient is well hydrated, comfortable and pain free before starting the procedure. The whole field of insertion from the side of the neck to the point of the shoulder and from the wing of the scapula to the nipple should be covered with a povidone-iodine pack for 3 h prior to the procedure (after adequate shaving). At the onset it may be worthwhile (but not essential) raising the footend of the bed by 20–30°, in order to improve venous filling, particularly if the state of hydration is sub-optimal. Another useful ploy is to provide support under the spine, so as to hyperextend the shoulders, a manoeuvre which separates the subclavian artery from the vein.

Using a fine needle local anaesthetic is introduced under the skin at a point just below and parallel to the junction of the medial one-third and the lateral two-thirds of the clavicle,

which coincides with the curvature in the bone. This is followed by the use of a standard 22 gauge needle inserted through the same point and gently advanced under the clavicle, pointing towards the opposite axilla. Local anaesthetic is infiltrated into the tissues, making sure by frequent withdrawal that a vessel has not been entered. The point entered serves as a useful landmark and will be referred to as the subclavian entry point (SEP). Using the fine needle and local anaesthetic the skin is entered at a second point 7–10 cm (3–4 in) away from the SEP, 2–3 cm below the acromion. This will be referred to as the catheter entry point (CEP) and this may vary depending on the physical size of the patient and the length of the available catheter. The subcutaneous tissue is infiltrated with anaesthetic between the CEP and SEP. A tiny incision is made at the CEP.

If the catheter is for short to medium term use then one can employ any one of the techniques, but it is worth incorporating a short tunnel. This can be achieved by using a long (6 in) needle with its outer cannula attached to a 5 ml syringe containing 2–3 ml of heparinized saline (5000 units l^{-1}). The needle is gently advanced towards the SEP until the operator can feel the tip against the clavicle. The needle is now withdrawn by 2 mm and the tip is then inserted into a deeper plane and then advanced in the same direction, so as to be just under the inferior surface of the clavicle, but parallel to the skin. From this point onwards the needle should only be advanced 1–2 mm at each step with aspiration of the syringe to detect entry into the vein.

Once blood is aspirated freely the syringe is detached from the needle and should reveal a free flow of blood. As far as possible the hub of the needle or cannula must be covered by the thumb of the operator, in order to minimize the remote chance of air embolism. The needle should be held as steady as possible with the non-dominant hand and the cannula gently advanced into the vessel with the other. It should go in smoothly and without resistance. If minor resistance is encountered it is worth gently rotating the cannula before advancing again. After the catheter has been inserted completely the needle is quickly withdrawn and the position of the catheter should be confirmed by demonstrating a free flow of blood by syringe aspiration.

Measurement of the distance between the CEP and the third

sternocostal junction on the side opposite to that of insertion will give an approximate measurement of the length of catheter required to have the tip floating freely in the SVC above the atrium. As the length of the catheter should be known prior to insertion, it will be possible to calculate the length of the catheter that should remain outside the skin. This completes the procedure for the first technique. It will be evident that this entails the presence of a relatively rigid catheter, which is more prone to produce mechanical complications.

For those employing the second technique, once the cannula has been introduced into the vessel as described, it need not be advanced more than 2–3 cm. After confirming a free flow of blood the indwelling catheter can be inserted through the cannula and into the central vein. After introducing it to a measured distance calculated as described above, the cannula can be withdrawn. The advantage here is that the catheter can be quite soft.

If employing the third technique, again the cannula need only be advanced 2–3 cm into the vein and after confirming free flow of blood, the guide wire inserted. The cannula may now be withdrawn and the definitive catheter inserted over the guide wire. By the procedure described above it is therefore possible to insert a catheter into the SVC via the subclavian vein, through a subcutaneous tunnel, all with one single entry point.

Medical insertion for long term use involves creating a longer tunnel with the catheter making an exit lateral to the sternal edge over the fourth or fifth intercostal space. The catheters are made of silicone (or similar material) and have a Dacron cuff for fixation and may be Broviac or Hickman type. Insertion technique combines the second and third methods; requires entering the vein with a relatively short needle, followed by insertion of a guide wire. A vein dilator and sheath are then passed over the wire, which is then withdrawn along with the dilator. The catheter is then passed into the vein through the sheath, which is then either withdrawn (in the case of a catheter with a detachable hub, e.g. S-Cath; the external portion is now tunnelled using a metal rod) or split apart (in the case of a catheter with an integral hub, e.g. Life-Cath; the external portion should have been tunnelled before insertion into the vein). Certain catheters are small

enough to be tunnelled through needles provided for that purpose (e.g. Nutricath-S).

It is very important to achieve adequate anchoring and fixation. The catheter must be flushed several times with heparinized saline during and just after insertion. The final position must always be confirmed by X-ray prior to use. Routine maintenance should include a flush of 50 ml of normal saline after use (before the catheter is capped off), followed by a 'heparin lock' of 2000 units injected into the catheter.

3.2 COMPLICATIONS

It goes without saying that the greater the expertise, the rarer the complications. Long term catheters should preferably be inserted by one who does it regularly. In spite of extensive use of methods to obtain vascular access, and considering the 'blind' nature of the insertion technique, complications are fortunately infrequent. They may be classified into two groups: mechanical and septic. The incidence of complications has been variously quoted as 3–5%.

3.2.1 Mechanical

1. Bleeding may be associated with the blind insertion techniques, particularly if by mistake an artery is damaged. Obviously the greater the expertise, the lower the chances of complications. In general a localized haematoma tends to resolve without any significant problem.
2. Pneumothorax or pneumomediastinum might result from trauma to the parietal layer of the pleura.
3. Erosion of the catheter tip through the vessel wall is a rare but dangerous complication. It can lead to bleeding into the mediastinum or infusion of fluid into the mediastinum, a potentially fatal event.
4. Similarly haemothorax or hydrothorax may occur.
5. Cardiac tamponade may be the result of similar trauma causing haemo- or hydropericardium.
6. Fracture of the catheter may occur after prolonged use and may potentially lead to ingress of air or infection.
7. Air embolism might occur due to air being sucked into the central vein if there is a somewhat high negative pressure in the chest.

8. Arterial puncture is not uncommon. It is recognized by the pulsatile flow of blood, though this might not be so obvious if there is marked hypotension. In addition to local bleeding, very rarely it can lead to aneurysmal dilation of the vessel.
9. Tracheal damage has been known to happen.
10. The brachial plexus may be traumatized.
11. Thoracic duct damage can lead to chylothorax.
12. Cardiac arrythmias may be precipitated due to mechanical irritation.
13. Venous thrombosis may set in around the catheter and this can lead to vena caval obstruction. It can be suspected by the appearance of collateral veins and impaired flow of the nutrient mixture. Rarely – and more seriously – the thrombus may propagate up the internal jugular and result in a stroke.
14. Recurrent blockage is a particular problem with the long term catheters. It is usually caused by gradual precipitation of tiny particles within the lumen. The result is the development of resistance to flow, culminating in complete obstruction. The catheter then needs to be replaced.

The cardinal rule during parenteral nutrition is to watch for any unexplained respiratory distress. The causes one must consider are: (a) cardiac failure/fluid overload; and (b) extravasation of fluid or blood into one of the visceral spaces – pericardium, pleura or mediastinum. Careful physical examination should distinguish one from the other. The safest course of action is to discontinue the infusion, examine the patient and obtain urgent chest X-ray and an ECG. If in doubt, injection of contrast into the catheter will demonstrate any extravasation.

3.3 Septic

Catheter related sepsis (CRS) remains a major problem in parenteral nutrition. Any fever, in the absence of an obvious focus of infection, must be attributed to CRS, until proven otherwise. The incidence varies, but is probably of the order of 5%. There is little doubt that the incidence can be diminished by two factors: tunnelling of the catheter and care of the catheter by a dedicated nurse specialist. Herein lies the

importance of a nutritional support team which can offer the expertise required for provision of both the factors mentioned.

CRS may occur at any time after catheter insertion. The incubation period is very short and there is usually no prodrome. There is an abrupt onset of fever which often rises to 40°C, associated with rigors and profuse sweating. There is no significant systemic finding to account for the fever, apart possibly from an inflamed catheter exit-site or tract. The commonest cause of CRS is staphylococcal infection, often by the skin organism *Staphylococcus epidermidis*. For this reason we recommend an anti-staphylococcal drug (usually flucloxacillin) as the first line of defence empirically, while awaiting culture and sensitivity. It is significant that Staphylococci possess the ability to secrete a protective 'slime' around themselves and colonize the catheter, causing recurrent and intractable infection.

It is mandatory to obtain specimens of skin swab (from the catheter site), blood and urine – and any other appropriate fluid – for culture, before giving the first dose of an antibiotic. The drugs should be administered through the catheter. Monotherapy is adequate if there is clinical evidence of infection from the skin, for example, cellulitis around the catheter site. When this is not the case depending on a single anti-staphylococcal agent may be risky; we recommend the addition of an aminoglycoside, such as gentamicin, which has a potent activity against gram-negative organisms as well as staphylococci.

Sometimes the patient may be in septicaemic shock. As this is potentially life-threatening, treatment should consist of broad-spectrum antibiotic cover; we recommend the combination described above plus one drug from one of the groups mentioned below.

1. Most recent penicillins – piperacillin, azlocillin, clavulanate-potentiated ticarcillin.

Or

2. Most recent cephalosporins – cefotaxime, cefuroxime, ceftazidime.
3. Anti-anaerobic – metronidazole, erythromycin – where there is bowel contamination, as in perforation.
4. Anti-fungal – ketoconazole, flucytosin, amphotericin – where there is a strong suspicion or evidence of such

infection, usually in immuno-compromised subjects.

After initiating treatment it is essential to follow up the culture and sensitivity and modify treatment appropriately. Duration of therapy may vary from 7 to 14 days, depending on the severity of infection and the speed of response. We recommend intravenous therapy until 48 h after the pyrexia has remitted, followed by oral therapy.

Persistence of the pyrexia beyond 48 h after starting treatment is a bad prognostic sign. It either signifies infection with an organism that is resistant to the antibiotics administered or the presence of heavy colonization of the catheter and its surrounding tract, which is unlikely to respond to treatment. If a positive culture isolates an organism which is sensitive to one of the antibiotics not hitherto administered, then it would be reasonable to stop the current drugs and switch to the appropriate one. If that is not the case (i.e. the cultured organism is sensitive to one of the present antibiotics) or if the culture is negative, then there is no option but to remove the catheter. There is certainly no justification for leaving the catheter in if the fever has not responded within a maximum of 3 or 4 days from the onset. Once a catheter has been removed, the tip must always be sent for culture and sensitivity. Re-insertion must be postponed as far as possible, except in patients who are critically dependent on that route of nutrition for survival.

4 *Paediatric aspects of parenteral nutrition*

A.H.B. Fyfe and F. Cockburn

Failure of the normal enteral feeding mechanisms in the human infant and child creates a situation in which normal physical, intellectual and emotional growth and development are compromised. Physical growth of the child is dependent upon an adequate supply of nutrient materials to allow cell division to proceed at a rate determined by genetic potential. Given that major organ function is compromised, parenteral nutrition can supply the required elements for growth. When organs such as the kidneys, liver, heart or lungs are damaged, or inadequately developed, then there are enormous difficulties in maintaining adequate growth. Full development of the central nervous system and intellectual maturation depend on an adequate nutrient intake given within a caring environment. Emotional growth and development are even more dependent upon the environment in which the child develops. Prolonged parenteral nutrition within hospital deprives the child of the full emotional support, which only a home environment with caring parents and other relatives can provide. Developments in technology have allowed some children to return home where they are cared for by their parents, initially with the help of nursing and medical professionals and sometimes independent of hospital care for months at a time.

In the healthy child changes in body size and proportion take place by cellular division and cellular migration. The younger the child the more rapid and evident are such changes. This growth and differentiation of organs takes place mainly by cell division and the rate of cell division within each organ is dependent upon the genetic control of that child's nucleoproteins, the provision of a well balanced and adequate

supply of nutrients and freedom from insult or injury. Permanent cellular and functional deficits of organs occur when a deficient or inappropriate supply of nutrients or a disease process interrupts the genetic potential for that organ. Although many of the vital organs have a remarkable capacity for compensatory growth at a later stage, the risk of permanent deficit increases the earlier in life that cell division is inhibited and the greater the degree of that inhibition. Emotional and intellectual, as well as physical growth may be stunted by starvation, insult and injury.

4.1 BODY COMPOSITION

The application of parenteral feeding techniques to very low birth weight (VLBW) infants has greatly improved the potential for ensuring undamaged survival. Many of the VLBW infants have been starved *in utero* because of maternal or placental dysfunction, and others are born prematurely. None of these infants have the reserves of nutrient which the normal term infant possesses. Table 4.1 gives the body compositions of two representative LBW infants who have grown appropriately *in utero,* but delivered at 28 and 34 weeks respectively with the values of a normal term (40 weeks) infant for comparison. The more immature infants have a relative excess of water related to the larger ratio of extracellular fluid (ECF) to intracellular fluid (ICF). As cell division proceeds the relative amount of extracellular water diminishes. At 28 weeks gestation water accounts for 85% of the infant's body weight and 50% of this water is extracellular. At 40 weeks water comprises approximately 70% of total body weight with about 40% being extracellular. This relative excess of water in the LBW infant confers no protection against dehydration since the surface area is relatively greater in the more immature infant and the obligatory daily turnover of water is up to 20% of the total body water pool. The relationship of surface area to body weight is shown in Table 4.2. As the child matures body water content gradually diminishes to the adult value of 60% of total body weight. The ratio of intracellular to extracellular water approaches the adult value by about 6 months of age (ECF approximately 20% and ICF approximately 40% of the total body weight).

There is a considerable increase in the body content of

Table 4.1 Body composition in preterm and term infants at birth

Gestation (weeks)	28	34	40
Body weight (g)	1000	2500	3500
Fat (g)	10	170	530
Fat-free body weight (g)	990	2330	2970
Extracellular water (g)	520	1088	1400
Total water (g)	850	1875	2400
Total water (g kg^{-1} fat-free BW)	859	805	808
Total water (g kg^{-1} total BW)	850	750	686
Carbohydrate (g)	5	14	34
Protein (g)	85	250	390
Minerals*			
Sodium (mmol)	94	200	286
Potassium (mmol)	42	108	185
Chloride (mmol)	68	139	192
Calcium (g)	6.3	19	33.6
Phosphorus (g)	3.9	11.9	19.6
Magnesium (g)	0.2	0.58	0.91
Iron (mg)	65	200	229
Copper (mg)	3.4	8.8	16.4
Zinc (mg)	20	40	70

* Expressed in terms of fat-free body tissue and adapted from data of Widdowson and Dickerson (1964)
BW = body weight

Table 4.2 Relationships between surface area (SA) and body weight (BW) in infant, child and adult

Body weight (kg)	*SA(m)*	*SA:BW*
2	0.15	0.075
3	0.20	0.067
5	0.25	0.050
10	0.45	0.045
20	0.80	0.040
50	1.50	0.030
70	1.75	0.025

minerals between 28 and 40 weeks of gestation. The distribution of these minerals changes as the ratio between ICF and ECF compartments alters. Different tissues have differing mineral contents, e.g. high concentrations of calcium and

phosphorus in bone and high concentrations of iron and copper in the liver. The body content of other elements involved in essential metabolic processes such as sulphur, chromium, selenium, molybdenum, manganese, cobalt, iodine and fluorine increases with maturation. The water soluble vitamins B and C transfer readily from mother to foetus so that by term the tissue concentrations of these vitamins exceed those of the mother.

Fat soluble vitamins A, D, E and K are present in relatively low concentrations in the newborn and deficits quickly occur unless adequate intakes are provided.

Of the total energy in a 1 kg LBW infant 350 kcal (1.47 MJ) are contained in protein and only 110 kcal (0.46 MJ) in fat and carbohydrate. In the normal term infant the total non-protein energy reserves are approximately 1430 kcal (6 MJ) kg^{-1}. In infants born preterm both fat and carbohydrate are almost entirely structural and in the absence of fresh nutrient supply tissue breakdown will commence within hours and growth cease. This is particularly true of the infant's tissue proteins as there is virtually no reserve of free amino acids in the LBW infant. In term infants delay in feeding is less critical because of the larger non-protein energy reserves, but again there is little reserve of free amino acids and new functional peptides and proteins such as hormones and enzymes can only be synthesized after destruction of structural proteins in organs such as muscle and liver to supply the required amino acids.

Many LBW infants will require ventilation in order to overcome problems of pulmonary and cardiovascular immaturity and after requirements for oxygen provision and carbon dioxide removal have been met the next immediate need for survival is an adequate water supply. A 28 week gestation infant might survive 3–4 days, the 40 week infant about 30 days and a well nourished adult up to 69 days if supplied with water alone. Growth will not proceed until a minimum balanced fluid and nutrient intake supplying at least 110 kcal (0.46 MJ) kg^{-1} day^{-1} is achieved. Supply of such an energy intake in a volume which can be tolerated by the immature cardiovascular system of the preterm infant creates a major challenge particularly if osmotic overload is to be avoided. In starvation a minimal catabolic energy release of 76 kcal (0.32 MJ) $kg^{-1}day^{-1}$ is necessary to maintain life. Establishment of growth is critical if success in parenteral nutrition is to be

achieved. Once growth is established the incorporation of nutrient materials into body tissues reduces the load of catabolic waste products on organs such as liver and kidney. The human foetus and infant are entirely anabolic creatures, poorly adapted for catabolic states.

The blood volume in the infant is relatively greater than in the adult. During the first year of life this is about 85 ml kg^{-1}, between 2 and 5 years 80 ml kg^{-1} and 75 ml kg^{-1} between 6 and 12 years. The 1 kg infant has a plasma volume of only 40 ml, which gives some indication of the difficulties which can arise in terms of depletion or overload of this small volume by fluid loss or infusions respectively.

4.2 IMMATURITY OF ORGAN FUNCTION

The skin is a major organ in the young infant in terms of absolute area, weight and importance. It is particularly liable to damage from minor trauma, hypoxia, hypothermia and infections. Water loss from the skin and lungs accounts for the greater part of fluid requirement in the unstressed infant (30–70 ml $kg^{-1}day^{-1}$), but may double when the environmental temperature is increased. Evaporative water loss accounts for approximately two-thirds of total body water requirement during the first 2–3 years of life. The preterm infant, because of skin immaturity and a large surface area relative to weight, is particularly prone to dehydration through excessive fluid loss. Normally during the first 2 weeks of life this degree of water loss diminishes as the skin becomes keratinized, but the use of inappropriate adhesive dressings in the fixation of skin electrodes and at infusion sites may result in the stripping of keratinized skin and a further increase in water loss.

4.2.1 Kidneys

In the human foetus new nephrons are developing up to the 35th week of gestation and further growth and development of the existing nephrons continues throughout the first 6 years of life. At birth the glomerular filtration rate (GFR) is approximately 20 ml min/1.73 m^2 in term infants and in preterm infants is 10.2–13.0 ml/min/1.73 m^2 at 28–30 weeks of gestation. During the early postnatal period the GFR rapidly matures even in preterm infants. A progressive rise in

systemic blood pressure and a decrease in renal vascular resistance in the postnatal period are responsible for this increase in GFR and in the renal blood flow. The creatinine concentration is elevated in cord blood probably reflecting maternal plasma concentrations. Thereafter, there is a rapid decrease in creatinine concentration during the first month. Preterm infants have higher initial plasma creatinine levels compared to term infants, though the rate of decrease is similar. An equilibrium state is usually obtained by about 28 days after birth. Creatinine output per unit of body weight increases throughout childhood and reflects the relative increase in muscle mass. The low GFR of the VLBW infants limits their ability to cope with extraordinary demands.

Tolerance to water and sodium is reduced because of renal immaturity and is markedly influenced by the osmotic load of nutrient intake and from tissue breakdown. During the first 3 days of life the kidneys make very little response to water load, but by the fifth day can usually dilute urine to about 50 mosmol kg^{-1} of water. Hypoxia, hypotension or other stress conditions will reduce renal efficiency. Urinary concentrations of 400 mosmol kg^{-1} are achieved in the newborn and by 3 months about 750–1000 mosmol kg^{-1} is achieved. Early exposure to high osmolality feeds will result in earlier maturation of the renal concentrating mechanisms. Sodium is excreted through glomerular filtration and reabsorption occurs in the proximal tubule, the ascending limb of Henle's loop and the distal tubule. The production of hypotonic urine by the foetus and young infant indicates a greater reabsorption of solute in the ascending limb. Inability of the preterm kidney to retain sodium has been attributed to deficient proximal reabsorption and to the incapacity of the distal tubule to cope with increased sodium loads despite high serum aldosterone concentrations. Vasopressin effects are found even in the VLBW infant and have been shown to influence tubular reabsorption appropriately. However, stress can produce inappropriate vasopressin release and fluid retention.

The kidneys and lungs play an essential part in the maintenance of acid–base balance. Respiratory disorders in young infants commonly produce a respiratory and metabolic acidosis which interferes with cell membrane function and tissue metabolism. Renal threshold for bicarbonate in the term infant is slightly lower than in the adult (21.5 v. 22.5 mmol l^{-1}).

Infusions of parenteral nutrients, by increasing the extracellular volume, may further decrease the renal threshold for bicarbonate and deficiency of potassium will increase the threshold.

The mature kidney excretes hydrogen ions in combination with ammonia (produced in the kidney from glutamine) as ammonium ions [(NH_4^+)] and the principal urinary buffer is disodium monohydrogen phosphate (Na_2HPO_4). Unless the phosphate intake is adequate the infant's capacity to excrete titratable acid is limited. The VLBW infant has a renal threshold for bicarbonate of approximately 18.5 mmol l^{-1} at birth and this increases to 20 mmol l^{-1} at 3 weeks. Values as low as 14 mmol l^{-1} should still be considered 'normal'. These smaller preterm infants tend to be more acidotic and have lower ammonium and lower titratable acid excretion rates than larger preterm and term infants. The lower response to acid loading in VLBW infants may be related to immaturity of the hydrogen ion secretory mechanisms or to a relative unresponsiveness of the distal tubule to aldosterone. There is a higher phosphate excretion rate during the first weeks of life due to either immaturity of the phosphate transport system or to the relative expansion of extracellular fluid volume inhibiting proximal reabsorption. It is essential to maintain an adequate phosphate intake to ensure normal bone growth and calcification as well as maintenance of renal acid excretion.

Renal mechanisms control potassium, sodium and chloride balance and the extracellular fluid volume, under the influence of antidiuretic hormone and aldosterone. Infants may have gross distortions of fluid and electrolytes when infused with unbalanced quantities of electrolytes or when there is tissue breakdown from injury and infections, particularly when the kidneys are poorly perfused or poorly oxygenated. Maintenance of good renal, gut and hepatic perfusion and oxygenation is a vital factor in promoting anabolism and growth. Hyperoxygenation may be as hazardous as hypoxia for it will decrease renal blood flow and aggravate a catabolic state.

Glucose, freely filtered at the glomerulus, is actively reabsorbed in the proximal tubule. Infusions of concentrated solutions of glucose may exceed the tubular threshold, but even in the VLBW infant tubules have a remarkable capacity to adapt when the quantities of glucose infused are increased slowly. Amino acids are efficiently reabsorbed at the proximal renal tubule even in immature infants and account normally for less

than 2% of total urinary nitrogen. Phosphate reabsorption in the proximal tubule is by an active process linked with glucose. Infusions of excessive quantities of amino acids can produce a urinary overflow of glycine, tryptophan, leucine and phenylalanine and this in turn can inhibit phosphate reabsorption.

Stressed preterm infants can develop negative potassium balance. There is normally (in LBW infants) a high urinary sodium/potassium ratio which decreases with gestational and postnatal age. Control of plasma potassium and renal excretion is dependent upon the renin–angiotensin–aldosterone system. Potassium losses can be exaggerated by the use of diuretics as well as by volume expansion and increased urine flow rates produced by parenteral nutrition. Excessive administration of potassium may cause hyperkalaemia and cardiac arrhythmias and conversely failure to provide potassium can rapidly lead to potassium depletion and hypokalaemia, causing muscular hypotonia and ileus.

4.2.2 Gastrointestinal tract

The function of the gastrointestinal tract (GIT) may be inadequate to sustain nutrition and growth in the young infant. Even when an adequate supply of human milk is available, a diminished ability to digest and absorb, together with abnormalities of gut hormone and enzymatic activity, can delay or prevent the synthesis of new peptides and proteins. There is in human milk a number of growth factors including epidermal growth factor, insulin-like growth factor and insulin, which promote growth of the GIT and other organs. How critical these factors are is uncertain as adequate gut growth and infant development are possible in the artificially fed infant deprived of human milk. When total parenteral nutrition is instituted these normal mechanisms are bypassed. The growth factors, endogenous gut enzymes and hormones and the exogenous enzymes and hormones from human milk are all involved in the normal growth and development of the gut. There may also be important interactions between gut polypeptides and similar peptides present in the paraventricular nuclei of the hypothalamus and other parts of the central nervous system.

4.2.3 Liver and exocrine pancreas

Exocrine pancreatic function is essential for normal digestion and utilization of enteral nutrients. Survival without pancreatic function is possible given an adequate replacement of digestive enzymes and insulin. This is necessary, for example, when there is subtotal removal of the pancreas in neonatal nesidioblastosis. The infant with meconium ileus due to cystic fibrosis will also have deficient or absent pancreatic enzyme production and require lipase and trypsin replacement. Bile salt production and circulation in the enterohepatic system is also essential to normal gastrointestinal function. During prolonged parenteral nutrition there is altered bile salt metabolism but the significance of changes in plasma bile concentrations and cholesterol is unknown. The immature infant's hepatic enzymes, which are normally 'switched on' near full term may not be functioning. For example, deficiency of hepatic glucuronyl transferase activity results in unconjugated hyperbilirubinaemia which can cause cellular damage particularly in the basal ganglia of the brain stem. Deficiencies of other enzymes such as hydroxyphenylpyruvic acid oxidase and cystathionine synthetase can result in hypertyrosinaemia and hypermethioninaemia which in turn may inhibit protein synthesis or cause cellular damage. Many other enzyme systems such as the amino transferases, the alkaline phosphatases and the cytochrome P450 are inactive or deficient in preterm infants and may result in, for example, failure of tissue growth and failure to excrete endogenous and exogenous toxins. Poor hepatic function can also reduce the production of fibrinogen and prothrombin, required for effective haemostasis, and of plasma albumin necessary for the maintenance of plasma oncotic pressure and the transport of lipids, vitamins, hormones and drugs. The half-lives of plasma proteins vary considerably, but unless synthesis is established, deficits quickly arise. Preterm infants and infants subjected to hypoxia, during or before birth, may have severe hepatic insufficiency as may older children with viral or toxic hepatic damage, so that any or all of these functions may be significantly impaired. A low plasma albumin in association with leaking immature capillaries or capillaries damaged by hypoxia, scalding or burns can result in gross fluid shifts and oedema.

4.2.4 Neuroendocrine systems

Endocrine function plays an important part in ensuring homeostasis. In the immature infant and in the older child who is critically ill endocrine function may be impaired, absent or inappropriate. This endocrine inadequacy may be aggravated by immaturity of hypothalamic, brain stem and autonomic nervous functions with failure of the homeostatic mechanisms controlling the distribution of blood and blood volume, body temperature, plasma osmolality and sodium, calcium and glucose concentrations. Haemorrhage can occur into the adrenal glands in states of asphyxia, hypotension and septicaemia resulting in acute adrenal insufficiency. These same conditions can further adversely influence the hypothalamic and pituitary control of the endocrine glands. In childhood hyperglycaemia due to diabetes mellitus is the commonest of the pancreatic endocrine disorders and can cause major fluid, electrolyte and metabolic disturbances. Hypoglycaemia may occur due to hyperinsulinism found in newborn infants of diabetic mothers or in association with islet cell tumours, and is commonly associated with lack of nutritional reserve and an inadequate supply of nutrients. Unless adequately fed before surgical procedures, young infants can have considerable metabolic disturbances from hypoglycaemia.

The role of enteric hormones such as glucagon, vasoactive intestinal peptide and gastrin is uncertain. The importance of these gut associated hormones in enterally and parenterally fed infants is unknown, but they might well be important determinants in the recovery of a damaged gastrointestinal tract and of nutritional homeostasis. Growth hormone does not appear to play an important part in body growth during the first months of life, but subsequently its deficiency results in delayed growth, particularly of long bones. During recent years an ever increasing number of growth promoting factors have been identified in the circulation. These factors are small polypeptides which have been shown to increase cellular division rates and protein synthesis. Once the specific role of these factors is determined they might prove useful additives in parenteral nutrition. Thyroxine is essential for normal cell division and may be deficient in the VLBW infant and is found in 1 in 4000 of the newborn population. Prompt recognition of the deficiency state is essential for normal growth and

Table 4.3 Allowances per kg body weight per day for total parenteral nutrition in infants and children (sufficient for growth in all but severe stress conditions). After Cockburn (1984).

Age (years)	*0–1*	*1–6*	*6–12*	*12–18*
Water (ml)	120–150	90–120	60–90	30–60
Energy (MJ)	0.38–0.50	0.31–0.38	0.25–0.31	0.13–0.25
Energy (kcal)	90–120	75–90	60–75	30–60
Glucose (g)	12–20	6.0–12.0	3.0–6.0	2.0–4.0
Fat (g)	2.5–4.0	2.0–3.0	2.0–3.0	2.0–2.5
Amino acids (g)	2.0–3.0	1.5–2.5	1.3–2.0	1.0–1.3
Sodium (nmol)	1.0–2.5	1.0–2.0	1.0–2.0	1.0–1.5
Potassium (mmol)	2.0–2.5	1.0–2.0	0.9–2.0	0.7–1.2
Calcium (mmol)	0.5–1.0	0.3–0.7	0.2–0.7	0.11–0.20
Magnesium (mmol)	0.15–0.40	0.08–0.20	0.06–0.20	0.04–0.08
Phosphorus (mmol)	0.4–0.8	0.20–0.50	0.18–0.50	0.15–0.25
Iron (μmol)	2.0–3.0	1.5–2.5	1.5–2.5	1.0–1.5
Copper (μmol)	0.2–0.4	0.1–0.3	0.1–0.3	0.07–0.12
Zinc (μmol)	0.5–0.7	0.4–0.5	0.4–0.5	0.2–0.4
Manganese (μmol)	0.8–1.0	0.7–0.9	0.7–0.9	0.6–0.8
Chlorine (mmol)	1.8–4.3	1.5–2.5	1.5–2.5	1.3–2.3
Iodine (μmol)	0.03–0.05	0.02–0.04	0.02–0.04	0.015–0.03
Vitamins (water-soluble)				
Thiamine (mg)	0.05	–	–	0.02–0.04
Riboflavine	0.10	–	–	0.03–0.05
Nicotinamide (mg)	1.00	–	–	0.20–0.50
Pyridoxine (mg)	0.10	–	–	0.03–0.05
Folic acid (μg)	20.00	–	–	3.00–6.00
Cyanocobalamin (μg)	0.20	–	–	0.03–0.10
Pantothenic acid (mg)	1.00	–	–	0.20–0.50
Biotin (μg)	30.00	–	–	5.00–10.00
Ascorbic acid (mg)	3.00	–	–	0.50–1.00
Vitamins (fat-soluble)				
Retinol (μg)	100.00	–	–	10.00–25.00
Cholecalciferol (μg)	2.50	–	–	0.04–1.00
Phytylmenaquinone (μg)	50.00	–	–	2.00–10.00
α-Tocopherol (mg)	3.00	–	–	1.50–2.00

development. Functional impairment of other endocrine organs such as the adrenal cortex and parathyroid must also be detected and managed with hormonal and/or mineral replacements.

4.3 FLUID AND NUTRIENT REQUIREMENTS

Table 4.3 gives the requirements for water, energy, carbohydrate, fat, amino acids, minerals and vitamins in infants and children. These allowances are sufficient for growth in all but severe stress conditions. Failure to achieve nutrient intakes within the range indicated can result in a catabolic state for which the infant is poorly equipped. If possible, catabolism should be prevented by providing adequate nutrition, by the gastrointestinal tract, but where this is not possible the parenteral route must be used.

Table 4.4 Estimated water expenditure (ml day^{-1}) in infants. Adapted from Fomon (1974) – assumes an average rate of growth, thermoneutral environment, low solute (breast milk) diet and an ability to concentrate urine to 1000 mosmol/kg water

Age (months)	1	4	12	36
Body weight (kg)	4.2	7.0	10.5	15
Growth (ml day^{-1})	18	9	6	5
Insensible loss, skin and lung (ml day^{-1})	210	350	500	600
Faecal loss (ml day^{-1})	42	70	105	140
Urine (ml day^{-1})	56	105	182	203

4.3.1 Water

Requirements for water depend upon loss from evaporation from skin and lungs, faecal losses, water necessary for renal excretion of solutes and water required for growth. Table 4.4 shows the estimated water expenditure (ml day^{-1}) in infants up to the age of 3 years. These values assume an average rate of growth, thermoneutral environment, low solute (breast milk) diet and an ability to concentrate urine to 1000 mosmol kg^{-1} water. Rates of water loss from skin depend on the surface area of the skin, movement of air over the surface and the vapour pressure of the water on the skin and in the adjacent air. Respiratory water loss depends on the rate and tidal volume of respiration and the difference in the humidity between the inspired and expired air. High rates of loss can occur in children ventilated with unhumidified air, nursed in dry environments or when there is extensive skin damage from infection, trauma and burns. For every gram of water vaporized 0.6 kcal of heat is released so that prevention of

evaporative loss helps preserve heat and energy as well as water. Calculations of fluid loss from fistulae, diarrhoeal stools, vomitus, etc., based on accurate measurements of these losses will allow a correct estimate of the total water requirements. In practice measurements of body weight give a good indication of acute water losses. Equally important are acute weight gains related to water retention and this is particularly true in the VLBW infant.

4.3.2 Carbohydrate

The requirement for carbohydrate intake in young infants is based on the average intake of breast fed infants during the first months of life, and thereafter on the mixed diet of a well-nourished growing infant and child, allowing for the very rapid rates of growth in the first year of life and at puberty. These assessments of requirement, like those of most other nutrients may not apply directly to an infant or child fed by the parenteral route. In practice, however, the enteral and parenteral requirements do not seem to differ greatly. Specialized carbohydrates such as the oligosaccharides found in human milk and required to sustain the bifidobacillus in the infant gut can be obtained only from human milk. Nonetheless adequate nutrition can be achieved even in the most immature of infants by supplying glucose as the sole source of carbohydrate. Glucose is the carbohydrate of choice for parenteral use because it is immediately available for use by the brain, prevents excessive sodium and water loss and causes insulin secretion which in turn has a major anabolic effect. Other sources of energy such as fructose, alcohol and the polyalcohols, sorbitol and xylitol have nothing to commend them as energy sources particularly in the child under the age of 2 years.

4.3.3 Fats

Preparation of vegetable oils in water with an emulsifier to stabilize the mixture contain concentrated supplies of energy in a small volume which can be made isotonic and can at the same time provide essential fatty acids and fat-soluble vitamins. Essential fatty acid deficiencies can occur very quickly in infants and although the commercially available fat

emulsions are relatively deficient in unsaturated fatty acids with a relative excess of oleic (C 18:1) and linoleic (C 18:2) acids, they appear to provide adequate nutrition in practice. There is, however, room for development of appropriate fat emulsions for parenteral use. Transient deficiencies in the acyl coenzyme A dehydrogenase enzymes may disturb intermediary metabolism, result in reduced energy output by the mitochondria and cause muscular hypotonia. It would seem rational to provide both essential and non-essential fatty acids for surfactant and prostaglandin synthesis as well as for structural lipid synthesis and as a source of energy. Excessively high concentrations of plasma free fatty acids can displace bilirubin from albumin and might increase the risk of kernicterus in the LBW, hypoalbuminaemic, jaundiced infant. In the absence of metabolic acidosis, septicaemia and circulatory failure most infants can utilize between 2 and 4 g fat $kg^{-1}day^{-1}$. There has been much speculation as to the stability of cellular membranes including vascular endothelium laid down, from the types of fats infused with intravenous emulsions, but as yet there is no hard evidence as to any adverse long term effects of prolonged parenteral lipid infusions.

4.3.4 Amino acids

Mixtures of crystalline L-amino acids available for parenteral use have a ratio of essential to non-essential amino acids of about 3.2 which corresponds to that found in the proteins of human milk. The ratio is higher than that for infant body proteins which is nearer to 2.8, but in practice it seems that any excess essential amino acids (EAA) are transaminated effectively with little loss of nitrogen as urea. Table 4.5 shows the estimated EAA requirements necessary for the promotion of growth and prevention of tissue catabolism in infants and children. In addition to the eight so-called 'essential' amino acids, histidine and probably tyrosine are essential for infants. Arginine is also necessary, particularly when glycine forms a large part of the non-essential amino acid component. Cystine and tyrosine are essential for the infant with immature hepatic enzyme activity. In older children with normal hepatic function cystine can be synthesized from methionine and tyrosine from phenylalanine. Taurine may also be essential in VLBW

Table 4.5 Estimated* requirements per kg per day for parenteral essential amino acids** in infants and children. After Cockburn (1984)

Age (years):	*0–1*	*1–12*	*12–18*
Threonine (mg) (mmol)	45–92 (0.38–0.77)	20–40 (0.17–0.34)	6–34 (0.05–0.29)
Valine	85–140 (0.73–1.19)	20–48 (0.17–0.41)	11–33 (0.09–0.28)
Cystine	15–55 (0.06–0.23)	17–35 (0.10–0.20)	11–27 (0.06–0.15)
Methionine	35–52 (0.23–0.35)		
Isoleucine	100–130 (0.76–0.99)	18–36 (0.14–0.27)	10–28 (0.08–0.21)
Leucine	75–230 (0.57–1.75)	38–60 (0.29–0.46)	11–49 (0.08–0.37)
Tyrosine	?		
Phenylalanine	50–100 (0.30–0.61)	17–35 (0.10–0.20)	13–27 (0.08–0.16)
Tryptophane	15–30 (0.07–0.15)	3–7 (0.01–0.03)	26–37 (0.01–0.02)
Lysine	110–160 (0.75–1.09)	41–74 (0.28–0.51)	9–59 (0.06–0.40)
Histidine	15–48 (0.10–0.31)	–	–
Total	545–1037 mg	174–335 mg	74–261 mg

* Values are based on average oral intakes and can only provide guidelines for parenteral use.
** In addition to the eight accepted essential amino acids, cystine, tyrosine and histidine are indispensable in the immature infant.

infants. If non-essential amino acids (NEAA) are not provided in proper amounts the body can usually synthesize them, but optimal utilization of EAA is established only when NEAA are provided in balanced quantities. The use of unbalanced amino acid solutions with excess or deficiency of EAA can result in failure of protein synthesis and severe tissue damage. Routine requirements for parenteral amino acids in the infant lie somewhere between 1.2 and 2.2 g $kg^{-1}day^{-1}$; in practice 2.5 g $kg^{-1}day^{-1}$ of a well balanced crystalline L-amino acid solution will promote growth in infants on total parenteral nutrition (TPN) where metabolic stress is not too severe. As the child grows older lesser amounts suffice (Table 4.5).

4.3.5 Minerals

The values for electrolyte and mineral requirements given in Table 4.3 are based on the data of Wretlind (1972) for growth in healthy children. In catabolic states infants and children are unable to tolerate high intakes of sodium and potassium, but once an anabolic state is achieved the quantities of sodium and potassium should be increased. Individual requirements can vary considerably so that frequent blood monitoring is recommended. Increased amounts of calcium, phosphorus, magnesium, copper, zinc and iron are required during periods of rapid growth in the first months of life and again at puberty. The preterm infant is particularly liable to develop mineral deficiency states.

Zinc is a component of the enzymes carboxypeptidase and carbonic anhydrase as well as being involved in nucleoprotein enzyme systems; and in the physiological actions of insulin. In the infant there is often a net negative balance of zinc even when large quantities are given. Intakes of zinc can fluctuate markedly, for it is frequently a contaminant of solutions. Optimal rates of infusion of zinc, copper, iron and manganese are not as yet known, but careful studies are beginning to allow tentative recommendations to be made. Copper is an essential element for the function of many enzyme systems including cytochrome oxidase, ascorbic acid oxidase, catalase, monoamine oxidase, tyrosinase and urease. It is thought to be particularly important in the newborn infant for its role in scavenging free oxygen radicals in the superoxide dismutase system. It is also essential for normal haemoglobin synthesis

and is found in plasma bound to caeruloplasmin, in the red cell to the protein erthyrocuprein and in the brain to cerebrocuprein. Iron, an integral part of porphyrin, is necessary for cytochrome, haemoglobin and myoglobin functions. It is also present in catalase and peroxidase. Manganese is necessary for normal activity of the enzyme pyruvic decarboxylase, arginase, leucine amino peptidase, alkaline phosphatase and of the enzymes of oxidative phosphorylation. When manganese is infused parenterally into young infants it is avidly retained and there is a strong positive balance (unlike copper, iron and zinc). Phosphorus is necessary for growth particularly of bone and teeth in the infant and deficiency can also reduce erythrocyte 2, 3-diphosphoglycerate and adenosine triphosphate, which in turn increase the red cell's affinity for oxygen.

Chloride is the major anion in extracellular fluid and its requirements vary in parallel with sodium but also depend on the amounts of anions given in the form of amino acid, phosphorus and sulphur. Iodine, necessary for normal thyroid function, must be provided in an amount adequate to allow normal growth and neurological development. Fluorine may not be an essential element although it appears to assist the normal development of bone and teeth. Sulphur is obtained from sulphur containing amino acids taurine, methionine and cystine. Cobalt is an integral part of vitamin B12. Optimal concentrations of trace elements required for long term infusion in children are uncertain and careful clinical observations are essential if toxic and deficiency states are to be avoided. Failure to supply individual minerals will quickly inhibit normal growth and development.

Care must be taken to avoid loading intravenously fed infants with potentially toxic minerals such as lead, cadmium and aluminium. Increased concentrations of aluminium have been demonstrated in infants receiving parenteral nutrition for only 3 weeks and there is a risk of aluminium toxicity with prolonged parenteral nutrition.

4.3.6 Vitamins

Vitamins influence a wide range of metabolic functions. Energy release and tissue function require these and other vitamins to enable the tissues and child to grow. Vitamins given parenterally may not be utilized (or function) in precisely

the same manner as vitamins absorbed from the gut. There is therefore some empiricism about the amounts of vitamins given parenterally in order to maintain metabolic processes. It is likely that thiamine which is necessary for carbohydrate metabolism and which is absorbed almost completely from the intestine, is required in an amount equal to the recommended oral intake of 0.05 mg/kg body weight/day. Riboflavin, an active component of oxidative enzymatic activities, is required in an amount of approximately 0.1 mg $kg^{-1}day^{-1}$. Nicotinamide, which can be formed from the amino acid tryptophan, has a daily requirement of approximately 1.0 mg $kg^{-1}day^{-1}$. It is a component of NAD and NADPH and is essential for glycolysis.

Pyridoxine (vitamin B6) is involved in protein, carbohydrate and fat metabolism. Deficiency interferes with tryptophan metabolism and can produce seizures particularly in infants. The recommended parenteral intake for infants is approximately 0.1 mg $kg^{-1}day^{-1}$. Folic acid and its metabolites together with the biopterins are necessary for normal phenylalanine metabolism, synthesis of purines and pyrimidines and for red cell maturation. Young growing infants require approximately 10 mcg folic acid $kg^{-1}day^{-1}$. Cyanocobalamin (vitamin B12) is an essential vitamin for normal central nervous system function and red cell production and the approximate daily requirements are 0.2 μg kg^{-1}. Pantothenic acid requirements are estimated at 1 mg $kg^{-1}day^{-1}$ and this vitamin is involved in carbohydrate and fatty acid metabolism, steroid hormone and porphyrin synthesis as well as being essential for normal acetylcholine function. Biotin, an essential nutrient for the urea cycle and for carboxylation, maintains an anabolic state in young infants when given at 30 μg $kg^{-1}day^{-1}$.

Ascorbic acid (vitamin C) is essential for normal collagen structure and for normal proline/hydroxyproline metabolism. It is also involved in the metabolism of phenylalanine, tyrosine and tryptophan particularly in the VLBW infant. It is essential for adequate p-HPPA oxidase activity and helps prevent the transient hypertyrosinaemia seen in the parenterally nourished preterm infant. Approximately 3 mg $kg^{-1}day^{-1}$ is required for infants on TPN.

Choline has not been demonstrated to be an essential nutrient in man although animals do not thrive well without it. As it is present in fairly large quantities in fat emulsions containing phosphatides and acts as a source of labile methyl

groups, it is unlikely that a deficiency would arise when lipid emulsions are used as a source of energy. It is estimated that the active growing infant will require approximately 150 mg choline chloride per day.

Carnitine is necessary for the mitochondrial oxidation of fatty acids. In general the rate of fatty acid oxidation in young actively growing infants is high during the postnatal period. The precise requirement for carnitine is unknown. In starvation states free carnitine concentrations in plasma and urine decrease rapidly, but acetyl carnitine increases in the plasma and there is a negative correlation between free carnitine and beta-hydroxybutyrate. Present parenteral nutrient solutions contain very little carnitine and sufficient carnitine should be provided to allow growing infants and children to maintain a plasma concentration of $>$ 20 mcmol l^{-1}. L-carnitine is now commercially available and it is likely that it will be added to fatty acid emulsions in the near future.

Fat soluble vitamins A, D, E and K are absorbed from the gut together with fat and the amounts absorbed vary with the type of dietary lipid. It is therefore difficult to assess the precise parenteral needs. Vitamin A, which is necessary for normal retinal and skin function, has to be given in the form of retinol at a dose of 0.1 mg $kg^{-1}day^{-1}$. The pro-vitamin A, carotenoid, cannot be used for intravenous nutrition.

The infant or child in hospital is unlikely to synthesize much vitamin D from 7-dehydrocholesterol in the skin and a daily intake of 2.5 mcg cholecalciferol per kg body weight must be supplied to prevent deficiency.

During TPN vitamin E requirements vary with the amounts of polyunsaturated fatty acid infused and it is estimated that about 1 mg of alphatocopherol per gram of polyunsaturated fatty acids is adequate. In the newborn infant haemolytic anaemia with red cell destruction and peripheral oedema can develop from vitamin E deficiency.

Vitamin K (Phytylmenaquinone) is essential for normal coagulation. It is involved in the production of prothrombin and coagulation factors, V, VII, IX and X. Requirements are uncertain, but it is estimated that approximately 50 mcg of vitamin K1 per kg bodyweight per day should be given with intravenous therapy. Infants and children on broad spectrum antibiotics will produce little endogenous vitamin K from bacterial action in the gut. Measurement of coagulation

factors and prothrombin time will indicate the vitamin K status.

4.4 CIRCULATORY AND METABOLIC DISTURBANCES

Normal infants may lose up to 15% of their ECF volume, equivalent to 10% loss of body weight, in the first 3–4 days after birth. There are usually no abnormal physical signs apart from a low grade pyrexia and reduced urinary output. Generally no treatment is necessary other than improving the feeding.

Diarrhoea with or without vomiting, results in rapid extracellular fluid loss causing loss of skin turgor in addition to reduced urinary output and low grade fever. When 5–10% of body weight is lost in 24 h a state of dehydration is reached which is critical to the infant. Skin turgor is then markedly reduced and the skin is slow to unwrinkle when released from a gentle pinch. The anterior fontanelle is sunken and eyeball tension is diminished. Reduced urinary output, dry mucous membranes and variable temperature control are usual and there is tachycardia with a low pulse pressure, but a normal pink colour and capillary refill. When 10–15% of body weight is lost within 24 h signs of peripheral circulatory failure appear. The skin is pale and mottled and feels cool. Capillary refill is slow after finger tip pressure blanching. Superficial veins are flattened and empty and severe tachycardia with poor peripheral pulse is a feature. Tachypnoea, a response to severe metabolic acidosis, can be marked and the infant is usually hypothermic.

In the majority of dehydrated infants there is isotonic dehydration in which there is a proportionate loss of extracellular water and electrolyte. Plasma sodium and osmolality are normal. Where losses are disproportionate there are differences in clinical findings. In hypertonic dehydration more water than electrolyte is lost, with an increase in plasma osmolality and sodium concentration (> 150 mmol l^{-1}). There is less than the expected degree of circulatory failure and subcutaneous tissue change. The high extracellular and plasma sodium concentrations cause cellular desiccation which tends to compensate for the extracellular water loss. Although dehydration is clinically less apparent (10% weight loss may cause no circulatory disturbance), signs of disordered central

nervous function may appear. Increased blood viscosity and a high haematocrit diminish effective cerebral blood flow and predispose to vascular thrombosis. Renal vessels may be involved as well as the cerebral venous sinuses. Co-existent metabolic acidaemia, hypoglycaemia or hyperglycaemia, raised blood urea and hypokalaemia can complicate the clinical picture. The infant is drowsy and when roused is irritable and sometimes jittery. Intracellular dehydration gives the skin, subcutaneous tissues and muscles a characteristic waxy, doughy feel. There is increased muscle tone which may progress to clonic and tonic seizures. Hypotonic dehydration is less common than the other forms of dehydration and there is almost always hyponatraemia (plasma sodium < 132 mmol l^{-1}). Severe circulatory disturbance with signs of peripheral circulatory failure and coma occur at lesser degrees of dehydration than in either isotonic or hypertonic dehydration states.

4.4.1 Management

Before proper nutrition and growth can be achieved adequate tissue perfusion with oxygenated blood is essential. Correction of hypovolaemia, dehydration, anaemia, acidaemia (respiratory and metabolic), hypoglycaemia and electrolyte disorder is the first priority. When blood is required for the infants in the first weeks of life it may be given partially packed (packed cell volume 60%). In conditions of gross metabolic disturbance and anaemia exchange transfusion with fresh whole blood can be used. Low sat albumin is available as a plasma expander for use in circulatory failure without anaemia and can be given to infants with plasma albumin concentrations of less than 28 g l^{-1}. In acute hypotension 5% low salt albumin may be infused at a rate of 15 mg kg^{-1} during the first hour. Each gram of albumin given will retain 12 ml of water in the vascular compartment, therefore, if further albumin is required great care must be taken to prevent circulatory overload.

No matter what the aetiology of the fluid and electrolyte disturbance, survival depends on the re-establishment of circulation and tissue perfusion. Survival of the infant with infective gastroenteritis depends more on the correction of fluid and electrolyte disturbances than on elimination of the offending organisms. Table 4.6 gives a schedule for the

Table 4.6 Treatment of isotonic dehydration

Therapy	*Time*	*Solution*	*Volume*
Emergency	0–15 min	10% glucose; Na^+ 75 mmol l^{-1} HCO_3 20 mmol/l; Cl^- 55 mmol l^-	20 ml kg^{-1}
	15–90 min	5% low salt albumin, or whole blood, or plasma	15 ml kg^{-1}
Deficit replacement	1.5–8 h	If 10% loss of body weight deficit is 100 ml kg^{-1} minus emergency 35 ml kg^{-1} = 65 ml kg^{-1} of a solution like half-strength Darrow's in 2.5% glucose	65 ml kg^{-1}
Maintenance + excessive	8–24 h	Same solution as for deficit replacement with added K^+, Na^+ and bicarbonate as decided by type of excess fluid lost and plasma biochemistry	100 ml kg^{-1} + vol. of fluid loss

treatment of isotonic dehydration. This form of management is only necessary when dehydration is moderate to severe (7–15% reduction in body weight). If there are signs of circulatory failure, blood is taken for biochemical analysis and an immediate infusion of 20 ml kg^{-1} of a 10% glucose solution containing sodium 75 mmol l^{-1}, bicarbonate 20 mmol l^{-1} and chloride 55 mmol l^{-1} should be given over the first 15 min. After this, 5% low-salt albumin, or whole blood if the patient is anaemic, can be given at a rate of 15 ml kg^{-1} during the next 60–90 min. If low-salt albumin is unavailable and the infant is not anaemic, plasma may be used at the same volume.

Replacement therapy is then continued after assessing the fluid volume required for deficit and maintenance. A 3.5 kg infant with a 10% deficit would have a 350 ml fluid deficit and would require an additional 350 ml (100 ml $kg^{-1}day^{-1}$) for maintenance, i.e. a total of 700 ml. If emergency treatment had been given with glucose/electrolyte mixture and low-salt albumin the volume of emergency treatment would be

subtracted from this total volume and the balance, about 580 ml in this example, would remain to be replaced. Infants with isotonic dehydration should be given a solution such as half strength Darrow's solution in 2.5% glucose, the replacement of the deficit taking up to 8 h. During the remaining 16 h the maintenance requirements together with provision for any excessive continuing loss should be given.

Infants with hypernatraemic dehydration have relatively small deficits of sodium with moderate to severe dehydration. If the ECF deficit is rapidly replaced water will enter cells freely and this can disrupt cell function. In the brain for example, this may produce cerebral oedema and convulsions. If circulatory failure is present in a hypernatraemic state this is corrected as for isotonic dehydration. Low-salt albumin is particularly useful and the use of plasma should be avoided. Deficit plus maintenance requirements for 2 days are calculated and this volume is given at a slow constant rate over a 48-h period. There must be no attempt at rapid correction of deficit. In the 3.5 kg infant with a 10% hypernatraemic dehydration 350 ml of fluid would be given to replace the deficit, less 120 ml emergency replacement fluid, and 350 ml for each day's maintenance. The total 930 ml volume would be given at about 19 ml h^{-1} over the subsequent 48 h. A suitable fluid for hypernatraemic dehydration is 0.45% sodium chloride (77 mmol sodium per litre) and 2.5% dextrose until urine flow is established. Once urine flow is established half strength Darrow's solution in 2.5% dextrose can be used. After about 1 h calcium gluconate may be given to correct any coexistent hypocalcaemia.

In infants with hyponatraemic dehydration there can be sodium deficits of up to 20 mmol kg^{-1}. The same emergency treatment as that used to correct isotonic dehydration is given and this can be followed by Darrow's solution at 40 ml kg^{-1} during the next 3–4 h. Subsequently, half strength Darrow's solution in 2.5% dextrose can be given to complete the estimated deficit and maintenance requirements for the remainder of the first 24 h.

Particular consideration must be given to the management of fluid and electrolyte problems in infants with burns, scalds and skin damage. Not only must the large surface area be considered, but the different body proportions must be remembered, particularly in relation to heat loss. The head and

Table 4.7 Some indications for parenteral feeding

1. Extensive reaction of small intestine (gastro-intestinal anomalies).
2. After cardiac and lung surgery or after repair of oesophageal atresia, diaphragmatic defect or gastroschisis.
3. Multiple trauma and burns.
4. Infections (meningitis and septicaemia).
5. Intractable diarrhoea (enteritis or disaccharide intolerance).
6. Ileus (gut infarction, peritonitis, necrotizing enterocolitis or severe metabolic upset producing electrolyte disorder).
7. Acute renal failure.
8. Ulcerative colitis and Crohn's disease.
9. Acute hepatic disease.
10. Immature infants intolerant of gastro-intestinal feeding.
11. Infants with severe respiratory difficulty (recurrent apnoeic attacks, idiopathic respiratory distress syndrome, aspiration and bronchopneumonia, pneumothorax and pneomomediastinum).
12. During and after removal of an endotracheal tube to reduce the risks of aspiration.
13. To complement enteral feeding in very immature infants.

neck of a newborn infant account for 19% of the surface area, compared with 9% in the adult. The lower limbs each comprise 9% in the newborn infant and 18% in the adult. The usual rule of 9's can be used in calculating the surface area of the trunk and upper limbs. In scalds, burns, dermal sepsis and epidermolysis bullosa there can be considerable protein loss.

4.5 PARENTERAL NUTRITION

Table 4.7 gives some of the indications for instituting parenteral nutrition. Once circulation is established and states of dehydration corrected, if enteral nutrition is not possible then parenteral nutrition must be considered (sometimes in addition to enteral nutrition). The given schedule is one of many recommended for use in infancy and childhood, based on the Stockholm regimen (Wretlind 1974). Table 4.8 gives examples of solutions for complete parenteral nutrition. The three basic solutions (dextrose, amino acid and lipid) can be given continuously at the appropriate constant rate through infusion pumps. The solutions are allowed to mix as near to the indwelling catheter as possible. In hospital practice we usually combine the dextrose and amino acid solutions in a

Table 4.8 Examples of solutions for Complete Parenteral Nutrition (volume per kg body weight per day)

Age (years)	0–1	1–6	6–18
Solution 1			
(a) Solution of L-amino acids with glucose 'Vamin 9' with	24–45 ml	22–30 ml	14–30 ml
(b) Electrolyte solution containing 0.15 mmol Ca, 25 μmol Mg, 0.5 μmol Fe, 0.15 μmol Zn, 0.25 μmol Mn, 0.075 umol Cu, 0.35 umol Cl, 75 μmol P, 0.75 μmol F, and 0.01 μmol I in 1 ml 10% Dextrose 'Ped-El'	4.0 ml	3.0 ml	2.0 ml
Solution 2			
(a) Fat emulsion 20% 'Intralipid 20%' with	15–20 ml	10–15 ml	10–15 ml
(b) Emulsion of fat-soluble vitamins containing 69 ug Retinol, 1 μg Ergocalciferol, 0.64 mg dl-α-tocopherol and 20 μg Phytomenadione in 1 ml 'Vitlipid N Infant' Daily dosage must not exceed 10 ml. In children older than 11 years 'Vitlipid N adult' (10 ml) to each 500 ml Intralipid is recommdended.	1.0 ml	1.0 ml	1.0 ml
Solution 3			
(a) Glucose 10% with 5.9 mmol Na, 1.5 mmol K, 0.09 mmol Ca, 0.3 mmol Mg, 4.9 mmol Cl and 0.6 mmol P and 1.6 mmol Lactate in 100 ml.	75–100 ml	70–90 ml	15–60 ml
with			
(b) Lyophilized water-soluble vitamins 'Solivito N' 3.0 mg Vitamin B_1, 3.6 mg Vitamin B_2, 40 mg Nicotinamide, 4.0 mg Vitamin B_6, 15.0 mg Pantothenic acid, 60 μg Biotin, 0.4 mg Folic Acid 5.0 ug Vitamin B_{12}, and 100 mg Vitamin C dissolved in 10 ml 10% Dextrose.	2 ml	1 ml	1 ml

single bag and infuse the fat emulsion (with fat soluble vitamins) as close to the indwelling catheter or cannula as possible. In the home situation we have recently used a one bag system combining all three solutions. Where prompt biochemical analyses and pharmacy based preparations of parenteral solutions are available then the one bag system may be possible even during the early acute management phase. Where these services are not available throughout the 24 h, then utilization of individual solutions allow the clinician to alter nutrient intakes in response to clinical and biochemical changes in infant and child. Lipid emulsions are usually

introduced after 12 h in VLBW infants and should never be given to an infant when the plasma pH is <7.28 as lipid is poorly cleared from the blood in this acidaemic state. When separate lipid infusions are given it is good practice to maintain the simultaneous continuous infusion of amino acids, glucose and mineral solutions for optimal utilization. The infusion of lipid emulsion may be discontinued at 0500 hours, blood being taken for biochemical estimations at 0900 hours when the lipid emulsion infusion can be recommenced. This allows the plasma to be checked for lipid content and prevents errors in biochemical estimation of other substances.

4.5.1 Clinical assessment

It is essential to know the initial weight of the infant and the weight after correction of circulatory disorder and dehydration states. Thereafter, the infant should be weighed daily. Occasionally this is difficult when an infant is connected to a ventilator, but such difficulties can be overcome. The fingers and toes should be warm and pink. Prompt refill of skin capillaries after blanching with fingertip pressure, together with peripheral warmth are indices of good peripheral circulation. Skin and core temperatures can be maintained by careful control of environmental temperature and humidity and by correction of circulatory disorders. Clinically detectable oedema is not uncommon, particularly in preterm infants, and depending on aetiology, the intakes of sodium and water may have to be reduced, albumin infused and a diuretic given. In the child requiring assisted ventilation measurements of arterial oxygen, carbon dioxide and hydrogen ion concentration will be required as a guide to ventilatory assistance. Tachycardia, bradycardia or arrhythmia may indicate circulatory failure, hypoxaemia or severe electrolyte disturbance. During the early stages of parenteral nutrition there should be continuous measurements of ECG, arterial and venous pressure measurements. Transcutaneous electrodes will measure continuously the PO2 and PCO2.

The child should be observed to determine liver size, distension of scalp veins, the presence of peripheral or pulmonary oedema, tachypnoea, tachycardia and cardiac arrhythmias. Urinary volumes should be measured and urine tested for osmolality and glucose concentrations in the first week or two of parenteral nutrition.

4.5.2 Biochemical assessment

Daily estimations of blood pH, plasma bicarbonate, sodium, potassium, chloride, glucose and urea concentrations and osmolality are usually necessary during the first 2–3 days of treatment. This allows the mineral composition of the infusion to be altered according to requirements. Plasma calcium, phosphorus, magnesium, ammonia and amino acid concentrations may be estimated twice in the first week. Thereafter, biochemical assessment may be less frequent if the clinical status is judged reasonable. Serum triglyceride concentrations during the infusion should not exceed 2.3 mmol l^{-1} and should be < 1.2 mmol l^{-1} 4 h after the discontinuation of the lipid infusion. According to progress and the child's ability to tolerate oral or gavage feeding the volumes infused parenterally are reduced stepwise as oral intake is increased. In general, metabolic complications during parenteral nutrition are no greater than those observed in enterally fed children. Long term survival and effective rehabilitation of children with near total absence of small bowel has been made possible by the introduction of a programme of TPN.

In the VLBW infant and in children on prolonged parenteral nutrition clinical assessments will require to be made regularly in order to avoid deficiency of vitamins and trace elements. The combination of careful clinical observation and biochemical estimations based on the clinical picture allows prompt correction of such deficiencies. Measurement of serum ferritin gives a good index of iron status. Measurements of white cell zinc, if available, will give a better picture of zinc deficiency state, otherwise plasma zinc and copper measurements together with measurement of plasma magnesium, phosphate, alkaline phosphatase, albumin, transaminase and bilirubin are recommended.

4.5.3 Metabolic complications

The risks of giving parenteral amino acids are negligible since the advent of crystalline L-amino acid solutions for use in paediatric practice. Hyperlipaemia from inadequate clearance of Intralipid from the circulation may cause fat accumulation in the lung. Preterm infants given fat infusions of 6 g $kg^{-1}day^{-1}$ can develop decreased oxygenation with no change in lung

mechanics. Increased free fatty acids in the circulation compete with bilirubin for binding to albumin and therefore the molar ratio of free fatty acid to albumin in plasma should be kept below 6. In order to avoid such complications Intralipid should be introduced in a dose of 1 g $kg^{-1}day^{-1}$ and gradually increased to 3 g $kg^{-1}day^{-1}$ given continuously over the 24-h period. It is inadvisable to use a higher rate of infusion. Cholestatic jaundice occurs in a variable number of young infants having parenteral nutrition. The aetiology is not established. In most children this resolves promptly when the parenteral nutrition is discontinued.

In spite of these and other complications related to the materials used and the invasive methods required for infusion, TPN can be life-saving in many instances of gastrointestinal failure. There is a definite mortality and morbidity and its use should be restricted to those infants and children in whom it is likely to be beneficial. It should not be used if adequate nutrition can be achieved by the enteral route. Used sensibly parenteral nutrition can be vital in securing undamaged survival in the sick and compromised child. Enteral nutrition should be introduced as early as possible and may initially be given by slow continuous infusion of human milk or an elemental or predigested milk substitute. It must be remembered that the intestinal mucosa requires to be nourished from its luminal aspect in order to be fully healthy and to grow. As the infant gut begins to tolerate larger volumes the parenteral intake can be gradually reduced and hopefully discontinued.

4.6 VASCULAR ACCESS IN THE INFANT AND CHILD – PRACTICAL ASPECTS

4.6.1 Sites and technique

(a) Umbilical artery

Immediately after birth the umbilical artery can be catheterized using a radio-opaque arterial catheter fitted with a Luer Lock. The catheter tip should be positioned within the descending aorta and can remain *in situ* for a week or more. Peripheral vascular occlusion with limb ischaemia has been seen occasionally in new born infants with umbilical arterial lines *in*

situ. Injection of drugs or withdrawal of blood samples through the catheter appears to predispose to this complication. We therefore make it a rule that these catheters should be reserved for continuous infusions of feeding solutions alone, with blood sampling and drug injections through a separate route. In the LBW infant, umbilical arterial catheterization has been implicated as one of the many possible aetiological factors in the serious disease of necrotizing enterocolitis. For this reason we recommend that this route be chosen only if really necessary and for as short a time as possible.

(b) Peripheral vein

It is quite possible in the neonate to maintain TPN by the use of peripheral venous cannulae, for periods up to 3 weeks. The following peripheral venous access sites can be used: the scalp, dorsum of the hand or foot, ventral aspect of the wrist, antecubital fossa, or the long saphenous vein at the ankle. A 24 or 26 gauge Teflon catheter would be suitable for this purpose. Prior puncture of the skin close to the vein allows the intravenous cannula to be inserted smoothly without resistance, and hence entry into the vein itself can be more readily appreciated by the operator. Fixation of the catheter to the skin must be adequate and splinting of the limb is usually necessary in an infant, preventing dislodgement of the cannula by movement of the child.

Redness around the entry site suggesting that the drip has 'tissued', or an increased pressure reading on the delivery pump, should be taken as indications for removal of the cannula and re-insertion at another site. In our experience these peripheral veins last for 24–72 h. Many of our infants can be maintained on TPN using this method alone. The main advantage is the lack of central catheter complications, which must be weighed against the necessity for frequent replacement of intravenous catheters.

(c) Peripheral vein access with catheter advancement to central vein

This technique is particularly useful in LBW infants, although its use can be extended to older patients. An appropriate vein

is selected either from the scalp, the external jugular, or the antecubital fossa. The skin is prepared with povidone-iodine and alcohol. Using a sterile technique the vein is entered with a 19 gauge needle. When free flow of blood is obtained, the catheter (23 gauge) is inserted through the needle and advanced along the vein into the right atrium. Graduation markings on the catheter allow accurate placement, the position being checked afterwards by X-ray. The needle is then withdrawn over the catheter and the system connected to the intravenous feeding apparatus using the detachable Luer lock compression hub (Vygon ECC Neonatal silicon catheter, Vygon Ltd, Cirencester, Glos, UK).

At the exit site the catheter must be fixed carefully by stitch or tape and scrupulous after-care of this site is essential to prevent infection or damage to the catheter. These catheters can remain *in situ* as long as necessary, their useful life usually being 3–4 weeks. The advantages inherent in central venous access are gained with only minimal interference to the sick neonate. Drawbacks include the limited infusion rate due to the narrow calibre and the possibility of the catheter 'losing its way' as it is advanced along the vein.

(d) Direct central venous access

In the event of peripheral venous access being impossible, or if prolonged parenteral nutrition is anticipated, direct access to major veins is necessary. Various techniques are available.

(i) Percutaneous puncture of subclavian or internal jugular vein using the Seldinger technique is a well tested method of achieving central venous access. The main disadvantage is the lack of a subcutaneous tunnel, resulting in an increased risk of infection and greater difficulty in fixation of the catheter. For relatively short term use it is a valid technique but it is not our first choice for parenteral feeding in children.

(ii) Modified Seldinger introduction with subcutaneous tunnel incorporated. Following skin preparation two small incisions are made; one just below the clavicle, the other medial to the nipple (Figs. 4.1–4.5). With the help of a trocar (Vygon Life-Cath-Broviac type) the feeding catheter is introduced until the fixation cuff is within the subcutaneous tunnel. Through the upper incision the subclavian vein is entered

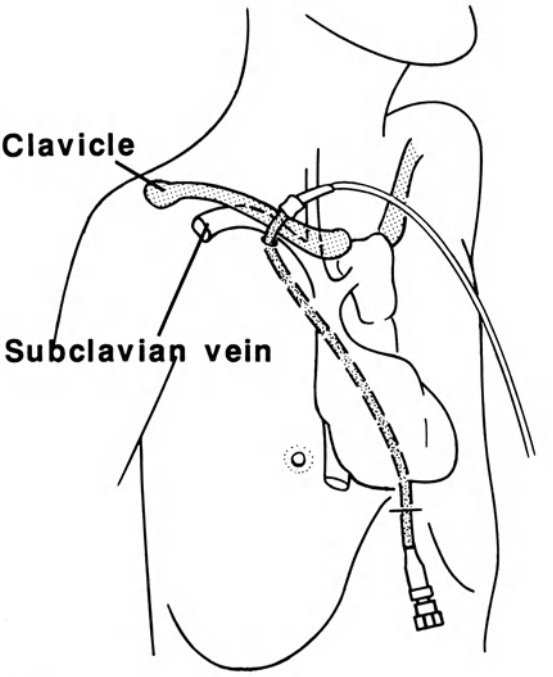

Figure 4.1

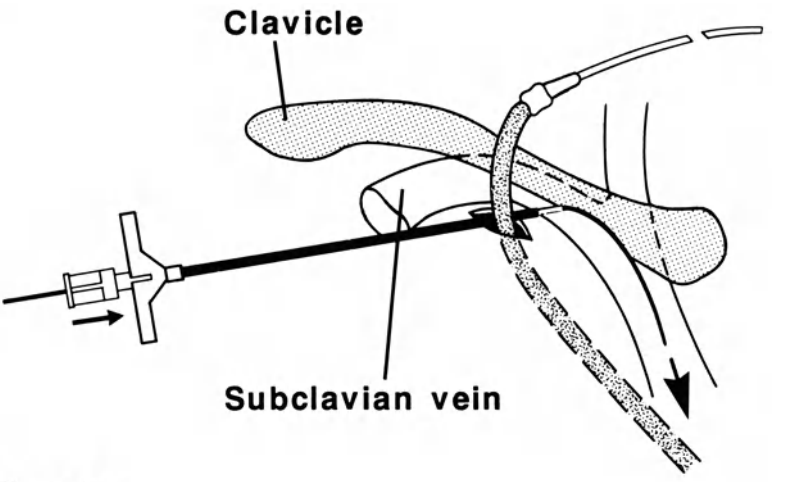

Figure 4.2

Figures 4.1–4.5 Modified Seldinger technique for subclavian vein catheterization

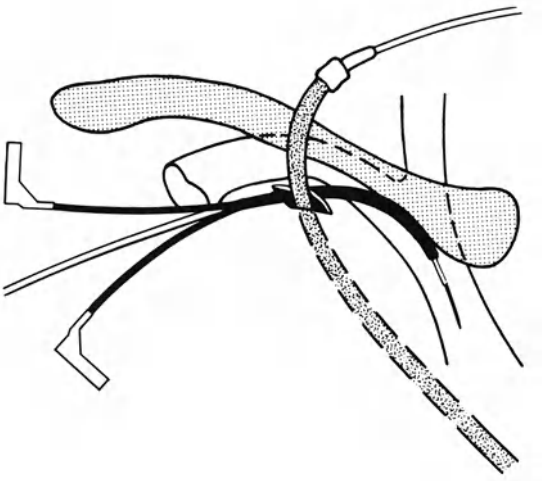

Figure 4.3

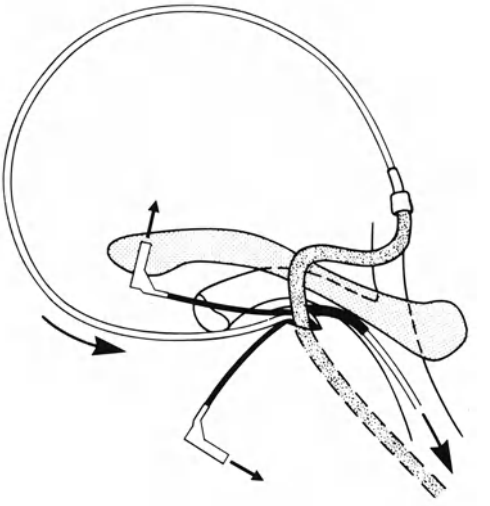

Figure 4.4

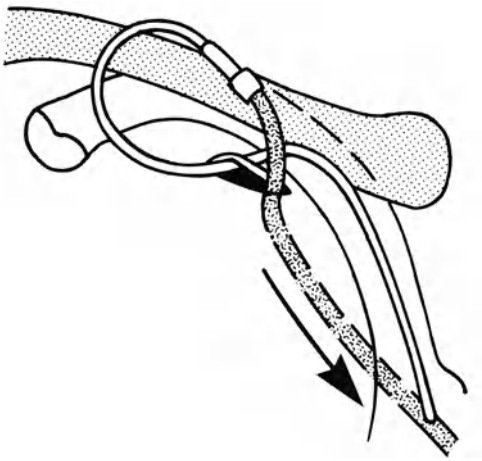

Figure 4.5

using the needle supplied. The guide wire is inserted and the needle withdrawn. Over the guide wire the dilator and sheath are passed into the vessel. The guide wire and dilator are then removed and the Broviac catheter is passed through the sheath into the vein. The sheath is pulled apart and gently removed allowing insertion of the rest of the catheter. The loop which is left can be straightened out by pulling on the proximal catheter until the fixation cuff is just within the exit wound. 'Blind' catheterization of the subclavian or internal jugular veins does carry a small but important morbidity. The recognized complications include pneumothorax, hydrothorax, haemothorax, haematoma and arterial puncture. With experience the incidence of these complications can be reduced to a minimum.

(iii) Direct surgical exposure of central veins. Cut-down exposure of the vein can be performed at many sites in the infant and child, but three access points have proved most useful. With the patient in the Trendelenberg position the external jugular vein can be seen in the neck, exposed surgically and used as an entry point for a Broviac or Hickman type catheter feeding down into the right atrium. The catheter

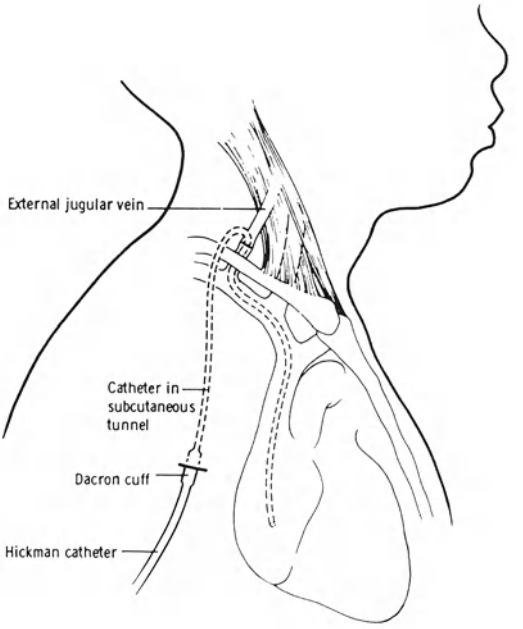

Figure 4.6 Surgical catheterization of the external jugular vein.

may turn towards the axillary vein, so if possible fluoroscopy should be used during the procedure. A subcutaneous tunnel can be led into the anterior chest wall (Fig. 4.6).

Direct surgical exposure of the internal jugular vein through a small transverse incision in the neck is often used in children. If possible the catheter should enter through a side-hole in the vein, controlled by a purse string suture. In neonates and infants the small diameter of the vein may render this impractical, so the vein has to be ligated proximal to the catheter entry point. Again a subcutaneous tunnel to the anterior chest wall is fashioned.

The long saphenous vein in the upper thigh can be identified and mobilized. A paediatric Broviac catheter is inserted into this vein and advanced into the inferior vena cava proximal to the renal veins; the position can be checked radiologically. With this approach the tunnel is led up onto the abdominal wall, well away from the napkin area (Fig. 4.7). With this technique occlusion of the inferior vena cava rarely occurs.

Any catheter fed into a central vein should be treated with

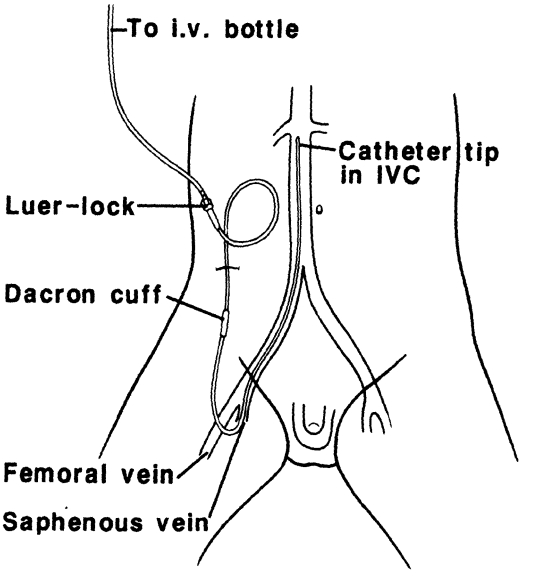

Figure 4.7 Surgical catheterization of the inferior vena cava.

great respect. Fixation at the exit site is essential, and this area is usually covered with a sterile adhesive, transparent dressing such as Op-Site (Smith & Nephew Ltd, Welwyn Garden City, Herts, UK). Daily change of nutrient bottles and administration must be performed in a sterile manner to avoid catheter sepsis. To reduce the risk of contamination we are at present trying a one-bottle feeding system, combining all the nutrients, vitamins, electrolytes and trace elements into one container. This greatly simplifies the administration of the nutrient, particularly for the child at home. Routine antibiotic prophylaxis is not recommended in children receiving parenteral nutrition.

4.6.2 Pumps and filters

It is essential in paediatrics to deliver accurately the correct quantity of intravenous solutions as the amount required by the neonate and LBW infant may be exceedingly small. Inaccuracies of as little as 0.1 ml h^{-1} in the infusion rate can cause major upset in the VLBW infant. Modern peristaltic pumps can deliver with fair accuracy quantities from 1–99 ml h^{-1}.

For example, the IVAC 560 variable pressure pump (IVAC Corporation, San Diego, CA, USA) is a sophisticated system which allows monitoring of the rate, total fluid volume infused and pressure at the site of delivery into the vein and has a range of delivery from 1 ml to 999 ml h^{-1}. For smaller quantities in the neonates we use the TREONIC IP4 syringe pump (Vickers Medical, Basingstoke, Hants, UK) which has a range of 0.1–99 ml h^{-1}. Routinely an IV filter/air eliminator with a 0.2 μm removal rating is used for parenteral nutrition. These filters remove particulate debris, microbial contaminants, together with air bubbles, and should be replaced daily for maximum effectiveness. Intralipid cannot be delivered through these filters.

4.6.3 Home parenteral nutrition in children (Fig. 4.8)

When prolonged parenteral nutrition is found to be necessary in the infant or child, treatment at home should be initiated if at all possible. Long hospitalization causes considerable stress for patient and parents, and may result in other siblings being neglected. Travelling to and from hospital is time-consuming, expensive and tiring. If the young patient is returned home for continuation of treatment, this has a very positive effect on his progress, and also relieves the parents of much of the stress experienced while their child is an in-patient.

Several important criteria must be met before home parenteral nutrition (HPN) is considered in a paediatric patient:

1. The infant should be well established on the parenteral nutrition regimen.
2. Parents must be intellectually and emotionally able to cope with the day-to-day management of the intravenous nutrition. This will require a period of training with respect to the function of the pump and the administration apparatus, together with the sterile technique required for catheter care. The parents should be taught how to deal with problems such as catheter fracture or blockage. Signs of sepsis should be explained and the parents advised to bring the child back to hospital if fever occurs.
3. Ready access to experienced medical and nursing staff in the hospital is essential.

Figure 4.8 A child undergoing home parenteral nutrition.

4. Parental support by Health Visitor, District Nurse, General Practitioner and Social Worker is essential and these other professionals must be kept informed about the ongoing and future management plans.
5. Home tuition may be necessary for the child on long term HPN.
6. We would recommend the appointment of a specialized liaison nurse who can visit regularly and advise these families, her base being the children's hospital. This nurse would normally visit the house on several occasions before the child is discharged, to ensure that the general hygiene is satisfactory. We recommend that there should be a refrigerator to store the nutrients and a telephone to ensure easy communication with the hospital.
7. Regular monitoring of the child's progress together with his nutritional and biochemical status is necessary – altering the regimen as necessary.

The hospital pharmacy supplies the intravenous solutions for these infants, the electrolyte contents being changed as advised by the physician or surgeon in charge. The nutrients are collected twice weekly from the pharmacy and stored in the domestic refrigerator. Flexibility as regards the timing of the infusion can allow most or all of the nutrition to be

delivered during sleeping hours, thus leaving the patient free for normal activities by day.

Patients on HPN show marked improvement in their nutritional status, many of them catching up to the 50th centile for weight and height after prolonged parenteral feeding. Infants who have episodes of sepsis requiring catheter changes, or who experience other complications, do show a delay in somatic growth. Once these problems are resolved and growth starts, rapid improvement is noted. So far there is little reported work on long term HPN in children, although deterioration in motor and language skills has been noted in some infants on prolonged HPN. Our experience is that the development in our patients proceeds normally, unless there has been prior neurological damage related to the initial disease process. Together with others we have seen marked improvement in the psychomotor development of our children once they are allowed home.

The common catheter-related complications do occur in patients on HPN, although apparently less frequently than in patients treated in hospital. If catheter sepsis is diagnosed removal of the catheter is often necessary. Blockage of the catheter can sometimes be cleared using urokinase, thus prolonging the useful life of the catheter. Fracture of the external portion of the catheter can be dealt with using commercially available repair kits.

Our experience with HPN in paediatric patients is that the initial effort necessary to set it up at home and to train the parents is more than offset by the marked improvement in well-being that the patient experiences on returning home. There is also an important boost to the parents' morale when they realize that they can contribute to their child's care in their own home.

SUGGESTED READING

Ament, M.E. (1981) in *Paediatric HPN. Home Parenteral Nutrition* (ed. E. Steiger), Pro Clinic, New York, p. 10.

Andrew, G., Chan, G. and Shiff, D. (1976) *J. Pediatr.*, **88**, 273.

Beckett, G.J., Glass, E.J., Callaghan, M.O., Elton, R.A. and Hume, R. (1985) *Clin. Chem.*, **31**, 1168.

Bergmann, K.E., Ziegler, E.E. and Fomon, S.J. (1974) in *Water and Renal Solute Load. Infant Nutrition* (ed. S.J. Fomon), W.B.

Saunders, Philadelphia, p. 246.
Cockburn, F. (1984) in *Parenteral Nutrition in Infants and Children. Textbook of Paediatrics* (eds J.O. Forfar and G.C. Arneil), Churchill Livingstone, Edinburgh.
Fomon, S.J. (1974) *Infant Nutrition*, 2nd edn, W.B. Saunders, Philadelphia.
Ganderer, M.W.L., Stellato, T.A. and Izant, R.J. (1982) *J. Paediatr. Surg.*, **17**, 580–4.
Goldberger, J.H., De Luca, F.G., Wesselhoeft, C.W. and Randall, H.T. (1979) *J. Pediatr.*, **94**, 325.
Kao, L.C., Cheng, M.H. and Warburton, D. (1984) *J. Pediatr.*, **104**, 429.
Lucas, A., Bloom, S.R. and Aynsley-Green, A. (1978) *Arch. Dis. Child.*, **53**, 731.
Morrice, J.J., Taylor, K.M., Blair, J.I. and Young, D.G. (1974) *Arch. Dis. Child.*, **49**, 898.
Ralston, C.W., O'Connor, M.J., Ameut, M., Berquist, W. and Parmelee, A.H. (1984) *J. Pediatr.* **105**, 842–6.
Witzelben, C.L., Pitlick, P., Bergmeyer, J. and Benoit, R. (1968) *Am. J. Pathol.* **53**, 409.
Wretlind, A. (1974) (a) Assessment of patient requirements. (b) Fat emulsions in *Parenteral Nutrition in Acute Metabolic Illness* (ed. H.A. Lee), Academic Press, London.
Wretlind, A. (1972) Complete intravenous nutrition: theoretical and experimental background. Suppl. 1. *Nutr. Metab.*, **14**, 57.

5 *Organization of parenteral nutrition in hospital and at home*

H.A. Lee

5.1 HOSPITAL ORGANIZATION

The first priority here is to educate clinicians (particularly, doctors in training) to recognize the situation when a patient might benefit from parenteral nutrition. The one absolute indication for TPN is gastrointestinal failure, though there may be other occasions when TPN is an important adjunct to therapy when the gut may be functional, e.g. in acute renal failure. Wherever possible it is agreed that enteral nutrition should be embarked upon as the main nutritional support system providing the gut is functional and the patient is co-operative.

At times there might be doubts as to which nutritional approach is most appropriate and most District General Hospitals now have a Nutritional Support Team that can give advice to clinicians about their patients and the best way of supporting their nutritional needs. It must be emphasized that the function of a Nutritional Support Team is not to take over the management of patients away from 'owning' clinicians but rather to offer advice, expertise and education to ensure the patients get the best possible nutritional support. This system also helps to standardize nutritional support methods throughout the hospital which, in turn, usually means a limited number of feeding regimens, which allows efficient bulk purchase of parenteral fluids, often with considerable cost benefit. It is important to note that Nutritional Support Teams are (and should be) multidisciplinary, consisting of physicians, surgeons, anaesthetists, pharmacists, biochemists and specialist

Table 5.1 Request for nutritional support

Patient's name ..... D.O.B: ..... Hosp. No: .....
Ward ..... Consultant: .....

Clinical Details:

Prescription:

Protein G/24 Hour Energy K/cal/24 Hour

Electrolyte: Na mmol/24 Hour K mmol/24 Hour

Enteral

Nasogastric – Preferably one of the standard regimens

Oral/sip feeds – Will be supplied by the Dietitian from a range of products

Parenteral

Preferably one of the standard regimens

Pharmacy must receive the day's prescription by 10.00 a.m. (based on the previous day's electrolyte results). If new requests for I.V. feeding arise over the weekend it is recommended that sequential feeding using bottles be undertaken.

Is feed to be administered via a central or peripheral line? Central/Peripheral

Is a central venous line in place? Yes/No

Standard Regimen I.V. or Enteral	Composition if different from standard	Start Time and duration	Signature	Date

In case of doubt or technical difficulty please contact the Nutrition Support Team through the Dietitian or the Clinical Nutrition Nurse (Mrs J. Collett) or Pharmacy.

For clinical advice please contact either Dr G. Venkat Raman or Professor H.A. Lee.

Please do **NOT** contact the Renal Unit.

Table 5.2 Parenteral feeding regimens

	Volume (ml)	Nitrogen (g)	Energy (kcal)	*Non-protein* Na	K	Ca (mmol)	Mg	P	Cl	Zn (μmol)
Central										
1. Vamin 9 Glucose	1000									
Glucose 10%	1000	9.4	1800	65	55	7.5	3.0	27.5	88	20
Intralipid 20%	500									
2. Vamin 9 Glucose	1500									
Glucose 10%	1000	14.1	2000	97.5	72.5	8.8	3.8	37.5	115	20
Intralipid 20%	500									
3. Vamin 14	1000									
Glucose 10%	500	13.5	2200	122.5	72.5	10	9.5	37.5	113	20
Glucose 50%	500									
Intralipid 20%	500									
4. Vamin 18 E.F.	1000									
Glucose 10%	500	18.0	2200	22.5	22.5	5	1.5	37.5	13	20
Glucose 50%	500									
Intralipid 20%	500									

Table 5.2 *contd.*

	Volume (ml)	Nitrogen (g)	Energy (kcal)	*Non-protein* Na	K	Ca (mmol)	Mg	P	Cl	Zn (μmol)
Peripheral										
P1 Vamin 9	1000									
Glucose 10%	1000	9.4	1500	65	55	7.5	3.0	35	88	20
Intralipid 10%	1000									
P2 Perifusin	2000									
Glucose 20%	500									
Intralipid 20%	500	10	1400	80	60	0	10	7.5	18	0

1. Peripheral access using an Abbott drum catheter or peripheral catheter can be used for **Peripheral** feeds P1 and P2 although for the **Central** feeds a central venous line is essential.
2. Ig.N=6.25g protein; requirement may be established by the following formula: 24 hour urinary urea (mmols) × 0.035 = g N.
3. Best mixed in a 3 litre bag in the pharmacy.
4. Infuse preferably by volumetric pump over 12–24 hours.
5. It is recommended that with peripheral line feeding a 5 mg Transiderm-Nitro Patch be placed close to the venflon site, the patch being changed every 24 hours.

nurses. This means that such a well balanced team can give appropriate advice on different aspects of parenteral nutrition.

In our District we have drawn up guidelines for clinicians to obtain information from and act upon as shown in Table 5.1. The Nutritional Support Team has amongst its membership two experts in the placement of central venous feeding lines which at times may be a deterrent for TPN for a Consultant clinician who may not have such expertise available amongst his own team. Every General Hospital should have a few doctors (both at Consultant and Registrar level) who are able to ensure that a safe central venous line insertion technique is always available and to allow for the education of new staff being recruited.

Table 5.2 outlines some of the parenteral feeding regimens available in our District. By printing such guidelines it encourages clinicians to be precise about the prescription of nutrition for their patients. There can be no place for the attitude of 'a bottle of amino acids and a few bottles of glucose'. It is hoped that by careful prescription, increasing knowledge of TPN would be obtained and this can only be to the benefit of the patients receiving such treatment. Clearly, different hospitals will have different feeding regimens to those mentioned here, but the principle is that a limited number of such regimens become familiar to the staff and the Nutritional Support Team, who can always advise with experience and expertise about their efficacy in given situations. It is worth noting in Table 5.2 that two regimens are available for TPN via a peripheral line. Thus, if for any reason a central line is not available, nutritional support can be maintained to some extent by a peripheral line. The duration of a peripheral line can be extended by the routine use of a patch which effects transdermal delivery of glyceryl trinitrate, such as Transidem-Nitro^{R}.

It is the policy of our Nutritional Support Team to ensure that prescriptions for TPN are received at the latest by 10 am in the Pharmacy to allow adequate preparation time and to ensure continuity of the feeding regimen. We are also insistent that a feeding line must be in place before TPN regimens are compounded and that an X-ray check of the position of a central venous feeding line is obtained before TPN is started.

All the feeding regimens referred to in Table 5.2 are stable and compatible and can be mixed in a 3 litre bag. Furthermore,

all these preparations have sufficient stability that they can be prepared on a Friday to cover weekends without fear of disintegration of the mixture. Many of these preparations are stable for up to 7 days, provided they are kept refrigerated at 4°C until used. However, when TPN is required at a time when pharmacy services are unavailable, then the Vitrimix (Kabi Vitrum) system provides a useful alternative. This permits simple ward 'compounding' by the nursing staff, whereby 250 ml of a lipid solution is transferred into a bottle containing 750 ml of an amino acid solution. Two litres of this preparation provides 14 g nitrogen and 1600 non-protein kcal. This may even be given as a peripheral infusion if central access is lacking.

The Pharmacy personnel have an important role to play to ensure that all prescriptions are compatible when making up a 3 litre bag and if there are any doubts they can either approach the clinician directly or through a member of the Nutritional Support Team. In this way inappropriate prescription of TPN can be avoided. It is equally important that TPN regimens should not be compounded, only then to be discarded, either because a line was not inserted for their infusion or there had been a change of heart! The daily cost of TPN in our District is between £60 and £70. If feeding bags are wasted a letter is sent to the appropriate clinician informing him of the financial waste.

There is no doubt that TPN can be cost effective and make the difference between life and death for many patients with gastrointestinal failure, not to mention diminishing complication rates and reducing the length of hospital stay in patients with other serious illnesses. With the advent of Nutritional Support Teams it should be possible for any clinician in any hospital to order at any time a TPN regimen on any patient requiring this therapeutic modality. The responsibility of the Team does not stop at providing a clinical service; it must also undertake an educational role and organize seminars, symposia, etc., particularly aimed at young professionals in training. Thirdly, the Team should engage in research and maintain regular contact with the academic world. The most important function of such a Team, of course, is to create awareness of the real dangers of nutritional deficiency which, all too often is lacking in health care professionals in hospitals today.

5.2 HOME TPN

Patients fall into two main groups: (a) those who will require long term HPN because there is no chance of recovery of intestinal function and (b) those who require semi-long term HPN who, after some months or even years, when the abdominal condition has settled down (or following re-establishment of bowel continuity) can return to normal feeding. Such was the case in two of our patients (Nos 2 and 6, Table 9.2). Although most patients will be receiving TPN in surgical wards, once it is considered that they will require HPN, then they should be referred to a specialist unit for training and acquiring informed knowledge of the treatment for their condition – rather analogous to those who develop end-stage renal failure and are referred to specialist centres for renal failure replacement therapy. Although the requirement for HPN is much smaller (1–2 new patients per million population per year) than for renal replacement, nevertheless I believe the numbers of patients who can benefit from HPN will grow, particularly with respect to the very young and the elderly. This trend has been seen in the recent returns from the UK National Registry of HPN patients (vide Chapter 9). Furthermore, I believe the idea of semi-long term HPN will be more widely recognized and accepted by surgeons, thus deterring them from operating on patients too early and so waiting until the abdominal disease has 'settled down'. HPN for cancer patients has not been as popular in this country as it has been seen in the United States, and may grow in future.

It must be recognized that HPN can not only keep patients alive in the long term, but also permit them to regain ideal body weight, restore them to good health and, indeed, when appropriate can make them fit enough to withstand further major reconstructive surgery. Nevertheless, for this treatment to be successful, careful training of the individual by dedicated staff and planning of their future requirements is necessary. Our policy in this Department has been to teach patients to do everything for themselves. This has meant that our patients are trained to prepare their own 3 litre bag, rather than depend on commercial companies. By so doing, we estimate we save £10 000 per patient per year and we are not aware of any inherent disadvantages with our system as compared to the commercially prepared solutions or those compounded in

the hospital pharmacy. Thus, in this chapter, I shall concentrate on HPN in the 'D-I-Y' sense, although making some reference to commercial companies that can offer a similar service.

5.3 TRAINING

The patient who needs HPN must be referred to a specialist unit, for one of the most vital aspects of training is to have nursing expertise with the techniques involved. For proper training it is essential to have a clinical nurse specialist dedicated to the various aspects of nutritional support. Before training starts it is of course imperative that a specific feeding catheter be placed by a surgeon or physician who is familiar with its insertion and use. Thus, a number of catheters are available, and are inserted via a subcutaneous tunnel. This tunnelling technique is important and the exit site of the catheter should be well away from the axilla, not beneath a breast fold and at a point that can be easily seen by the patient and easily fixed to the skin. Again, the exit site is important with respect to cosmetic appearance, particularly in the female. Training in catheter care and maintenance of the catheter is almost the exclusive role of the clinical nurse specialist.

Then, once the patient is familiar with catheter care and using heparin 'locks', attention is then paid to teaching the patient the theory behind the need for feeding via the particular route, the potential risks and a knowledge of what their requirements are likely to be. When the formal training begins, a doctor and/or nurse should visit the patient's home to ensure there is adequate space for preparation of the bags and for storage of fluids and other disposable equipment. The training period on average takes about 2 weeks and most patients adapt remarkably quickly to the idea of treating themselves, firstly in the hospital and then at home. They are made to appreciate that when they are home they are not forgotten and that the nutritional support team are always available should problems arise and they have an open door access to the specialist unit. The nurse specialist plays a crucial role as the first port of call for the patient.

Patients are told clearly that they must not hesitate to contact the unit if they have any problems, these relate particularly to catheter care. Thus if redness, pain or swelling occurs

anywhere along the catheter track, they must immediately report to the unit. The same applies if they develop a temperature, particularly associated with rigors. When flushing the catheter, patients soon come to appreciate if there is any resistance. In general, patients are advised to contact the unit early in case of problems, rather than procrastinate.

Training initially covers daytime hours but then, before going home, the practice of overnight feeding is started so that there is minimal interference with their daily routine, particularly for those going out to work. The recommended duration for overnight feeding is between 8 and 10 h; more rapid infusion may result in considerable diuresis and loss of some nutrients, not to mention sleep! The preparation time for the 3 litre bag is approximately 25 min and the clearing up takes about 10 min. During the training period, it is important that patients have a clear understanding of aseptic techniques and are encouraged to become confident about their ability to cope. As with most patients who have to start home therapies, there is always anxiety at the beginning, both in the patient and the partner or next of kin and, therefore, considerable psychological support during the training period is necessary for a successful outcome. More details about the patient training are given in Chapter 6.

5.4 PLANNING

As indicated above, when the patient starts training, visits are made to the home to ensure there is enough space for aseptic preparation of the feeds and for storage of the ingredients. Of all the patients treated in our Unit so far, we have only had to consider the need for rehousing in one single patient. As stressed above, the machinery (pumps) requirements for HPN are minimal, though storage space for fluids and other disposables is sometimes a problem. Again, bearing in mind that 3 litre bags in hospital are prepared under strict aseptic techniques with laminar flow hoods, etc., it is important that some recognition is given to this aspect at home.

It is totally impracticable and unnecessary to have laminar flow hoods installed in patients' homes, but they do need a preparation area which can be kept clean and uncontaminated from other household goods (see Figs. 5.1 and 5.2). Thus, basically all that is required is some storage shelving, a

Table 5.3 Basic adaptations for HPN

1. Adequate shelving; easy cleaning
2. Room heater (wall mounted or free standing)
3. Preparation surface at least 4ft × 2 ft
4. Mobile drip stand
5. Small domestic refrigerator for storing Intralipid and Heparin
6. Plastic collection bags for disposables. Bag holder
7. Two 2-gang electric power points
8. Adequate cupboard space for storing disposables and bottles
9. Small handwash basin

refrigerator (for keeping fat emulsions and heparin) and a work surface where the ingredients for the preparation of the 3 litre bag can be placed. Such a work surface should be about 4 ft long and 2 ft wide and may be of a collapsible design so that once preparation has been completed it can be folded down. The room in which the 3 litre bag is going to be prepared should have a simple wash basin installed so that hand washing can be easily done at close proximity. Preferably the room should have some heating, e.g. a small wall mounted 2 kW electric heater. No special floor requirements are necessary. Provision for disposal of bags and lines after a feed have to be thought of and bags provided and the local health authority informed so that collection can be arranged. A list of the basic requirements for home planning are shown in Table 5.3. The average cost of such home adaptations is approximately £400. A list of the disposable items, together with their cost, is shown in Table 5.4 and shows how the total annual cost has been derived for patients in our Department. In Tables 5.5a and 5.5b an order form is shown on which the patient indicates at the end of each month what supplies he/she will need for the following month's treatment.

It should be stressed that once patients are ready to go home very few alterations are made thereafter to their home maintenance nutritional regimen. Indeed, patients are told not to make any changes to their regimen without prior consultation with the physician in charge. As for the delivery of goods, either an arrangement is made with the hospital delivery service or patients agree to come in once a month to collect their requirements. Most patients are more than happy to do this. Once the room is ready the patient then goes home and

Table 5.4 Home parenteral nutrition

MSE Cost *CSSD Cost* *MSE Items*	*Cost per Day* £	*Cost per Year* £
Accusets	3.39	1237.35
Non/surgeon gloves × 4	1.48	540.02
Syringes × 14	1.48	365.00
Needles × 14	0.25	91.25
Administration sets	0.95	346.75
Primapore dressings	0.01	3.65
Vygon caps	0.14	51.10
Face masks × 2	0.14	51.10
3 litre bags TPN bags	6.50	2372.50
Plus:		
Hypofix × 1 roll every 6/12	2.17	4.34
Catheters × 1 every 6/12–12 mths	32.00	64.00
Clamps – 1 per week		60.32
Yellow sacks (×7) per week	0.27	14.45
Blue towels (×2) per week	1.38	71.76
		£5273.59
CSSD items		
Gallipots	0.05	18.25
Paper towels	0.12	43.80
Gauze	0.16	58.40
Cotton balls	0.07	25.55
'Q' tips	0.07	25.55
		£171.55
Grand total		
MSE		£5273.59
CSSD		171.55
Total revenue cost per patient		£5445.14
Non-revenue costs		
Cost of house conversion for fridge, electrical points, heating		
Approximate cost		400.00
Cost of imed pump		1495.00
Annual cost per patient		£7340.14
Drugs, TPN fluids and additives		12 000.00
Total annual cost (1st year)		£19 340.14
Total annual cost subsequent years		£17 446

for the first one or two TPN bag preparations the nurse specialist is in attendance to provide moral support. Most patients elect to prepare their 3 litre bag in the room that has been adapted and then move the pump to their bedroom, sleep in their normal bed (with the spouse) and feed overnight. The IMED 922E pump has all the alarms required to safeguard the patient from any error. Indeed, over the past 15 years in the management of patients in our Unit, not one single error has occurred with overnight TPN.

The alternative approach to what has been mentioned above is to select patients in the same way, and teach them about all aspects of catheter care and maintenance and then to use one of the commercial compounding services offered by companies (such as Baxter or Geistlich), who will prepare the 3 litre bags according to the patient's requirements (based on clinician prescription) and arrange for their delivery on a fortnightly basis. There is no doubt that this method works extremely well and units who use the compounding services have been well satisfied with services rendered. However, this does cost on average £10 000 per patient per annum more and this is a significant additional cost. At the time of writing there is no agreed supra-regional funding for HPN in this country; this is simply taken on board by District General Hospitals from their existing funds. Therefore, such cost savings as can be effected by our method are important, particularly if more patients are to be treated.

The arguments against the 'D-I-Y' approach have been: (a) safety to the patient; (b) sterility of bags prepared; and (c) imposition on patient time. We have shown conclusively that our technique is not dangerous for the patient, we have had no instances of infection arising from badly prepared bags and it is our view that the amount of time the patient spends in bag preparation is acceptable.

5.5 ORGANIZATION OF HPN

There can be no doubt that a few specialist centres must be established in the UK to cope with patients requiring HPN. Indeed, there are currently 14 such centres, although 75% of some 200 patients so far treated have been based on seven centres only. The value of such centres is to have expertise concentrated in a limited number of units whereby a small

Table 5.5a Home parenteral nutrition patient – stores order form

Name and Address	We are unable to guarantee delivery of orders received less than seven days before delivery date	
Item	*Approx. quantity per month*	*Enter amount required*
KabiVitrum 3 litre bags	40 bags	
Accusets	40	
Sterets	2 boxes	
Alcowipes	2 boxes	
Op-site 6 cm × 8.5 cm	as required	
Basic dressing pack	15	
Surgical gloves: Size	100 pairs	
Sterile container (MSU pot)	4	
Plastic bags for waste disposal (large yellow)	32	
Kleenex hand towels	8 packs	
Small sterile foil receivers	40	
Gauze squares 7.5 × 7.5 cm	70	
Sterile paper towels	100	
Plastic syringes 2 ml	35	
Plastic syringes 5 ml	35	
Plastic syringes 10 ml	120	
Green needles No. 1	1 or 2 boxes	
Disposable masks	1 or 2 boxes	
Micropore tape 1″ wide	as required	
Large brown paper bags	as required	
60 ml plastic syringe	as required	
Plastic syringes 20 ml	as required	
I.V. Solution administration sets	as required	

number of patients can be optimally treated. Furthermore, this allows for careful auditing of procedures used, for improving techniques and watching cost accountability. Over the years, HPN has become rationalized in very much the same way as renal replacement therapy which overall has made things easier for the patient. By having a limited number of centres it can be argued that sufficient data can be accumulated to be used as evidence to encourage the government to provide specific sums of money for this treatment. Clearly, it would

Table 5.5b Home parenteral nutrition order form

Name ..... Delivery date .....
Address ..... No. of days required .....
..... Hospital .....

We are unable to guarantee delivery of orders received less than seven days prior to delivery date

Item	*Requirement*	*Pharmacy*
Intravenous infusions		
Aminofusin 10%, 500ml		
Glucoplex 1000, 1 litre		
Glucoplex 1600, 1 litre		
Intralipid 10%, 500ml		
Intralipid 20%, 500ml		
Sodium chloride 0.9%, 500ml, with potassium		
Sodium chloride 0.9%, 500ml		
Sodium chloride 0.9%, 100ml		
Vamin glucose, 500ml		
Vamin glucose, 1 litre		
Vamin-N, 500ml		
Additions		
Addamel, 10ml		
Folinic acid 3mg in 1ml		
Heparin 100u/ml, 1ml ampoule (box of 10)		
Potassium chloride, 20 mmol in 10ml		
Sodium chloride 0.9%, 2ml		
Solivito, 10ml		
Vitlipid, 10ml		
Zinc sulphate 40mg in 1ml		
Other items		
Povidone iodine		
Savlodil sachets 25ml		

Doctor's signature .....
Date .....

be distressing if at this time of financial stricture on the National Health Service, patients who could benefit from this therapy were turned down because other interests were competing for the same money which could treat these patients. I believe that money must be set aside so this form of treatment can be developed in a rational way. In the UK, by the setting up of the UK HPN Registry we have the wherewithal to co-ordinate developments for the future.

6 *Patient training and nursing aspects*

J. Collett

The role of the nutritional nurse specialist can be divided into four categories:

Clinical practice
Education
Administration
Research

For the majority of the patients receiving home parenteral nutrition (HPN), their intravenous catheter is their life-line. The clinical decision to commence long term HPN is not taken lightly, but once made, the nurse has an extremely important part to play. She is involved firstly in training both the patient and the relatives, secondly with catheter placement, thirdly with catheter maintenance and fourthly with patient monitoring. It is important to adopt a team approach before commencing HPN training. This does not mean that a crowd of nursing and medical staff proceed to the patient's bedside, which can be daunting, but that specific team members approach the patient knowing their own role and that of their colleagues. The patient's confidence and peace of mind are secured by a united team – conversely, unnecessary insecurity and apprehension can be created by a disjointed team.

Research into the relationship between education and post-operative pain has shown that a well prepared patient is less anxious and requires less analgesia. Using this analogy the patient and relatives who are counselled by an experienced team in preparation for HPN are more able to comprehend and accept the system's intricacies. The patient should be encouraged to ask as many questions as possible, e.g. 'Will I be able to lead a normal life and how will it affect my family?'

'Will I be able to eat and what will happen to my bowels?' 'Is this nutrition as good as eating?' 'What happens if I can't cope?'

A specially produced booklet with easy-to-understand diagrams not only helps the educator explain the complexities of catheter insertion and why the catheter should be treated with greatest respect, but allows the patient time to 'digest' the information and come up with more questions.

6.1 CATHETER INSERTION

A full explanation must be given prior to catheter insertion because the patient's co-operation will be necessary during the procedure. The patient will be asked to lie supine with head and neck extended or head tipped downwards and to stay in this position for up to half an hour. His face may be partially covered by sterile towels. During the insertion he may be asked to hold his breath or perform a Valsalva manoeuvre. It is important, therefore, that he is totally aware of what is going to be asked of him – and practised in the case of the Valsalva manoeuvre. (This will require him to breathe out through a closed mouth and closed nose, thus increasing intrathoracic pressure diminishing the risk of air embolus. The manoeuvre has been likened to 'bearing down'.)

The day before insertion a povidone iodine patch test is applied to the forearm and the proposed cannulation area (the front of the neck, shoulder and upper chest between the sternum and the axilla) is shaved. If the patch test is negative a povidone iodine soak is applied to the area 3 h prior to insertion. It is therefore very important that the whole team knows which vein is to be used, i.e. internal/external jugular, subclavian, left or right.

The insertion is usually performed in theatre, but can be performed in a treatment room under theatre conditions. This fact must be explained to the patient to eliminate alarm at the sight of theatre greens. Once again the nurse and doctor work as a team, it helps if the nurse can anticipate the doctor's requirements so that the procedure time is not extended unnecessarily. A second nurse should stay close to the patient to provide psychological support.

6.1.1 Trolley for central line insertion

(a) Insertion equipment

Trolley preparation – two trolleys are required:

Trolley I (prepared as per theatre technique).
Luxan sheet/green towels – for catheter insertion.

Trolley II Suture set pack for flushing, suturing and dressing.

Trolley I

1 single sterile paper towel
1 luxan sheet cover
1 gown
2 green towels } central line pack
1 paper towel
1 small receiver
Gauze squares
Cotton wool balls
Povidone iodine – alcohol not aqueous
1 scalpel
10 ml 2% lignocaine
× 1 10 ml syringe
× 1 G19 needle
× 1 G25 needle
Extra cotton wool balls – if required
Extra gauze squares – if required
Central line
2 ml syringe
1 catheter clamp
Gloves, surgical
1 face mask

Trolley II

Suture set pack
Silk suture (curved needle)
Gloves surgical – for dressing procedure
500 ml N/saline + 20 000 units heparin – mixed
Syringe 50 ml for withdrawing heparin/saline mix from ½ litre bag
1 × G19 needle
20 ml syringe
Small receiver (for heparin/saline mix)

Primapore dressing or Op-site
1 catheter Luer cap
Hypafix
Cotton wool balls

Following insertion, a bag of fluid (dextrose 5% or normal saline) is attached and the bag is then brought down below the level of the right atrium – a blood flash back is observed, this test will confirm venous catheter position and an X-ray should confirm the catheter's distal end in the superior vena cava.

6.2 PATIENT TRAINING

Theoretical patient training has already begun – practical training starts from the time the nurse applies the first dressing following catheter insertion. From that moment there must be continuity in team approach and much reiteration. The golden rule to follow is, 'Do as I do and say'.

The training is divided into four stages:

1. line dressing;
2. catheter flush and feeding line connection;
3. catheter flush and heparin lock;
4. 3 litre bag preparation/pump priming.

6.2.1 Catheter dressing

The key to a successful dressing technique involves:

1. adequate hand washing;
2. use of sterile gloves;
3. adequate site cleaning time (30s);
4. adequate site drying time (30s);
5. a supportive, easy to apply, easy to remove dressing.

6.2.2 Redressing central venous catheter entry site

Unless the dressing becomes wet, loose or soiled it should be renewed three times weekly, or twice weekly if the tunnelled line is well established. The first dressing should be renewed within the first 24 h of catheter insertion.

An occlusive island type dressing, e.g. Primapore wound pad, is recommended because it is easy to apply and remove.

It is particularly useful when applied to the tunnelled line. Alternatively, an Op-site membrane dressing may be applied – the renewal protocol remains unchanged, i.e. within the first 24 h and then three times weekly.

(a) Equipment

1. Dressing pack
2. Sterile cotton wool buds (CSSD Pack)
3. Gloves, surgical
4. Primapore dressing or Op-site
5. Povidone iodine alcohol solution
6. Chlorhexidine spirit
7. Extra cotton wool balls – if required
8. Gallipot
9. Hypafix

(b) Action	*Remarks/rationale*
1. Wash hands	
2. Clean trolley using sterile technique	
3. Equip trolley	
4. Open packs, pour out lotions	
5. Remove old dressing, observe catheter site for signs of infection. Take a swab if there is any sign of infection	Any redness, swelling or discharge should be noted – and medical staff should be alerted
6. Wash and dry hands to elbows	Infections such as septicaemia, endocarditis can be caused by a poor hand washing technique
7. Apply sterile gloves	
8. Use a gauze to support catheter 3 cm from entry site	To prevent catheter displacement during cleaning
9. Using chlorhexidine gently clean entry site with cotton buds or cotton wool ball. *Do not drag on catheter,*	There is often a light sterile serous discharge, which may be blood stained for a couple of days after the

removing any matter that has collected around catheter. Discard cotton wool ball/bud. Allow to dry for 1 min	catheter insertion. Any debris is a potential source of infection and must be removed
10. Place Povidone iodine soaked cotton wool ball over entry site	Entry site is protected whilst remaining area is cleaned
11. With Povidone iodine or Chlorhexidine carefully clean all skin area and catheter to be covered by dressing	The slightly 'tacky' Povidone surface aids dressing fixation but it must be dry before dressing application
12. Remove cotton wool ball from entry site wait approximately 30 s for Povidone spirit to completely dry	Drying time is as important as cleaning time because it allows the bacteria to agglutinate and die
13. Apply dressing as illustrated	Read dressing guidelines before application
14. Use Hypafix to support catheter	

6.2.3 Central line dressing

(a) Primapore

Dressings used are:

Primapore – adhesive wound dressing

Sizes: 8.3 × 6 cm
12 × 8.25 cm

This sterile dressing comprises a Hypafix square with a central Melolin dressing. It adheres well and is removed painlessly; therefore it is ideal for both entry site protection and catheter support.

(b) Primapore/Hypafix

Dressings used are:

Hypafix – retention sheet

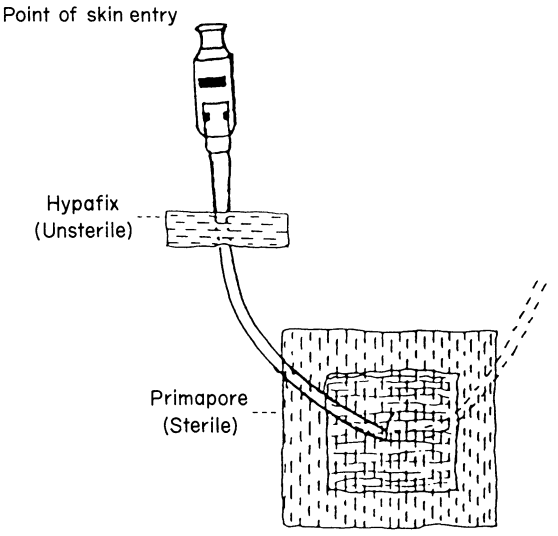

Figure 6.1 Feeding catheter in place with dressing.

Sizes: 5 cm × 10 m
10 cm × 10 m

This dressing is UNSTERILE and should not be used near the catheter point of skin entry. However, its elastic supportive quality is ideal for catheter hub support to prevent catheter drag and displacement (Fig. 6.1).

The patient has now had his central line inserted, he has seen the catheter disconnected, flushed and reconnected and has actually redressed the entry site. The time has now come for training stages 2 and 3.

- Catheter flush and feeding line connection.
- Catheter flush and heparin lock.

He knows what to expect because he has already witnessed both procedures, but is still not ready psychologically to actually handle stages 2 and 3 on his own central line. For this reason a teaching apron has been developed, which consists of a simple plastic apron with several central lines protruding from the bib.

Both procedures are repeated on the bib as many times as desired until the patient feels confident enough to tackle his own central line.

The key to a successful disconnection technique is four-fold:

1. Adequate hand washing
2. Use of sterile gloves
3. Adequate hub cleaning time (30 s)
4. Adequate hub drying time (30 s)

Although it is best to have the patient in complete control of line care it is most important that a spouse or relative (or whoever the patient wishes), is able to share the training. Sometimes the relative will take full responsibility (in case of physical disability), in which case there must also be a third person trained, just in case unforeseen commitments arise when at home.

6.2.4 Connecting primed pump to patient

(a) Equipment

1. Basic pack
2. Ampoule N/saline 10 ml
3. Syringe 10 ml
4. Needle G19
5. Chlorhexidine or Alcowipe
6. Gloves, surgical
7. Hypafix
8. Alcowipe

(b) Action	*Remarks/rationale*
1. Plug pump into mains, clamp catheter.	Many units use an extension set to avoid damage to the catheter by repeated clamping.
2. Wash hands, prepare work surface using aseptic technique. Open packs, pour out chlorhexidine, or open Alcowipe, place in lotion receiver. Apply gloves. Clean neck of ampoule with second Alcowipe and snap open.	To minimize the risk of introducing infection into the catheter.

3. Load syringe with N/saline 10 ml	
4. Hold catheter with gauze. Clean hub with chlorhexidine or Alcowipe for 30 s, allow to dry for 30 s. Place sterile towel under catheter. Check clamp is still secure on catheter	Drying time is as important as cleaning time because it causes the bacteria to agglutinate and die
5. Use second gauze square to disconnect feeding line/or Luer lock. Slowly flush catheter with N/saline. Connect feeding line – turn on pump	Line has to be unclamped and reclamped during this process. By flushing the line prior to feed-connection, catheter patency is checked – any resistance should be reported
6. Support catheter with hypafix	To prevent dragging and displacement.

6.2.5 Central line heparin flush

(a) Equipment

1. Basic pack
2. Gloves, surgical
3. Chlorhexidine or Alcowipe
4. Syringe 2 ml
5. Syringe 50 ml
6. N/saline 50 ml ampoule
7. Heparin 2000 units (2 ×1000 units = 2 ml)
8. Needles G19
9. Luer lock cap
10. Alcowipe

If intermittent feeding is used, i.e. to run over anything less than 24 h, heparin flush must be added to ensure catheter patency.

(b) Action (note *Remarks/rationale* earlier)

1. Clamp catheter.
2. Wash hands. Prepare work surface using aseptic technique.

Open packs, pour out chlorhexidine, or Alcowipe, place in lotion receiver. Wear gloves, clean neck of ampoules with second Alcowipe, snap open.

3. Load 2 syringes, one with N/saline 50 ml and one with heparin 2000 units in 2 ml.
4. Hold catheter with gauze, completely clean hub with chlorhexidine or Alcowipe for 30 s. Allow to dry for 30 s. Place sterile towel under catheter. Check clamp is still secure on catheter.
5. Using second gauze square to disconnect giving set line, slowly flush the line first with N/saline and then with heparin. Cap the catheter with Luer lock cap.
6. Support catheter with hypafix.

The last procedure to be taught is how to make up the 3 litre bag. At first sight this might appear most complicated, but if each stage is tackled systematically, it is by no means too difficult. The problem long term is not that the routine is forgotten, but that patients might tend to cut procedural corners. So it is most important to stress that making the 3 litre bag today should be identical to making the 3 litre bag in 6 years time.

Another point to be considered is the area at home where the 3 litre bag will be made; it should not be used as a general meeting place, this rule particularly applies whilst the bag is being made up.

6.2.6 Making a 3 litre bag

(a) Equipment

1. cap
2. mask
3. IV bag
4. 1 litre Glucoplex (or carbohydrate source)
5. 0.5–1 litre Intralipid (fat source)
6. 1 litre Vamin (or nitrogen source)
7. additives
8. needles G19
9. syringes
10. Alcowipes

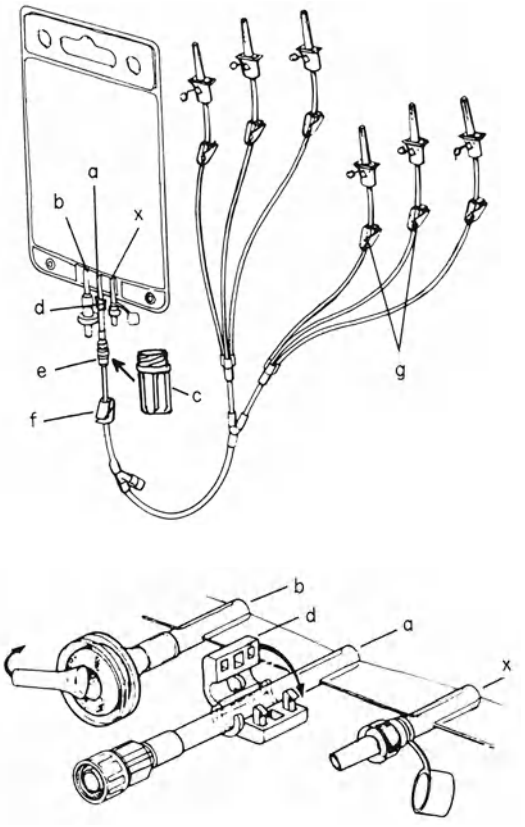

Figure 6.2 3 litre bag with connections and clamps.

11. 1 Ampsnap – optional
12. 1 giving set with pump cassette (for IMED pump)

(b) IV bag showing connections and clamps (Fig. 6.2)

a = Filling tubes
b = Giving set point
c = Luer lock cap
d = Clamp
e = Luer lock point
f = Clamp
g = Spiked tubing clamp
x = Additive point – never used

(c) Action	*Remarks/rationale*
1. Wash trolley, drip stand with soap and water	Infections such as septicaemia can be caused by poor hand washing technique
2. Put on mask – using Alcowipe clean work surface and IMED pump, set volume to 3053, set ml/h at 000	
3. Assemble equipment. Apply bottle holders	
4. Clean hands with Alcowipe, apply gloves. Open 3 litre bag. Close G clamps. Put cap packet into 3 litre container. Place to one side	
5. Open cassette – attach empty bag to top shelf of trolley. Open up giving set, turn off roller clamp. Connect giving set and cassette together, check that both cassette connections are secure, place in pump. Lay chamber end of giving set on the work surface. Place cassette tubing into attached cassette bag (this acts as a receiver for priming)	Cassette bag should be peeled back just enough to allow set to fall onto sterile surface
6. Snap off 'B' giving set point on 3 litre bag. Insert spike in centre of bung – *do not touch spike*. Check that particles of rubber have not shed. Place bag at back of work surface	Simple handling errors at the conclusion of the procedure are eliminated if the system is connected initially. The bag should be discarded if particles are present, as this could cause an embolus
7. Remove protective cap from Intralipid swab with	Drying time is as important as the cleaning time as it

Alcowipe (30 s) allow to dry	causes the bacteria to agglutinate and die
8. Swab Solivito and Vitlipid. Using Ampsnap, snap off Vitlipid top. Open 10 ml syringe and needle. Draw up Vitlipid in syringe. Add it to the Solivito and mix and withdraw into syringe. Add to Intralipid	
9. Select a line 'G', remove protective sheath. *Do not touch*. Insert spike into rubber bung of bottle	
10. Remove protective cap from Vamin swab with Alcowipe (30 s) allow to dry	
11. Swab trace element ampoules (e.g. Additrace, calcium, magnesium). Draw up solutions into separate syringes, add to Vamin	
12. Select a line, remove protective sheath. *Do not touch spike*. Insert spike into rubber bung of bottle	
13. Remove protective cap from Glucoplex swab with Alcowipe	
14. Swab the additive ampoules (e.g. Addiphos, potassium) draw up solutions into syringes add to Glucoplex	Addiphos should not be added to the same solutions as Addamel, it causes precipitation (particle formation)
15. Select a line 'G', remove protective sheath. *Do not touch*. Insert into rubber bung of bottle	
16. Hand bottles and bags on drip stand leave 3 litre bag on trolley	
17. Open clamps from Vamin,	

Glucoplex and allow fluid to drain into 3 litre bag. As the bottles empty close G clamps so air does not enter the bag	
18. Finally open clamp from Intralipid and drain into 3 litre bag	Intralipid must not be added to the IV bag at the same time as Glucoplex/Vamin because it affects the stability of the feed causing fat globules
19. Close F clamp and snap shut D clamp	
20. Open small packet containing screw cap	
21. Unscrew filling line and discard. Place screw cap on end of clamped tube, screw securely	
22. Discard empty bags, bottles, needles, syringes and line	
23. Holding 3 litre bag securely, gently rotate until fluid is well mixed. Cover bag to protect from light. Hang on drip stand	
24 Set volume to 3053, set ml h^{-1} to 000. Open roller clamp. Prime chamber. Switch on pump – press purge button, keep pressing until air has been cleared from the line. Double check that the line is free of air bubbles *never mute the alarm*. Turn off pump. Set ml h^{-1} to 250. Continue as in 6.2.4.	Once made the feed should be commenced within 6 h as the vitamins start to degrade if exposed to light

6.3 PATIENT MONITORING AND PITFALLS

The central line *should only be used for the feeding regimen.* The 'TPN only' bed label should be clearly visible on the bed head. No further addition should be made into the catheter – a peripheral line should be used for other solutions. The catheter should not be used for the collection of blood specimens.

Action	*Remarks/rationale*
1. Temperature, pulse, blood pressure – 4 hourly in the immediate post-insertion period	Infection, haemorrhage, trauma pneumothorax are all complications of central line insertion therefore the patient is monitored. If pyrexia occurs blood culture through the catheter

If, when at home, the patient complains of chills and feeling unwell, the patient should take his temperature and contact the nutritional team immediately.

2. Blood sugar monitoring via a glucometer – initially t.d.s. for baseline then less frequently; for those on HPN at each clinic visit	Some regimens of parenteral fluids can lead to hyperglycaemia. If blood sugar is 13 mmol l^{-1} or above on two occasions a venous blood sample should be checked by the laboratory. Either insulin infusion or injections may be required

Both hyperglycaemia and hypoglycaemia can occur at home. If the patient complains of thirst, drowsiness and passing excessive amounts of urine, he should contact the nutritional team. Conversely if the patient complains of dizziness, excessive sweating or irritability, this could indicate hypoglycaemia and he should also contact the nutritional team.

If the feed is actually in progress the pump could be incorrect so should be checked. Or if the feed has finished there could be rebound hypoglycaemia in which case the feed should not be stopped suddenly.

3. Daily weight initially. For those on HPN, at each clinic visit	A steady weight gain is the best indication that the body is utilizing the infused nutrition. Excessive weight gain over a short period is likely to represent fluid retention and should be reported

Once an individualized feeding regimen is established the patient's weight should be steady. Any undue swelling or puffiness should be reported to the nutritional team immediately.

4. Accurate fluid balance	Correct fluid replacement can be assessed and fluid overload eliminated if accurate records are kept
5. Catheter dressing	Following catheter insertion the dressing should be renewed within the first 24 h as there is always an exudate at the catheter insertion point. The dressing should then be changed three times weekly (Mon., Wed., Fri.) or twice weekly if the tunnelled line is well established, unless there is evidence of the dressing becoming wet, loose or soiled

If there is any pain, discharge or swelling around the catheter site, the patients should take their temperature and contact the nutritional team.

6.3.1 Catheter fracture/cracking

This is very serious, as it could lead to an air embolism or septicaemia. The line should be clamped proximal to the break and the nutritional team contacted immediately. Catheter hub cracking is often caused by an over-enthusiastic twist of the

Luer lock. Care should be taken when showing the connection procedure, to emphasize the importance of a gentle but firm technique.

6.3.2 Catheter disconnection

If air enters the line it can cause an air embolus. The patient will become suddenly breathless and feel faint. The line should be clamped at once, the patient should lie down and elevate their legs. The nutritional team should be contacted immediately.

6.3.3 Catheter blockage

If during the normal saline flush, prior to feeding commencement, more force than usual is required on two consecutive occasions, the catheter is probably starting to get blocked. The nutritional team should be kept informed of the likely outcome. If blockage occurs during feeding follow instructions as for pump occlusion alarm.

6.3.4 Pump problems

(a) Power cuts

In some pumps batteries will take over in the case of mains failure and the pump will continue to function normally for 4–6 h. If the power cut is prolonged, i.e. during the night whilst feeding is in progress the pump audio low battery alarm will sound. Disconnect feed and contact the nutritional team immediately for a replacement pump.

(b) Pump occlusion alarm

First check that the giving set clamps are not closed, if they are, open clamps and turn off the pump, re-set and then re-start. If the occlusion is in the catheter DO NOT disconnect feed but use the 'heparin lock' procedure and inject through the additive port on the giving line nearest to the catheter. The port must be cleaned for 30 s and allowed to dry for 30 s prior to injection. To prevent the flush running up the line the giving set clamp must be applied above the additive port. If

the catheter remains blocked, cap catheter and contact the nutritional team.

6.3.5 Embolus detector (air in the line)

The air must be removed either by catheter disconnection and purging, in which case a strict aseptic technique must be used, or by withdrawing the air through the additive port. The port must be cleaned for 30 s and allowed to dry for 30 s prior to needle insertion. N.B. The pump must never be purged with the line connected to the catheter. The giving line and cassette junctions should be checked to eliminate loose Luer lock fittings.

6.3.6 Home facilities/storage

At the start of the training the nutritional nurse visits the home to assess the facilities, i.e. are the WC and hand basin in close proximity. Arrangements can be made through the hospital to install a separate sink unit perhaps in the bedroom or in the area chosen for feed preparation. An electrical point may be required for the pump. Is there a suitable cool cupboard (pantry) to store the TPN solutions, i.e. Vamin, Intralipid, Glucoplex? Is there a cool room cupboard to keep the Addamel in and will the refrigerator, to store the Vitlipid and Solivito, fit in the work area?

6.3.7 Other equipment supplied

Wall units
Work surfaces
Pump
Drip stand
Refrigerator

6.3.8 Ordering supplies

An order form is completed every 4 weeks and sent to the hospital by the patient. The patient must be informed of any prescription alteration so that the correct regimen can be supplied.

6.3.9 Supplies problems

Running out of supplies should not occur, but if it does contact the nutritional team at once.

6.4 THE FIRST DAYS AT HOME

On the patient's first day at home, the nutritional nurse will visit and stay to watch the first feed made and the first feed connected. The patient will feel very vulnerable in the early days and will need much support. The active message for the patient is 'when in doubt do not struggle'.

6.4.1 Special home considerations

(a) Work

Because the feed is given overnight there is no reason why a full working day cannot be achieved.

(b) Mouth care

Even though very little oral diet if any is taken, regular visits to the dentist must be maintained. Mouth washes and teeth cleaning must be continued as usual – at least twice a day.

(c) Showering – bathing – swimming

When showering, a Primapore dressing is quite adequate. For bathing or swimming, a membrane dressing, i.e. Op-site/ Bioclusive must be applied over the catheter insertion site prior to immersion and changed immediately following.

(d) Sports

Contact sports such as rugby, wrestling or football are not recommended, but sports such as cricket, golf and fishing can be easily pursued.

(e) Pets

Animals should be kept out of the 3 litre bag preparation area

– special precaution should be taken when holding cats to prevent the flexed claws puncturing the central line.

(f) Holidays

Whenever leaving the home area, the nutritional team should be informed and the hospital nearest to the holiday residence located. Unless there has been a previous arrangement made with the hotel, the most convenient form of holiday is self catering because adequate storage facilities are usually supplied, i.e. fridges.

(g) Sex

Normal sexual relations can be resumed although participation is not recommended whilst the feeding is in progress!

(h) Diet

There are no hard and fast rules regarding oral food intake and it is up to the individual to restrict the quality and quantity to sensible limits, without developing diarrhoea.

6.5 PSYCHOLOGICAL PROBLEMS

Anybody deprived of the nurturing comfort of eating can develop psychological problems. It is unlikely that the question of depression would have been discussed during the preliminaries of training and if it had, the patient would have been too preoccupied learning the practical techniques to be unduly affected by food deprivation.

As the training programme is brought to a successful conclusion, patients are suddenly faced with the prospect of intravenous feeding for the rest of their lives and are confronted with a potential social obstacle. Everything seems to centre around food, Christmas parties, wedding banquets and we even eat at funerals. Meal times are historically the one occasion when the whole family are still able to sit down together.

It is worth noting that the psychological deprivation syndrome is not only restricted to patients who are receiving intravenous feeding. Patients who are naso-gastrically fed or who have a gastrostomy can also be affected.

6.6 CONCLUSION

The role of the nutritional nurse has been shown to improve patient care physically and psychologically. This unique position offers a specialist service bridging the gap between the hospital and the community.

7 *Practical aspects of patient monitoring during intravenous feeding*

H.A. Lee

Although intravenous nutrition has become simplified particularly with the advent of 3 litre bags and TPN is much more widely used, nevertheless there is a need to carefully monitor such patients. The degree of monitoring will of course, depend upon the seriousness of the underlying condition for which a patient is being treated, often at its most extreme in Intensive Care Units. Clearly, for patients on home TPN the degree and frequency of monitoring is much reduced and a similarity can be drawn here between the degree of observation required for patients being managed for acute renal failure and those maintained by regular haemodialysis in their own homes.

Again, it is important to remember that in a patient on TPN, complications can occur which are likely to be due to underlying end organ failure rather than specifically due to the TPN ingredients used. It also makes sense to monitor such patients carefully for clinical and laboratory signs of the underlying disease or indeed of any new problem that might arise. In the old days there was a tendency to give a drop of water with a pinch of salt as a sole intravenous regimen and, equally now, one must be careful not to give too much nitrogen with excessive calories in the false belief this is all that is required for complete TPN. It must be noted that TPN regimens are designed to fulfil 24 h requirements and, therefore, it is essential the infusion rate should be on time, not too fast or delayed. This of course, is particularly crucial in paediatric practice.

Thus during TPN, overall consideration must be given to anthropometric measurements, electrolyte and water balance,

nitrogen and energy metabolism. There must be regular assessments of renal and hepatic function, as many critically ill patients are likely to have compromised renal and/or hepatic function. This may be further compounded by the concomitant use of toxic antibiotics. Thus, a patient may become jaundiced whilst receiving TPN and it may be thought to be due to the feeding regimen when, in fact, a glance at the drug chart may reveal he is also receiving erythromycin or rifampicin.

One of the most troublesome complications of TPN is infection which usually relates to bad technique, particularly at the angio access site. Therefore, it is all too simple to blame TPN for infection arising in such patients when, in fact, they may have underlying intra-abdominal sepsis, chest infection or other sources of infection (which may themselves lead to colonization of the feeding catheter). Therefore, it is important to ensure there are no other reasons for a patient developing complications.

7.1 PHYSIOLOGICAL MONITORING

As discussed earlier it is important to assess a patient's nutritional status so that baseline information is available and against which progress can subsequently be measured. Thus, careful documentation of vital signs – pulse, respiration, blood pressure, temperature and peripheral perfusion – are all important. Many patients will be oedematous at the outset of their treatment and this may be due to a simple inanition, leading to hypoalbuminaemia or, there may be excessive blood losses, proteinuria or decreased albumin synthesis by the liver, at a time of increased catabolic rate. The temptation to use too many diuretics must be resisted (unless of course, there is true congestive cardiac failure) and at the outset it may be important to restore serum oncotic pressure by an albumin infusion – though, one must be aware that little of such infused protein will remain long in the intravascular circulatory space. Furthermore, one must not expect rapid restoration of serum oncotic pressure as a result of intravenous feeding. A patient can well go into positive nitrogen balance days before, if not weeks before, the serum albumin returns to normal. Thus, it is useful to measure the mid-arm circumference (muscle protein reserve) and the tricep skin-fold thickness (fat reserve) not only initially but thereafter once weekly. A limited number of

observers should make such measurements to minimize error. Careful assessment of the patient's fluid balance in terms of intake and output (urine, diarrhoea, aspiration, wound drainage) is important if both over and under hydration are to be avoided, likewise electrolyte imbalances. Blood counts, electrolytes, renal and hepatic functions should be monitored daily in the acutely ill patient – diminishing in frequency to once in 2–3 months in the stable patient on HPN.

As mentioned in an earlier chapter, a 24-h urine collection and measurement of the urea excretion rate is a useful handle to the patient's catabolic status. It is therefore sensible (not a difficult laboratory measurement) to undertake once or twice weekly 24-h urine collections to measure this index. The importance of daily weight measurement cannot be overemphasized – rapid changes in weight are due to fluid volume shifts and not due to sudden loss of structural proteins and 'burn up' of tissue energy reserves. Critically ill patients should be measured, therefore, on weigh-beds if at all possible. Nevertheless, when assessing the 24-h urine urea excretion rate, one must be mindful in severely ill patients of the contribution from the absorption of massive haematoma, absorption of blood from the gut, and absorption from large areas of necrotic tissue. Careful clinical examination usually makes these points fairly obvious.

7.2 ELECTROLYTE MONITORING

Probably the commonest complication of any intravenous therapy regimen is that of hyponatraemia – often treated erroneously by the infusion of normal or hypertonic saline. Commonly the cause of hyponatraemia in a critically ill patient is relative over-hydration, whether or not he be oedematous. This may result from inappropriate ADH secretion as a result of cerebral or intrathoracic injury and/or infection or, as a result of drug therapy. Alternatively it may be true hyponatraemia related to excessive sodium loss from the gut (e.g. enterocutaneous fistula). The difference can be established by measurement of sodium concentration in urine and other effluents, osmolality of urine and plasma. It is also important to be aware of the entity of pseudo hyponatraemia caused by excess of lipid (due to infusion prior to sampling) or protein (e.g. paraproteinaemia). For this reason it is important

that lipid infusion is terminated at least 6 h before blood sampling. The simplest way of managing water excess is not by giving more saline but by simply restricting water intake and, of course, treating the underlying condition or removing the incriminating drugs. Hypertonic saline should only be given when there is severe hyponatraemia causing cerebral symptoms and signs, with a serum sodium of less than 115 mmol l^{-1}. Obviously true hyponatraemia should be corrected by adding sodium chloride to the feeding regimen in appropriate amounts. Occasionally hypernatraemia may result from excessive sodium loading in the intravenous feed and occasionally, because of the large sodium content of some intravenous antibiotics, for example, carbenicillin. Rarely hypernatraemia may be associated with inadequate water provision, excessive water loss (diabetes insipidus) or hyperosmolar diabetic state. When this complication occurs, it is usually a simple matter to correct it with intravenous 5% dextrose combined, if necessary, with a reduction in the sodium content of the feed.

7.3.1 Hypokalaemia and hyperkalaemia

Fortunately, hyperkalaemia is a very rare complication of TPN and it is only likely to occur in those patients who have a degree of renal insufficiency or who are receiving concomitant potassium sparing diuretics. The obvious way to treat this is by eliminating potassium from the intravenous feed, or avoiding the use of solutions which have potassium incorporated. A much more frequent problem is that of hypokalaemia which can have serious adverse effects on both skeletal and cardiac muscle, and renal function. This usually occurs because of inadequate potassium provision when planning an intravenous regimen or not making adequate allowances for gastrointestinal losses. Hypokalaemia is a difficult problem to correct with precision though the rule of thumb the author has used for many years without complication is that if the serum potassium is below 3 mmol l^{-1} then a patient has at least a 10% total body deficit of potassium and a replacement (80–120 mmol day^{-1}) can be safely made over 24 h, usually with ECG monitoring. Another common clinical error is to correct hypokalaemia too slowly for fear of complications.

7.3.2 Hypophosphataemia

A decade ago this was quite a common problem with TPN. However, with the advent of phosphorus containing energy solutions (e.g. Glucoplex, Intralipid) and the development of new phosphate supplement solutions, (e.g. Addiphos), this problem is becoming increasingly rare. A number of amino acid solutions may also contain some phosphate. Formerly, hypophosphataemia was often seen in a TPN regimen deriving energy from glucose only. The detection of hypophosphataemia is particularly important for this may impair weaning a patient off a ventilator or conversely, may induce coma, and respiratory insufficiency, thus making ventilatory assistance mandatory. It has long been understood that hypophosphataemia is associated with a reduction in the red cell 2, 3-diphosphoglycerate and adenosine disphosphate which is associated with increased red cell affinity for oxygen, shifting the oxygen dissociation curve, leading to tissue and cerebral hypoxia. Therefore, at the beginning of TPN treatment, the serum phosphate should be measured at least thrice weekly.

7.3.3 Hypoalbuminaemia

Hypoalbuminaemia is one of the most common markers of clinical malnutrition. However, it is a mistake to believe that intravenous feeding will rapidly restore serum albumin and inappropriate to try and correct this by massive infusions of expensive albumin solutions. In many critically ill patients the capillary bed is excessively 'porous' and the albumin simply drifts into the extravascular, extracellular fluid compartment providing little change either to serum oncotic pressure or to the circulating plasma volume.

7.3.4 Trace (essential biological) elements

Much has been learned about these elements in the past decade and there are now appropriate solutions available whereby the requirements of zinc, copper, manganese, chromium and selenium can be catered for. There is uncertainty about the basic requirements, particularly in neonates and young infants. Again, in the past, there has been considerable confusion about the interpretation of serum

essential biological elements, though this, too, has become clearer and laboratory facilities are available in many district general hospitals. Certainly, with respect to zinc, copper and selenium, it makes excellent metabolic sense to add these ingredients to a TPN regimen from the beginning for their own specific deficiency state can have adverse effects on nitrogen balance. Trace element status should be measured at least once a fortnight initially; in HPN patients, once in 3–6 months.

Zinc deficiency has now become well recognized in adult practice having formerly been discovered to be the source of acrodermatitis enteropathica in children. The syndrome in adults is a very florid presentation usually with eczematous lesions around the mouth, in the axillae and in the scrotal areas, development of Beau's lines on the fingernails, general apathy, depression and failure to achieve nitrogen balance even when adequate provision is made. There is now general agreement that 100 μmol day^{-1} of zinc should be provided and measuring the serum zinc, or even preferably the white cell zinc concentration once weekly during TPN is useful.

Copper deficiency is much less common these days with TPN, but where it does occur, it has a marked influence on normal haematopoiesis and on a number of metabolic reactions since copper is an important component of oxidation/reduction enzyme systems. There is general agreement that adults should receive between 5 and 10 μmol day^{-1}.

Magnesium losses are particularly associated with inflammatory diseases of the bowel, diarrhoea and excessive nasogastric aspiration or enterocutaneous fistulae losses. Magnesium is found in most TPN solutions, it is easy to give and approximately 0.5 mmol g^{-1} of nitrogen per day is required. Nevertheless, it is important to measure serum magnesium 3 times weekly where gastrointestinal losses may be high and extra supplements of magnesium are required.

In the past 5 years much has been learned about selenium requirements. It is unlikely that severe selenium deficiency will occur in under 8 weeks on TPN. However, thereafter supplements should be made. Certainly, one must be mindful of this potential complication in any patient who has been on HPN. Selenium deficiency is recognized by a fall in the serum concentration of selenium and reduction in red cell glutothione peroxidase. Administration of 800 nmol day^{-1} of selenium should correct any deficiency and rapidly correct any clinical signs.

Cardiomyopathy is the most serious complication of selenium deficiency, while skeletal myopathy is still a fairly rare phenomenon. It may occur as early as 30 days from the beginning of TPN or may take several years.

Chromium is now recognized to be an essential biological element with respect to glucose metabolism. The general consensus view for daily requirements of this element is 200–400 nmol daily. However, a word of warning here, before chromium additions are actually made. Some amino acid solutions have highly variable concentrations of chromium, varying between 42 and 1454 nmol l^{-1}. Glucoplex (a glucose solution) has been shown to have chromium concentrations varying between 81 and 238 nmol l^{-1}. In some patients from our unit, excessively high chromium concentrations have been noted in their serum, though no supplements have been made. However it was not possible to ascribe any particular symptoms to the excesses measured, and the toxic potential of chromium remains to be elucidated. Manganese deficiency has not been met with in adult practice. This is probably because sufficient amounts appear as a contaminant in the parenteral solutions.

In conclusion, essential biological element deficiency is more likely to occur in those patients who: (a) have been critically ill; (b) have become malnourished; (c) have started TPN late and without appropriate supplements being added to the regimen; and (d) are on long term HPN. Nevertheless, as previously indicated, if one is aware of the problem, laboratory facilities are now available in many district general hospitals (if not in specialist reference centres) to make the appropriate measurements and the supplements are available for addition to TPN 3 litre bags.

7.4 LIVER FUNCTION

Liver function should be assessed at the outset of TPN and at least once weekly thereafter. If a patient does become jaundiced or the liver function tests do become abnormal, it may be incorrect to assume that the TPN regimen is the sole cause. Many infections (particularly occult intra-abdominal ones) can cause cholestatic jaundice. Likewise, many drugs used in critically ill patients have the same potential. Not infrequently patients will be recalled to theatre, may sustain hypotensive

episodes during surgery and this, too, can lead to a degree of liver damage. Nevertheless, about 1% of all patients on long term TPN will develop cholestatic jaundice which may be irreversible. Indeed, 2 of our patients successfully established on HPN died from this complication. Many studies have been conducted over the years to try and incriminate the amino acid solution, the amount of glucose given, the amount of fat infused, vitamin, essential biological element deficiencies or even infusion of particulates. At the end of the day, no satisfactory conclusion has been drawn about the cause of this very distressing complication, albeit infrequent in TPN.

Where a patient is known to have liver impairment, then clearly care must be taken with the total loading of energy, particularly with carbohydrates and infusion of massive amounts of amino acids avoided. There may be a case in such patients, thus far not proven, to use solutions with a higher concentration of the branched chain amino acids. It is timely to recall that both the liver and the kidney are the major organs concerned with the metabolism of lactic acid and if either renal and/or hepatic failure occur then there is increased risk of lactic acidosis. Finally, all clinicians should be aware that at the beginning of intravenous feeding, if a particular patient has become malnourished, there may be an elevation of liver enzymes which does not imply cellular damage but simply reflects the phenomenon of induction of hepatocellular enzyme activity as a result of the infused nutrient substrates. A similar phenomenon has been described with the introduction of enteral feeding.

7.5 RENAL FUNCTION

Occasionally patients receiving TPN may become 'uraemic' with a considerable elevation of the serum urea concentration, with little or no change in the serum creatinine. Such elevation is not usually associated with any change in serum potassium, or evidence of metabolic acidosis. This urea:creatinine divergence may or may not be the result of intravenous feeding, unless of course vast amounts of intravenous nitrogen are being infused (greater than 24 g day^{-1}). It may be that the patient is being given an antibiotic such as tetracycline which interferes with the incorporation of amino acids into nucleic acid synthesis and, therefore, an increased rate of deamination.

Table 7.1 Advantages of combined glucose/fat energy regimen over glucose-only energy regimen in parenteral nutrition

Smaller osmolar load
Less chance of hyperosmolar dehydration syndrome
Less likelihood of hyperglycaemia/glycosuria
Need for additional insulin less common
Less risk of fatty liver
Less water gain compared to glucose only
Greater positive effect upon protein anabolism
Remains within individual energy substrate tolerance limits
Less risk of hypercarbia and respiratory compromise
Improves weaning time in patients on ventilators
Catabolic state not exacerbated by excess noradrenaline secretion
Less demand upon myocardium to meet increased oxygen requirements by increased cardiac output in glucose-only regimens
Overall requirements for monitoring decreased

Where excessive amounts of amino acids are infused, particularly in the elderly, then excess urea production will soon exceed the excretory capacity of the kidney and give the divergence referred to. Again, the blood urea may rise simply because of excessive absorption of blood from haematoma, gastrointestinal haemorrhage or excessive catabolism. Another important aspect is that some patients may be receiving steroids and these can increase the albumin degradation rate by 15%.

7.6 LUNG FUNCTION AND ACID–BASE CONTROL

With the current increase in the usage of 3 litre bags in TPN practice where energy is derived on a 50–50 basis from fat and carbohydrate, fewer acid–base problems are being seen. The metabolic/nutritional advantages to be obtained from such combined regimens are shown in Table 7.1. Thus, not only are the risks of hypercarbia and respiratory acidosis lessened by using combination regimens but other complicating aspects of TPN, e.g. requirements for insulin, are diminished.

Although previously metabolic acidosis has been associated with some amino acid preparations which had high cationic amino acid content (e.g. arginine, lysine) these are no longer seen. Likewise, hyperammonaemia which has been particularly described in children on TPN is no longer seen as

ammonia contamination of crystalline amino acids does not occur, as had been the case with the earlier casein hydrolysates. Likewise lactic acidosis from infused fructose is a thing of the past. Earlier disturbances of folate metabolism associated with a high methionine content of some amino acids is also no longer seen.

The question of acid–base balance is always important, particularly in patients on ventilators. Nonetheless, one has to remember that factors other than the TPN regimen will give disturbances of blood gas measurements such as the state of lung and cardiac function, type of ventilator used, ventilator setting and peripheral perfusion. Finally, it is worth reiterating that both liver and kidneys are the principal organs for gluconeogenesis and for removal of lactate from the circulation.

7.7 HAEMATOLOGICAL MONITORING

Most patients will have a full blood profile estimation once or twice a week as part of the monitoring of their underlying condition. However, with respect to TPN it is worth checking the prothrombin time once a week initially. Again, the usual reminder must be given that some drugs can have a haematopoietic suppressant effect as, indeed, can septicaemia and ill health *per se*. If a patient does develop a bleeding diathesis during intravenous feeding, this may be related to vitamin K deficiency, which is easily correctable but may also be due to other problems such as underlying liver disease or thrombocytopenia unrelated to the TPN regimen.

7.8 RADIOLOGICAL MONITORING

From a radiological standpoint the only important aspect of monitoring is to demand an initial chest X-ray immediately after catheter placement to ensure that it is in the right location. Indeed, it should be a mandatory rule in hospitals that no TPN regimen should be started unless such an X-ray has been obtained. Patients on HPN should have an annual chest X-ray as a screening procedure. In the event of any suspicion of central venous thrombosis, there should be no delay in getting bilateral upper limb venography. Skeletal X-rays may be indicated if there is any doubt of osteodystrophy (bone pains,

Table 7.2 Optimal monitoring during intravenous nutrition in hospital

1. *Clinical/physiological*
   - Vital signs – pulse, respiration, blood pressure, temperature
   - Central venous pressure (not mandatory)
   - Body weight (weigh-bed invaluable)
   - Fluid balance (careful input and total output recordings; allowances for insensible losses)
   - Check for presence of oedema
   - Weekly mid-arm muscle circumference (skeletal muscle protein) and skin-fold thickness (fat, energy reserves)
   - Photography (once in 4–8 weeks)
2. *Biochemical*
   - Serum urea, creatinine and electrolytes (daily)
   - SMA 12/60 profile* (every 2 or 3 days)
   - Serum lactate, pyruvate (in unexplained anion gap)
   - Blood glucose (once or twice a week if euglycaemic; frequent daily checks if hyperglycaemic)
   - Serum trace elements – Mg, Cu, Mn, Zn, Se (at least weekly)
   - Serum transferrin and complement C3 (weekly)
   - Serum and urine osmolality (if indicated)
   - Serum lipid profile – triglycerides, cholesterol, HDL cholesterol (weekly or fortnightly)
   - 24-h urine urea, creatinine, sodium, potassium (twice or thrice a week)
   - Acid–base balance (frequency varies according to whether patient is on a ventilator and has accompanying liver or renal failure)
   - Any specific test determined by illness (e.g. serum amylase)
   - Serum (and urine) amino acid profiles (rarely, in the presence of chronic liver or renal impairment)
3. *Haematological*
   - Full blood counts (daily or less frequently depending on circumstances)
   - Clotting screen (frequently depends on clinical indications)
   - Serum B_{12}, folate (rarely)
4. *Mechanical (daily, during infusion)*
   - Line inspection (filter changes, care with connections)
   - Flow rates
   - Catheter insertion point
   - Pump checks
   - Meniscus levels in bubble traps

Table 7.2 *contd.*

Back-flow up 'piggy-back' lines (particularly with solutions of low density, e.g. fat emulsion – avoided by use of 3 litre bags)
5. *Microbiological*
Blood cultures (once a week – or more, if indicated)
Viral agglutination titres (when indicated)
Observe for candida or other fungal infections
6. *Radiological*
Chest X-ray – must have initial one immediately after catheter insertion; subsequently one a week depending on clinical condition
Special tests such as venography to be undertaken if clinically indicated.

For patients on long term HPN, we recommend monitoring the clinical, biochemical, haematological and microbiological parameters listed above at every outpatient visit; every 2–3 months. Mechanical aspects listed must be monitored by the patient every single day. Radiological monitoring is recommended at least once a year.
*Includes albumin, total protein, calcium, inorganic phosphate, bilirubin, aspartate aminotransferase, alkaline phosphatase, urate.

pathological fracture or progressive rise in serum alkaline phosphatase). Some units recommend annual echocardiography to detect mural thrombus formation, but this has not been a problem in our unit.

7.9 GENERAL POINTS

Clearly, from the foregoing discussion it can be appreciated that many of the metabolic disturbances hitherto associated with TPN are now avoidable. Nevertheless, adequate monitoring is required and the frequency of this depends both on the underlying condition of the patient and to a lesser degree on the TPN regimen being used (see Table 7.2).

As a general rule, all vitamin supplements should be given from the beginning of any TPN regimen for the simple reason that biochemical detection of vitamin deficiencies is difficult and only available in a few specialized centres. Fortunately, with vitamin additions, as per current recommendations for

TPN, these are not likely to cause any complications. When any complications occur with a TPN regimen, a few simple thoughts must be answered: (1) Is the patient receiving too much energy, i.e. above 2500 kcal day^{-1}? (2) Is the patient being flooded with nitrogen, i.e. receiving more than 24 g of nitrogen daily in the mistaken belief that the urea nitrogen output has to be matched even at 40 g day^{-1}!? (3) Is end organ failure occurring because of the patient's underlying condition? (4) Are adequate amounts of trace elements being given? (5) Are there other agents such as antibiotics being given causing the problem?

One important complication to be on the look out for is infection setting in through the catheter. However, there is no justification for immediate removal of the catheter should a pyrexia set in. It is mandatory to carry out at least three sets of blood cultures, prior to starting empirical antibiotic treatment. At the same time it is essential to try and locate other foci of infection, such as the urinary tract. If there is no other obvious source of infection then catheter related sepsis may be assumed and treatment started with broad spectrum cover which must include an antistaphylococcal agent. If this fails to control the fever, only then should removal of the catheter be considered.

7.10 HOME PARENTERAL NUTRITION

Clearly, by the time a patient goes home he will be in a metabolically stable state and therefore the frequency of monitoring will be much less. It is the author's policy that when patients first go home they are seen at monthly intervals for the first 3 months and thereafter at 2–3 monthly intervals. The approach to monitoring patients on HPN should be multidisciplinary and follow-up should be by one or two doctors with a special interest, with a specialist nurse in attendance. One has to monitor not only the underlying disease, but also the overall nutritional status of the patient with respect to weight, anthropometry, intake and other nursing/surgical problems associated with line care. At such visits patients have routine haematology and biochemistry (inclusive of zinc, copper and magnesium and only rarely chromium, selenium and manganese).

One of the important features to monitor is the development

of cardiovascular complications in patients on HPN. Many of these patients tend to become obese and/or hyperlipidaemic. Hence an annual check of their lipid status and an electrocardiogram. Appropriate reductions in the total caloric intake/amount of fat infused must be made. Thrombosis around the feeding catheter, particularly in the right atrium, has been described and must be looked for. Rarely infective endocarditis can set in and present a diagnostic challenge.

As will be seen from the results of the UK TPN Registry half the patients on HPN die of recurrence or extension of their primary disease. This is particularly true for patients with malignancy and therefore an annual chest X-ray is recommenced.

A few long term home patients may experience bone disturbances which currently are ill understood and there is little specific treatment that can be given.

The mental and psychological status of the patient should not be forgotten, for long term HPN can be stressful, not only for the individual but also for the spouse. Nevertheless, if a patient is not getting back to work (assuming he is of working age) then one must interview the patient carefully for any other problems that are not immediately apparent on a simple clinical examination or biochemical surveys.

Finally, with HPN it is useful if the Clinical Nurse Specialist makes a visit to the home once every 3 months just to ensure that the home TPN room is being kept in a very clean state as well as conferring with the spouse about any problems that might not surface at a routine clinic visit.

8 *Complications of parenteral nutrition*

G. Venkat Raman

While accepting that parenteral nutrition is of enormous benefit in many potentially lethal situations, it is important to be aware of the complications that may be associated with the procedure. The list is long but it is worth emphasizing that they are rare and for the most part reversible. They can be categorized into two groups: vascular and metabolic. The vascular complications have been dealt with in an earlier chapter. This discussion will therefore concentrate on the metabolic and haemodynamic complications of TPN.

8.1 FLUID OVERLOAD

Infusion of large volumes of fluid as TPN obviously carries with it the danger of fluid overload and cardiac failure. This is particularly true in patients with pre-existing ischaemic or valvular heart disease and in patients with renal impairment, who are unable to excrete a water load. Under these circumstances one has to be particularly careful, particularly in the elderly. In borderline cases one might be able to manage with concurrent administration of a loop diuretic such as frusemide. If this is not adequate with florid pulmonary oedema, or the patient is oliguric, then the fluid will need to be removed either by haemodialysis or by haemofiltration.

8.2 HYPOVOLAEMIA

TPN often presents a large osmolar load to the circulation, which in the presence of normal renal function can lead to an osmotic diuresis with consequent volume and sodium depletion. This is more prone to happen if the total volume is

infused over a relatively short period and can be mitigated if the duration of infusion is prolonged adequately. If the latter measure is not successful then one has to consider reducing the osmolar load of the fluid. Fortunately, this problem tends to be self limited. Sub-clinical hypovolaemia may only be detectable by measurement of postural fall in blood pressure, which makes postural measurements an important part of clinical assessment in these patients.

8.3 SODIUM IMBALANCE

Hyponatraemia may occur as a result of an osmotic diuresis produced by TPN, particularly when the feed contains inadequate amounts of sodium. This is even more likely to occur when diuretics are administered in an attempt to tackle hypoproteinaemic oedema. Routine monitoring of electrolytes is therefore important and the problem can be simply solved by addition of extra sodium chloride to the feed. Offending drugs must be discontinued. Persistent and unexplained low serum sodium levels must alert one to the possibility of pseudohyponatraemia, caused for example, by hyperlipidaemia. Hypernatraemia has been encountered on occasion and is usually related to a hyperosmolar dehydration state secondary to the infusion of large volumes of highly concentrated dextrose, analogous to the situation that arises sometimes in elderly diabetics. The condition can be reversed by administration of isotonic or hypotonic dextrose.

8.4 POTASSIUM IMBALANCE

Hypokalaemia can occur during TPN, on the same basis as hyponatraemia; osmotic diuresis, inadequate supplementation and diuretic excess. It is corrected in the same way by addition of potassium supplements. Hyperkalaemia is rarely a problem as long as renal function is normal. In patients with acute or chronic renal failure, this becomes a major problem, frequently encountered as a number of currently available parenteral solutions have variable quantities of potassium incorporated at the stage of manufacture. In patients with renal failure, therefore, it is important to check the potassium status before starting nutrition and, if necessary, use potassium free solutions. If there is a modest degree of renal function with a urine output

of more than 1200 ml day^{-1}, then hyperkalaemia may be managed by administration of loop diuretics such as frusemide. If the serum potassium is greater than 6.5 mmol l^{-1} and/or there is evidence of oliguria, then other measures will have to be tried (glucose–insulin infusion, sodium bicarbonate, calcium, beta-2 agonists, oral ion exchange resins and dialysis).

8.5 GLUCOSE DISTURBANCES

It is not unusual to find hyperglycaemia during TPN, and sometimes this can persist even after discontinuation, resulting in a true diabetic state. The causal factors include a rate of infusion higher than the body's ability to metabolize glucose, impairment of utilization by stress (trauma, infection), liver or pancreatic disease and drugs (cephalosporins, diazoxide, steroids). Hyperglycaemia can be ignored in the short term as it is likely to correct itself, but if it does persist after a week of TPN and if the blood concentration is persistently greater than 12 mmol l^{-1} then treatment with insulin must be considered. There is still controversy regarding the question of whether or not to use insulin routinely during the acute phase of an illness when patients are commenced on TPN. Under the conditions described above it is reasonable to use low dose intravenous insulin infusion (1–6 units h^{-1}) with a target blood glucose of 6–12 mmol l^{-1}. It is worth emphasizing the dangers of hypoglycaemia.

Rebound hypoglycaemia can occur following the cessation of feed, due to an insulin over-shoot. Fortunately this is rare and can be corrected by administration of dextrose. If the problem becomes recurrent then the feeding schedule must be altered so as to taper off the feed over a few hours, rather than sudden cessation.

8.6 ACID–BASE DISTURBANCES

Metabolic acidosis is unusual with the currently used TPN solutions, but has been reported in the past, related to administration of fructose, sorbitol or ethanol used as energy substrate, leading to accumulation of lactic acid. The use of dextrose and fat emulsion as energy substrate overcomes this

problem. If it does occur for any reason, it can be corrected by administration of sodium bicarbonate.

8.7 HYPOPHOSPHATAEMIA

This may occur due to inadequate phosphate supplementation in the feed, particularly when hypertonic glucose administration drives phosphate into the cells. Addition of adequate amounts of phosphate to the feed will correct the situation.

8.8 HYPERURICAEMIA

This was encountered when sorbitol, fructose or xylitol were used as energy substrates and is rarely seen today.

8.9 HYPERLIPIDAEMIA

Hypertriglycerideaemia (Type V hyperlipoproteinaemia) is a common problem associated with TPN, particularly in the long term. Hypercholesterolaemia is less predictable. The long term implications of these abnormalities with regard to increased cardiovascular risk is at present unknown. With increasing experience in the field definitive evidence might be forthcoming, with appropriate therapeutic implications. For patients on long term TPN we advocate regular screening of the lipid status and in the presence of persistent abnormalities treat them in the logical way one would treat any other patient: by reduction in the lipid component of the TPN to a minimum (500 ml of Intralipid 10% twice a week) and control of obesity by reduction in the total caloric intake. It is not uncommon to see HPN patients who are over-nourished! We have not found it necessary so far to resort to lipid lowering agents, whose absorption may, in any case, be severely impaired by the lack of adequate bowel.

8.10 TRACE ELEMENT DEFICIENCIES

Medical science is rapidly learning more about the physiological role of trace elements, mainly due to experience with long term parenteral nutrition. Deficiency states (or toxicity) can only be established by sophisticated blood tests. Many of the currently available solutions incorporate variable amounts

of some of these elements. Many elements occur as contaminants during manufacture and may even be present in excessive amounts – we have seen one example where chromium levels were very high. Additional supplements of specific trace elements are now commercially available, examples being zinc and selenium. With identification of specific roles and deficiency states, many more of these trace elements are likely to become commercially available. Clinical aspects have been dealt with in an earlier chapter.

8.11 ESSENTIAL FATTY ACID DEFICIENCY

Linoleic and linolenic acids are both thought to be essential to man and need to be provided in adequate amounts in the diet; the latter is the precursor of arachidonic acid, which gives rise to prostaglandins. Though considerable amounts may be present in adipose tissue a state of deficiency (EFAD) can be precipitated by impaired mobilization secondary to hyperinsulinaemia produced by hypertonic glucose infusions. Arachidonic acid is a 20-carbon fatty acid with four double bonds and when the essential precursors are deficient, the use of oleic acid as substrate gives rise to the abnormal appearance of an alternative 20-carbon eicosatrienoic acid with three double bonds.

EFAD was identified in man during the early days of TPN when fat emulsions were avoided (due to the adverse reactions to emulsions derived from corn and castor oils). Today we have an eminently safe preparation which will ensure the prevention of this deficiency. It can still occur if the source of energy in the feed is solely carbohydrate in nature. Clinical features of EFAD include dry scaly skin, rash, loss of hair, platelet abnormalities and a neurological syndrome resembling sensorimotor neuropathy. The diagnosis is supported by the finding of an abnormally high trienoic to tetraenoic acid ratio in the plasma, which should be less than 40%. The abnormality is simply corrected by the inclusion of a fat emulsion which contains both substances, in the nutritional regimen. We recommend providing enough EFA to account for 5–10% of the total calories. In practice this can be achieved by the administration of as little as 2 l of a 10% fat emulsion such as Intralipid, per week; we recommend *at least* twice that amount for routine maintenance nutrition (in the absence of significant hyperlipidaemia).

8.12 THE CHINESE RESTAURANT SYNDROME

This is a syndrome of sudden and self-limited circulatory dysfunction manifested by pallor, sweating, tachycardia, tremors and hypotension. It is thought to be due to the rapid infusion of glutamic acid present in nitrogen based fluids. No specific treatment is indicated.

8.13 ANAEMIA

In the earlier years of parenteral nutrition, when solutions based on linseed oil and cottonseed oil were used, the occurrence of a chronic low grade haemolytic anaemia was described. Nowadays the fat emulsions generally used are based on soya bean and this complication does not arise. Macrocytic anaemia has also been described in alcohol based feeds in the past, due to impaired folate metabolism. Again this does not apply as ethanol is no longer used as a source of energy – at least not parenterally!

8.14 HYPERCALCAEMIA

The exact pathogenesis of this entity during TPN is not clearly understood. There is no demonstratable hyperparathyroidism or vitamin D toxicity. Fortunately it is self limited and has not been shown to produce any adverse effects.

8.15 TPN OSTEODYSTROPHY

This curious syndrome has been predominantly documented in North America, occurring in patients on long term TPN. The symptoms include bone pains and pathological fractures. There are physical and radiological signs of osteomalacia. The exact nature of the disease is poorly understood. There are conflicting views on the role of vitamin D in this problem. There is some evidence to suggest that there may be resistance requiring large doses of the vitamin. On the other hand the syndrome is said to be reversed (paradoxically) by exclusion of vitamin D from the feeds and this has been attributed to vitamin D toxicity or excessive end-organ sensitivity. It is significant, however, that a similar picture may arise in patients with chronic renal failure on long term haemodialysis whose

'dialysis bone disease' is now attributed to aluminium intoxication. In some cases of TPN osteodystrophy aluminium deposition along the osteoid seam has been demonstrated and that may indeed be the explanation for this disease. Further research is required in this area and at present there is no known treatment.

8.16 CHOLELITHIASIS

This is a recognized complication of long term TPN. The exact mode of pathogenesis is unclear, but may relate to impaired flow of bile or to altered bile salt/acid metabolism. This can lead to the usual complications such as cholecystitis and obstructive jaundice.

8.17 INTRAHEPATIC CHOLESTASIS

This sinister complication is often a harbinger of death. It usually occurs in patients on long term treatment. Often, during the early weeks of TPN, a rise in the liver enzymes (aspartate transaminase and alkaline phosphatase) is noted and this seems to be a non-specific and harmless phenomenon. Fatty liver may be seen on histology and in itself may not be a clinical problem.

However, the appearance of jaundice with a persistently raised serum bilirubin and features of obstructive jaundice, in the absence of demonstrable extrahepatic obstruction by gall stones, is an ominous sign. The condition often progresses to liver failure and death. Histology of the liver reveals a picture of intrahepatic cholestasis. An aetiological agent has not been clearly delineated, though there have been suggestions that it may relate to conditioned deficiency of taurine or choline. There is the real possibility that it may be the result of inadvertent toxicity caused by excessive infusion of some obscure trace element.

There is no known treatment, apart from cessation of TPN and reversion to oral feeding. Exclusion of specific components such as lipids, or change to alternative preparations have proven futile, though worth a try. Steroids have not been of any benefit in our experience. The potential role of trace elements (deficiency or toxicity) in this condition is worthy of serious consideration.

8.18 MISCELLANEOUS

Miscellaneous deficiencies of metabolites have been suggested or identified during TPN – tyrosine, choline, taurine, cysteine and carnitine. The exact significance has not been established firmly and requires further investigation.

9 *Prognosis and outcome*

G. Venkat Raman and H.A. Lee

TPN does not automatically mean permanent or life-long dependence on it for survival. The vast majority of patients started on TPN (over 90%) will only require the treatment for days or weeks, rarely months. Even of those who go on to HPN, roughly half will be off the treatment within 1 year, either due to remission of the primary disease (e.g. Crohn's disease) or death. Only a tiny minority will therefore be on the long term HPN programme.

The typical example of short term TPN is that of a patient with an intra-abdominal problem requiring surgery (such as cholecystectomy), in whom the pre-operative nutritional state is sub-optimal and who warrants nutritional support for 10–14 peri-operative days. Examples of patients requiring medium term TPN include those with acute exacerbation of Crohn's disease and cancer chemotherapy, when nutritional support may be required for up to 8 weeks. In some circumstances such as enterocutaneous fistulae or colostomy following bowel resection, long term TPN may be required for several months, subsequently bowel continuity may be restored and TPN discontinued.

In all these situations, TPN is necessary to tide patients over periods of lack of bowel function. 'Weaning' patients back onto the enteral feeding may sometimes be difficult. The longer the patient has been on TPN and the greater the bowel loss, the more difficult this is likely to be. It is important therefore, to remember that sudden cessation of TPN with commencement of oral feeding is likely to result in problems. TPN should be continued while oral intake is gradually increased over several days. We would recommend either reducing the TPN to alternate nights, or reduce the volume, to suit the individual patient. The starting enteral feeding regimen must be relatively 'light', consisting of easily

digestible foods and avoiding foods abundant in fat or protein.

If supplemental feeds are used, it is important to start with half strength (diluted by water). There may be some merit in using pre-digested preparations such as Reabilan[R]. When it is established that the patient is consuming enough without any evidence of diarrhoea or malabsorption, only then would it be safe to discontinue TPN. If bowel has been resected, a certain amount of diarrhoea may be unavoidable. There is little doubt that temporary hospital TPN, though expensive, can save many lives which would otherwise be lost. Furthermore, quite apart from providing vital nutrition, TPN probably has a salutary effect on the healing of many self-limiting conditions such as inflammatory bowel disease, by providing complete bowel rest.

9.1 UK HOME TPN REGISTER

This was set up in 1977 to document the national incidence of HPN, the causes leading to it, the associated complications and the long term outcome. From January 1977 to May 1987, 241 patients had been registered (101 male and 140 female) and the treatment was being offered in 12 centres. Of the 241 that had started HPN, however, only 103 were continuing on the treatment at the time of reporting.

The age distribution was as follows:

9 (4%) cases below the age of 10
60 (25%) between the ages of 11 and 30
126 (52%) between the ages of 31 and 50
43 (18%) between the ages of 51 and 70
3 (1%) over the age of 71.

The major diagnoses of conditions in this series were:

Crohn's disease: 103
Mesenteric vascular disease: 31
Malignancy: 15
Pseudo-obstruction: 14
Radiation enteritis: 14
Volvulus: 9
Pancreatic disease/malabsorption: 9
Ulcerative colitis: 7
Systemic sclerosis: 7

Table 9.1 Quality of life on home parenteral nutrition

Grade	*Description*	*No.*
1	At work full-time or looking after home and family unaided	100
2	At work part-time or looking after home and family with help	46
3	Unable to work but able to cope with HPN unaided and go out occasionally	70
4	Housebound, needs major assistance with HPN	16
Other	e.g. infants	9

By and large HPN has been very successful and rewarding in this country. Patients have enjoyed a good quality of life as illustrated in Table 9.1.

Just over half the patients come off the treatment for various reasons. Most were able to return to oral feeding. Fifty subjects died in the period mentioned and the causes are set out below. Half of those that died did so within the first 6 months of starting home TPN.

HPN related deaths	
Septicaemia	6
SVC thrombosis	3
Hepatic failure	3
Endocarditis	1
Post-operative	1
Disease related deaths	
Recurrence/continuation of malignancy	13
Complication/exacerbation of disease	13
Post-operative	4
Other deaths	
Road traffic accident	2
Cardiac arrest of unknown cause	2
Cerebral haemorrhage	1
Carcinoma of the bronchus	1

Our own figures for HPN in Portsmouth are given in Table 9.2 and refer to 14 patients treated. The importance of this particular group of patients as compared to those from the

Table 9.2 Patients on home parenteral nutrition, managed by the Portsmouth Unit

Case No	*Duration on TPN (months)*	*Indication for TPN*	*Number of catheters*	*Outcome*
1	10	Volvulus of small bowel	1	Died (cerebral haemorrhage)
2	10	Multiple enterocutaneous fistulae	1	Bowel function restored
3	66	Superior mesenteric arterial occlusion	8	Died (carcinoma bronchus)
4	3	Carcinoma of bladder with vesico-colic fistula	1	Bowel function restored
5	1	Diverticula disease with colectomy	1	Bowel function restored
6	9	Multiple enterocutaneous fistulae secondary to Crohn's disease	3	Bowel function restored
7	11	Superior mesenteric arterial occlusion	2	Died (myocardial infarction)
8	4	Venous infarction of small bowel	1	Died (hepatic failure)
9	50	Venous infarction of small bowel	7	Continuing on TPN
10	9	Acquired megacolon	2	Died (hepatic failure)
11	30	Ulcerative colitis with colectomy and secondary small bowel infarction	7	Died (myocardial infarction)
12	13	Carcinoma of stomach with peritoneal sclerosis	1	Died (carcinomatosis)
13	2	Desmoid tumour of small bowel	1	Bowel function restored
14	4	Carcinoid syndrome with bowel obstruction	2	Died (Bronchopneumonia)

UK TPN Registry is that they are all maintained by the do-it-yourself approach (*vide supra*) and none of these patients developed infections that could be attributed to their method. Furthermore, throughout the period they were observed no electrolyte abnormalities occurred.

As for the future, it is likely that the growth of home TPN will exceed the current level of 1–2 per million population. TPN in hospital will be used more and more with advances and expansion in the various branches of medicine and surgery. With the development of Nutritional Support Teams and technical advances TPN has become both essential and cost effective. It is our view that TPN should no longer be seen as super erudite treatment for the hospital malnourished, but a standard mode of treatment as cautiously but as simply given as antibiotics.

Suggested reading

American Medical Association (1979) Multivitamin preparations for parenteral use. *J. Parenteral and Enteral Nutr.*, **3**, 258–62.

American Medical Association (1979) Guidelines for essential trace element preparations for parenteral use. *J. Parenteral and Enteral Nutr.*, **3**, 263–7.

Baker, J.P., Detsky, A.S., Wesson, D.E. *et al.* (1982) Nutritional assessment. *N. Engl. J. Med.*, **306**, 969–72.

Blackburn, G.L. and Thornton, P.A. (1979) Nutritional assessment of the hospitalized patient. *Med. Clin. N. Amer.*, **63** (5), 1103–15.

Butterworth, C. and Blackburn, G. (1974) Hospital malnutrition and how to assess the nutritional status of a patient. *Nutrition Today*, **10**, 8.

Coburn, J.W. and Klein, G.L. (eds) (1985) *Metabolic Bone Disease in Total Parenteral Nutrition*, Urban and Schwarzenburg, Baltimore, Munich.

Cuthbertson, D.P. (1942) Post shock metabolic response. *Lancet*, **i**, 433–6.

Dudrick, S.S., Wilmore, D.W., Vars, N.M. *et al.* (1968) Long term total parenteral nutrition with growth, development and positive nitrogen balance. *Surgery*, **64**, 134–42.

Goodgame, J.T. (1983) A critical evaluation of the results of total parenteral nutrition in various states: Cost and Benefit, in *Surgical Nutrition*, (ed. J. E. Fischer), Little, Brown, Boston.

Heatley, R.V., Losowsky, M.S. and Kelleher, J. (eds) (1986) *Clinical Nutrition in Gastroenterology*. Churchill Livingstone, London.

Hill, G.L. (ed.) (1981) *Nutrition and the Surgical Patient. Clinical Surgery International II*, Churchill Livingstone, Edinburgh.

Irving, M., White, R. and Tresadern, J. (1985) Three years' experience with an intestinal failure unit. *Ann. R. Coll. Surg. Engl.*, **67**, 2–5.

Jeejeebhoy, K.N. (ed.) (1983) *Total Parenteral Nutrition in the Hospital and at Home*. CRC Press Inc., Florida.

Jeejeebhoy, K.N., Langer, B, Tasalles, G. *et al.* (1976) Total parenteral nutrition at home: studies in patients surviving four months to five years. *Gastroenterology*, **71**, 943–53.

Karran, S.J. and Alberti, K.G.M.M. (eds) (1980) *Practical Nutritional Support*, Pitman Medical, London.

Khawaja, H.T., Campbell, M. and Weaver, P.C. (1988) Effect of transdermal glyceryl trinitrate on the survival of peripheral intravenous infusions: A prospective double blind controlled study. *Brit. J. Surg.*, **75**, 1212–15.

Klein, G.L., Targoff, C.M., Ament, M.E. *et al.* (1980) Bone disease associated with parenteral nutrition. *Lancet*, **ii**, 1041–4.

Klein, G.L. and Rivera, D. (1985) Adverse metabolic consequences of total parenteral nutrition. *Cancer*, **55**, 305–8.

Knaus, W.A., Zimmerman, J.E., Wagner, D.P. *et al.* (1981) APACHE, acute physiology and chronic health evaluation: a physiologically based classification system. *Crit. Care Med.*, **9**, 591–7.

Knaus, W.A., Draper, E.A. and Wagner, D.P. (1985) APACHE II: A severity of disease classification system. *Crit. Care Med.*, **13**, 818–29.

Knochel, D.P. (1985) Complications of total parenteral nutrition. *Kidney Internat.*, **27**, 489–96.

Lee, H.A. (ed.) (1974) *Parenteral Nutrition in Acute Metabolic Illness*, Academic Press, London.

Lee, H.A. (1986) Practical aspects of intravenous feeding, in *Clinical Nutrition in Gastroenterology* (eds R.V. Heatley, M.S. Losowsky and J. Kelleher), Churchill Livingstone, London.

Lee, H.A. (1988) The nutritional management of renal disease, in *Nutrition in the Clinical Management of Disease* (2nd edn) (eds J.W.T. Dickerson and H.A. Lee), Edward Arnold, London.

Mughal, M. and Irving, M. (1986) Home parenteral nutrition in the United Kingdom: a report of 200 cases. *Lancet*, **ii**, 383–6.

Pennington, C.R. (1988) Home parenteral nutrition. *Intensive Therapy and Clinical Monitoring*, **9**, 122–8.

Rudman, D. and Bleies, J.C. (1983) Nutritional requirements. Assessment of nutritional status. Protein and energy undernutrition, in *Harrison's Principles of Internal Medicine*, McGraw-Hill, London, pp. 426–39.

Rudman, D. and Williams, P.J. (1985) Nutrient deficiency during total parenteral nutrition. *Nutrition Reviews*, **43** (1), 1–13.

Rainford, D.J. (1987) Trends in management of acute renal failure, in *Current Approaches: Renal Failure* (eds. H.A. Lee and S.W. Parker), Inprint (Litho) Ltd, Southampton, pp. 26–30.

Rees, R.G.P., Payne-James, J.J., Grimble, G.K. *et al.* (1988) Energy and nitrogen requirements in patients receiving nutritional support. *Intensive Therapy and Clinical Monitoring*, **9**, 204–8.

Schneider, H.A., Anderson, C.E. and Coursin, D.B. (eds) (1977) *Nutritional Support of Medical Practice*, Harper and Row, London.

Scribner, B.H., Cole, J.J., Christopher, D.G. *et al.* (1970) Long-term parenteral nutrition. *J. Am. Med. Ass.*, **212** (3), 457–63.

Shenkin, A., Fell, G.S., Halls, D.J. *et al.* (1986) Essential trace element

provision to patients receiving home intravenous nutrition in the United Kingdom. *Clin, Nutr.*, **5**, 91–7.

Shike, M., Harrison, J.E., Sturtridge, W.C. *et al.* (1980) Metabolic bone disease in patients receiving long-term total parenteral nutrition. *Ann. Intern. Med.*, **92**, 343–50.

Smith, R. (1987) Special nutritional problems, in *Oxford Textbook of Medicine*, Oxford University Press, Oxford, pp. 8.51–8.58.

Soroff, H.S., Pearson, E. and Artz, C.P. (1961) An estimation of the nitrogen requirements for equilibrium in burned patients. *Surg. Gyn. Obst.*, **112**, 159–72.

Sutherland, A.B. (1956) The nutritional care of the burned patient. *Brit. J. Plast. Surg.*, **8**, 68–74.

Wilkinson, A.W. (1963) Historical background of intravenous feeding. *Nutritio Dieta*, **5**, 295.

Glossary of available products

Three litre bags

Obtained from various solution manufacturers, e.g.

Geistlich and Sons, Chester
Travenol (Baxter), Thetford
KabiVitrum Ltd, Uxbridge.

Volumetric pumps

IMED series, e.g. model 922H
Travenol (Baxter) pumps.

TPN solutions

(a) Nitrogen sources

(i) Vamin series – KabiVitrum Ltd
(ii) Aminoplex series – Geistlich and Sons Ltd
(iii) Synthamin series – Travenol (Baxter)
(iv) Amino acid solutions – McGAW Laboratories, Irvine, California
(v) Amino acid solutions – Pfrimmer and Sons Ltd, Erlangen, West Germany.

(b) Energy sources

(i) *Glucose*
Many companies produce a whole range of different concentrations of glucose. Many hospital pharmacies produce their own. Glucoplex series (Geistlich and Sons) are particularly useful as they contain phosphorus and zinc.
(ii) *Fat*
Soybean fat emulsions (triglyceride) are manufactured and distributed world-wide by:

KabiVitrum Ltd – Intralipid 10% and 20%
Travenol (Baxter) – Travemulsion 10% and 20%.

Vitrimix system (KabiVitrum) consists of a 250 ml bottle of Intralipid 20% which can be vacuum-transferred to a litre bottle containing 750 ml of amino acid–glucose solution, to make up 7 g of nitrogen and 800 non-protein kilocalories.

(c) Micronutrient solutions

Additives to ingredients of 3 litre bags. All major parenteral nutrition companies manufacture:

(a) Trace element solutions
(b) Vitamin preparations.

Some companies, e.g. KabiVitrum, offer a comprehensive range of trace element preparations, e.g. Addamel, Additrace, Ped-el (infants); vitamin preparations, e.g. Soluvite-N (water soluble) and Vitlipid N (fat soluble) and phosphorus preparations, e.g. Addiphos.

(d) Compounding manufacturers

All the major companies referred to above provide compounding facilities so that prepared 3 litre bags can be delivered direct to patients' homes according to individual prescriptions.

Some hospital Pharmacy Departments (e.g. Royal Victoria Hospital, Newcastle, and Queen Alexandra Hospital, Portsmouth) offer a similar compounding service to hospitals and homes in their own regions.

Vascular catheters for parenteral nutrition

Included here is a list of catheters commonly used in St Mary's Hospital, Portsmouth. There is an enormous variety available and operators are advised to get familiar with a few.

1. Drum-Cartridge Catheter – Abbott Ireland, Eire.
   A popular peripheral-to-central catheter which can be inserted into an antecubital vein and advanced into the central venous system. Particularly useful in situations where direct access to the central venous system is lacking. Limited by tendency to thrombophlebitis, hence for short term use.
2. Secalon T – British Viggo, Swindon, Wilts.
   Polyurethane stiff catheter for short term use – simple insertion procedure (over-the-needle); for subclavian rather than internal jugular approach.
3. Abbocath-T – Abbott Hospitals, North Chicago.
   An easy to insert catheter (over-the-needle) for short term use, which can be tunnelled in by starting at a distance of 10 cm away from the point of entry into the subclavian vein; not recommended for the internal jugular.
4. Multicath – Vygon (UK) Ltd, Cirencester, Glos.
   Triple lumen catheter made of 'Flexane', a refined form of polyurethane. Very useful in the intensive care situation for multiple simultaneous infusions. For short term use.
5. Wallace Flexihub Cannula – Medical Assist Ltd, Colchester, Essex.
   For internal jugular catheterization, for short term use. Has a protective sleeve surrounding the cannula. Catheter-over-needle approach.
6. Centrasil – Travenol Laboratories, Deerfield, Illinois.
   Silicone elastomer catheter for internal jugular use. Cannula within a cannula, for short term use.

7. Leader Cath – Vygon (UK) Ltd, Cirencester, Glos.
   Inserted by Seldinger technique, suitable for internal jugular as well as subclavian veins. For short to medium term use.
8. Secalon Seldy – British Viggo, Swindon, Wilts.
   Polyurethane soft catheter for short to medium term use – incorporates a lock to close off the lumen during manipulation. A short tunnel can be incorporated.
9. Nutricath S – Vygon (UK) Ltd, Cirencester, Glos.
   For medium to long term use. Silicone catheter inserted through a needle preferably into the subclavian vein. Can be tunnelled through the same needle, with a detachable hub which is attached at the end of procedure. Relatively narrow diameter, hence not recommended for HPN.
10. Cuff-Cath – British Viggo, Swindon, Wilts.
    Silicone elastomer catheter for long term use, including HPN. Inserted by initial introduction of a guide wire into the subclavian vein, followed by a vein dilator and sheath, finally by introduction of the catheter through the sheath. The external portion tunnelled by a metallic rod to produce a tunnel.
11. Life-Cath – Vygon (UK) Ltd, Cirencester, Glos.
    Silicone catheter for long term use, including HPN. Initial tunnelling of catheter followed by insertion of guide wire into the subclavian vein, then vein dilator and sheath, followed by introduction of catheter; the sheath is then simply torn off.
12. Wallace Venous Access Catheter – Medical Assist Ltd, Colchester, Essex.
    Silicone catheter for long term use. Surgical insertion through either one of the jugular veins or the cephalic vein. With a strong integral titanium hub.
13. Infuse-A-Port – Infusaid Inc., Norwood, Montana, USA.
    Implantable device for long term use, for TPN or chemotherapy. Inserted surgically into a jugular vein, with a subcutaneous implant on the chest wall, which can be needled directly through a septum.

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