

## Nutritional Support of Children in the Intensive Care Unit

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Nutritional support is an integral and essential part of the management of 5-10 percent of hospitalized children. Children in the intensive care unit are particularly likely to develop malnutrition because of the nature and duration of their illness, and their inability to eat by mouth. This article reviews the physiology of starvation and the development of malnutrition in children. A method of estimating the nutritional requirements of children is presented. The techniques of nutritional support, including enteral, peripheral, and central parenteral nutrition are discussed in detail. Appropriate formulas are given for different age groups. Electrolyte, vitamin, and mineral supplements are discussed. Guidelines are provided for choosing between peripheral and central total parenteral nutrition. A monitoring protocol is suggested and complications of nutritional therapy are reviewed. Safe and effective nutritional support requires considerable investment of time and effort by members of the nutrition team.

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Adequate nutrition in hospitalized patients is recognized as an important factor in prompt recovery from illness or injury. The rapidity with which malnutrition can develop in seriously ill patients has also become apparent [1,2,3]. The majority of children admitted to the intensive care unit (ICU) are transferred to a regular floor within three to four days. During this brief stay in the ICU, attention is appropriately directed to their primary medical problems and nutrition is of secondary concern. However, children who have been hospitalized for some time and are admitted to the ICU because of a new complication may be malnourished already and children who stay in the ICU for more than five to seven days are likely to develop nutritional deficiencies, since normal feeding is rarely possible. About one-third of children admitted to our ICU stay for more than a week. Nutritional support is of prime importance for these patients.

Most of the data which documents the rapid appearance of malnutrition and the rate of energy expenditure and protein loss in seriously ill or traumatized patients has been obtained from adults. There is very little direct information about the metabolic response to trauma and sepsis in children, so conclusions about indications for nutritional support and nutritional requirements are derived from adult data and must be regarded as tentative. Nevertheless, it seems likely that the metabolic effects of illness are similar in children and probably occur more rapidly because of their higher metabolic rate and limited endogenous caloric reserves.

### PHYSIOLOGY OF STARVATION

The metabolic events of normal nutrition and fasting have been studied and reviewed by Cahill and his colleagues [4,5]. Under normal conditions, sufficient

calories and protein are ingested to meet the body's needs for energy, for amino acids to replace protein lost through normal turnover, and, in children, for growth. Fasting man must turn to endogenous caloric reserves to provide metabolic fuel. Small amounts of carbohydrate are stored as glycogen—less than 1,000 kilocalories (Kcal) in adults and about 1 percent of body weight in children [4,6]. Fat is the major storage form of energy. Protein can also be burned for energy, but all body proteins have essential structural or metabolic functions, and the goal of nutritional homeostasis is to preserve lean body mass and prevent net loss of protein.

During fasting, most organs derive their energy from the oxidation of fatty acids and/or ketone bodies produced from fatty acids in the liver. The central nervous system, however, is an obligate glucose user under ordinary conditions. In the absence of carbohydrate intake or significant stored carbohydrate, the only source of glucose is gluconeogenesis from amino acids, most of which are supplied by the breakdown of skeletal muscle protein. In adults, this demand for glucose results in the catabolism of about 75 grams of protein a day during fasting [4].

At this rate, the loss of body protein would reach lethal levels (about one-third of lean body mass) in two to three weeks. As starvation progresses, however, several adaptations take place which act to conserve lean body mass. The most important of these are (1) a gradual decrease in metabolic rate, and (2) progressive ketosis. The serum concentration of ketone bodies rises during starvation. In high concentration, these fat-derived, water-soluble molecules cross the blood-brain barrier and can be utilized as an energy source by the central nervous system [7]. These adaptations, when fully operative, allow starving man to survive for two to three months [4].

These observations apply to otherwise healthy individuals. Adaptation to starvation does not take place, or occurs only to a limited degree, in sick, fasting patients. Illness and injury increase metabolic energy expenditure and the hormonal milieu of stress favors glycogenolysis and gluconeogenesis [8,9]. The rise in serum insulin which accompanies the elevated blood glucose inhibits the rise in serum ketone body concentration which is necessary if the brain is to use fat as its primary fuel [10,11]. Thus, production of glucose and concomitant loss of protein continue at a high rate in sick, starving, hospitalized patients.

Two other factors must be considered—namely, the increase in metabolic rate associated with severe illness and trauma, and the protein-sparing effect of carbohydrate.

Cuthbertson first demonstrated that injury (long-bone fracture) is accompanied by an increased loss of nitrogen [1]. Moore, in a series of elegant studies summarized in his book, clearly documented the hypermetabolic state characteristic of injury and severe illness and the rapid wasting of body mass which occurs [2]. More recently, Kinney and his colleagues, using indirect calorimetry, have quantified the increased energy expenditure in these patients [12,13]. From these and other data we can conclude that the metabolic rate is increased 20–30 percent by skeletal trauma, 30–50 percent by multiple trauma or sepsis, and 50–100 percent by thermal injury, depending on the extent of the burn [14]. The duration of this hypermetabolic response ranges from a few days in simple trauma to several weeks in patients with major burns or severe, recurrent infectious complications. Thus, the seriously ill patient who is starved not only cannot decrease his metabolic rate but has increased energy and protein requirements. Under these circumstances, potentially lethal loss of lean body mass can occur in two weeks or less.

Hospitalized patients are rarely totally starved since most intravenous fluids contain 5 percent glucose, or 50 grams per liter. Gamble demonstrated the protein-

sparing effect of carbohydrate in 1947 when he found that nitrogen excretion was considerably reduced in fasted subjects who were given 100–150 grams of glucose [15]. This amount of glucose supplies a major part of the energy requirements of the central nervous system, thereby reducing, but not eliminating, the need for gluconeogenesis. Nitrogen loss is not totally eliminated, however, because of the inefficiency of normal protein turnover and the continuing need for some glucose. O'Connell et al. found that nitrogen excretion was reduced by 50 percent in fasted subjects who were given 150 grams of glucose daily [16]. Increasing the glucose intake to 600 grams per day did not allow significantly greater nitrogen conservation.

How can these observations be applied to children? As noted above, there are very few studies of the physiology of starvation in children, but we can make some reasonable estimates. Body composition studies have yielded somewhat variable results, depending on the techniques used, but in general fat constitutes about 20 percent of body weight [6,17,18]. A major exception is the small premature infant. Heird and Winters estimate that a 1.0 kg premature infant has only 1 percent body fat, or 10 grams [19]. Protein makes up about 10 percent (dry weight) of total body weight [6,18]. In infants, about half the total protein is in muscle and half in organs. The proportion of protein in muscle gradually rises to about 90 percent in adults [17].

Since the central nervous system is the major organ which requires glucose as metabolic fuel, the brain metabolic rate is the major determinant of the need for gluconeogenesis during starvation. In adults, the brain accounts for about 25 percent of basal metabolic rate. In newborn infants, however, 65–75 percent of basal energy is expended by the brain [17]. This proportion decreases gradually during childhood as other organs grow more rapidly and consume more energy (Fig. 1).

Table 1 summarizes data from a variety of sources about body composition, basal metabolic rate, and brain metabolic rate for patients of various ages. From these data one can very roughly estimate the number of days in which one-third of body protein will be catabolized in an individual who is totally fasted and has no adaptation to starvation. These conditions are not encountered clinically and there are a number of assumptions involved in deriving these numbers, but the table does give an approximate idea of the rate of body wasting and clearly illustrates the nutritional disadvantage of infants and young children.

When should nutritional support be started? Provision of enough glucose (100–150 g/day in adults) to meet the metabolic requirements of the brain has been shown to reduce nitrogen losses by one-half [16]. The nitrogen-sparing effect of car-

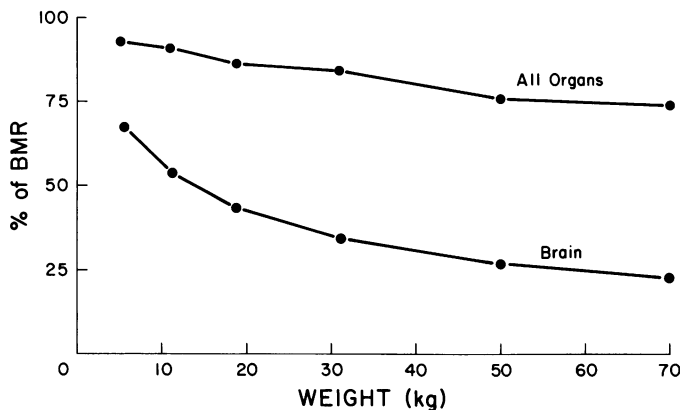


FIG. 1. The brain accounts for about two-thirds of the basal metabolic rate in neonates. Brain metabolic rate as a percentage of BMR declines more rapidly than total organ metabolic rate, reaching a plateau of about 25 percent in adults.

TABLE 1  
Body Composition and Energy Requirements

	Term Infant	Child			Adult 70 kg
		10 kg	30 kg	50 kg	
Total caloric reserves (Kcal)	6,500	21,200	51,300	72,000	95,400
As protein (Kcal)	1,500	4,000	12,000	20,000	28,000
BMR (Kcal/kg/day)	55	53	40	30	25
(Kcal/day)	190	530	1,200	1,500	1,800
Brain MR as % of BMR	65%	50%	40%	30%	25%
Brain energy (Kcal/day)	125	260	480	450	450
No. of days to catabolize 1/3 of protein stores	4	5	8	15	21

Data adapted from [6,17,18,19]

bohydrate may be even greater in children since the brain consumes a much higher proportion of total metabolic expenditure, but this has not been studied. Maintenance intravenous fluids containing 10 percent glucose will provide all the fuel necessary for brain metabolism in infants, while 5 percent glucose solutions will provide about two-thirds of the central nervous system requirements in children [17]. This simple expedient of adding glucose to maintenance intravenous fluids is routine clinical practice and probably at least doubles the length of survival in fasted patients [19].

On the other hand, imminent death from starvation should not be the end-point for starting nutritional support. Nutritional needs should be attended to before the numerous complications and potentially irreversible changes of severe malnutrition develop. For patients who have some oral intake or are receiving protein-sparing quantities of glucose, the number of days shown at the bottom of Table 1 is a reasonable estimate of the maximum time after which full nutritional support is essential. The addition of protein, vitamins, and minerals to the intravenous infusion will further slow the rate of catabolism of endogenous body protein, but it has been shown repeatedly that patients are in negative nitrogen balance unless their complete protein and caloric requirements are met [20,21,22].

In practice, 5 percent or 10 percent glucose is used in all intravenous fluids. If the child will be taking nothing by mouth for more than a few days, protein, vitamins, and minerals are added on the third to seventh day, depending on age. If the child is not eating by the number of days shown in Table 1, complete nutritional support is instituted by the most appropriate route. The number of days shown must be reduced considerably for children who have already lost weight prior to hospitalization or who have increased metabolic requirements.

### INDICATIONS FOR NUTRITIONAL SUPPORT

Notably absent from this article is a table listing diseases for which nutritional support is indicated. Protein-calorie malnutrition is the only disease which is treatable by nutrition. The indication for nutritional support is to treat or to prevent malnutrition. Many children who have congenital gastrointestinal anomalies, necrotizing enterocolitis, chronic diarrhea, inflammatory bowel disease, tumors, or who need mechanical ventilation in the ICU will require nutritional support but it is

TABLE 2  
Estimation of Energy Requirements

Basal = $(55 - 2 \times \text{age}) \times \text{kg} =$	_____
Maintenance, 20% $\times$ basal =	_____
Activity, 0-25% $\times$ basal =	_____
Sepsis, 13%/1°C $\times$ basal =	_____
Simple trauma, 20% $\times$ basal =	_____
Multiple injuries, 40% $\times$ basal =	_____
Burns, 50-100% $\times$ basal =	_____
Growth/Anabolism, 50% $\times$ basal =	_____
Total =	_____

well to remember that nutrition is an adjunct, albeit an essential one, to the primary management of the underlying disorder. Nutritional support is indicated in any patient whose spontaneous oral intake is inadequate for a length of time which is inadequate for that patient as outlined in the previous section.

### ESTIMATION OF METABOLIC REQUIREMENTS

Many formulas have been derived and proposed to estimate metabolic expenditure. These are more or less accurate but are cumbersome to use clinically. The author prefers to use a simplified formula based on age and weight, recognizing that all such formulas only approximate actual energy expenditure and that there is considerable leeway in the amount of calories which can be given to achieve a satisfactory clinical result (Table 2).

The formula:

$$\text{BMR (Kcal/day)} = (55 - 2 \times \text{age in years}) \times (\text{weight in kg})$$

assumes a linear decline in metabolic rate per kg body weight from birth to 15 years, after which the adult value of 25 Kcal/kg/day is used. The values for basal metabolic rate (BMR) calculated from this formula closely parallel measured BMR in children (Fig. 2) [23]. The formula underestimates BMR in older children by about 5 percent, but the values are close enough for clinical use. The formula is also reasonably accurate for young children who are between the tenth and ninetieth percentiles for weight, but the error becomes significant (10 percent) in children over ten years of age who are under- or overweight. For these children it is probably more accurate to use the age for which their weight would be at the fiftieth percentile rather than their actual chronologic age.

The energy necessary to maintain equilibrium is always higher than the basal metabolic rate calculated from any formula, in part because basal metabolism standards are determined in healthy, trained subjects. Minimal muscular activity, anxiety, and external stimulation usually increase the metabolic rate even in unstressed patients in the hospital. Feeding further increases resting energy requirements. The specific dynamic action, or the energy cost of metabolizing nutrients, is generally estimated at 10 percent of the calories consumed [24]. Thus the caloric intake necessary to maintain energy equilibrium in the fed but resting, unstressed patient is higher than basal. An increment of 20 percent added to the basal metabolic rate is adequate to account for these factors [25].

Additional calories must be allotted to provide energy for activity. This increment may be 50 percent or more of basal energy expenditure in very active children involved in competitive sports or an active camp program. For children in an intensive

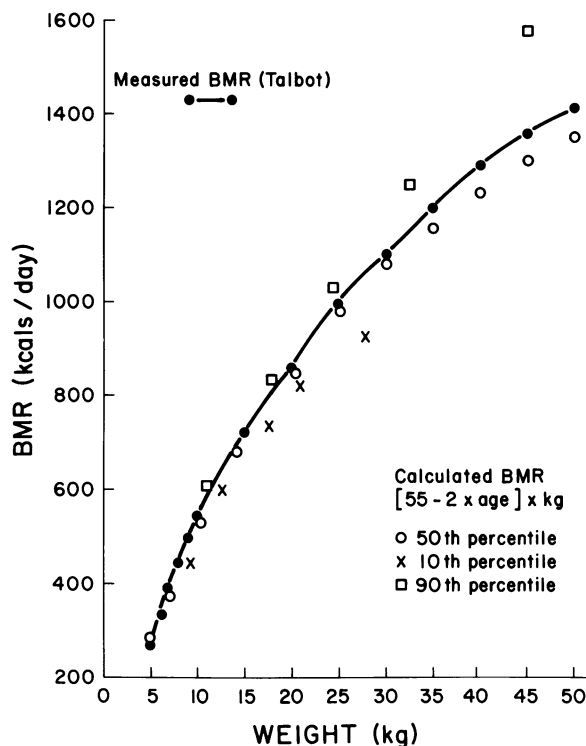


FIG. 2. The formula,  $BMR = [55 - 2 \times \text{age in years}] \times \text{kg}$ , closely approximates measured BMR (Talbot, [23]) for children whose weight is at the fiftieth percentile for age (*open circles*). The formula is also reasonably accurate for children in the tenth (*X*) and ninetieth (*squares*) percentiles up to about age ten years.

care unit, this increment is more likely to be in the range of 0–25 percent. The lower value would be appropriate for a child who is comatose and treated by mechanical ventilation and muscle-paralyzing drugs. The upper value is about right for a child who is active in bed and perhaps ambulating two or three times a day [26].

Energy requirements are further increased by illness and injury. As noted in the introduction, this question has not been well studied in children and we must extrapolate from studies in adults. Energy expenditure is increased 20–40 percent by sepsis and fever [13,27]. We have traditionally added 13 percent per  $1^{\circ}\text{C}$  of fever as suggested by DuBois [27]. Simple trauma (e.g., long-bone fracture) entails approximately a 20 percent increment in metabolic rate [1,26], while multiple injuries (skeletal and visceral) increase energy expenditure by 40–50 percent [26]. Burns impose the most severe metabolic demands, increasing metabolic rate by 50–100 percent depending on the extent of thermal injury [28]. This hypermetabolic state may persist for several weeks until the burn wound is covered with skin.

Growth is a unique requirement of children. During the few days of acute illness in the ICU, growth is not a major concern and may not even be possible because of the marked hormonal changes which accompany severe stress. However, for children who need nutritional support for longer periods, it seems desirable to provide additional calories for growth. The spontaneous intake of healthy children during rapid growth spurts (infancy and adolescence) is about twice basal energy expenditure, and an increment of 50 percent is adequate for the slower growth during middle childhood. Blackburn et al. have reported that a 50–75 percent increase above basal energy requirements is necessary to achieve anabolism and restoration of lean body mass in severely malnourished adults [25]. This regrowth may be analogous to normal growth in children. In practice, we try to increase caloric intake

above basal levels by 100 percent in neonates and 50 percent in older children who require continuing nutritional support during the convalescent stage of their illness.

The protein intake of normal healthy growing infants taking an ad lib diet of breast milk is about 2 g/kg/day [29], and is somewhat higher with proprietary formulas. Studies in our nursery have shown that a protein intake of 2.5 g/kg/day is adequate for growth in infants who are receiving total parenteral nutrition [30]. The protein requirement for normal adults is 0.6–0.8 g/kg/day, assuming an adequate intake of energy and other nutrients [31]. Requirements for children gradually decline from 2.0 g/kg/day to adult levels as age increases except that protein intake increases substantially during the adolescent growth spurt. Protein requirements are also increased by severe illness and trauma. Enteral and parenteral nutrient solutions suitable for use in children are designed so that adequate protein is supplied if energy intake is calculated appropriately. Extensive burns, massive trauma, and severe sepsis may increase nitrogen losses even more than energy requirements and it is often recommended that nutrient formulas having a lower calorie-to-nitrogen ratio be used in these circumstances. In practice, this is rarely necessary in children but should be considered if the hypermetabolic state persists for a long time.

## TECHNIQUES OF NUTRITIONAL SUPPORT

### *Enteral Feeding*

Nutritional support is defined as the provision of nutrients to patients who cannot take an adequate diet by mouth. One-half to two-thirds of all patients who require nutritional support can be managed by enteral feeding, which is preferable to parenteral nutrition because of lower cost, greater safety, and greater metabolic efficiency.

Many special enteral diets can be taken by mouth, but feeding through an indwelling nasogastric tube is usually necessary, particularly for patients in the ICU. Tube feedings have a poor image and are often rejected by physician and patient alike. Several principles of management are necessary to make tube feedings safe, effective, and reasonably comfortable.

The smallest tube which will allow passage of the enteral formula should be used—usually 6 or 8 French. Standard large-bore tubes designed for gastric decompression are wholly unsuitable as feeding tubes. They are very uncomfortable for patients, cause erosion of the nares and pharyngeal irritation, and disrupt the lower esophageal sphincter, promoting gastroesophageal reflux, esophagitis, and aspiration. Small tubes are not totally free of these problems but are much safer and generally well tolerated. Most of the newer feeding tubes on the market are made of soft, pliable, non-reactive material and are provided with stylets or other mechanisms to facilitate passage.

Enteral feedings should usually be administered by continuous infusion. Bolus feedings are easier for the nursing staff (and parents) to manage and are appropriate for stable patients who require long-term tube feeding (mostly neurologically impaired patients). However, they tend to cause gastric retention and diarrhea and are unsuitable for acutely ill patients in the ICU. Numerous studies have shown the greater efficacy of continuous infusion [32,33,34]. A constant infusion pump simplifies management. Only the amount of nutrient formula which will be administered in eight hours should be placed in the infusion bag or bottle since bacterial growth occurs rapidly when these solutions are open to the air at room temperature [35].

If possible, the head of the bed should be elevated 20–30 degrees to discourage gastroesophageal reflux. It is also important to aspirate from the tube periodically to measure gastric residual and determine whether the stomach is emptying properly. As a rule of thumb, the aspirate volume should be no more than the amount which is infused in two hours. Gastric residual should be measured every four hours initially but can be checked less frequently if the volume remains small after a day or two. This safeguard is especially important in patients who are comatose and cannot complain of abdominal discomfort.

In recent years many new enteral feeding products have appeared on the market. Most are safe and effective, but several points must be noted. Products which contain lactose should be avoided since most acutely ill patients are lactose-intolerant. The sodium content of some formulas is unacceptably high for use in children and patients with cardiac disease or cirrhosis. Finally, most of the enteral formulas are designed for adults and the vitamin and mineral composition is not well suited to long-term use in young children. Infants under a year of age should be given standard or special infant formulas.

The types of enteral formulas are listed in Table 3. Supplemental formulas are not nutritionally complete and are intended only to give additional calories and protein. The same end can often be achieved at less expense with routine items from the kitchen.

Standard enteral formulas are balanced, nutritionally complete liquid diets which can be used as the sole nutrient intake for long periods of time. They are composed of complex proteins, fats, and carbohydrates, supplemented with vitamins and minerals, and require a relatively intact digestive tract. Their advantages include low osmolality, palatability, and low cost. The great majority of patients who require enteral feeding will tolerate these basic formulas.

Elemental, or chemically defined, liquid diets are composed of less complex nutrients. The simplest formula, Vivonex (Eaton Laboratories, Norwich, NY), contains only glucose, crystalline amino acids, and a small amount of linoleic acid, plus vitamins, electrolytes, and minerals. Others have slightly more complex sugars and proteins and often have medium chain triglyceride (MCT) oil which is absorbed directly into the portal venous system and does not require the action of bile. MCT oil is a good source of calories but does not provide essential fatty acids. The three main advantages of elemental formulas are (1) little or no active digestion is required, (2) stimulation of bile and pancreatic secretions is minimal, and (3) stool volume is very low. Elemental diets often can be used successfully in patients who have enterocutaneous fistulas, distal intestinal obstruction, inflammatory bowel disease, or other gastrointestinal disorders in whom more complex formulas are not tolerated. On the other hand, elemental diets offer no particular advantage in patients whose gut is relatively intact but who require tube feedings for some other reason. In these patients, controlled studies have shown no significant difference in

TABLE 3  
Types of Enteral Formulas

Supplemental
Standard (nutritionally complete)
Elemental
Concentrated
Special function



stool frequency or volume between elemental diets and standard, less expensive formulas [36].

The major disadvantage of elemental diets is high osmolality. One gram of glucose has the same caloric value as one gram of sucrose but has twice as many osmotically active molecules and many times more molecules than one gram of complex carbohydrates. The same principle applies to amino acids and protein. Hypertonic formulas are rapidly diluted in the gastrointestinal tract by secretion of water from the mucosa, which often leads to gastric retention or osmotic diarrhea. Elemental diets are more expensive than standard formulas (though far less costly than parenteral nutrient solutions). They are also less palatable and, therefore, less acceptable for oral use. Elemental diets may be very useful in selected patients but should not be used for routine enteral feeding.

Most of the standard and elemental diets contain one calorie per milliliter. Patients who are fluid-restricted because of cardiac or renal disease or who require multiple intravenous lines for constant infusion of cardiotropic drugs, administration of antibiotics, or central venous and pulmonary artery pressure monitoring may not tolerate enough enteral formula to meet their caloric needs. One simple principle in these patients is to make certain that at least some calories are provided in whatever fluids are given. All intravenous fluids should contain 5 percent or 10 percent glucose. If more calories are needed, one of the concentrated enteral formulas may be used. Ensure-Plus (Ross Laboratories, Columbus, OH) contains 1.5 cal/ml. A new product, Magnacal (Organon, Inc., West Orange, NJ), provides 2 cal/ml, using a mixture of complex carbohydrates, protein, and fat. The concentrated formulas are relatively hypertonic and must be used carefully, but may be invaluable in selected patients.

Table 4 shows the enteral diets used at Yale-New Haven Hospital for purposes of comparing composition, caloric density, calorie-to-nitrogen ratio, sodium content, osmolality, and cost. There are other equally effective products on the market.

Two special function formulas merit brief mention. Amin-Aid (McGaw

TABLE 4  
Comparison of Enteral Formulas

	Ensure	Isocal	Vivonex	Vivonex HN	EnsurePlus	Magnacal
<b>Carbohydrate</b>						
Source	Sucrose				Sucrose	Sucrose
	Corn syrup	Corn syrup	Glucose	Glucose	Corn syrup	Maltodextrin
% total cal	55%	50%	91%	84%	53%	50%
<b>Fat</b>						
Source		Soy				
	Corn oil	MCT oil	Safflower oil	Safflower oil	Corn oil	Soy oil
% total cal	32%	37%	1%	1%	32%	36%
<b>Protein</b>						
Source	Casein	Casein			Casein	Casein
	Soy	Soy	Amino acids	Amino acids	Soy	Soy
% total cal	14%	13%	8%	15%	15%	14%
Kcal/ml	1.0	1.0	1.0	1.0	1.5	2.0
Cal/N ratio	175:1	195:1	300:1	150:1	167:1	178:1
Na (mEq/L)	32	22	37	33	46	43
Osmolality (mOsm/kg)	460	300	550	800	600	590
Cost /1,000 cal	\$2.05	\$2.42	\$5.20	\$9.97	\$1.57	\$2.20

Laboratories, Irvine, CA) is designed for patients in renal failure and contains essential amino acids, 1.9 Kcal/ml, and *no* electrolytes or vitamins. Hepatic-Aid (McGaw Laboratories, Irvine, CA) is formulated for patients who have severe liver disease. It is rich in branch-chain amino acids and low in aromatic amino acids which may correct the abnormal plasma amino acid pattern commonly seen in patients with liver disease and allow more protein to be administered without exacerbating hepatic failure. Hepatic-Aid provides 1.6 Kcal/ml and has a low electrolyte content. Both of these formulas are expensive, hypertonic, and nutritionally imbalanced. They are totally inappropriate for routine use and should be given only to selected and carefully monitored patients.

Patients who have deranged bowel function because of intrinsic gastrointestinal disease or the effects of systemic illness often will not tolerate large volumes of full-strength formula at the outset, particularly when hypertonic solutions are used. Feedings should start with small volumes of dilute solution. We usually begin with one-quarter or less of the desired hourly volume and dilute the formula to about 150 mOsm/kg (i.e., half-strength or one-quarter strength, depending on the osmolality of the formula). It is generally best to advance feedings by small, frequent (every four to eight hours) increments rather than by larger increases less frequently. We usually increase concentration in increments of one-eighth or one-fourth strength (75–150 mOsm/L) and volume by 20–25 percent of the final desired amount. If gastric retention or diarrhea occurs, we reduce volume and/or concentration by one or two steps and advance more slowly. Most patients can progress to full feeding in 48–72 hours, though some individuals never tolerate the full-strength solution. If fluid tolerance is not a problem, larger volumes of three-fourths or even seven-eighths strength formulas may be given to achieve adequate nutrient intake.

### *Parenteral Nutrition*

The three major classes of nutrients (protein, carbohydrate, and fat) are available as intravenous solutions and can be administered in various combinations to provide adequate nutrition to patients who cannot tolerate enteral feeding. The original intravenous protein solutions were hydrolysates of casein or fibrin. Casein hydrolysates are still available and are effective and relatively inexpensive. However, the newer crystalline amino acid solutions provide a more balanced and appropriate mixture of amino acids and, at least theoretically, have higher biologic availability. Crystalline amino acid solutions are supplied in concentrations of 5–10 percent and can be mixed with glucose, minerals, and vitamins. Glucose is the preferred carbohydrate source because of ready availability, low cost, and the fact that most other carbohydrates must be converted to glucose before they can be metabolized. Alcohol has been used effectively and provides more calories (7 Kcal/g) than glucose (4 Kcal/g) but has potentially toxic effects on the liver and central nervous system.

Intravenous fat emulsions are prepared from soybean or safflower oil, stabilized with egg phosphatides, and made isotonic with glycerol. The 10 percent solutions provide 1.1 kilocalories per ml. Both solutions are safe and effective and are rich in linoleic acid, the primary essential fatty acid. The size of the fat particles is similar to normal chylomicrons and the emulsions are quite stable. They cannot, however, be mixed with other nutrients since this would destroy the emulsion.

*Peripheral Vein Nutrition* Amino acids, glucose, electrolytes, vitamins, and minerals can be combined in appropriate quantities and infused into a peripheral vein so long as the total osmolality of the solution does not exceed the tolerance of

TABLE 5  
Caloric Density of Parenteral Nutrition Solutions

Glucose concentration	5%	10%	12.5%
Protein concentration	4%	3%	2%
Caloric density (Kcal/ml) (approximate)	0.33	0.45	0.5
Osmolality (mOsm/kg) (including electrolytes)	800	914	903

the vein (usually about 1,000 mOsm/Kg). Since glucose is particularly irritating to veins and likely to cause thrombophlebitis, its contribution to osmolality is most important. Neonates often tolerate glucose concentration as high as 12.5 percent, while the limit is usually 10 percent in children and 5 percent in adults. The caloric density of these solutions is shown in Table 5. It can be seen that adequate calorie intake cannot be achieved by infusing these solutions at conventional rates. For example, a neonate who receives 100 ml/kg/day of the 12.5 percent dextrose-2 percent protein solution will get only 60 Kcal/kg/day, and an adult receiving 3 liters of the 5 percent dextrose-4 percent protein solution will get only 1,000 Kcal/day. High-volume infusion (twice the maintenance rate or more) of these dilute solutions occasionally may be successful [37], but most patients who are given this volume eventually develop fluid overload and electrolyte derangement.

Fat emulsions are isotonic, non-irritating to veins, and have a caloric density of 1.1 Kcal/ml (2.0 Kcal/ml for 20 percent solutions). By adding the maximal allowable amount of fat (Table 6) to the peripheral infusion regimen, it is possible to achieve adequate caloric intake in a reasonable volume of fluid. Table 7 gives several examples of peripheral parenteral nutrition regimens. It can be seen that infusion at rates which provide maintenance fluid needs yields an inadequate intake of calories and protein and that fat contributes an inordinately high proportion of the total calories. Infusion at 1½ times the maintenance rate, which most patients will tolerate, provides adequate nutrients and a better balance of fat and carbohydrate calories.

The protein-glucose solution and the fat emulsion ideally should be administered into separate peripheral veins. This is often impractical in children and it is acceptable to "piggyback" the fat emulsion into the tubing from the protein-glucose solution. The Y-connection between the two should be close to the site of venipuncture to minimize mixing. It is also essential to administer both solutions by continuous infusion pumps to prevent back-up of one solution into the other. There is continuing controversy about the relative merits of steel "butterfly" needles and plastic catheters for peripheral total parenteral nutrition (TPN). Plastic cannulas tend to remain in place longer but in our experience cause a higher incidence of throm-

TABLE 6  
Daily Allowance of Fat Emulsions

	Fat (g/kg/day)	10% Emulsion (ml/kg/day)	20% Emulsion (ml/kg/day)
Infant	4	40	20
Child	3	30	15
Adult	2	20	10

TABLE 7  
Sample Peripheral Parenteral Nutrition Regimens

Infant			
	Volume (ml/kg/day)	Amount (g/kg/day)	Calories (Kcal/kg/day)
D 12.5 P2	60	1.2 (protein)	5
		7.5 (carbohydrate)	25
10% fat emulsion	40	4.0 (fat)	44
Maintenance rate	100		74
D 12.5 P2	110	2.2 (protein)	9
		13.8 (carbohydrate)	47
10% fat emulsion	40	4.0 (fat)	44
1.5 × maintenance	150		100
30 kg Child			
	Volume (ml/day)	Amount (g/day)	Calories (Kcal/day)
D 10 P3	800	24 (protein)	96
		80 (carbohydrate)	272
10% fat emulsion	900	90 (fat)	990
Maintenance rate	1,700		1,358
D 10 P3	1,600	48 (protein)	192
		160 (carbohydrate)	544
10% fat emulsion	900	90 (fat)	990
1.5 × maintenance	2,500		1,726

Hydrous glucose provides 3.4 Kcal/g.

bophlebitis. More important, the venipuncture site should be examined regularly and changed at least every 48 hours since even occult thrombophlebitis can lead to bacteremia and systemic sepsis. The use of peripheral vein "cutdowns" for total parenteral nutrition is discouraged since occult thrombophlebitis is a real risk with long-indwelling peripheral intravenous catheters and it is prohibitive to perform a new cutdown every 48 hours. If peripheral venipuncture sites are no longer available, a central venous catheter should be placed.

*Central Vein Nutrition* In 1967, Dudrick et al. reported the successful long-term infusion of hypertonic glucose into the superior vena cava (SVC) [38]. The high-volume blood flow in the SVC dilutes the glucose and protects the vein from phlebothrombosis and thrombophlebitis. Most central TPN solutions contain 20 percent to 25 percent glucose and provide about 1 Kcal/ml; solutions providing up to 2 Kcal/ml can be used in patients who require severe fluid restriction.

The principles for placement and care of the central venous catheter which Dudrick et al. [39] outlined in their original report have proved to be sound and essential to safe long-term catheterization [40]. Placement of the catheter must be by meticulous aseptic technique. The operator wears cap, mask, sterile gown, and gloves. The catheterization site is scrubbed as for a surgical procedure and draped carefully. Adequate lighting and instruments are essential. If these criteria cannot be met at the bedside or in the treatment room, the procedure should be performed in the operating room. Infants should be restrained in the proper position. Frightened

children may need to be sedated. Under no circumstances should the procedure be attempted in uncooperative, combative children because the risks of complications and contamination are too high. Safe catheterization may on rare occasions require the use of general anesthesia.

The author believes that silicone rubber is the material of choice for central TPN catheters. There have been no prospective studies comparing different catheter materials, but silicone rubber is less thrombogenic than polyethylene, polyvinylchloride, or Teflon and does not stiffen at body temperature [41,42]. Its pliability also favors its being flow-directed into the SVC rather than passing into an internal jugular or subclavian vein.

Percutaneous catheterization of a subclavian vein is the preferred method for placing a central TPN catheter in adults and older children. There have been several reports of subclavian catheterization in neonates [43,44,45] but this should not be attempted until the operator has abundant experience with larger patients. The technique in children is essentially the same as in adults. The neck and shoulders are extended by placing a small towel between the scapulae and the head is turned to the opposite side. The patient is placed in the Trendelenberg position to distend the vein and to decrease the risk of an air embolus. The skin and subcutaneous tissue are infiltrated with 1 percent lidocaine. In children over the age of three years a kit containing a 14 g introducer (Teflon catheter with internal needle) and 16 g silicone rubber catheter is quite satisfactory (Centrasil, Travenol Laboratories, Deerfield, IL). The skin is punctured a bit lateral to the midpoint of the clavicle and 1 cm below it. The needle is directed toward a point just above the sternal notch and is carefully passed between the clavicle and first rib to enter the vein. When blood can be aspirated freely, the Teflon catheter is advanced into the vein, the needle is withdrawn, and the silicone rubber catheter is passed through the introducer. Once the silicone catheter tip is in the vein, the metal stylet is slowly withdrawn as the catheter is advanced. The floppy tip of the catheter will thus be flow-directed into the SVC. The correct distance to advance the catheter should be estimated ahead of time. The ideal position for the catheter tip is at the junction of the SVC and right atrium, which is about halfway between the sternal notch and the xyphoid. The catheter is placed on the sterile drapes with its tip at this point and the correct distance to the skin puncture site is marked. When the catheter has been advanced to this length, the Teflon introducer is withdrawn. Adequate fixation of the catheter is essential to prevent accidental dislodgement and especially to minimize to-and-fro motion of the catheter at the entry site, since this causes skin irritation and encourages local staphylococcal infection which may colonize the catheter. The catheter is secured with tape (either cloth tape which has been gas-sterilized or the tape which is included in commercial dressing change kits). The skin below the entry site is painted with benzoin. Several one-inch strips of tape are placed directly on the skin. The catheter is placed over this tape and secured to it with several additional pieces of tape. This tape-to-tape method is more reliable than suturing. An antiseptic ointment is applied to the exit site and a large occlusive dressing is placed.

In neonates and infants a jugular vein is cannulated by cutdown. The neck is extended and the head is turned to the opposite side. A skin crease incision is made over the sternocleidomastoid muscle halfway between the sternal notch and the mastoid process. The external jugular vein is readily identified in the subcutaneous tissue and can often be cannulated. Frequently, however, the catheter will not advance around the acute angle between the external jugular vein and the subclavian vein. In that case the cervical fascia is incised and the anterior border of the ster-

nucleidomastoid muscle is retracted laterally. The internal jugular vein is deep to the anterior border of the muscle at this point and can be isolated by careful blunt dissection and controlled by looping it with silk threads. The common facial vein can usually be identified and isolated where it enters the jugular vein superomedially. The facial vein can be cannulated in all except the smallest premature infants, thus eliminating the need to ligate the internal jugular vein. After the catheter has been advanced the previously determined correct distance, the vein is tied gently around it. The free end of the catheter is tunneled subcutaneously for several centimeters so that the skin exit site is well removed from the venotomy. The skin is closed with absorbable subcuticular sutures, and the catheter is taped and dressed as above.

A solution of 5 percent or 10 percent dextrose in water is connected to the catheter hub and all joints are secured with tape. A portable chest X-ray is obtained to ascertain the position of the catheter tip. If it is too far in (right atrium or beyond) it can be withdrawn the appropriate distance (using the same meticulous sterile technique), retaped, and redressed. If the catheter is not far enough in or has been directed into a jugular or subclavian vein, it must be removed and a new catheter placed on the opposite side. If the catheter has been placed by cutdown, a fresh catheter can usually be placed through the same venotomy. Under no circumstances should a catheter be left in the wrong position since the incidence of venous thrombosis, thrombophlebitis, and sepsis is unacceptably high. Once the proper catheter position has been documented, infusion of the nutrient solution may begin.

Proper catheter care is equally important to minimize complications. The "lifeline" should be a closed sterile system at all times. Piggy-backed solutions, Y-connectors, and three-way stopcocks are not allowed. The intravenous tubing is changed once a day after soaking its junction with the catheter hub with povidone-iodine solution. The line is not entered for any other reason and should not be used to draw blood, administer medications, or measure central venous pressures. The dressing is changed three times a week by nurses trained in the correct technique. Masks are worn by all persons in the room. The old dressing is removed; then sterile gloves are worn for the rest of the procedure. The skin and catheter are cleaned with alcohol and then painted with povidone-iodine solutions. Povidone-iodine ointment is applied, and a new occlusive dressing is placed. If the catheter exit site must be inspected at other times, the same technique is used. If it is necessary to irrigate the catheter, the operator should wear mask and gloves and soak the tubing catheter joint with povidone-iodine solution before disconnecting. The catheter is gently irrigated, taking care to protect the sterility of both the tip of the intravenous tubing and the inside of the catheter hub.

*Central Vs Peripheral TPN* The choice between central and peripheral TPN is often difficult and must be made on an individual basis. Several general principles can be applied:

1. Peripheral TPN is safer than central TPN since catheter complications are avoided and sepsis is less common. However, thrombophlebitis and sepsis do occur with peripheral TPN. Failure to give adequate nutrition by the peripheral route can also lead to serious complications.

2. The difficulties in achieving adequate caloric intake by the peripheral route have already been mentioned. Thrombophlebitis and infiltration require frequent restarting of intravenous lines, sometimes two or three times a day in infants. Intravenous sites become harder to find. The intravenous line is often used to ad-

minister medication, which requires interrupting the nutrient infusion for 20–30 minutes several times a day. Large fluid volumes are necessary to achieve adequate caloric intake. Faubion et al. reported that actual caloric intake was only 89 percent of calories ordered, and that the amount of calories ordered was usually inadequate [46]. Only 30 percent of the infants in their study received adequate nutrition, as judged by weight gain. If the peripheral route is chosen, it is essential to (a) order maximum doses of fat emulsion, (b) give as much volume as the patient will tolerate, and (c) calculate *actual* caloric intake daily to assure that intake is adequate.

3. Central TPN catheters should not usually be placed in patients who have other indwelling central lines. Central venous pressure and Swan-Ganz catheters are not placed and maintained with the strict aseptic technique required for TPN catheters and are more likely to cause sepsis which may seed the TPN catheter. Peripheral TPN is used in these patients until the other catheters can be removed. Nutrition is of secondary importance during the first five to seven days following major illness or surgery, which is the period when intensive monitoring is most essential.

Thus, peripheral TPN is safer and central TPN is more reliable. In general, the central route should be selected for patients who (a) will not tolerate large fluid loads (cardiac failure, renal failure, and the like), (b) are expected to require long-term TPN (more than two weeks), (c) have limited sites for peripheral intravenous lines, or (d) have caloric requirements substantially higher than maintenance needs, either because of hypermetabolic states or established malnutrition. The peripheral route is more likely to be adequate if TPN is initiated early before malnutrition has developed. Peripheral TPN is adequate for about 75 percent of infants and children who require total nutritional support. Peripheral TPN is somewhat more expensive than central TPN because of the high cost of fat emulsions.

**TPN Solutions** Since fluid, electrolyte, and nutrient requirements vary with age, it is necessary to tailor TPN solutions to different age groups. Three standard solutions are suitable for most patients—one for infants (to about 10 kg), one for children (10–40 kg), and one for adolescents (and adults). The composition of these solutions is shown in Tables 8 to 10. The concentration of any constituent can be changed to meet individual needs. For peripheral TPN the glucose concentration is reduced to 5 percent, 10 percent, or 12.5 percent by substituting sterile water for a portion of the 50 percent glucose. The calcium concentration is reduced in peripheral TPN solutions since calcium is especially likely to cause skin sloughs.

The solutions are prepared in the pharmacy under a laminar flow hood, using meticulous sterile technique. The rapid growth of bacteria and especially fungi in the TPN solutions at room temperature has been well documented [47,48]. The incidence of *Candida* sepsis complicating TPN in the early 1960s was a direct consequence of careless admixture and has been largely eliminated by central preparation of solutions.

### *Administration*

**Rate of Infusion** The formula for estimating energy requirements has been given in Table 2. From this formula and the caloric content of the solution being used, the appropriate infusion rate can be calculated. Ongoing fluid losses (e.g., nasogastric tube drainage) are replaced with appropriate solutions, *not* by increasing the rate of the nutrient mixture. The TPN solution is administered by a constant infusion pump to assure a steady flow of nutrients and, with central catheters, to prevent backup and clotting of blood in the catheter. An occluded catheter must be irrigated—which

TABLE 8  
TPN Solution for Infants

	Concentration per Liter
Calories	760
Protein equivalent (Travasol)	19.6 g (2%)
Dextrose	200 g (20%)
Na <sup>+</sup>	25 mEq
K <sup>+</sup>	24 mEq
Cl <sup>-</sup>	35 mEq
Ca <sup>++</sup>	11.3 mEq
Mg <sup>++</sup>	4.8 mEq
P	7.8 mM
Lactate	10 mEq
Acetate	12 mEq
Zn	2.2 mg
Cu	150 µg
Mn	110 µg
Cr	1.5 µg
I	37 µg
Vitamins A	5,000 u
D	500 u
E	2.5 u
K	0.2 mg
Folate	0.25 mg

At a rate of 150 ml/kg/day, this solution provides  
114 Kcal and 2.6 g protein per kg per day.

TABLE 9  
TPN Solution for Children  
(10–40 kg)

	Concentration per Liter
Calories	940
Protein equivalent (Travasol)	30 g (3%)
Dextrose	250 g (25%)
Na <sup>+</sup>	35 mEq
K <sup>+</sup>	36 mEq
Cl <sup>-</sup>	62 mEq
Ca <sup>++</sup>	8 mEq
Mg <sup>++</sup>	4 mEq
P	7.8 mM
Lactate	10 mEq
Acetate	18.7 mEq
Zn	3 mg
Cu	200 µg
Mn	150 µg
Cr	2 µg
I	50 µg
Vitamins A	3,000 u
D	300 u
E	1.5 u
K	0.2 mg
Folate	.25 mg



TABLE 10  
TPN Solution for Adolescents and Adults

	Concentration per Liter
Calories	1,020
Protein equivalent (Travasol)	39 g
Dextrose	250 g
Na <sup>+</sup>	35 mEq
K <sup>+</sup>	30 mEq
Cl <sup>-</sup>	35 mEq
Ca <sup>++</sup>	4.6 mEq
Mg <sup>++</sup>	5.0
P	15 mM
Acetate	68 mEq

The following vitamins are added to *one liter* per day:

MVI concentrate* (A,B,C,D,E)	2.5 ml
Vitamin K	1 mg
Folic acid	5 mg

*Upon request*, the trace element mixture (Zn, Cu, Mn, Cr, I) will be added to *one liter* per day.

\*MVI: USV Pharmaceutical Corp., Tuckahoe, NY

increases the risk of sepsis—or replaced. *Sudden cessation of 25 percent glucose infusion because of catheter occlusion may lead to profound hypoglycemia and seizures.*

**Glucose** Most patients will not tolerate large volumes of 20–25 percent glucose initially. The central venous catheter is often the only intravenous line in children and must therefore be used to provide maintenance fluid requirements. Treatment is started with a TPN solution containing 10 percent glucose and advanced by 5 percent increments daily, provided there is no glycosuria.

**Fat** There is no particular advantage to the routine use of fat as a calorie source in patients receiving central TPN since 20–25 percent glucose solutions have approximately the same caloric content as 10 percent fat emulsions. Fat emulsions are not administered via the central catheter since that would require either piggy-backing or interruption of the glucose infusion, neither of which is desirable.

However, biochemical evidence of essential fatty acid deficiency develops within one week of fat-free TPN in infants and children. This can be prevented by giving 2 percent of total calories as linoleic acid [49]. Soybean oil emulsions contain 50 percent linoleic acid. Infusion of the maximum daily dose of soybean oil emulsion (Table 6) by peripheral vein once or twice a week is adequate to prevent essential fatty acid deficiency. Safflower oil contains 75 percent linoleic acid so somewhat smaller quantities are adequate.

**Iron** Iron is not routinely added to TPN solutions because of the risk of anaphylactic reactions to intravenous iron. Bleeding, blood sampling, and illness all contribute to the rapid development of iron deficiency anemia. Periodic blood transfusions or intramuscular iron therapy may be necessary.

### Monitoring

Careful monitoring is essential to the safe use of TPN. Observation of the patient is most important—hourly by the nursing staff and at least three times a day by a physician. General appearance, level of activity, sense of well-being, and skin turgor are noted. Vital signs are recorded at least every four hours. Intake and output are measured and urine specific gravity and glucose content are determined every four to eight hours. Daily weights are obtained. Length and head circumference of infants are measured once a week.

The frequency of laboratory tests throughout the course of treatment is determined by the occurrence of specific abnormalities and complications. More frequent determinations should be made during the initial stabilization period and the interval between tests increased if no problems arise. A suggested protocol for laboratory monitoring is shown in Table 11. The laboratory should be equipped for microchemical analysis to minimize iatrogenic blood loss. Blood cultures are obtained if the patient develops fever, appears clinically septic, or has unexplained glycosuria.

### COMPLICATIONS

Complications of nutritional support fall into five general categories related to: (1) enteral feeding tubes, (2) enteral formulas, (3) central venous catheters, (4) sepsis, and (5) metabolic problems.

Complications of *indwelling nasogastric feeding tubes* include incorrect placement (e.g., trachea, esophagus), nasal erosion, gastroesophageal reflux, esophagitis, and aspiration. These can be eliminated for the most part by careful placement of the smallest possible tube.

The major *untoward effects of enteral formulas* are gastric retention and diarrhea. Gastric retention is often a result of feeding too much too fast. A reduction in volume or concentration of formula and then a more gradual increase may resolve the problem. The secondary consequences of gastric retention (vomiting and aspiration) can be avoided by frequent measurement of gastric residual.

Diarrhea may be the result either of malabsorption or osmotic overload. It is often difficult to determine which of these is at fault and the treatment is exactly opposite. Elemental and semi-elemental diets are hypertonic and cause diarrhea when

TABLE 11  
Laboratory Monitoring During TPN

Hematocrit, hemoglobin	Daily for four days
BUN, glucose	then
Electrolytes	Two times/week
Bilirubin, SGOT, NH <sub>3</sub>	
Alkaline phosphatase	
5' nucleotidase	Once/week
Ca, Mg, P,	
Total protein, albumin	Once/week
Patients receiving fat emulsion:	
Serum fat emulsion level	Daily
Cholesterol, triglyceride	Once/week

fluid enters the gut to reduce intraluminal osmolality. A more complex, less hypertonic formula is indicated.

Malabsorption is usually an indication to try a more elemental diet. Stool pH < 5 and/or a positive test for reducing substances in the stool suggest carbohydrate malabsorption (note that sucrose is not a reducing sugar, however). There is no simple test for fat malabsorption, yet fat is probably the most common culprit in malabsorption diarrhea. A 72-hour stool fat content of more than 10 percent of ingested fat is diagnostic of fat malabsorption and dictates changing to a formula which contains medium chain triglyceride oil or no fat at all. Watery green stools suggest bile acid diarrhea due to incomplete reabsorption of bile salts and may respond to treatment with cholestyramine or bismuth subsalicylate (Pepto-Bismol) (Eaton Laboratories, Norwich, NY). From a practical standpoint, the trial-and-error method is often the only way to determine the best formula. In general, we find that most patients do well with the fairly complex, nearly isotonic formulas and that the elemental diets should be reserved for patients who clearly have malabsorption.

Finally, both gastric retention and diarrhea of whatever cause may mean that the gut is unable to tolerate any enteral feeding. In that case, parenteral nutrition is indicated.

*Complications Related to the Central Venous Catheter* Pneumothorax, hydrothorax, arterial puncture, and hemorrhage usually occur as a result of over-zealous attempts to cannulate the subclavian vein. If the catheter will not pass after three or four attempts, it is wise to start over on the opposite side. Cardiac arrhythmias and perforation of the heart can be prevented by not allowing the catheter tip to enter the right atrium. Leakage of fluid from the venipuncture site in the subclavian or jugular vein may cause an apical pleural effusion or an accumulation of fluid in the interstitial spaces of the lung, which we identified with six of 82 catheters in infants [50]. Periodic chest X-rays are obtained to look for these complications, which usually resolve if the catheter is removed promptly.

Venous thrombosis is the most common complication of central catheters in children in our experience (18 of 82 catheters) [50]. Phlebothrombosis is more common in young children than in adults because of the relatively small size of the central veins. It is manifested by edema of the head, neck, and shoulder of the cannulated side. The thrombosis usually resolves and the vein recanalizes if the catheter is removed. Permanent caval thrombosis is less common (four of 82 catheters) but may be a contributing factor in the development of hydrocephalus [50,51].

The risk of catheter complications can be minimized by proper positioning. In our study in infants, complications of a minor and transient nature occurred with 22 percent of catheters which were correctly positioned in the SVC. Seventy percent of catheters whose tips were in a tributary vein or the right atrium caused complications. All of the serious complications (pleural effusion, permanent caval thrombosis, arrhythmias) were in this group [50].

*Sepsis* is the most feared complication of TPN. In the late 1960s catheter sepsis rates as high as 40–50 percent were reported [52,53,54]. Over 50 percent of the infections were fungal, mostly *Candida albicans*, a ubiquitous organism which grows rapidly in TPN solutions. After central aseptic preparation of solutions became standard practice, the incidence of contaminated bottles became negligible, and sepsis rates declined dramatically to about 10 percent in most institutions. Large hospitals with extensive experience and TPN teams which assure adherence to rigid protocols have reported catheter sepsis rates as low as 2–3 percent [55].

Catheter sepsis is defined as blood and catheter tip cultures positive for the same

organism or fever for which no other cause can be found and which resolves when the catheter is removed. Infection which originates from the catheter is usually the result of a break in technique or local skin irritation at the skin entry site. *Staphylococcus epidermidis* is the most common organism. Strict adherence to the principles of catheter placement and care outlined above will reduce the likelihood of sepsis from this source. A more common cause of sepsis in TPN patients is bacteremia from some other focus of infection which may secondarily seed the catheter. The only way to rule out catheter sepsis is to remove the catheter and culture its tip. In our experience [unpublished data], the catheter tip is sterile in almost half of these cases and the catheter is not involved in the septic process. Gram-negative organisms predominate. While this type of catheter sepsis cannot be prevented, early removal of the catheter is essential to prevent further dissemination of infection.

Patients who have central TPN catheters in place and develop fever are examined carefully for possible sources of infection, and blood cultures are obtained. Foci of infection are treated appropriately with antibiotics and drainage. The catheter is removed and cultured if the blood culture is positive, if the patient has clinical signs of overwhelming sepsis, or if there is persistent (longer than 24 hours) unexplained fever. This policy eliminates the need to remove catheters for every febrile episode but assures prompt removal of infected catheters.

The cornerstone of treating catheter sepsis is removal of the catheter, since sepsis will not resolve with an infected foreign body in the bloodstream. Conversely, removal of the catheter is usually sufficient treatment. Antibiotics are not indicated unless there is evidence of invasive sepsis or continuing bacteremia. It is preferable to wait until blood cultures have been negative for 48 hours before placing another catheter, although in patients who have no other venous access, a new catheter may have to be inserted immediately.

While sepsis is primarily a complication of central catheters, thrombophlebitis and bacteremia may also occur with peripheral TPN. We have seen three cases of clinical sepsis in which the same organism was recovered from the blood and the peripheral intravenous catheter.

We have recently reviewed our experience with the *metabolic* complications of TPN in infants and children [56]. Only the most common will be discussed here. Most of the metabolic problems can be prevented by careful technique and monitoring. Early detection and correction of metabolic abnormalities avoids the need for heroic treatment of major derangements.

Glucose intolerance is uncommon except in diabetics, premature infants, or children who are extremely ill and have high circulating concentrations of the stress hormones. Slight glycosuria (trace to 1+) is common and does not cause an osmotic diuresis. A greater degree of glucose spillage calls for a reduction in the rate of glucose administration and then a more gradual increase. If glycosuria persists, 10 units of regular insulin are added to each 1,000 ml of TPN solution. Further adjustments of insulin dosage are made on the basis of blood glucose determinations and the degree of glycosuria.

Fluid overload, manifested by edema, hyponatremia, and congestive heart failure is also most common in premature infants and severely stressed children. Fluid restriction is safer and more effective treatment than administration of diuretics. Glucose *concentration* can be increased to maintain caloric intake, unless the patient is also glucose-intolerant which, unfortunately, is often the case.

Abnormalities of sodium, potassium, and chloride are usually related to the underlying disease and can be corrected by appropriate adjustments in the TPN solution. Patients who are malnourished often develop significant hypomagnesemia and hypophosphatemia when central TPN is initiated and they become anabolic. It may be necessary to double the amount of these elements in the TPN solution.

Deficiency of the most common trace metals should be preventable by including adequate quantities in the TPN solution. The clinical manifestations of deficiency of other trace minerals and human requirements for them will undoubtedly be defined in time. Vitamin deficiency has not been a significant problem.

Elevation of the blood ammonia concentration, usually mild, occurs in 70 percent of infants and children who receive TPN [57]. The cause is unknown but it does appear to be dose-related. The significance of hyperammonemia, which is usually asymptomatic, is also unknown. Blood ammonia concentrations up to 250  $\mu\text{g}/\text{dl}$  (normal 150  $\mu\text{g}/\text{dl}$ ) are probably acceptable; at higher levels, protein intake is reduced. Abnormalities of liver function are also common in patients who are receiving TPN. Cholestatic jaundice occurs in 20–30 percent of premature and full-term infants [58] and occasionally occurs in older children and adults. Mild elevations of the transaminases are common in older patients. The cause of these abnormalities is unknown, though duration of TPN appears to be important. The abnormalities occasionally resolve without any change in therapy and may improve if protein intake is reduced or the balance of fat and carbohydrate calories is changed. Recent studies suggest that this complication may be related to excessive glucose infusion and may be alleviated by giving a portion of the calories as fat emulsion [59]. The only consistently effective treatment is discontinuation of TPN and resumption of oral feeding.

Fat emulsions are generally safe in recommended doses. Premature infants and very sick children may not clear the emulsion from the serum efficiently. A high serum concentration leads to destabilization of the emulsion, coalescence into larger fat globules, and fat embolization. The fat overload syndrome is characterized by fever, headache, myalgia, thrombocytopenia, pulmonary and hepatic failure, and, in extreme cases, death. Visual inspection of the serum for turbidity is of limited value; serum concentration of fat emulsion, as determined by nephelometry, is more reliable. A serum concentration of less than 150  $\mu\text{g}/\text{dl}$  is safe.

Even if the fat emulsion is cleared from the serum, the free fatty acids and triglycerides which result from cleavage of the fat may not be metabolized, particularly in hypoxic patients. A high plasma concentration of free fatty acids may interfere with bilirubin binding by albumin and impair pulmonary diffusion. Therefore it is important to monitor the metabolites of fat emulsions. Serum triglyceride concentration, which is readily available in most laboratories, correlates well with free fatty acid concentration, and should be measured regularly.

## SUMMARY

The onset of malnutrition can be both rapid and insidious in patients in the intensive care unit. Young children and children who have major trauma or sepsis are at particular risk for malnutrition. Treatment of the primary disease is of paramount importance initially, but provision of adequate nutrition is an essential goal after the first five to seven days of hospitalization.

There are many potential complications of nutritional support, some of which may be life-threatening, but they are well known and can usually be prevented or

mitigated by careful monitoring. On the other hand, complications of malnutrition may be more subtle and harder to document, but it is likely that poor nutrition contributes substantially to morbidity and mortality, particularly in patients who are hospitalized for more than two weeks.

At least half of all patients who need nutritional support can be managed by the enteral route which is cheaper, safer, and probably more effective than parenteral feeding. Peripheral parenteral nutrition, using fat as a major calorie source, is adequate to *maintain* nutrition in patients who are not hypermetabolic. Patients who are already malnourished or who require more than maintenance calories should have a central catheter placed.

Understanding, experience, and meticulous attention to detail are essential to achieve safe, effective, and appropriate nutritional support. A nutrition team should have overall responsibility for the nutrition program and should be available for advice and consultation for individual patients.

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