Review article

Intensive Care Medicine

Intensive Care Med (1993) 19:129–136

A sensible approach to the nutritional support of mechanically ventilated critically ill patients

J. W. Christman and R. W. McCain

Department of Veterans Affairs and Department of Medicine, Vanderbilt University, Nashville, Tennessee, USA

Received: 3 February 1992; accepted: 6 November 1992

Abstract. *Objectives:* The goal of this review is to educate physicians in the details of nutritional support of mechanically ventilated critically ill patients.
Design: The subtopics of this review include: introduction, goals of nutritional treatment, assessment of nutritional status, estimation of nutritional requirements, estimation of protein requirements, recommended approach to the initial nutritional regimen, route of nutrition, and monitoring the response to nutrition.
Setting: The information is primarily germane to the medical management of patients with acute respiratory failure superimposed on chronic lung disease and malnutrition.
Conclusion: Malnutrition is prevalent in mechanically ventilated critically ill patients. Undernutrition is associated with respiratory muscle weakness and may contribute to ventilator dependency. Overnutrition may increase CO_2 production and increase ventilatory demands. This review advocates a titrated approach to nutritional management based on protein balance. Careful monitoring is necessary to ensure a regimen which maintains or improves body protein composition. Preliminary data exists which indicates that careful nutritional support may improve clinical outcome but more information is needed to recommend a universal approach.

Key words: Nutrition – Lung – Mechanical ventilation

Nutritional management is an essential element in the supportive care of critically ill patients. A conservative estimate is that 30%–50% of hospitalized individuals have clinical evidence of malnutrition [1–5] and preliminary evidence indicates a relationship between initial nutritional status and in-hospital mortality [6]. Physiologic stress is associated with elevated serum concentrations of catecholamines and corticosteroids which have profound effects on metabolism. Gram-negative bacteremia, which is prevalent in mechanically ventilated patients, is associated with the appearance of tumor necrosis factor, interleukin-1, and interleukin 6 in the peripheral circulation [7]. These cytokines are thought to mediate the effects of endotoxemia including effects on protein metabolism, nitrogen balance and the development of a nutritionally depleted state [8–13]. Undernutrition is associated with decreased muscle function which may lead to respiratory muscle weakness and ventilator dependency. Overnutrition is associated with increased carbon dioxide production which increases the amount of ventilation necessary to maintain steady state arterial blood gases [14]. Several studies have shown that nutritional intervention appears to improve the success in weaning from mechanical ventilation [15–18], yet to our knowledge there are no prospective studies confirming this observation. If this finding proves to be true and can be generalized to other types of critical illnesses, then aggressive nutritional management may lead to improved outcome for patients admitted to the critical care unit. Critically ill patients are typically dependent on doctors to provide most or all of their basic nutrients. The ability of physicians to empirically determine nutritional requirements has recently been questioned [19–23]. At least one study has shown that iatrogenic perpetuation of malnutrition in the critical care setting occurs with a surprising frequency [24].

Many hospitals have developed an integrated approach to nutritional management that combines the input of a nutritional team with that of the primary care doctors and nurses to assess a patients nutritional status and recommend appropriate supplementation. The use of indirect calorimetry in the clinically setting can provide further insight into the nutritional needs of critically ill patients and in many cases is used to guide nutritional management. The precise information provided by indirect calorimetry may lead to improved patient survival but confirmative clinical data is not yet available. This article will review the basic principles of nutritional management which pertain to mechanically ventilated critically ill patients. Simple schemes for estimating the initial nutritional status and requirements of patients will be discussed and methods for evaluating the clinical response to nutritional support will be proposed. The current scientific data which supports careful nutritional

therapy in the critical care setting will be provided when available.

Goals of nutritional treatment

Mechanical ventilation is typically applied to patients as a supportive treatment modality for acute respiratory failure with hypercarbia, hypoxemia, or both. The first goal of nutritional treatment is to prevent or minimize the loss of respiratory muscle mass and function while specific therapy is directed at improving the underlying pulmonary pathology. Nutritional treatment must incorporate an understanding of basal nutritional requirements and the effects of acute respiratory failure with mechanical ventilation on energy requirements. A patient can only be weaned from mechanical ventilation when adequate oxygenation is coupled with a sustainable respiratory workload. The respiratory workload is determined by the elastic properties of the thorax and lungs and the resistive properties of the airways. The maintenance of steady state arterial blood CO_2 levels is dependent on the rate of production and efficiency of elimination. CO_2 production is increased in agitated, tachypneic, febrile patients who are being overfed with a diet based on carbohydrates. The efficiency of CO_2 elimination is decreased when the lung pathophysiology results in perfusion which is relatively decreased compared to ventilation. The ability of respiratory muscles to perform the necessary work of breathing is determined by respiratory muscle mass and function. Maintenance of respiratory mass and function should result in earlier weaning for the same degree of lung disease.

Patients typically present with respiratory failure in conjunction with malnutrition and may have various degrees of underlying chronic lung pathology. The goal of nutritional treatment in these patients is to increase or improve respiratory muscle mass and function. This process is more difficult and requires more time. Inadequate nutrition may prolong mechanical ventilation by failing to restore respiratory muscle strength and endurance while excessive nutrition may also prolong mechanical ventilation by increasing CO_2 production and the necessary work of breathing to maintain a steady state of CO_2 in arterial blood.

Assessment of nutritional status

A perceptive history and physical examination remains the mainstay of nutritional assessment (Table 1). The loss of body weight is a major sign of malnutrition. Recent loss of more than 10% of the usual body weight (10–20 pounds) is the most important finding and reflects severe malnutrition. Loss of 25%–50% of body mass in a non-obese patient is life threatening. Yet, a reliable weight history is often difficult to obtain in acutely ill patients and the effect of malnutrition on body weight may be masked by fluid retention in patients with chronic heart, lung, renal, and/or liver disease. Further, in an affluent society, carbohydrate indulgence may mask a protein deficient state and make the nutritional assessment more difficult. A history of decreased food intake attributed to anorexia, dysphagia, nausea or vomiting may clarify the events leading to nutritional depletion. A chronic wasting illness, the use of corticosteroids, and alcoholism commonly contribute to malnutrition. Poverty, depression, and ignorance of basic nutritional principles, can result in chronically decreased nutritional body stores, which are further depleted in the presence of an acute illness. A directed physical examination can complement the nutritional history. Body fluid stores can be estimated by orthostatic blood pressure and pulse measurements but this is difficult to measure in mechanically ventilated critically ill patients. Similarly, estimation of skin turgor and mucous membrane moisture may give ambiguous or misleading information.

Table 1. Assessment of nutritional status

History
Weight loss
5%–10% mild to moderate malnutrition
>10% severe malnutrition
Decreased food intake
Depression, psychiatric disease, or dementia
Anorexia, inanition, lassitude
Dysphagia, nausea, vomiting, diarrhea
Presence of chronic illness
Cancer
Chronic renal failure
Chronic obstructive or interstitial lung disease
Congestive heart failure
Chronic therapeutic use of corticosteroids
Alcoholism
Physical examination
Muscle weakness and/or wasting loss of subcutaneous fat stores
stigmata of chronic liver disease
Jaundice
Cutaneous telangiectasia
Ascites
Signs of specific nutritional depletion
Ophthalmoplegia
Cheilosis
Glossitis
Edema
Peripheral neuropathy

Body nutritional stores can be estimated by examining the degree of muscle wasting and the amount of subcutaneous fat tissue. Careful anthropometric measurements, such as triceps skinfold thickness (TSF) and mid-arm muscle circumference (MAMC), are useful indicators of chronic malnutrition. These values estimate the body's fat stores (TSF) and lean body muscle mass (MAMC), respectively. Measured TSF and MAMC values are compared to age and sex-specific standards [25]. The elderly are a group with an increased risk of malnutrition and a proclivity for critical illness. TSF and MAMC standards have not been derived for the very elderly, older than 75 years. Standards for dietary intake are not available and changes associated with malnutrition may also be a function of normal aging.

Several simple laboratory measurements can be used to further evaluate a patients nutritional status. Serum electrolytes and renal function testing indicate the adequacy of body salt/water content. The adequacy of body stores of magnesium, phosphate, and calcium, should be

assessed initially since they are often depleted in severely malnourished patients. Depletion of these divalent ions is associated with respiratory muscle weakness which may perpetuate ventilator dependency [26–29]. The serum albumin can be used to estimate visceral protein mass which is a reflection of nutritional stores but has several limitations. Albumin is a reverse phase reactant meaning that its synthesis is depressed during an acute illness. This may be mediated by tumor necrosis factor (TNF) and interleukin 1 which increase mRNA steady state levels for acute phase reactants and decrease the expression of the mRNA for albumin [8, 11]. Albumin is redistributed from the vascular to the interstitial compartment in the presence of a diffuse capillary leak conditions such as sepsis syndrome [30]. This increases albumin's volume of distribution and results in lower serum concentrations. The molecular weight of human serum albumin (67 kilodaltons) is near the threshold for selective permeability of glomerular filtration and the barrier properties of the alveolar-capillary membrane and other organs. The serum albumin will further decline if albumin deficient intravenous fluids are given to support the circulation of these patients. Thus, low serum albumin levels can be explained by the sequestration of albumin to the interstitial spaces, increases in the obligatory insensible urinary loss, and decreases hepatic synthesis. Since the circulating half life of albumin is 18 days, it takes several weeks for a serum albumin measurement to reflect nutritional changes. For this reason several authors have suggested the measurement of larger proteins with shorter circulating half lives which are not acute phase reactants such as retinal binding protein, thyroid binding protein, or transferrin as a better method of estimating protein balance [31–33].

Bioelectrical impedance is a relatively new and noninvasive method which allows a bedside quantitative estimation of lean body mass. This methods exploits the difference in electrical conductance of body fat and fat-free tissues to estimate human body composition. The method has been well validated in young adults from age 18–50 where predictive regression curves have been established [34]. Predictive formulas based on measurements in young adults grossly overestimate fat-free body mass and hence underestimate fat mass in elderly patients. Recently, accurate predictive formulas have been established in children and in the elderly [35] but have not yet been applied systematically to a critical care population.

Estimation of nutritional requirements

The energy expenditure (EE) is defined as the number of kilocalories expended over a 24 h period. This value is usually estimated from a predicted basal energy expenditure (BEE) which is multiplied by an empirically derived "stress factor". The BEE can be accurately predicted by the Harris and Benedict formula [36]. This formula relates the BEE to an individual's age, sex, and body size (Fig. 1). Stress factors are traditionally estimated proportional to the level of physical activity and the specific disease state of the patient. However, availability of accurate clinical measurements of the EE such as metabolic cart

$$\text{REE(males)} = 66.473 + (13.7516 \times W) + (5.0033 \times H) - (6.755 \times A)$$

$$\text{REE(females)} = 655.0955 + (9.5634 \times W) + 1.8496 \times H) - (4.6756 \times A)$$

where: W = weight in kilograms; H = height in centimeters; A = age in years

Fig. 1. Harris-Benedict equation

studies has questioned the validity of these estimates [18, 20, 37]. EE is clinically measured by indirect calorimetry utilizing metabolic cart which measures concentrations of oxygen and carbon dioxide in inhaled and exhaled gas. By multiplying these concentrations by the exhaled minute ventilation, the metabolic cart can accurately determine the rates of oxygen utilization and carbon dioxide production, respectively. The Weir equation converts this primary data into an estimation of the EE (Fig. 2) [38]. In a sedated patient on a stable diet, the EE should reflect the resting energy expenditure (REE). Yet, there is considerable variability in the EE which results during the metabolic stress of routine ICU diagnostic and therapeutic studies [39–41]. Sleeping patients utilize 10% less oxygen than awake but resting patients and 25% less oxygen than active patients [39]. In our experience, it is difficult to measure a true REE (TREE) in critically ill patients without intravenous sedation. Longer periods of measurement may more reliably reflect the TREE and may be of more clinical value than trying to measure an accurate REE.

Another potentially confounding factor is the phenomenon of diet-induced thermogenesis (DIT). DIT refers to the energy expenditure BEE that is needed for absorption, processing, and storage of nutrients [42]. DIT is dependent on the composition of the formula, ranging from 30%–40% for proteins, 6%–8% for carbohydrates, and 2%–3% for lipids [42]. The DIT of continuous enteral feeding is minimal providing that the intake ranges between 1 and 1.3 times the fasting rate of REE [43]. DIT is lower with high-fat compared to high-carbohydrate enteral formulas [44]. Thus, DIT for a selected calorie load can be minimized by the use of high fat continuous infusion enteral diet.

The inaccuracy of predictive formulas for nutritional assessment can lead to inappropriate and potentially detrimental feeding regimens [20, 39, 40]. Makk et al. have shown that 41% of patients are underfed and 27% overfed when traditional formulas are used to estimate nutritional requirements [37]. In critically ill patients with lung disease, underfeeding may perpetuate respiratory muscle weakness while overfeeding results in excessive carbon dioxide production requiring an increased work of breathing necessary to achieve steady state ventilation. Even the most catabolic patients, such as those with severe sepsis, have only a modest increase (approximately 25%) in their caloric requirements over their calculated

$$EE = 1440 \times ((3.941 \times VO_2) + (1.11 \times VCO_2))$$

where: *1440* = min/24 h; VO_2 = O_2 utilization/min; VCO_2 = CO_2 production/min

Fig. 2. Weir equation

BEE [19]. Foster et al. compared measured EE to 191 published predictive equations in 100 patients receiving TPN [45]. These authors found an average of 1076 ± 660 h kilocalories/day in excess of the actual measured EE were being administered to these patients and suggested that the cost of TPN could be cut by 22% by utilizing metabolic cart studies routinely [45]. Thus, it appears from the literature that predicitve formulas overestimate caloric expenditures and that lack of appropriate attention to nutrition by the responsible physicians frequently results in undernutrition [24, 37, 45].

The accuracy of indirect calorimetry is dependent on many variables [46]. The accuracy is reduced in patients who require exceedingly high inspired oxygen concentrations. For example, a person with a surface area of 1.7 m^2 has a resting oxygen uptake of approximately 240 ml. This same person inspiring 100% oxygen with a minute ventilation of 10,000 ml/minute would have an oxygen uptake representing only 2.4% of the total amount available (240 ml/10,000 ml × 100%). The measurement of such a small fraction approaches the limits of the instrument. In practice, the clinically available metabolic carts are not accurate with inspired oxygen concentrations greater than 50% – 60%. Other sources for errors include, system leaks, the effect of water vapor pressure, changes in the compliance of the ventilator tubing, and errors in calibration. There have been no studies addressing whether routine use of indirect calorimetry improves the outcome of an ICU stay. At present, indirect calorimetry may be better viewed as an investigative tool than a necessary part of routine patient care. We advocate periods of measurement of 6 – 24 h and only in selected patients who are most likely to benefit from indirect calorimetric measurements, such as those who fail to respond to conventional empiric nutritional management by the second week of their illness.

Estimation of protein requirements

An important benefit of supplementary calories in the ICU is the utilization of exogenous dietary protein for nitrogen building and the sparing of endogenous protein. Protein requirements are linked to protein losses and demands of individual patients. Because there are no endogenous stores of protein, most protein loss comes from functioning muscle. Many studies have shown that loss of body muscle mass is associated with a profound weakness of respiratory muscles [47 – 54] and may be a major factor in the failure of certain patients to wean from mechanical ventilation [15 – 18]. The utilization of exogenous protein as substrate for anabolism is energy dependent and requires non-protein calories in the form of either carbohydrates or fats. Therefore, exogenous protein should not be used as a calorie source. Typically, 25 – 35 kilocalories of non-protein calories are necessary for the metabolic utilization of each gram of protein. A critically ill patient requires from 1 to 2 grams of a high biologic quality protein per kilogram of body weight proportional to the degree of metabolic stress. There is substantial confusion in the literature regarding the employment of ideal predicted body weight, usual body, and acutal body weight in the calculation of protein requirements [40]. The use of the ideal predicted body weight obviates confusion and standardizes the approach to patients within a single institution.

Recommended approach to the initial nutritional regimen

There is no universally agreed upon method of initiating nutrition in critically ill patients. We recommend initiating nutrition within the first 24 – 48 h of a critical illness. A reasonable starting place, for most critically ill patients, is 1 g protein and 25 non-protein kCal/kg of ideal body weight. Thus, a 70 kg patients should receive 70 g of protein and 1750 kCal of non-protein calories. This value represents a 10% – 15% increase over the predicted BEE using the Harris Benedict equation. In patients with multiple trauma, major burns, sepsis, or pancreatitis, this starting regimen may be increased by up to 25% (90 g of protein and 2240 kCal of non-protein calories). The adequacy of this initial selection can then be determined and appropriate adjustments made as needed.

Visceral protein measurements and nitrogen balance determination are inexpensive methods to monitor the adequacy of nutritional supplementation. Serial measurements of visceral proteins should show a definite trend toward improved protein synthetic function. For example, weekly measurements of transferrin, which has a circulating half life of 7 days, should increase if protein and caloric requirements are being met. If direct transferrin measurements are unavailable they can be estimated by measuring the total iron binding capacity (TIBC) using the formula: transferrin = (0.8(TIBC) – 43). Measurements of thyroid binding protein and retinal binding protein, which have half lives of 2 days and 12 h respectively, may give a more rapid indication of clinical improvement and the adequacy of nutritional management than proteins with longer half lives such as albumin and transferrin [32, 33]. A second method for determining the adequacy of protein intake is the nitrogen balance study (Fig. 3). This method requires an accurate 24 h measurement of total urinary urea nitrogen (UUN) and urine volume. Measurements of UUN on spot urine are not always accurate due to hour to hour variations of urea excretion. Nitrogen loss of 4 g/day is usually entered into the nitrogen balance equation for insensible losses primarily from stool and skin. This estimation should be increased in patients with protein losing diarrhea, open surgical wounds, large burns, or psoriasis. Protein present in removed pleural or peritoneal fluid should also be measured and in-

Nitrogen Balance = (dietary nitrogen) – (excreted nitrogen) – (insensible nitrogen loss)

where: *dietary nitrogen* = (g of protein intake)/6.25;
excreted nitrogen = UUN [(mg/dl) × total volume (l/day) × 10 (dl/l)];
insensible nitrogen loss = 4 g/day

Fig. 3. Nitrogen balance study

cluded in the calculation of nitrogen balance. The goal of nutritional management is to achieve a positive nitrogen of 1 to 2 g/day. We recommend an initial nitrogen balance study after one or two days of nutrition. If a patient is found to be in negative nitrogen balance, then the increase in protein requirements can be estimated by adding 2 to the absolute value for nitrogen balance and multiplying by 6.25. For example, if the nitrogen balance is -2 g/day, then $((2+2)\times 6.25 = 25)$ g protein should be added to the dietary intake in order to achieve a 2 g positive nitrogen balance. In addition 25 nonprotein kCal for each additional gram of protein must be added to the diet in order to utilize this increased protein as a substrate for endogenous protein sparing rather than a caloric source. Thus, a nitrogen balance study can provide quantitative information regarding the adequacy of nutrition 48–72 h from the initiation of nutrition. Additional considerations are necessary in severely malnourished patients. For example, Wernicke's encephalopathy may be precipitated in patients with marginal thiamine stores by the nasogastric feedings, glucose containing intravenous fluids, or initiation of TPN [55].

Route of nutrition

Nutrition can be given either enterally or parenterally. Enteral feeding is preferred because of lower cost, fewer serious side effects, and a greater tolerance for errors. The disadvantages of enteral feeding are that it requires a functioning, intact gastrointestinal tract, may cause diarrhea, and has an attendant risk of pulmonary aspiration. The available enteral routes include oral, nasogastric, and gastroenterostomy feedings. Voluntary oral protein and caloric supplements may be adequate in patients who are not severely ill or mechanically ventilated but are often unreliable. In these patients the adequacy of oral feedings should be rigorously documented by at least 3 consecutive daily calorie counts. Forced enteral feeding requires a nasogastric tube. Weighted silastic nasogastric tubes are thought to have a lower complication rate than larger, more rigid, vented tubes. A chest radiograph must be performed following placement of silastic nasogastric tubes prior to feeding since placement into the lung parenchyma is not uncommon and difficult to assess by auscultation. Forced enteral nutrition can be delivered either as a bolus or constant infusion. The later is usually preferable due to ease of delivery via a constant infusion pump.

Four types of enteral feedings are available, polymeric, semi-elemental, elemental, and modular. Polymeric preparations are balanced diets which include all of the essential nutrients (Table 2). A large number of commerical preparations are available that vary in price, caloric density, osmolality, lipid: carbodhydrate ratio, fiber content, and relative amounts of simple versus complex carbohydrates. Most polymeric formulas contain 30% fat and 70% carbohydrates, have an osmolality of approximately 350 mOsm/l, and contain 1 kCal/ml. Preparations varying in these parameters are available for patients with special needs. These preparations are lactose-free since lactase deficiency is common in critically ill patients. The available feedings contain the recommended amounts of vitamins and micronutrient, but may not be sufficient to treat patients with depleted states. Semielemental and elemental feedings use small peptides or essential amino acids, respectively, as a protein source. These preparations can also substitute simple for complex carbohydrates and mean chain trigylcerides (MCT) for larger lipids if necessary. Elemental preparations have much higher osmolarity which may limit their clinical utility. There is no convincing data at present to recommend the routine use of semi-elemental or elemental enteral preparations in critically ill patients. However, there is theoretical basis and anecdotal experience which indicates that these preparations may be better absorbed during critical illnesses and in the early postoperative period. They are most useful for patients with abnormal gastrointestintal tracts with a reduced absorptive surface area (i.e. short bowel syndrome). Further, investigation is necessary to make specific recommendations regarding their use in specific clinical situations. Modular feedings can be used to supplement a specific component of a polymeric feeding such as carbohydrates, fats, or protein in patients with additional requirements.

Table 2. Essential nutrients

Water and electrolytes (Na^+, K^+, Cl^-, Ca^{++}, PO_4^{2-}, Mg^{2+})
Non-protein calories
Lipids
Carbohydrates
Protein
Vitamins
Fat soluble (thiamine, riboflavin, pantothenic acid, niacin, pyridoxine, biotin, folacin, cobalamin, ascorbic acid)
Water soluble (D, E, A, K)
Trace minerals (I, Chr, Fe, Mn, Cu, Zn, Fl, Se)
Essential fatty acids
Linoleic acid
Linolenic acid

Total parenteral nutritional (TPN) is indicated when enteral feedings are not capable of reaching target levels. The use of TPN has been recently studied in malnourished patients requiring major surgery and only in patients with severe nutritional depletion was there clear evidence of efficacy [56]. The decision regarding TPN administration to patients who can tolerate partial NG feeding is arbitrary and data supporting its use anecdotal. In our opinion, a common error of clinical management is the anticipation over days that enteral feeding will soon reach the target level. The reasons for inadequate enteral nutrition are numerous but typically include large gastric residuals, severe diarrhea, and frequent elective diagnostic or therapeutic procedures. Enteral feeding should be continued if possible since partial enteral feeding may promote better emptying of the gall bladder, titrate gastric acidity, and retain normal histology and function of the small intestine. These caveats aside, TPN can be used to either supplement enteral feeding or to provide all of the necessary micro and macronutrients. TPN requires

the aseptic placement of a central venous line which can be placed safely in a critical care setting but has an alarming number of potential serious complications [57, 58]. TPN should only be initiated after assessing that the catheter tip is appropriately positioned in the thorax by chest radiography.

Most hospital pharmacies offer a standard and low volume high caloric density TPN preparation. The standard formula typically contains a 3.5% amino acid solution (35 g of protein/l), 25% dextrose (250 g/l), and a total of 850 non-protein kCal/l (dextrose has 3.4 kCal/g). Two l/day will deliver 1 g protein/kg/day and 1700 kCal (24 kCal/g of protein) to a 70 kg person. The addition of 500 ml/day of 10% intralipids (10% intralipids has 1.1 kCal/ml) will increase the non-protein kCal to a total of 2,250 kCal (32 kCal/g of protein). Low volume high caloric density preparations typically contain a 5% amino acid preparation (50 g of protein/l), 35% dextrose (350 g/l), and 1,200 non-protein kCal/l. This preparation is indicated in patients intolerant of excess volume (i.e. oliguric renal failure), since 1.5 l/day contains 75 g of protein and 1800 non-protein kCal (24 kCal/g of protein). Electrolytes, vitamins, and trace minerals must be added to these preparations to balance the diet and meet routine dietary needs.

The theory of using branched chain amino acids (BCAA) in hypermetabolic states is based on the in vitro observation that BCCA may inhibit muscle degradation and stimulate muscle protein synthesis [59–62]. If these observations can be extrapolated to the in vivo state, then BCAA therapy may decrease nitrogen wasting associated with catabolic states such as trauma, surgery, sepsis, or burns. The use of BCAA is, however, controversial. Oki and Cuddy carefully reviewed 18 studies of utilizing BCAA in hypermetabolic states [62] and noted that there was considerable intra and interindividual variability in nitrogen balance with only a slight improvement in the utilization of nitrogen resulting from BCAA nutritional support. Thus, BCAA therapy is not routinely indicated but may be tried in patients with an extremely high loss of urinary nitrogen in an attempt to promote better utilization of amino acid substrates for protein sparing.

For patients receiving only TPN, intralipids must be administered at least twice per week to prevent essential fatty acid deficiency. Intralipids can be given daily as either a 10% (550 kCal/500 ml) or a 20% (1100 kCal/500 ml) solution to supplement non-protein kilocalories. The ratio of lipid/carbohydrate calories in either enteral or parenteral nutrition determines the respiratory quotient which is the relationship between carbon dioxide production and oxygen utilization. Increasing the percentage of lipid kilocalories relative to dextrose kilocalories will decrease the amount of carbon dioxide produced. This reduces the minute ventilation needed to maintain a steady state partial pressure of carbon dioxide in arterial blood ($PaCO_2$). The optimal balance of lipid/carbohydrates which spares endogenous protein mass is unknown. Glucose appears to be somewhat superior to mixed glucose/lipid preparations in sparing protein [63] but is also associated with greater production of CO_2. Several authors have suggested that up to 60% of the non-protein calories can be reasonably obtained from lipids (63–67], although this area remains controversial. Critically ill patients can maintain protein balance using a variety of nutritional mixtures ranging from lipid free carbohydrate mixtures to a lipid/carbohydrate ratio of at least 1:3 [63]. Interestingly, apparently healthy individuals exist north of the Arctic Circle, where virtually all non-protein kilocalories are obtained from animal fat. Factors other than protein balance may be important when choosing lipids over cabrohydrates. Over-utilization of carbohydrates as an energy source can result in fatty liver infiltration and abnormal liver function test [68]. There are several reports that large volumes of glucose containing TPN can markedly increase CO_2 production and lead to dire clinical consequences [69, 70]. However, there are no reports that minimizing the respiratory quotient by manipulating the lipid/carbohydrate ratio alters the course of a critical illness or accelerates weaning from mechanical ventilation.

Monitoring the response to nutrition

In addition to serial visceral proteins and nitrogen balance studies (see above) there are a number of routine measurements which should be made in patients who receive either enteral or parenteral nutrition. Determination of daily weights and fluid balance are essential. TPN is associated with an obligatory intravenous fluid load in patients who are usually receiving other fluids associated intravenous pharmaceutical preparations and resuscitation. It is unnecessary to add "maintenance fluids" to a TPN regimen since this fluid and electrolytes is included in the TPN preparation. Tracking the exact amount of fluid flux in critically ill patients is difficult but essential to avoiding gross volume expansion. Serial measurements of electrolyte, divalent ions, blood counts, clotting studies, renal function test, liver function test, and glucose are sufficient for patients receiving either enteral or parenteral nutrition (see Table 3).

The initiation of TPN requires special attention for potential adverse effects. Glucose intolerance is a feature of many acute illnesses and can be worsened by TPN. Thus, patients receiving TPN require frequent measurement of serum glucose and urinary glucose reductions. There measurements can be decreased when a stable steady state is reached. Hyperglycemia can be easily treated by a constant infusion of insulin which may be added to the TPN preparation. Alternately, regular insulin can be given on a sliding scale tailored to an individual patient's serum glucose level. Insulin preparations with a longer half life should be used only with caution since insulin requirements can change quickly. When initiating intralipid therapy, the patient should be closely observed since anaphylactic-like reactions to intralipids have been reported. In addition, a lipid clearance study is necessary to ensure that lipemia doesn't occur as the result of the infusion.

The composition of nutrients can have a pharmacologic effect on the respiratory system. Intralipids are relatively contraindicated in severe hypoxemic respiratory failure since subtle abnormalities in pulmonary function

Table 3. Laboratory monitoring of TPN

Prior to initiation of TPN and twice weekly thereafter
Serum electrolytes, glucose, BUN, and creatine
Serum phosphate, calcium, and magnesium
Liver enzymes and function test
Clotting studies
Complete blood count with differential and platelet count
Serum albumin and transferrin levels
Upon initiation of TPN
Hourly glucose and urinary reductions
When using intralipids:
Lipid test dose with observation
Begin with a rate of 1 ml/min
Observe for evidence of acute toxicity
dyspnea, cyanosis, cutaneous allergic phenomenon, nausea, vomiting, headache, flushing, sweating, fever, dizziness/hypotension
Lipid clearance study
Draw serum triglyceride level 6 h post infusion
At the time of a suspected line related infection
At least two separate peripheral blood cultures
Urinalysis and culture
Chest X-ray and (if positive) sputum evaluation culture of the TPN catheter tip

studies have been shown to occur during intralipid infusion [71–73]. Protein appears to increase ventilatory drive which can been accentuated by the use of amino acid preparations which are enriched in BCAA [74, 75]. van den Berg et al. have suggested that a high-protein enteral diet may stimulate the ventilatory response and accelerate weaning from mechanical ventilation [76], but this should be only considered in patients with adequate respiratory muscle strength and endurance to sustain steady state CO_2 regulation in arterial blood. Future, prospective controlled clinical studies will be necessary to make specific recommendation based on the pharmacologic effects of nutrients.

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J. W. Christman, MD
Center for Lung Research
Vanderbilt University
Nashville, TN 37212
USA