Nutrition in the Critically Ill Patient

George L. Blackburn, M.D., Ph.D.,* Baltej S. Maini, M.D.,† Ellison C. Pierce, Jr., M.D.‡

 Significant advances in the diagnosis, surgical treatment and postoperative care of the critically ill patient include an invaluable contribution by therapeutic nutrition. Most patients survive a single episode of stress, but repeated insults by anesthesia and surgery often lead to prolonged illnesses beset with complications, one of which, malnutrition, can add substantially to the morbidity and mortality of these patients. Elective and semielective surgical procedures can transform mild categories of malnutrition (particularly protein-calorie malnutrition§) into clinically significant states, where immune-defense mechanisms are impaired, wound healing is delayed, and ultimate recovery is adversely affected.¹ The failure of physicians to carry out proper nutritional assessment plays a major role in the high incidence of hospital malnutrition, which can no longer be ignored.²,³

It is the purpose of this paper to review the metabolic changes associated with the different phases of illness and to identify objectively and correct the specific nutritional deficits created by such responses. The products and techniques utilized in present-day nutritional strategy are reviewed, with particular reference to the adjustments necessitated

* Associate Professor of Surgery, Harvard Medical School; Director, Nutrition Support Service, New England Deaconess Hospital, Boston, Massachusetts.
† Research Associate, Cancer Research Institute, New England Deaconess Hospital, Boston; Visiting Physician, Clinical Research Center, Massachusetts Institute of Technology, Cambridge, Massachusetts.
‡ Chairman, Staff Anesthesia, New England Deaconess Hospital; Clinical Instructor, Anesthesia, Harvard Medical School, Boston, Massachusetts.

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Publication No. 591, Cancer Research Institute, New England Deaconess Hospital, 194 Pilgrim Road, Boston, Massachusetts 02115.
Address reprint requests to Dr. Blackburn.
§ International Classification of Diseases Adapted for Use in USA (ICDA), 1968.

Protein–Calorie Malnutrition (ICDA No. 268). Loss of body cell mass, primarily muscle tissue and body fat reserves. Without stress, visceral protein functions will remain intact.

Kwashiorkor (ICDA No. 267).

Selective loss of visceral protein such as albumin and transferrin (iron-binding protein).

Impaired cell-mediated immunity and fatty liver are common characteristics of this disease.

by multiple-organ dysfunction. Many of these observations are still investigational, and possible clinical applications are suggested. It is hoped that they will generate enough interest so that research in this important field can be developed further. For an in-depth review, the reader is referred to a number of excellent monographs, manuals and books that are now available.⁴–⁸

Metabolic Response to Injury

Over the years, the metabolic response to injury has been the subject of extensive research; notable among the studies are those of Cannon,⁹ Cuthbertson,¹⁰ Moore,¹¹,¹² and Kinney.¹³ The induction of anesthesia initiates the response to injury, while most surgical procedures 60–90 minutes in duration do not augment this stress further.¹⁴ The changes in body composition secondary to trauma are characterized by a biphasic hormonal response (fig. 1). In the initial or acute phase, the hormonal effects are mediated through the sympathetic nervous system. There is a release of catecholamines from the adrenal medulla and sympathetic nerve endings, with consequent inhibition of insulin secretion but a marked stimulation of glucagon secretion.¹⁵ This is accompanied by an increase in the release of ACTH by the pituitary, which in turn stimulates the production and release of adrenocortical hormones. The hormonal interplay results in peripheral protein catabolism and gluconeogenesis.¹⁶,¹⁷ Epinephrine and glucagon provide a strong glycogenolytic stimulus, and oxidation of fat is increased, secondary to the lipolytic effect of catecholamines. Glucocorticoids and other pepptides antagonize the peripheral action of insulin, leading to a sacrifice of lean tissue (protein breakdown) in favor of maintaining adequate levels of free amino acids for visceral protein synthesis and energy fuel substrates (fig. 2).

The duration of the acute phase, though usually one to three days, also depends upon the severity of injury and the presence of sepsis and associated malnutrition. The more predominant and immediate factors, however, include hypovolemia, pain and fever. A deficit of peripheral energy fuel substrates in severely traumatized patients with sepsis has been shown recently by O'Donnell et al.¹⁸ This corroborates the observation that body cell mass can be conserved by providing branched-chain amino acids and ketone bodies, a deficiency of which can prolong illness

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and delay recovery. Once the crisis has passed, the adaptive phase follows: insulin levels are lower, blood glucose falls, and the levels of catecholamines and glucocorticoids return to normal. Body mechanisms now turn to different sources of energy, and the appearance of ketone bodies in the blood and urine suggests accelerated lipolysis and associated ketogenesis. There is an increase of approximately 30% per cent in the utilization of fat as a fuel for energy demands, since the stores of glycogen are now depleted. Seventy-two hours postoperatively more than 80% per cent of the energy requirements can be provided by fat.

**Nitrogen Metabolism**

The nitrogen (protein in g ÷ 6.25) necessary for tissue protein synthesis, erythropoiesis, wound healing and cellular and humoral immune function is provided by redistribution of muscle protein. This interrelationship basically entails catabolism of muscle protein and release of gluconeogenic precursors for utilization by the liver. The more important demands for visceral or secretory protein synthesis are, in turn, met by the liver (fig. 3). The efficiency of this mechanism is influenced by the extent of injury and the type of nutrient intake. It becomes extremely important to keep these changes in mind when designing nutritional therapies, so that the adaptation to the physiologic response to injury is enhanced (table 1).

**Salt and Water Metabolism**

Shifts in body fluid and electrolyte compartments are an inevitable consequence of these physiologic hormonal and metabolic alterations. However, a decrease in the “functional” extracellular space produces a hypovolemic response, which entails conservation of water. This physiologic response is exaggerated by the activation of the renin–angiotensin system initiated by hypovolemia. Under the influence of aldosterone and glucocorticoids, retention of sodium (and water) occurs. Renal water retention, despite a decrease in plasma osmolarity, occurs secondary to the secretion of antidiuretic hormone, expressed as “negative free water clearance”. Outlined in detail below, infused hypotonic solutions (e.g., 5 per cent dextrose in water or ½ physiologic saline solution, either of which provides free water) are major contributors to an inappropriate antidiuretic effect.

Considerable fluid, rich in both colloid and crys-
Fig. 3. Functional redistribution of body cell mass after injury provides nitrogen for protein synthesis. Arrows reflect the net release (−) in grams from collagen, gut, and muscle, as well as uptake (+) of amino acids into tissues whose net anabolism is associated with survival. The conversion of protein to glucose and urea is a trivial source of energy but is an important role of the liver to produce heat necessary to maintain core temperature.

tallloid, is lost into the “third space” in the area operated on and other interstitial spaces. The fluid shift represents a redistribution of the body’s extracellular fluid and therefore must be replaced appropriately. Although one would expect glucocorticoids and aldosterone to increase renal excretion of potassium, the net effect during the acute phase of injury (in the absence of excessive gastrointestinal losses) is that of maintaining normal serum potassium. Significant extrusion of intracellular potassium secondary to muscle injury, protein catabolism, blood transfusions and absorption of blood from serous cavities is responsible for maintaining serum potassium concentration. Once diuresis becomes manifest (a sign of the adaptive phase of injury), renal potassium excretion increases and supplementation becomes necessary (40–60 mEq/day).

Normal extracellular potassium and relative hyponatremia are present during the acute phase. During surgical injury at this stage, an antagonistic effect of the high glucagon:insulin ratio teleologically counteracts this aldosterone response. This response in simple starvation has been best categorized by Boulter et al. A further mechanism may be the obligatory cation coverage of anions metabolically generated during starvation and resulting in natriuresis, as is discussed below.

**Nutritional Support of the Critically Ill Patient**

**Nutritional Assessment**

The association of excessive morbidity and mortality with malnourished states has been well documented. The mechanism is best understood as being one where the intake of nutrients is inadequate to meet the excessive demands placed by stress and injury. It becomes important, therefore, to recognize the early signs of malnutrition or those of specific nutrient deficiencies. Nutritional assessment should now be an integral part of the evaluation of all hospitalized patients, particularly those scheduled for surgical procedures. The anesthesiologist can play an important role in the nutritional and metabolic assessment of high-risk patients. Such surveillance can minimize the risk of elective or semielective surgical procedures, and must become a part of routine preoperative evaluation.

A diagrammatic representation of the key constituents of the whole body is made in figure 4. An assessment includes characterization of the following compartments:

**Lean Body Mass.** A simple and accurate method of assessing the skeletal muscle compartment is to measure the mid-arm muscle circumference. Estimation of the creatinine–height index (CHI) also indicates the quantity of muscle stores and is a sensitive measure of protein depletion in cachectic and marasmic states. In obese or edematous patients,

**Table 1. Metabolic Responses to Injury**

<table>
<thead>
<tr>
<th>Key Physiologic Functions</th>
<th>Nutrients</th>
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<tbody>
<tr>
<td>1. Homeostasis</td>
<td>Oxygen</td>
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<tr>
<td>A. Ventilation</td>
<td>Fluids</td>
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<tr>
<td>B. Circulation</td>
<td>Electrolytes</td>
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<tr>
<td>C. Cardiovascular</td>
<td>Caloric substrate</td>
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<tr>
<td>D. Energy state</td>
<td>Protein and micronutrients</td>
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<tr>
<td>II. Tissue repair</td>
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<td>III. Host resistance and</td>
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height/weight index may not provide an accurate estimate of nutritional status, and therefore has limited application.

Fat Stores. Fat mass can be adequately measured by triceps skin fold. Given the fact that each pound of fat contains 3,500 kcal, only a severe loss (<75 per cent of standard) represents significant depletion.

Visceral Protein. In stress conditions, loss of secretory or visceral proteins occurs rapidly. Estimation of serum albumin and preferably transferrin (the iron-binding protein), indicates the extent of depletion of this vital tissue compartment. The cellular immune system also reflects important visceral function. Measurement of total lymphocyte count together with delayed cutaneous hypersensitivity to recall antigens (streptokinase-streptodornase, mumps, and candida) is particularly useful.

Extent of Hypermetabolism. The amount of urinary urea nitrogen excreted per 24–48 hours is a valuable indicator of the severity of hypermetabolism. Figure 5 shows the urinary urea nitrogen in different clinical states after 24 hours on a protein-free diet. The relationship between urea nitrogen excretion and metabolic rate is due to the obligatory oxidation of body cell mass that occurs with stress and starvation. Thus, energy expenditure and extent of hypermetabolism (percentage above normal) can be predicted from the simple clinical determination of urea nitrogen in a 24-hour or, more precisely, in a 48-hour urine collection. Simultaneous determination of creatinine–height index can also be accomplished.

Preoperative Nutritional Support

Routine preoperative evaluation of patients by an anesthesiologist includes checking the chest x-ray, electrocardiogram, hematology and chemistry profiles. A low serum albumin (<3.5 g/100 ml), depressed lymphocyte count (<1,500/cu mm) and a history of recent weight loss are indicators for the more detailed nutritional assessment described above. By using these simple techniques, adequate estimates of the risk associated with anesthesia and operation can be determined and postoperative complications avoided. Given the fact that these tests are simple, quick, and easily obtained at minimal cost, they must become a part of standard patient evaluation.

Once moderate (60–75 per cent of standard) or severe (<60 per cent of standard) nutritional deficits have been identified and characterized, nutritional support is mandatory prior to elective or semi-elective surgical procedures. Rarely will a significant nutrition problem exist without protein and calorie depletion (protein–calorie malnutrition). It must be emphasized that a period of at least ten days, but preferably two to three weeks, is necessary for an objective response to nutritional therapy. When a satisfactory result has been obtained (return of cellular immunity, elevation
of serum albumin and lymphocyte count, and gain in weight), the patient can then be considered in view of the usual risk factors appropriate for the procedure, but with the hazards of malnutrition eliminated, or at least minimized. Malnutrition is associated with increased incidences of infection, intestinal anastomotic leaks, and utilization of critical care units and other support services. One should assess the consequences of the failure to treat malnutrition in terms of cost, morbidity and mortality. It becomes essential to recognize malnutrition early, repair the deficit, and minimize complications.

Fluid and electrolyte therapy is an essential part of nutritional support. The value of ensuring an adequate intravascular volume by administering crystalloid solution preoperatively (15 ml/kg body weight), to minimize the risk of operative hypotension, has been described. Such precautions are of particular value in procedures that involve aortic cross-clamping. The risk of hypotension during induction of anesthesia is also reduced by ensuring a proper state of hydration. Elderly patients, especially those who undergo several days of mechanical preparation of the bowel for intestinal operations, become easily dehydrated, and preoperative fluid and electrolyte repletion is necessary.

Operative Therapy

An excellent study of the intraoperative requirements for fluid and electrolytes has been provided by Thompson. Ringer's lactate (or acetate) solution is administered at the rate of 500 ml/hour as maintenance fluid, and blood is replaced as indicated. Although these guidelines were initially provided for aortic-iliac surgery, they remain true for most major surgical procedures. Additional crystalloid and albumin is provided as determined by the presence of coexistent crush injuries, fractures, and sepsis in organs or serous cavities.

Patients receiving intravenous hyperalimentation (IVH) preoperatively are best managed by reducing the hyperalimentation solution to a minimal flow rate (20–50 ml/hour) on the morning of operation. IVH is associated with increased water retention, which is largely extracellular water. Thus, during IVH, additional preoperative hydration is usually not needed. There is often an administration of glucose-containing solutions intraoperatively, which results in elevation of blood glucose. The hyperglycemia evoked by the stimulus of anesthesia and surgery is exaggerated during IVH, and the potential risks of hyperglycemia, glycosuria, and nonketotic hyperosmolar dehydration must be guarded against by careful monitoring of serum and urinary glucose. Patients receiving IVH who need insulin are often best treated by discontinuing IVH on the day prior to operation and maintaining them on a dextrose-free solution, viz., physiologic saline or lactated Ringer's solution or isotonic amino acids.

Diabetic patients scheduled for routine surgical procedures are easily managed by withholding insulin on the morning of operation and maintaining them on dextrose-free solutions intra- and postoperatively. Ketosis is produced, and mild transient acidosis may occur, but it is easily buffered by the use of sodium acetate or lactate. Some insulin-dependent diabetic patients require insulin for the control of blood sugar. The provision of insulin in sugar-free intravenous solutions containing amino acids or protein represents the most efficient regulation of blood glucose in diabetics. The classic objections to this practice have not been supported by our experience. Very little insulin is bound to glass when the solution contains protein or amino acids. Since only 10–15 units of insulin per 1,000-ml bottle are needed, the inadvertent discontinuation of the infusate has not
resulted in hypoglycemia, which is seen frequently when using subcutaneous administration of insulin and maintaining the patient on a 5 per cent glucose solution. A regimen for controlling blood sugar in diabetic patients during the perioperative period (while administering dextrose-containing infusates) entails the administration of half the usual daily dose of intermediate insulin on the morning of operation, and the other half in the recovery room. Supplemental doses of crystalline insulin are given as dictated by blood sugar estimation.\textsuperscript{74}

**Postoperative Nutritional Support**

*Fluid and Electrolyte Therapy.* Shires has emphasized the importance of the "functional extracellular fluid volume" in surgical trauma.\textsuperscript{20} More recently, Shizgal has demonstrated the value of administering physiologic saline solution in such circumstances.\textsuperscript{23} Accumulation of nonfunctional extracellular fluid may represent as much as 28 per cent of the body weight, resulting in a substantial reduction of the effective extracellular fluid. Increased glucocorticoid and aldosterone activity in the acute phase postoperatively is known to result in renal retention of sodium. The ensuing diminution of natriuresis can be overcome by preoperative salt loading, as has been demonstrated by Marks et al.\textsuperscript{38} By maintaining an infusion of balanced salt solution, renal sodium retention is not increased.\textsuperscript{38} The effect of vasopressin on free water retention,\textsuperscript{22} together with the formation of metabolic (free) water, would appear to preclude the need for administering additional free water, \textit{viz.}, 5 per cent dextrose in water, except in patients who have burns, kidney dysfunction, cirrhosis, heart failure, or conditions associated with osmotic diuresis. In most situations, balanced isotonic salt solution seems to be the most appropriate maintenance fluid.

Veeverbrants and Arky\textsuperscript{37} demonstrated that the fluid and electrolyte losses of early fasting can be reversed by the refeeding of carbohydrates, more slowly by administering protein, and not at all by feeding fat. The role of aldosterone in the antinatriuretic effect of carbohydrate refeeding is controversial, but administration of spironolactone (aldosterone antagonist) exaggerates the natriuresis of fasting and blocks the antinatriuresis of refeeding, as shown by Boulter et al.\textsuperscript{24} An excellent study by Sigler\textsuperscript{29} showed that in fasted individuals, obligatory sodium coverage of metabolically generated anions (ketoacids) and acid phosphate (H\textsubscript{2}PO\textsubscript{4}) is the mechanism responsible for the natriuresis of fasting. On refeeding with glucose, these subjects showed a decrease in organic acid anions.

The above observations have an important bearing in designing postoperative fluid and electrolyte therapy. The intraoperative and immediate postoperative periods (acute phase of injury) are associated with a hormonal response designed to reduce muscle breakdown and release amino acids.\textsuperscript{17} Associated with this response is the increased release of organic anions. If isotonic, glucose-free physiologic electrolyte solutions are provided, fat mobilization and ketogenesis will occur, adding to the anions excreted by the kidney. Consequently, an obligatory cation coverage (sodium from the electrolyte solution) will offset the classic aldosterone effect observed after operation where only free-water (5 per cent dextrose in water) and hypotonic electrolyte solutions (usually \frac{1}{2} physiologic saline solution) are given. It is important to note that the hyponatremia and decreased sodium excretion after surgical procedures are largely iatrogenic. More effective management of fluid and electrolytes, based on current understanding of the metabolism of starvation and surgical injury, supports the use of dextrose-free salt-containing solution.\textsuperscript{17} Similarly, refractory clinical states associated with excess fluid retention can be dramatically reversed by starvation regimens. The use of small amounts of isotonic electrolytes is effective even in cardiopulmonary-bypass operations.\textsuperscript{30} Once the acute phase of injury has passed, the most effective solution is one containing protein rather than glucose, allowing starvation ketosis to continue until the patient can return to a full diet. The important new observations regarding energy metabolism enable one to design fluid and electrolyte therapy that can enhance diuresis and natriuresis and thereby minimize circulatory overload, dilutional hyponatremia, and related cardiorespiratory complications.

*Respiratory Functions.* The effect of ketosis on carbon dioxide (CO\textsubscript{2}) response has been studied in obese patients.\textsuperscript{39} Although no such study of patients in the postoperative state is available, depressed sensitivity to carbon dioxide, especially in obese patients with CO\textsubscript{2} retention, may be overcome by ketogenic regimens. As a corollary, clinical semistarvation regimens such as 500-calorie diets containing glucose have been seen to depress the hypoxic ventilatory response, an effect that is abolished upon refeeding.\textsuperscript{40} Ketogenic fluid regimens, on one hand, and hyperalimentation, on the other, need to be investigated relative to their roles, in respiratory failure postoperatively. It is conceivable that some pulmonary problems after general anesthesia may be overcome by metabolic manipulation. This subject deserves investigation.

The classic indication for the use of glucose during anesthesia is the impression that glucose protects the liver from potential toxic effects of anesthetic agents.
This observation is apparently based on *in-vitro* experiments dealing with the metabolism of liver slices and has been extrapolated to conclude that glucose will benefit the liver during anesthesia. No *in-vivo* or clinical studies exist to support this hypothesis. Also, it is important to know that the physiologic response to anesthesia is *hyperglycemia* even without glucose infusion. The effect of glucose infusion is to increase the glucose flux and turnover with the production of fat in the liver. Very little increased consumption of glucose (*i.e.*, oxidation to CO$_2$ and water) occurs.$^{31,42}$

**Protein-Calorie Therapy.** Nutritional therapy is an essential component of present-day life-support systems, and basic knowledge in this field is essential. Having reviewed the metabolic response to injury, and the designing of fluid and electrolyte therapy based on such a response, it becomes essential to understand the development of a nutritional support plan for the critically ill patient (table 1).

A large variety of protein and non-protein caloric sources are available to the practicing physician involved in the care of the traumatized patient.$^{49}$ The following factors must be considered in formulating a nutritional therapy plan:

- Category and extent of malnutrition
- Extent of hypermetabolism and presence of sepsis
- Protein and caloric requirements
- Goal of nutritional support
- Presence of a functioning gastrointestinal tract
- Appetite
- Route of delivery of nutrients (central vs. peripheral vein)
- Presence of specific organ dysfunction necessitating restriction of volume or nutrients

Figure 6 is a logic tree that enables the designing of rational nutritional therapy on an individual basis. Parenteral feeding, which provides glucose calories at a rate of 40–45 kcal/kg/day and protein (1.5 g/kg/day), produces positive nitrogen balance in slightly to moderately catabolic patients. In contrast, oral intakes of 35–40 kcal/kg/day result in positive nitrogen balance. This difference is related to the greater efficiency of enterally-absorbed nutrients and the obligatory lipogenesis that occurs with intravenous dextrose infusion.$^{34,48}$ In patients who have severe burns, caloric requirements in excess of 45 kcal/kg/day have to be provided. In routine conditions, excessive calories result in diminished net protein utilization (NPU)$^{**}$ and fatty liver.$^{46,30}$

Since utilization of dietary protein is less efficient in stress conditions than during convalescence, 16 per cent of the calculated caloric needs are provided by protein, to give a nitrogen:calorie ratio of 1:150. Conventional defined formula diets$^{49}$ provide a 1:300 nitrogen-to-calorie ratio, wherein 8 per cent of the calories are supplied by protein. These products are satisfactory for maintenance therapy only. This ratio is increased to 1:150 in the high-nitrogen diets, which are most useful in stressful and catabolic states. In nitrogen-accumulation disorders (primarily renal failure), the nitrogen–calorie ratio is changed to 1:450 or 1:700, described below.

**Protein-sparing Therapy.** When the ability to sustain nutrient intake adequate to meet energy requirements and minimize protein catabolism is not practical or possible, preservation of body cell mass is made feasible by utilization of stored energy reserves, namely body fat. This adipose tissue reserve is adequate in most patients and can meet the energy requirement for several days to weeks. So long as protein depletion has not already resulted in significant protein malnutrition, considerable preservation can be achieved by the infusion of near-isotonic (3.5 per cent) crystalline amino acids together with appropriate cofactors and micronutrients.

The interrelationships of protein, fat, and carbohydrates during fasting and semistarvation have been described by Blackburn and Flatt.$^{47,48}$ During starvation, protein stores are progressively spared while the body gradually adapts to the use of non-protein calories, namely free fatty acids and ketone bodies, as fuel substrates.$^{49}$ This protein sparing may be diminished using hypocaloric carbohydrate-containing nutrients, because of the subsequent increase in circulating insulin and associated peripheral insulin resistance. Fat mobilization is inhibited by insulin, and the body accordingly turns to fuels from skeletal and visceral protein during periods of hypocaloric intake. In the well-nourished individual, this effect may be justified, because the normal response to injury prevents the effective utilization of exogenous nutrients in the immediate posttraumatic phase. However, in the malnourished patient, to whose already debilitated condition the stress of operation or infection has been added, the catabolic phase must be minimized so as to affect the outcome favorably. Significant amounts of body protein can be spared by the parenteral infusion of isotonic amino acids with appropriate electrolyte, vitamin, and mineral additives. By this technique, visceral protein synthesis is maintained, while body fat is mobilized (1 pound of body fat provides approximately 3,500 kcal).

Protein-sparing therapy is provided by isotonic amino acids delivered through a peripheral vein as a 3 or 3.5 per cent solution with vitamin, mineral and

$^{**}$ NPU = Net Protein Utilization, refers to the percentage of dietary protein absorbed and retained in the body.
Fig. 6. Logic tree, depicting the use of feeding molecules in nutritional support.28 (Reproduced with permission.)

electrolyte additives. The solution has an osmolarity of <600 mOsm/ml and is well tolerated by peripheral veins. The addition of glucose increases the osmolarity and thus may result in phlebitis, considering that the mineral additives also contribute to the osmolarity (approximately 280 mOsm/ml). Although addition of 5 per cent dextrose to the amino acid solution may improve nitrogen balance, any such improvement is primarily due to improved uptake of nitrogen by muscle. The aim of therapy, however, is to encourage visceral protein synthesis. Since it is unknown how clinically significant this difference is, it merits study.

Protein-sparing therapy is indicated for short periods for the hypermetabolic patient from whom IVH is being temporarily withheld, but is of little benefit in management of the severely catabolic patient, for whom IVH is definitely indicated. The failure to develop ketonuria in two to three days, accompanied by hyperglycemia (>100 mg/100 ml), indicates carbohydrate intolerance and insulin resistance, seen with severe sepsis and major stress.50 Patients may manifest mild metabolic acidosis, which is easily corrected by the addition of sodium acetate. A transient increase in blood urea nitrogen does not require treatment.

Amino-acid infusions represent a satisfactory means to preserve lean body mass of patients in the starved state, and minimize catabolism (as opposed to rebuilding body cell mass with IVH). It remains the clinician's judgement to decide the duration of this therapy. It may be necessary to convert to forced-feeding regimens if the stress-producing condition persists. On the other hand, many patients may have adequate preservation of body cell mass, particularly visceral
organisms, and even reversal of early malnutrition with protein-sparing therapy. The clinical condition of the patient together with the nutritional status and extent of hypermetabolism provides the basis for any alteration in treatment plans (Fig. 7).

The catabolic signals in the immediate postoperative state are sufficiently strong to prevent synthesis of body cell mass, and all therapies aim to preserve body tissue. During the anabolic phase, however, forced-feeding regimens encourage cellular synthesis and the rebuilding of body cell mass. Protein-sparing therapy, on the other hand, can successfully reduce catabolism and maintain visceral protein for a limited period. The use of dextrose-free amino-acid solutions fits well with the current understanding of the hemodynamic response to stress and injury. This therapy may also provide better preservation of functional extracellular volume and renal function.

Intravenous Hyperalimentation. The development of intravenous hyperalimentation (IVH) by Dudrick et al. in 1968 has proved to be one of the most significant advances in the care of critically ill patients. Tailoring the hyperalimentation solution to meet a patient's individual requirements also allows appropriate adjustments of specific organ dysfunction, which is often present in patients receiving intensive care.

Table 2 lists the usual composition of the IVH solution in use at the New England Deaconess Hospital. The constituents of a trace mineral mixture are shown in table 3. The role of TPN++ in pre- and postoperative repletion, septic states, intestinal fistulas, burns, and short-bowel syndrome cannot be overemphasized.

Central venous hyperalimentation: delivery of 25 per cent dextrose and 4.25 per cent amino acids mixed as a hypertonic solution into the superior vena cava through a catheter placed in the subclavian vein is generally referred to as "hyperalimentation," originally described by Dudrick. The rate of delivery is gradually increased to meet the goal of daily protein and caloric requirements over three to four days. Complications of central venous hyperalimentation are listed in table 4 and the principles of management also described.

The lipid system: Intralipid has been used for several years in Europe, and has been the subject of a recent review. The peripheral-vein method utilizes three per cent amino acids with 5 per cent dextrose, with which 10 per cent Intralipid (soybean oil emulsion

Fig. 7. Criteria for designing nutritional therapy. The timing and nature of nutritional therapy are determined both by nutritional assessment and by evaluation of the clinical status necessitating such therapy. (Reproduced with permission.)

with egg yolk phospholipid) is administered. Besides its use via central vein catheterization ("50-50" fat:carbohydrate system of Jeejeebhoy), it can also be administered through a peripheral vein. The latter method employs 3 per cent amino acids and 5 per cent dextrose in one bottle, with which 10 per cent fat is "piggybacked" at a distal "Y"-connector into a peripheral vein. This system provides approximately 30 per cent calories from glucose and 70 per cent from fat.

Complications from Intralipid are limited to phlebitis, minor disorders of platelet adhesiveness, febrile reactions, and pigment deposition in the reticuloendothelial system. Specific indications for the use of Intralipid as opposed to IVH with hypertonic dextrose and amino acids have been developed by the authors. Since larger volumes of fluid are necessary to deliver isocaloric amounts of Intralipid, comparison with hypertonic dextrose, its use for critically ill and septic patients may often be limited. The bacterial flora that grow in Intralipid may exceed the variety seen with hypertonic dextrose, and caution must be exercised.

Specific Problems in the Critically Ill Patient

Renal Failure. This complication is one of the major causes of morbidity and mortality in abdominal aortic-aneurysm operations. Renal failure is also often associated with systemic sepsis and shock. The use of IVH in patients with postoperative renal failure has

++ TPN (Total Parenteral Nutrition) is a general term that incorporates all techniques for parenteral feeding. This includes various combinations of intravenous fat, glucose, peripheral-vein infusions, and home hyperalimentation, etc.
been described by Abel et al.\textsuperscript{57,59,60} The principle is adapted from that applied by Giordano to management of patients with renal failure, where endogenous urea is recycled as a source of protein synthesis.\textsuperscript{68} However, protein intake of high quality or a mixture of crystalline amino acids (20–30 g/day) with a nitrogen-to-calorie ratio between 1:450 and 1:700 is most effective.\textsuperscript{61,62} The available amino-acid solutions are quite effective and consistent with the Giordano–Giovanetti diet, which “supplemented essential amino acids” to a regular low-protein diet. Kopple\textsuperscript{63} has demonstrated optimal protein intake in chronic renal failure (creatinine clearance <5 ml/min) to be 20–25 g/day. This value is similar to that observed by most investigators during acute renal failure. Solutions that consist exclusively of essential l-aminocids are now available. Defined formula diets such as Aminade\textsuperscript{88} may be used for the same purpose, when the gastrointestinal tract is functional and there is no contraindication to their use. Response to such therapy is manifested by lowering of blood urea nitrogen and creatinine, easier control of hyperkalemia, hyperphosphatemia and hypermagnesemia, less frequent need for dialysis, and above all, lowered morbidity and mortality.\textsuperscript{57,59,60}

*Hepatic Failure*. An inability effectively to metabolize the aromatic amino acids (tryptophan, tyrosine, and phenylalanine) is seen in hepatic failure. Also, levels of branched-chain amino acids (leucine, isoleucine and valine) are lowered in the serum because of excessive peripheral utilization.\textsuperscript{64} An interesting avenue of approach to this problem is through the use of a nutrient solution with a low level of aromatic amino acids, but a high concentration of branched-chain amino acids. This may not only enhance recovery from hepatic failure, but provide optimal synthesis of brain neurotransmitters in hepatic encephalopathic states.\textsuperscript{65} Special intravenous solutions and diets in hepatic failure will, in all likelihood, prove to be an invaluable adjunct to the measures used in combating this difficult disease process, which carries with it a discouragingly high failure rate from most forms of treatment.

Currently, 2 per cent crystalline amino acids with 20 per cent glucose solution, the latter partially substituted or supplemented with Intralipid, or a combination of enteral and parenteral feeding, represents the best available therapy. The provision of protein-free hypertonic glucose is contraindicated, given its adverse effect on hepatic function.\textsuperscript{66,73}

*Cyclic Hyperalimentation*. This means of providing IVH delivers parenteral feeding with hypertonic dextrose and amino acids for approximately 12 hours each day. During the remaining period, dextrose-free solutions (saline or 5 per cent amino acids) are provided. The development of a “postabsorptive state” allows the mobilization and utilization of calories stored during the glucose phase. Improved visceral function, which accompanies reversal of hepatic steatosis, is observed.\textsuperscript{46} Patients receiving long-term

\footnotesize{\textsuperscript{88} Aminade\textsuperscript{\textregistered}, McGaw Laboratories, Irvine, California.}
IVH benefit from this method, but its use is not recommended for patients who have severe hypermetabolism or those requiring insulin for the control of blood sugar.

Myocardial Dysfunction. A cardiotoxic effect of intravenous hyperalimentation may be extremely important in the control of shock associated with sepsis and severe trauma. The basis for therapy is similar to the rationale for glucose, potassium and insulin (GKI) therapy in septic and cardiogenic shock.66,67 GKI may indeed provide a boost to the cardiovascular system that is either refractory or not optimally responding to other cardiotoxic agents. In addition, nutritional support of the patient with cardiac cachexia has a major role, and is best carried out with "high-density" sources of protein and calories. A reversal of the malnourished state over three to four weeks can improve the outcomes of major cardiac-surgical procedures.68 Despite the fact that infusion of exogenous glucose results in only a modest increase in its oxidation,41,42 the shuttle of glucose moieties through various metabolic pathways, particularly the Cori (glucose–lactate) cycle, would appear desirable, especially during states of shock and hypodynamic "low-flow" sepsis.

Pulmonary Insufficiency. The manufacture of high-calorie and high-protein feedings, concentrated in a small volume of fluid, has made the delivery of IVH in conditions requiring fluid restriction relatively easy. When vigorous diuresis must be carried out, as in post-traumatic pulmonary insufficiency, high-density feedings (providing >1 kcal/ml) can support body cell mass adequately, while providing <1,000 ml total water. Also, salt-poor albumin can be added to the nutrient solution, but is generally wasteful and unnecessary unless it is used to promote circulatory homeostasis. Large doses of potassium may be easily administered as part of the IVH mixture, to combat the hypokalemia from diuresis. The lipid system has no application in this instance, for two reasons. First, large volumes of fluid are necessary to provide Intralipid, glucose, and protein in amounts sufficient to produce nitrogen balance. Second, there may be difficulty in the clearing of fat particles by the damaged pulmonary endothelium, and pulmonary diffusion may be decreased. Both these accompanying effects are undesirable in the management of this disorder.

Sepsis.69,70 Hypermetabolic states associated with sepsis are an important indication for the use of IVH, despite the poor efficiency in utilization of the infused protein. In addition, the presence of carbohydrate intolerance during sepsis exaggerates this effect. The role of nutrition is most important in maintaining body cell mass during the onset of a critical illness, as anabolism of vital tissues is difficult under the

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### Table 3. Trace Elements for Parenteral Use

<table>
<thead>
<tr>
<th>Element</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc</td>
<td>2 mg</td>
</tr>
<tr>
<td>Copper</td>
<td>1 mg</td>
</tr>
<tr>
<td>Manganese</td>
<td>0.4 mg</td>
</tr>
<tr>
<td>Iodide</td>
<td>0.056 mg</td>
</tr>
</tbody>
</table>

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### Table 4. Complications of Intravenous Hyperalimentation and Guidelines for Management

<table>
<thead>
<tr>
<th>Complication</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Pneumothorax</td>
<td>Removal of catheter, needle aspiration, ? closed thoracostomy</td>
</tr>
<tr>
<td>Hemotorax</td>
<td></td>
</tr>
<tr>
<td>2. Subclavian-vein thrombosis</td>
<td>Removal of catheter, add heparin to HA solution</td>
</tr>
<tr>
<td>3. Hyperglycemia</td>
<td>Add insulin to HA solution, capillary blood glucose every 6 hours</td>
</tr>
<tr>
<td>4. Hyperosmolar nonketotic hyperglycemia</td>
<td>Slow or stop HA infusion, insulin, treatment of associated fluid and electrolyte disorders</td>
</tr>
<tr>
<td>5. Metabolic acidosis</td>
<td>Decrease sodium chloride in solution and substitute sodium acetate</td>
</tr>
<tr>
<td>6. Hypokalemia</td>
<td>Potassium in adequate amounts (especially during anabolic or recovery phase)</td>
</tr>
<tr>
<td>7. Hypophosphatemia</td>
<td>Appropriate supplements daily</td>
</tr>
<tr>
<td>Hypomagnesemia</td>
<td></td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td></td>
</tr>
<tr>
<td>8. Essential-fatty-acid deficiency</td>
<td>500 ml Intralipid twice weekly, ? cyclic hyperalimentation</td>
</tr>
<tr>
<td>9. Trace mineral deficiency</td>
<td>Appropriate supplements daily</td>
</tr>
<tr>
<td>10. Catheter sepsis</td>
<td>Establish diagnosis, remove catheter after other sources of sepsis have been ruled out, and reinset catheter after 48 hours.</td>
</tr>
</tbody>
</table>
strong catabolic hormonal influence. Failure to provide nutrients necessary for optimal physiologic activity required to maintain homeostasis is the major cause of the high morbidity and mortality in sepsis. Hyperalimentation of patients with sepsis must be monitored with care, and sites of infection such as the lung, peritoneum and urinary tract must be ruled out prior to incriminating the central venous catheter as the source of sepsis.

When catheter-related sepsis is confirmed, the catheter must be removed, and hyperalimentation resumed after 48 hours. Fever usually subsides after removal of the catheter, and antibiotics are not routinely indicated. Patients who show evidence of septic shock while receiving IVH are best dealt with by immediate removal of the catheter as a precautionary and/or therapeutic measure, followed by resumption of nutritional support once hemodynamic stability has been achieved and antibiotic therapy instituted. The incidence of catheter-related sepsis can be kept less than 4 per cent by good mechanical cleansing of the catheter and catheter site. The importance of maintenance of an aseptic technique and limited breaking of the tubing by "piggybacking" must be emphasized.

**Enteral Hyperalimentation**

It is the aim of most nutritional support plans to utilize the gastrointestinal tract whenever possible, since it is likely that better visceral protein synthesis may result.

By the time gastrointestinal function has returned, participation by the anesthesiologist will be limited. Most commercially available preparations for adult use provide about 1 kcal/ml in their recommended concentrations. Maintenance diets provide a nitrogen-calorie ratio of 1:200 or 1:300, while the high-nitrogen formulas make available a nitrogen-calorie ratio of 1:150 for anabolic needs. This may be lowered to 1:100 for management of sepsis and severe stress. Feeding modules of predigested protein and hydrolyzed starch enable one to compound nutrition prescriptions to fit most clinical situations.

Recently, silastic feeding tubes with mercury tips that allow easy passage and are satisfactory for long-term use have become available. The judicious creation of a feeding jejunostomy or gastrostomy with procedures where prolonged postoperative problems are anticipated considerably facilitates the delivery of nutrients. This is more important where naso-gastric intubation can compound pulmonary problems by causing "silent aspiration," particularly in the presence of an endotracheal tube or a ventilator. Tube feedings as a constant infusion are to be encouraged, and high-density feedings can be delivered with ease at a slow rate with minimal complications from the hypertonosmolar solution. Detailed discussions of enteral feeding can be found elsewhere.

**Conclusions**

Nutritional support of the critically ill patient can improve health and organ function and have a significant impact on survival. An awareness of a patient's nutritional status by the team of surgeon, anesthesiologist and internist helps to identify disease-related malnutrition, and objective responses to nutritional repletion can be measured with relative ease. An understanding of the metabolic alterations after trauma or sepsis can help the practicing physician correct the deficits created during the various phases of injury. In management of the critically ill patient, careful attention must be given to formulating nutritional support plans that allow recovery of associated organ dysfunction. Elective and semielective anesthesia and surgical procedures must be delayed until an adequate plan for the support of organ homeostasis can be developed and instituted. The availability of many modalities of nutritional support enables one to do this quite effectively, so that wound healing, convalescence and the final outcome of operation are influenced in a favorable manner.

**References**

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57. Abel RM, Abbott WM, Fischer JE: Intravenous essential L-amino acids and hypertonic dextrose in patients with