Paparella: Volume I: Basic Sciences and Related Principles

Section 7: General Surgical Principles

Chapter 31: The Rational Use of Applied Nutrition in the Surgical Setting

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The rational application of nutrition to surgical patients is founded on the metabolic response to injury and its effects on body nitrogen. At one end of the spectrum it the patient with simple starvation of whom the application of the principles of nutritional support are appropriate. At the other end is the patient with hypermetabolism and organ failure who requires metabolic support to achieve effective results with a minimum of complications. In both cases, the aim is to prevent malnutrition (an inappropriate reduction in body nitrogen) from becoming a major cofactor in organ dysfunction and in morbidity and mortality.

The distinction between nutritional and metabolic support is that in metabolic support, mediator systems obligate and modulate metabolism to control the flow and utilization of the metabolic substrates: glucose, fat, and amino acids. With neuroendocrine activation, the resting energy expenditure (the energy required to sustain life) increases. The respiratory quotient, the relationship of CO_2 produced to O_2 consumed, approaches 0.8, indicating the oxidation of carbohydrate, fat, and amino acids for energy production. There is an obligatory catabolism accompanied by a reduction in total body protein synthesis. Hepatic protein synthesis is increased as is hepatic ureagenesis. The responsiveness to exogenous nutrition usually seen in starvation states is not present. Thus, exogenous glucose is not able to turn-off hepatic gluconeogenesis and lipolysis in adipose tissue, and has little effect on muscle and visceral proteolysis.

Because of these basic differences in metabolism, two general responses occurred when starvation feeding principles were applied in these cases. First, the expected nutritional results were not uniformly realized, such as nitrogen retention and support of visceral protein synthesis. Second, new complications arose, ranging from pulmonary failure to hepatic failure and the multiple organ failure syndrome. Principles of metabolic support evolved. The major distinction is that the substrate doses are adjusted to accommodate the metabolic response to injury. Thus, the glucose load is reduced, the fat load is increased, and the amino acid load is increased.

Priorities in Application

The metabolic response to injury is a dynamic process. In the presence of dead or injured tissue, perfusion deficits, and infection, the metabolic response is activated. It tends to peak at 2 to 3 days after injury and then to abate after another 3 to 4 days. When the response continues, a complication has occurred, usually an infection. If controlled, the response again abates. With repeated episodes, persistent states of hypermetabolism and organ failure can ensue.

A number of factors have been found to activate the metabolic response to injury. These factors include dead tissue, injured tissue, severe perfusion deficiencies, and invading microorganisms (infection). Any of these factors can induce the metabolic response to injury with its clinical, physiologic, and metabolic characteristics. The link between the activating events and the response is the mediator systems: the central nervous system, the macroendocrine system, and the microendocrine or cell-cell mediator system. They act to regulate metabolic pathways, substrate flow, and utilization with results such as

1. Lipolysis with reduced ketogenesis.
2. Increased gluconeogenesis; a reduction in the fraction of caloric expenditure coming from glucose.
3. An increase in lactate and pyruvate production from peripheral tissues.
4. Increased catabolism of the mobile amino acid stores in muscle, viscera, and connective tissue.
5. Increased peripheral branched chain amino acid oxidation and a mass efflux of the non-branched chain amino acids from the periphery to the liver.
6. Increased hepatic protein synthesis and urea-genesis.

Because of the dynamic nature of the process, it became necessary to develop a system for categorizing the degree of metabolic response present. The degree of metabolic response is not well predicted from the clinical setting or from the various kinds of injury severity scores. It requires the measurement of metabolic response variables, such as urinary area excretion, oxygen consumption, blood sugar levels, or any other variable whose metabolic characteristics are known. Once accomplished, metabolic support regimens follow logically. Thus, support can be adjusted to meet the existing metabolic requirements with the minimum of risk. For instance, a patient may go from starvation to high level septic stress, maintain that state for several days, and then revert to a starvation pattern as the response abates.

There is a need to prioritize the application of the support principles depending on the ranking of that support in the overall scheme of the various treatment modalities in the care plan. Immediately following injury, exogenous substrate support has a low priority. After control of hemorrhage, resuscitation, and necessary surgery, there is a suggestion that early feeding may modulate the metabolic response to injury and improve outcome. The emphasis during this phase is upon the restoration and maintenance of perfusion and oxygen transport. As the hypermetabolic phase of the response to multiple trauma is entered, the priority ranking of substrate support moves up. In the presence of preexisting malnutrition, the priority ranking moves up faster, because one of the goals of treatment is to prevent the development or progression of malnutrition. Once malnutrition is present, its alleviation is difficult. The nature of the patient's injuries needs to be considered because it influences when eating might occur, the route of nutrient administration that might be used, and the kind of nutrient that might be used. Thus, the plan for nutrition may range from none in the setting of a previously well-nourished patient with no severe injuries who is expected to eat in 3 to 4 days; to early aggressive support in a patient with multiple injuries pancreatitis and sepsis who was previously malnourished and not expected to ear in 3 to 4 weeks; to the use of early tube feedings in patients after head and neck surgery.

Rational clinical judgment must prevail.

Nutrient Requirements

Once the decision is made to institute nutritional and metabolic support, the existing energy and substrate requirements of the patient need to be met. With the activation of the neuroendocrine axis, the mobilization of such substrates as essential fatty acids, vitamins, and glycogen is inhibited and deficiency states can occur if these substances are not exogenously supplied. In the case of stress, there is increased mobilization and loss of metabolically important substances such as nitrogen, vitamins, trace elements and minerals such as calcium, magnesium, and zinc. Consequently, deficiency states can develop very rapidly, with overt malnutrition occurring within days in the presence of hypermetabolism.

Energy Requirements

Energy expenditure must be met if energy equilibrium is to be maintained. There are two basic methods for estimating calorie needs. One is the use of the Harris-Benedict equations; the other is by expired gas analysis. The Harris-Benedict equations were derived from population analysis and take into account the patient's age, sex, height, and weight. The number calculated is the basal energy expenditure (BEE), which is the energy expended in the resting, nonstressed state after an overnight fast. In the presence of metabolic stress in which energy demand increases, the BEE must be multiplied by a stress factor to achieve an estimate of the energy needs. Although there is some continued controversy, low stress requires a multiplier of 1.3; moderate stress, a multiplier of 1.5; high-level stress, a multiplier of 1.8 to 2.0; and advanced hypermetabolism, a multiplier of 2.5. The equations are:

Men: BEE = 66 + (13.7 x Wt) + (5 x Ht) - (6.8 x A)

Women: BEE = 655 + (9.6 x Wt) + (1.7 x Ht) - (4.7 x A)

Wt = weight (kg) Ht = height (cm) A = Age (years)

Expired gas analysis applies the principles of indirect calorimetry. The carbon dioxide production and oxygen consumption are measured and from them the respiratory quotient (R/Q) and resting energy expenditure (REE) are calculated. The R/Q represents the ratio of CO_2 production to O_2 consumption. Different fuel utilizations have characteristic ratios: fat, 0.7; glucose, 1.0; and protein, 0.8. An R/Q exceeding 1.0 indicates a net CO_2 production characteristic of net lipogenesis. The REE represents the actual energy expenditure at the time of measurement. As such, it requires no correction for the degree of metabolic stress.

BEE is easy to use, does not require technical equipment, allows calculations to be arrived at rapidly, and is not expensive. However, it is not very accurate in the presence of metabolic stress. REE is quite accurate in most settings; measures oxygen consumption, which can be used to determine the degree of hypermetabolism; and measures the R/Q so that combustion can be

monitored and the administration of excess calories and excess glucose can be avoided. The measurement, however, requires significant labor and technology; it is expensive, and cannot be used reliably in a number of clinical settings such as with inspired oxygen concentrations over 50 per cent in intubated patients and an FIO_2 over 20 per cent in nonintubated patients.

In both cases, the values are estimates of energy expenditure that allow a rational beginning of support to occur. Monitoring of response and outcome needs to be done to tailor the regimen to the particular needs of the patient.

Glucose Requirements

In starvation states, the nonprotein calories can be supplied as glucose alone or as some combination of glucose and exogenous fat. In the first case, fat would be given in amounts only to prevent essential fatty acid deficiency; in the latter case, the fat is being given as a caloric source along with glucose. If glucose is given in excess of demand or total calories are given in excess of demand, net lipogenesis occur, the R/Q exceeds 1.0, minute ventilation increases, hepatic steatosis occurs, and catecholamine excretion markedly increases. A direct, linear relationship exists between the glucose load and CO_2 production. In isotopic studies, the maximum usable glucose load seems to be 5 mg/kg/min. In general, 20 to 25 nonprotein kcal/kg/day provides a reasonable working estimate. The ratio of nonprotein calories to each gram of nitrogen administered approximates 150/1. In settings of glucose intolerance as in diabetes, fat can be substituted for more glucose calories, with a resultant reduction in glucose tolerance.

In stress states, the BEE increases and total glucose oxidation increases but the fraction of total energy expenditure derived from glucose decreases. Even though glucose production is increased and peripheral uptake is normal, the entrance of glucose into the Krebs cycle is reduced and it becomes recycled as lactate and pyruvate. In addition, exogenous glucose is less able to reduce the rate of gluconeogenesis. For these reasons, the glucose load is reduced, with fat making up the difference in calories.

Fat Requirements

The current intravenous fat preparations are emulsions of triglycerides of the essential fatty acids. They are used in nutrition and metabolic support to prevent or treat essential fatty acid deficiency or as calorie sources.

In starvation states, it is necessary to give a certain amount of essential fatty acid to prevent essential fatty acid deficiency. Evidence of the deficiency can range from scaling of skin to impaired wound healing, increased susceptibility to infection, capillary fragility, thrombocytopenia, fatty infiltration of the liver, and alterations in mentation. The requirement is necessary for the inhibition of lipolysis from the insulin response to the high glucose infusions. In patients with glucose intolerance, as in diabetes mellitus, or in patients in whom CO_2 production can be a problem, as in those with advanced lung disease, the fat formulations can be substituted for glucose as part of the calorie source. Providing up to 60 per cent of the

nonprotein calories as fat seems to be well tolerated. When 2 to 3 gm/kg/day are given, adverse effects can occur, particularly hepatic steatosis.

In stress settings, it has been observed that the plasma changes of essential fatty acid deficiency (low arachidonic acid and a high oleic acid) are present from the onset of the stress, presumably a reflection of the hormonal milieu. The exogenous fat emulsions are somewhat effective in controlling this problem and are also effective in controlling this problem and are also effective calorie sources. It has also been shown that they have a protein-sparing effect that is equivalent to glucose. Thus, fat can be used for 30 to 40 per cent of the nonprotein calories.

When using the intravenous fat preparations, it is important to monitor their clearance. This is particularly true in patients with higher levels of stress in whom triglycerides intolerance can develop. In general, a 50-gm intravenous fat load over 12 hours would be cleared by 8 to 10 hours after infusion, either measured by plasma lipemia or triglyceride level. When intolerance occurs, administration can be altered to continuous 24-hour infusion and, in some patients, intolerance disappears. Otherwise, when this stage reached, the administration of lipid emulsion must be stopped.

This late phase of organ failure seems to be the stage of over liver failure and is characterized by triglyceride intolerance, rapid rises in lactate, an endogenous R/Q over 1 with net endogenous lipolysis, rapid reductions in amino acid clearance and hepatic protein synthesis, and a marked increase in catabolism and ureagenesis with prerenal azotemia regardless of whether or not metabolic support is used. This stage is almost uniformly fatal and has no good means of metabolic support. The primary fuel seems to be amino acids.

Protein Requirements

With the onset of starvation, glucose becomes the initial fuel for energy production. When glycogen stores are rapidly depleted, amino acids become the prime source of carbon for the hepatic and renal production of glucose. The source of the amino acids is the mobile amino acid pools in muscle, connective tissue, and the viscera. Within several days, adaptation occurs, the basic principle of which is to spare the amino acid pools by substituting other sources of carbon for glucose, thereby slowing the loss of lean body mass, with a resultant reduction in urinary nitrogen excretion. The sources of this carbon reside mainly in mobilized fat and in the production of ketone bodies by the liver. In addition, glucose oxidation becomes reduced and the glucose recycles as lactate, and glycerol becomes available as a gluconeogenic substrate.

Exogenous glucose or fat, or both, produces a reduction in the mobilization of amino acids in starvation. If amino acids are also supplied, along with vitamins, electrolytes, minerals, and trace elements, positive nitrogen balance and calorie balance can be achieved, particularly within a program of exercise.

With the activation of the mediator systems, total body protein synthesis falls; hepatic protein synthesis increases with production of the acute phase reactants. Catabolism increases

with an increased efflux of amino acids from the periphery. The rate of total body protein synthesis can be increased through the administration of exogenous amino acids; equilibrium with the catabolic rate can be achieved, a phenomenon reflected in the achievement of nitrogen equilibrium (2 to 4 gm of positive nitrogen balance). Reducing the rate of absolute catabolism with exogenous amino acids appears to be relatively ineffective. Increasing the amino acid load beyond this equilibrium point appears to increase both the rates of anabolism and catabolism without a significant change in the equilibrium. The amino acid load necessary to meet the demands of energy production and protein synthesis and to achieve nitrogen equilibrium increases with the amount of metabolic stress present.

Research has shown that the increased oxidation of amino acids was primarily in the peripheral tissue and includes the branched chain amino acids leucine, isoleucine, and valine; that there was a marked increase in the peripheral efflux of the non-branched chain amino acids that correlated with hepatic toxicity; and that there was an excess of gluconeogenic amino acids at a time of increased gluconeogenesis. For these reasons the amino acid formulas were redesigned to increase the amount of branched chain amino acids up to 45 to 50 per cents, and to reduce the amount of non-branched chain and gluconeogenic amino acids. In randomized, prospective, double-blind testing in clinically matched patients at the same level of metabolic stress, the modified amino acids produced better nitrogen retention, improved hepatic protein synthesis, and resulted in less urea production than the standard amino acid formula.

Electrolyte Requirements

The regimen for nutritional and metabolic support must include adequate amounts of sodium, potassium, phosphorus, magnesium, calcium, chloride, and acetate. Adequate amounts of the intracellular electrolytes are especially important because they are necessary for proper metabolic function and anabolism. The requirements for the critically ill patient may differ from that usually prescribed for the starvation patient, because the former patient may have problems such as renal failure, losses from nasogastric tubes or fistulas, sepsis, and acid-base imbalance.

Acid-base imbalance may be affected by the amount of chloride and acetate present in the parenteral solution. For example, the amino acids in these solutions are present in the form of acetate salts to prevent metabolic acidosis. However, if acidosis is present or appears, additional acetate may be added as the sodium or potassium salt. If alkalosis is present or appears, it may help to increase the concentration of chloride by adding sodium or potassium chloride and to decrease the concentration of acetate.

Vitamin, Mineral and Trace Element Requirements

The actual requirements for vitamins, minerals, and trace elements during acute stress are unknown. It is usually recommended that an adequate daily intravenous dose be administered, except to patients in renal failure, in whom trace elements should not be given more than two times a week to prevent accumulation of potentially toxic amounts.

The American Medical Association's Nutrition Advisory Group has established guidelines for daily intravenous doses of vitamins, minerals, and trace elements. There are a number of commercial preparations that meet these guidelines, including MVI-12 (USV laboratories) and MVC9 + 3 (Lypho-Med, Inc.).

Also available are several multitrace element products, all of which contain zinc, copper, manganese, and chromium and meet the Advisory's Group's recommendations, i.e. Multi-Trace Metal Additive (IMS). In stress states, increased amounts of calcium, magnesium, and zinc are lost in the urine. Plasma levels must be used if appropriate amounts of these minerals are to be maintained and deficiency states avoided.

Route of Administration

The route of administration is usually determined by the patient's condition, the access available, and the skill and preference of the practitioner. There are advantages and disadvantages to both the enteral and the parenteral routes. From the point of view of nutritional efficacy, all other things being equal, both routes give comparable results.

The enteral route requires access by a feeding tube. Gastric feeding in stressed patients, who usually have gastric atony, is associated with a high incidence of aspiration. If gastric feeding is to be done, the practitioner must demonstrate that the patient has adequate gastric motility, particularly when enteral formulas with a high fat content are used. In addition, the small bowel has been found to absorb well, even in the presence of ileus. Therefore, the general recommendation is to place a feeding jejunostomy at surgery or to pass a feeding tube past the pylorus either at surgery or to pass a feeding tube past the pylorus either at surgery or by endoscopy or fluoroscopy. It is not recommended to use the large bore polyvinyl chloride salem sumps that are left in place after surgery for tube feeding. If left in place for longer than 7 to 10 days, there is a high risk of causing nasopharyngeal irritation, esophageal erosion, and even otitis media. To avoid these problems, a small bore (i.e. 8 French) Silastic tube should be placed as soon as possible after surgery. Great caution must be exercised when attempting to pass the small Silastic stiletted feeding tubes in patients with tracheostomies, because the feeding tubes have a tendency to enter the trachea. The enteral route is also much cheaper to use than the parenteral route. There is an incidence of diarrhea, usually less than 15 to 20 per cent. With a good regimen of administration and choice of product, most cases of the diarrhea are controllable and do not require the discontinuation of the tube feedings.

Enteral formulas may be delivered as bolus feedings, intermittent feedings, or as a continuous infusion. The type of feeding tube, its location, and the amount of formula needed per day determine the feeding method to be used. With the bolus feeding method, feedings are given four to six times a day. Each feeding is rapidly instilled over a matter of minutes via a bulb or plunger syringe. Volumes generally range from 250 to 500 mL per feeding. This method is not recommended for most patients because bloating, cramping, diarrhea, nausea, and vomiting are frequent side effects.

Intermittent feedings differ from bolus feedings in that, in the former method, each feeding is given over 30 minutes to 1 hour by slow gravity drip. Volumes should not exceed 400 mL per feeding for optimal tolerance. This method is well suited for patients who can receive gastric feedings, have a normal gastrointestinal tract, and are not critically ill.

Continuous infusions are generally administered via an enteral feeding pump. Feedings are infused continuously over 16 to 24 hours a day, with hourly rates of administration not exceeding 125 mL/hour. This method is appropriate for critically ill patients and those who are being fed via the small bowel.

Recent data indicates that tube feedings can be used as an effective form of prophylaxis in stress ulceration of the stomach. Animal studies indicate that use of the tube feeding method very soon after a severe burn may lessen the magnitude of the metabolic response to injury. In the presence of hepatic cholestasis or biliary sludge, tube feeding can be an effective remedy. With the initiation of tube feedings, levels of alkaline phosphatase, gamma glutamyl transamylase, and bilirubin may rise transiently.

The parenteral route ensures that nutrient actually was delivered into the bloodstream. It is expensive and has a number of complications. Incompatibilities are frequent problems. The practitioner would be well advised to seek the advice of a clinical pharmacist when these questions arise.

Irrespective of the route of administration, appropriate monitoring must be done to achieve an appropriate clinical response with a minimum of complications. This is particularly important in the first several days of therapy and with changes in the condition of the patient. It is necessary to achieve nitrogen equilibrium (2 to 4 gm of positive nitrogen balance) with an improvement in visceral protein status at a BUN less than 100 to 125 mg/dL and an R/Q less than 0.9 if positive mortality/morbidity outcomes are to be achieved. Sometimes, however, the clinical setting prevents the attainment of these goals, as in settings of oliguric renal failure or severe hypermetabolism and organ failure, or cardiogenic states. In other clinical situations, the disease process may not allow the nutritional benefits to be realized, even when the nitrogen retention goal is achieved. The latter event is a poor prognostic sign, as in cases of rampant organ failure and cancer cachexia. Nonetheless, these are goals to be achieved for the greater benefit of most patients.