Nutritional support of the pediatric trauma patient

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KEYWORDS
Pediatric trauma; Nutrition support; Energy expenditure; Enteral nutrition

Training in trauma surgery and critical care emphasizes that recovery after critical illness depends on adequate oxygen delivery. This emphasis is correct but incomplete. Oxygen is indispensable, but chemically it is simply an ash can for spent electrons, useless to the cells without substrate fuel to burn. The neurons in a child’s brain will die nearly as quickly when deprived of dextrose as when deprived of oxygen, and hypoglycemia can significantly shorten the duration of hypoxia tolerated by the brain.1 Similarly, repair of injury cannot take place in either a hypoxic or a catabolic state. Catabolic protein breakdown and depletion of energy slow healing and can extend and complicate injury. This implies that an inadequate supply of energy and protein can be viewed as another form of shock. It is no wonder then that, after the ABCs of trauma resuscitation, nutrition support can be the most important determinant of outcome in the critically injured child.2 The strategy for substrate delivery should be similar to that for oxygen delivery: goal-directed therapy based on remeasurement after medical interventions.

The pediatric trauma patient differs in important ways from the adult patient. For instance, major trauma induces dramatic metabolic aberrations in both children and adults but to rather different magnitudes.3 These responses are magnified in the context of the large differences in nutritional needs between children and adults even in uninjured conditions. Treating injured children according to the same quantitative heuristics for protein and energy supply one might use in an adult will not provide adequate support. Because oversupply of fluid, protein, and carbohydrate in a child carries high risk of new complications, imprecise substrate delivery can lead to iatrogenic injury. By contrast, understanding the differences between carbohydrate and protein metabolism in the injured child allows the clinician to avoid the potential complications related to either underfeeding or overfeeding, thereby speeding recovery.

This review describes the physiological and metabolic alterations in the pediatric trauma patient with particular attention to specific differences in children’s needs (when known). The physiological rationale or clinical evidence for practical interventions is described.
Catabolic response to trauma

The physiological response to trauma is accompanied by a constellation of metabolic changes. The degree of response is proportional to the severity of injury. Cuthbertson and Tilstone classically describe two phases of metabolic response to trauma: ebb and flow. The initial ebb phase, lasting approximately 3-5 days after injury, is characterized by decreased cardiac output, temperature, blood pressure, and oxygen consumption. This is followed by the flow phase, with increased cardiac output, increased core temperature, and elevated expression of catabolic hormones. Muscle protein breakdown and protein turnover during this phase are vastly elevated. Children also appear to display similar ebb and flow physiology but with important differences.

The major hormonal changes during the flow phase include increased levels of serum glucagon, cortisol, and catecholamines, (eg, epinephrine, norepinephrine, and dopamine). These oppose the anabolic effects of insulin, mobilizing endogenous sources of protein, carbohydrate, and fat to provide essential substrate intermediates and energy necessary to fuel the ongoing inflammatory response.

One of the most important of these hormones is glucagon. Glucagon induces glycolysis and gluconeogenesis to boost circulating serum glucose. Children, especially infants, have more restricted hepatic glycogen stores, particularly in the context of their higher per kilogram metabolic rate. Limited glycogen stores can be quickly depleted, increasing reliance on gluconeogenesis, or the generation of glucose from noncarbohydrate carbon substrates, including lactate, glycerol (derived from free fatty acids), and glucogenic amino acids (such as alanine and glutamine). On a per kilogram basis, gluconeogenesis is more important to infants and children, perhaps because of the proportionately larger nature of the brain (which demands an uninterrupted and large supply of glucose or ketones). Glycolysis, the conversion of glucose to pyruvate, produces lactate and alanine, both of which serve as substrate for the endogenous regeneration of glucose through the Cori and alanine cycles.

Provision of exogenous glucose from nutritional support does not halt gluconeogenesis after injury. Instead, glycolysis and gluconeogenesis continue to alter carbohydrate metabolism during acute metabolic stress. Excess glucagon can produce hyperglycemia, strips the liver of glycogen reserves needed to buffer blood glucose levels, and contributes to protein loss by driving gluconeogenesis.

Cortisol is also elevated after major injury because of adrenocorticotropic hormone release from the anterior pituitary. Cortisol induces muscle proteolysis through associated cytokine release (predominantly interleukin-6 and tumor necrosis factor, both released following activation of macrophages) and gluconeogenesis. As with glucagon, cortisol drives new glucose synthesis by stripping amino acids, especially alanine and glutamine, from skeletal muscle and the gut. These amino acids contribute three-carbon units to the liver for conversion to glucose.

This loss of glutamine is particularly important. Glutamine depletion has been observed during critical illness in adults and children, appearing surprisingly early during intensive care unit (ICU) stays. In addition to its roles in gluconeogenesis and synthesis of nucleic acids, glutamine acts as the primary oxidative fuel for enterocytes and lymphocytes. Therefore, glutamine depletion is believed to damage intestinal and immune function in critically ill or injured patients. These observations provide the rationale for glutamine supplementation, which will be discussed in greater detail below.

Catecholamines (including epinephrine, norepinephrine, and dopamine) released from the adrenal medulla by the sympathetic nervous system leads to both hyperglycemia and lipolysis. Catecholamines contribute to hyperglycemia indirectly through the suppression of pancreatic secretion of insulin and directly by promotion of glycogenolysis (eg, conversion of skeletal muscle glycogen to lactate). Lactate acts as a substrate for the Cori cycle in the liver, where it is converted to glucose. Catecholamines also induce lipolysis, or the breakdown of fat into free fatty acids and glycerol. Glycerol can then be used to produce glucose via gluconeogenesis, whereas free fatty acids are used directly for energy.

Although children are threatened by these catabolic effects on carbohydrate and fat stores, the real danger lies in protein catabolism. Although both fat and carbohydrate can be stored, there is no such thing as a “protein store.” Therefore, protein catabolism always results in some kind of diminished capacity, whether the proteins are clotting factors, immune factors, or actin–myosin chains. This effect is magnified in children whose lean body mass is smaller relative to body size. Without provision of adequate substrate in the form of dietary protein after major injury, loss of diaphragmatic and intercostal muscle can lead to ventilatory compromise (manifesting, for example, as extubation failure) in less than a week. The heart appears to be protected initially, but after loss of approximately one-third of lean body mass, loss of cardiac muscle may lead to decreased cardiac performance and even fatal arrhythmias.

The best way to attenuate protein catabolism is to repair the injury by early surgical intervention and to lessen the physiological injury by early goal-directed restoration of perfusion. In the presence of injury, nothing (including oversupply of protein) will halt the increased protein catabolism. However, the provision of adequate calories and protein can decrease recovery time and prevent late complications (eg, infection, wound dehiscence, decubitus ulcer, delayed healing, and prolonged rehabilitation), and it is to these ends that nutritional support is directed.

Means and ends of nutritional support in pediatric trauma

Early nutrition in the pediatric trauma patient can ameliorate the deleterious effects of excessive protein catabolism by

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speeding the rate of recovery (function, wound healing) and decreasing the risk of late complications (infection, dehiscence, death). These are the ends we wish to achieve. Here, we are mostly concerned with the means of achieving those ends. These means can be distilled into a few simple imperatives:

1. Feed early;
2. But not too much;
3. Give enough protein;
4. Feed the gut; and
5. Use additives and specific formulations aimed at reducing damage from reactive oxygen species and improving gut function.

**Feed early**

Feeding the injured child may be delayed by a number of obstacles, including interruptions in feeding caused by clinical instability, airway management, and radiologic and surgical procedures. Too often, children in the ICU do not receive enough calories, even when feeds with proper calories have been ordered. One study in critically ill pediatric patients noted that delivery of the energy prescription was inadequate in >50% of all enteral nutrition days. Unfortunately, clinicians rarely pay enough attention to the actual calories delivered, focusing instead on nutrition ordered. By contrast, in units where “substrate delivery” shares similar emphasis to other organ systems, this error is far less likely to occur. Sometimes the chaotic nature of the first few postinjury days prevents immediate provision of calories. For example, the gut may be unavailable because of ileus secondary to abdominal injuries, surgical repair, abdominal compartment syndrome, or ongoing shock and pressor support (discussed below). Gastric feedings may be hindered by gastroparesis in response to a head injury. Patients may lack adequate venous access for anything but correction of shock. For these reasons, in the first day or two after injury, it is not unreasonable to “let the dust settle.”

Nevertheless, initiation of nutrition support should begin as soon as the patient has been initially resuscitated and stabilized. In general, a reasonable rule of thumb is to ensure some form of nutritional support on postinjury day (PID) 1 whenever possible, but no later than PID 3. Evidence suggests that early attention to nutrition reliably improves recovery (Figure 1). For example, in patients suffering from traumatic brain injury (TBI), feeding to achieve caloric goals within 48 hours was associated with a reduction in infectious morbidities in adults and accelerated neurologic recovery at 3 months postinjury.

In cases where enteral nutrition is contraindicated (eg, gastrointestinal obstruction, prolonged ileus, high output/proximal enterocutaneous fistula, intractable diarrhea or vomiting, high-dose inotropic agents), total parenteral nutrition (TPN) should be initiated. Recall that the profound metabolic changes that accompany trauma elicit a magnified effect in children whose lean body mass is smaller relative to body size and whose metabolic needs vastly outweigh that of an adult on a per kilogram basis. Feeding early, whether enterally or parenterally, is one of the best ways of feeding enough.

**But not too much**

Provision of adequate calories is the first step in providing appropriate nutrition support. Protein retention is augmented by the provision of adequate calories, especially when protein intake is marginal. But children handle energy differently than adults. Not only do they have a far higher per kilogram metabolic power than adults, but the energy is partitioned differently. Small children and babies devote more energy to maintenance of body temperature, and they use large fractions of total energy expenditure for growth. For example, healthy infants use approximately 30%-35% of calories for growth, whereas 2 year olds use only 2%-5% of total energy intake for growth. Approximately 5 kilocalories (kcals) in excess of resting energy expenditure (REE) are needed to build about 1 g of new tissue. This growth energy is the first to be diverted during major illness or injury.

One of the prime differences between children and adults is that children do not show increased overall energy consumption in response to trauma. Instead, calories that would normally be used to support growth are shunted to support the hypermetabolic response, yet there is no significant increase in the overall per kilogram energy needs of the injured child. This does not mean the energy expenditure is not increased during high fever or sympathetic storm or seizures; bedside estimates of energy expenditure must be adjusted to clinical context. Nevertheless, this finding shows
that injury per se does not directly increase the child’s energy expenditure, and the practice of adjusting energy estimates by an additional “stress factor” to account for the trauma is an error.

Overfeeding occurs when the amount of calories administered exceeds the amount necessary for metabolic homeostasis. Some clinicians believe that “more is better” and resort to oversupply of calories and nutrients to overcome injury. But provision of excessive calories cannot overcome or reverse the metabolic changes that accompany trauma and actually exposes the patient to several risks, including the following:

1. Increased carbon dioxide (CO$_2$) production, resulting in increased work of breathing and ventilatory failure;
2. Hyperglycemia;
3. Hyperinsulinemia;
4. Increased hepatic workload;
5. Increased hepatic fat deposition; and
6. Immunosuppression.$^5,6$

Overfeeding increases VCO$_2$ (the volume of CO$_2$ produced), producing hypercapnia, increased work of breathing, acidosis, and delayed extubation. Excessive glucose intake leads to rising insulin levels, resulting in decreased fatty acid oxidation, reduced ketogenesis, increased glucose oxidation, and increased lipogenesis.$^5$ Serum transaminase levels subsequently increase, reflecting hepatocellular injury.$^{12}$ Lipid overfeeding with long-chain triglycerides inhibits bacterial clearance in the reticuloendothelial system,$^{13}$ whereas excessive caloric delivery can cause immunosuppression, perhaps by forcing hyperglycemia. There appears to be a direct association between hyperglycemia and impaired granulocyte adhesion; chemotaxis and phagocytosis; and decreased immunoglobulin function and complement fixation in vitro.$^{5,14}$

Determination of energy expenditure would decrease the risks of overfeeding and underfeeding. Unfortunately, methods for measuring or estimating energy expenditure in humans, especially small humans, are historically difficult. Clinically, the gold standard of determination of energy expenditure is by indirect calorimetry based on measurements of oxygen (O$_2$) consumed in relation to CO$_2$ produced per unit time. Indirect calorimetry returns REE—that is, energy expended by a sedated, (typically) fasting patient. Sometimes these circumstances match the clinical context, but often they do not, leaving the clinician with a misleading measurement.

REE can also be estimated through the use of predictive equations, including Harris–Benedict, World Health Organization, Schofield, and White (Table 1). Unfortunately, these estimates diverge from measured energy expenditure, differing by >10% (over or under) in critically ill children.$^{15,16}$

Caloric requirements can vary based on the type of trauma and can change during the child’s convalescence. For instance, the clinician may suppose that a child on a ventilator after injury will have lower energy needs, reasoning that the ventilator supplants the work of breathing. But a child with acute respiratory distress syndrome (ARDS) after pulmonary contusion may actually have higher energy requirements because of metabolic demands imposed by the inflamed lungs themselves. Children with traumatic brain injury further illustrate the point. Although children with

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Equations for calculation of resting energy expenditure</th>
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<tr>
<td><strong>Equation</strong></td>
<td><strong>Harris–Benedict (kcal/d)</strong></td>
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<tr>
<td></td>
<td>Males</td>
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<tr>
<td></td>
<td>$66.4730 + [5.0033 \times \text{height (cm)}] + [13.7516 \times \text{weight (kg)}] - [6.7550 \times \text{age (y)}]$</td>
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<tr>
<td></td>
<td>Females</td>
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<tr>
<td></td>
<td>$655.095 + [1.8496 \times \text{height (cm)}] + [9.5634 \times \text{weight (kg)}] - [4.6756 \times \text{age (y)}]$</td>
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<td><strong>WHO (kcal/d)</strong></td>
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<tr>
<td>Males</td>
<td></td>
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<tr>
<td>0-3 y</td>
<td>$[60.9 \times \text{weight (kg)}] - 54$</td>
</tr>
<tr>
<td>3-10 y</td>
<td>$[22.7 \times \text{weight (kg)}] + 495$</td>
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<tr>
<td>10-18 y</td>
<td>$[17.5 \times \text{weight (kg)}] + 651$</td>
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<tr>
<td>Females</td>
<td></td>
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<tr>
<td>0-3 y</td>
<td>$[61.0 \times \text{weight (kg)}] - 51$</td>
</tr>
<tr>
<td>3-10 y</td>
<td>$[22.5 \times \text{weight (kg)}] + 499$</td>
</tr>
<tr>
<td>10-18 y</td>
<td>$[12.2 \times \text{weight (kg)}] + 746$</td>
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<tr>
<td><strong>Schofield (MJ/d)</strong></td>
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<tr>
<td>Males</td>
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<tr>
<td>3-10 y</td>
<td>$[19.59 \times \text{weight (kg)}] + [130.3 \times \text{height (m)}] + 414.9$</td>
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<tr>
<td>10-18 y</td>
<td>$[16.25 \times \text{weight (kg)}] + [137.2 \times \text{height (m)}] + 515.5$</td>
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<tr>
<td>Females</td>
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<tr>
<td>3-10 y</td>
<td>$[16.969 \times \text{weight (kg)}] + [161.8 \times \text{height (m)}] + 371.2$</td>
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<tr>
<td>10-18 y</td>
<td>$[8.365 \times \text{weight (kg)}] + [465 \times \text{height (m)}] + 200.0$</td>
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<tr>
<td><strong>White (kJ/d)</strong></td>
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<tr>
<td>Males</td>
<td></td>
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<tr>
<td>3-10 y</td>
<td>$[17 \times \text{age (months)}] + [48 \times \text{weight (kg)}] + [292 \times \text{temp (°C)}] - 9677$</td>
</tr>
</tbody>
</table>

Conversion factors: MJ $\times$ 238.846 = kcal, kJ $\times$ 4.186 = kcal.
Abbreviations: kcal, kilocalories; kJ, kilojoules; MJ, megajoules; REE, resting energy expenditure.
severe TBI may show a transient (1-5 days) increase in overall energy expenditure, these demands may be tempered by therapies used in the treatment of TBI. Sedation, chemical paralysis, and barbiturate coma all decrease energy expenditure. Numerous studies have shown that patients receiving sedation had an energy expenditure measured at between 89% and 120% of estimated REE, whereas those not receiving sedation had energy expenditures measured at 138%-160% REE. It has been proposed that fentanyl and Versed, two widely used sedatives in children, alter the metabolic response to trauma by blunting the initial increase in stress hormones and decreasing plasma catecholamine levels. Whatever the mechanism, serial measurements of calorie needs via indirect calorimetry may be the only means to objectively control for these changes.

Unfortunately, indirect calorimetry often is simply not available or not feasible. If measurement is unavailable, and current estimation methods are unreliable, and the penalty for inaccurate calorie supply is high, what strategy should be followed? In general, we follow a strategy of weight-based calorie estimation plus repeated measures of weight and laboratory values, or “measure–intervene–measure.” A simpler heuristic equation allows quick bedside estimate of calorie needs based on body mass alone

\[ E = 200 \times M^{-0.4} \]

where \( M \) is body mass in kg, and \( E \) is energy. Note that this function returns kcals/kg/day; total kcals/day is determined by multiplying the answer by mass (or adding 1 to the exponent). This power law equation captures the nonlinear relationship between mass and metabolic power and can be calculated quickly at the bedside for patients of any body mass. When using TPN, about 15% of this estimate should be subtracted to account for gut \( \text{Vo}_{2} \), or the “thermogenic effect of food.”

This equation does not account for extremes of age (prematurity), body habitus (severe failure to thrive, obesity), or clinical condition (seizures, fevers, paralysis). No estimate equation can account for these, and it is a serious error to employ this equation, or any estimate equation, out of clinical context. Instead, this equation acts as a good first approximation, to be followed by updated estimates based on serial measurements of clinical data. For example, following this equation, a 12-kg child with a head injury would be started at 74 kcal/kg/day, but this number might be adjusted upward if the child was having frequent seizures or downward if the \( \text{CO}_{2} \) and blood urea nitrogen (BUN) were rising, or if the calorie source was TPN.

**Give enough protein**

The single most important nutritional intervention following pediatric trauma is the provision of adequate protein. Proteins undergo a constant state of degradation and resynthesis known as protein turnover. Even at baseline, protein turnover is greater than protein synthesis, and turnover is much higher in newborns (>6 g/kg/d) than adults (3.5 g/kg/d). After injury, the protein flux is even higher. The high rate of protein turnover increases the pool of amino acids available for energy and other responses, producing a net redistribution of amino acids away from skeletal muscle to the wound, acute phase reactants, and the liver (Figure 2). This increased supply of amino acids allows for the synthesis of acutely needed enzymes, serum proteins, and glucose. Synthesis of positive acute phase proteins involved in the inflammatory process, such as C-reactive protein (CRP), fibrinogen, and haptoglobin, are increased, whereas downregulation of negative acute phase proteins, including albumin, retinol binding protein, and prealbumin, occurs concurrently. In this circumstance, prealbumin and albumin levels do not reflect nutritional status: they are depressed due to ongoing physiological injury and inflammation. Rather than being purely pathologic, freeing amino acids during stress probably translates to maximal adaptability and seems likely to have conferred an evolutionary advantage in cases of injury and other stresses.

Even if this response allows for short-term advantage, the result of “recruiting” functioning proteins is to degrade their function, prolonging the patient’s recovery. Early and adequate enteral or parenteral protein supply aims to shorten this recovery time. Nutrition regimens should aim to provide 15%-20% of total calories as protein because reductions in nitrogen loss have been demonstrated at this level of intake. This translates to approximately 2-3 g/kg/d for infants and children under 2 years of age, 1.5-2 g/kg/d for children ages 2-13 years, and 1.5 g/kg/d for adolescents. This amount of protein has been shown to support resistance to infection, replenish preexisting or injury-driven depletion, maintain muscle mass, and support replacement of exudative losses to promote wound healing.

![Figure 2](image-url)

**Figure 2** There is no “protein reserve.” After injury, catabolism of functional protein increases the flux through a tiny free amino acid pool, driving most amino acids toward the liver for conversion to glucose. Supply of adequate dietary protein allows rebuilding of functional protein, but oversupply cannot force anabolism.

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Note that, in certain severely stressed states, including major burn injury, additional protein may be required.

But more is not always better. Toxicity has been noted in patients who receive an oversupply of protein. For example, neonates receiving greater then 6 g/kg/d exhibited azotemia and pyrexia.21 Oversupply of protein may be detected by rising BUN, rising serum osmolarity, and acidosis.

Recovery can also be heralded by trends in laboratory values. It is our practice to follow serial measurements of CRP, prealbumin, and albumin. As CRP levels fall, it is expected that prealbumin and albumin will rise if nutritional needs (both calorie and protein) are being met. As with calorie requirements, protein needs should be serially evaluated through laboratory measurements and nitrogen balance studies (where feasible) as needs change throughout the course of recovery. In patients suffering from TBI, protein catabolism appears to peak 8-14 days postinjury.22

Feed the gut

Enteral nutrition is the preferred method of feeding whenever clinically possible. Early provision of enteral nutrition forestalls the breakdown of glycogen and fat stores, attenuates the effects of protein breakdown, blunts the innate inflammatory response, promotes immune competence, decreases infections, and limits the risk of bacterial translocation.24-26 Enteral nutrition itself has numerous physiological advantages over parenteral nutrition, including the following:

1. Decreased bacterial translocation;
2. Maintenance of gut mucosal integrity;
3. Decreased infectious complications;
4. Improved nitrogen retention;
5. Enhanced wound healing; and
6. Improved immune response.7,8

The cells of the liver, spleen, and pancreas can be supplied via either the enteral or parenteral routes, whereas enterocytes can only be nourished by nutrients delivered to the gut lumen. Luminal nutrients maintain villus structure, potentiate absorption, and strengthen the gut immune barrier.27

Because of these advantages, clinicians often deliver “trophic feeds” to patients who cannot absorb all of their nutrition from the gut. However, confusion exists regarding the provision of “trophic” feedings in pediatric patients who range from a few kilograms to over 100-kg body mass. Therefore, some “low rate” of feeds, say 7 mL/h of a 1-kcal/mL formula, could be insufficient to feed the enterocytes in a large teenager but approach total daily calories in an infant. A better heuristic is needed for pediatric patients.

Because trophic feeds are intended to supply just enough nutrients into the bowel lumen to nourish the enterocytes, estimating intestinal oxygen consumption gives an estimate of trophic feeds for different sized patients. Before a meal, the splanchnic blood flow accounts for approximately 25% of cardiac output and Vo2 (therefore, of total energy expenditure) regardless of patient size.28-30 The splanchnic organs consist of the small and large bowel, stomach, liver, spleen, and pancreas. Assuming that approximately half of splanchnic blood flow is to the gut, trophic enteral feeding rates of 12% of total estimated calories would be adequate to nourish the enterocytes. So, trophic feeds for a 4-kg infant would be around 12% of per kilogram daily calories, or

\[ \frac{200 \times 4^{-0.4}}{3}\times 0.12 = 13.8 \text{ kcal/kg/d} \]

Assuming the baby is being fed formula containing 0.67 kcal/mL (or “20-cal/oz” formula), the enteral feeding rate would be

\[ \frac{13.8 \text{ kcal/kg/d} \times 4 \text{ kg}}{0.67 \text{ kcal/mL} \times 24 \text{ h/d}} = 3.4 \text{ mL/h}, \]

or about 3 mL/h. Similarly, a 20-kg child would need about 6 mL/h of a formula with 1 kcal/mL (“30-cal/oz”), and a 55-kg child would need around 11 mL/h of a similar formula.

Clinicians are often reluctant to give enteral feeds to any patient who requires inotropic support (eg, to treat low systemic vascular resistance or to boost cranial perfusion pressure in TBI), because imposing additional work on the gut could worsen intestinal ischemia. The gut’s particular sensitivity to ischemia lies in part in the structure of its vasculature. Arterial blood flow from the celiac artery, superior mesenteric artery, and inferior mesenteric artery, with branches from the celiac and superior mesenteric arteries, supplies the gut. Smaller branches form plexuses in the serosa and submucosa of the small bowel. The anatomical arrangement of the villus, with the artery and vein lying parallel but flowing in opposite directions, creates countercurrent gas exchange of oxygen within the villus.30 As a result, there is a lower partial pressure of O2 at the tip of the villus, leaving enterocytes here more susceptible to hypoxia from vasoconstriction.29 Inotropes with strong alpha-agonist activity appear to potentiate this ischemia by shunting blood away from the mucosa.

The high metabolic activity of the splanchnic region accounts for around 25% of oxygen consumption in the body but also the lowest oxygen extraction ratio (3%) of any tissue bed in the body.30 Taken together, these ratios reveal the dependence of the splanchnic bed on blood flow. Meanwhile, digestion and absorption of food increases the metabolic rate of the gut. In response to a meal, splanchnic oxygen consumption in the human can double while oxygen extraction remains the same.30 Because oxygen extraction remains constant, this increased demand is met by increased blood flow to the gut, producing the well-known phenomenon of postprandial hyperemia.31 However, in any circumstance where intestinal blood flow is limited (eg, high-dose alpha-agents, poor cardiac performance, redistributive shock, etc.), oxygen demand can exceed oxygen supply, leading to bowel ischemia and even necrosis. Feeding in such circumstances would worsen ischemia and make bowel injury more likely.
Nevertheless, the presence of alpha-agents alone is not a contraindication to enteral feeds. For example, low doses of norepinephrine and dobutamine simultaneously appear to improve splanchnic perfusion in children. It is reasonable to consider enteral feeding when vasopressor agents are at steady or decreasing doses. There are strategies that can attenuate “intestinal work” and still supply good nutritional support. In particular, enteral feedings should have the lowest available osmolarity, should not contain insoluble fiber (which can produce bloat, distension, and even constipation), and should be initiated at low continuous rates with steady but cautious advancement. Intolerance from ischemia will be signaled by ileus, abdominal distension, and occult blood in the stool.

Use additives and specific formulations

Severe trauma directly and indirectly causes immunologic dysregulation, increasing the risk of infection, sepsis/systemic inflammatory response syndrome, and multiple organ failure. There is evidence that some substances can modify these responses in clinically desirable ways, suggesting that such “immunonutrition” has an important role in trauma care. Numerous studies in adult trauma patients demonstrate that nutritional additives can strongly improve outcomes. Although not all tested in pediatric trauma patients, supplements demonstrated to have significant positive effects in adult-sized patients may improve outcomes in small patients as well. Immunonutrients with potential benefit in trauma are summarized in Table 2.

Antioxidants

Reactive oxygen species (ROS) play a central role in ischemia/reperfusion injury and the systemic inflammatory response that accompanies critical illness and trauma. ROS, or free radicals, include hydroxyl (HO), the superoxide anion, and hydrogen peroxide (H2O2). Restoration of oxygen to ischemic tissues after resuscitation from shock leads to the generation of ROS as byproducts of membrane lipid metabolism and from leakage of electrons from mitochondrial electron transport chains. During the systemic inflammatory response (as seen after trauma), the production of free radicals outpaces cellular defenses (eg, superoxide dismutase), resulting in oxidative injury of cellular proteins and nucleic acids, induction of apoptosis, induction of lipid peroxidation that destroys cellular membranes, and organ injury manifested by ARDS and multiple organ failure.

Fortunately, inflammatory damage can be blocked by antioxidants.

Among the more potent of these endogenous antioxidant defenses are vitamin E, vitamin C, and selenium. Vitamin E is a collection of lipid-soluble tocopherols and tocotrienols obtained from plant oils. Tocopherols are readily incorporated into cellular membranes, where they interrupt lipid peroxidation and alter intracellular signaling pathways that rely on ROS. Vitamin C, or ascorbic acid, is a water-soluble antioxidant capable of scavenging free radicals, especially HO and H2O2. Both vitamins C and E may also reduce the incidence of infectious complications by restor-

<table>
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<th>Table 2 Use of immunonutrients in pediatric trauma</th>
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<tr>
<td><strong>Immunonutrient</strong></td>
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<td>------------------</td>
</tr>
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<td>Whey protein</td>
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<td>Glutamine</td>
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<td>Antioxidants (selenium, vitamin C, vitamin E)</td>
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Abbreviations: LOS, length of stay; RDA, recommended daily allowance.
Glutamine supplementation has been associated with numerous potential benefits in critically ill patients, including the following:

1. Enhanced insulin sensitivity;
2. Decreased free radical availability;
3. Enhanced heat shock protein;
4. Maintenance of the intestinal mucosal barrier; and
5. Preservation of muscle mass.

Glutamine, a conditionally essential amino acid, is the preferred fuel source of enterocytes and plays a key role in the intermediary metabolism of the gut mucosa. Orally administered glutamine is entirely metabolized by the enterocytes and does not appear in the circulation. Glutamine also plays a crucial role in maintaining mucosal integrity through the reversal of shock-induced splanchnic vasoconstriction even after systemic shock resuscitation. In addition, glutamine has been shown to induce antioxidant enzymes (e.g., glutathione peroxidase) and activate kinases necessary for proliferation of enterocytes.

The evidence supporting glutamine supplementation is strong. A systematic review of glutamine supplementation performed by Novak et al found that surgical patients receiving glutamine had significant reductions in infectious complications and length of stay. McQuiggan et al explored the effects of supplementing enteral glutamine to patients with major torso trauma beginning on PID 0. Patients were randomized to receive either 0.5 g/kg/d of glutamine or an intact whey protein supplement via a nasogastric (NG) tube. Enteral nutrition was started for both groups starting on PID 1-2. Not only was glutamine well tolerated with no adverse effects, but patients receiving glutamine showed significantly fewer instances of high NG output, abdominal distention, and total instances of intolerance (including diarrhea and vomiting). By PID 7, patients receiving glutamine were tolerating approximately 30% more enteral nutrition than controls, and none of the patients receiving glutamine required TPN.

Omega-3 fatty acids

The active components of omega (ω)-3 fatty acids are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA and DHA displace arachidonic acid from cellular membranes, promote the synthesis of less inflammatory eicosanoids (including thromboxanes and prostaglandin E₂), and inhibit proinflammatory mediators (such as iNOS). In an animal study conducted by Oz et al., rats receiving nutrition containing EPA-DHA and fructooligosaccharides (prebiotic short-chain fibers) lost considerably less weight and had significantly less rise in serum transaminases and hepatic pathology following injection of lipopolysaccharide (LPS). LPS released by colonic microorganisms leads to upregulated ROS and inflammation, mimicking systemic inflammatory response syndrome in humans. Singer et al found that patients with acute lung injury receiving enteral nutrition containing EPA and gammalolinolenic acid showed significant improvement in oxygenation, compliance, and decreased duration of ventilation. Overall, supplementation with ω-3 fatty acids may help protect the lungs against systemic inflammation.

Whey protein

Numerous studies have found significantly faster gastric-emptying time in formulas containing hydrolyzed whey compared with formulas containing mostly casein. After digestion in the stomach, casein curdles, whereas whey remains liquid. In the stomach, casein behaves like solids, which have a slower gastric-emptying time than liquids. In the small intestine, casein breaks down into beta-casomorphones, a form of opioid not produced after feeding hydrolyzed whey formulas. It has been postulated that these opioid peptides decrease gastrointestinal motility through...
direct interaction with gut opiate receptors. 52,53 Because children are already at risk for disordered gut motility after trauma (eg, ileus, gastroparesis after TBI, etc.), using a whey-based enteral formula may improve tolerance.

Conclusions

Nutrition support after trauma is often neglected, but adequate substrate delivery remains one of the most powerful and straightforward interventions available to protect and heal an injured child. Inadequate calorie and protein supply is best understood as an avoidable form of shock. Children are different, and the differences must be implemented into nutritional strategy. In comparison with adults, the following is true about children:

- Have higher energy expenditure per kg of body weight;
- Require more gut perfusion to absorb calories, leaving them more vulnerable to mucosal ischemia;
- Do not increase energy expenditure in response to injury, instead shunting energy from growth (protein synthesis) while keeping total energy expenditure about the same;
- Exhibit higher rates of protein turnover after injury; and
- Have far lower capacity to tolerate protein loss without complications, such as infection, prolonged intubation, delayed healing, etc.

Reasonable nutrition strategies for children include the following:

- Early feeding (eg, initiation of substrate delivery on PID 1, attempt to reach goal calories by PID 3);
- Enteral feeding (whenever safe, defaulting to TPN otherwise);
- Feeding strategies that minimize intestinal work and intolerance: whey protein, low osmolarity, no added insoluble fiber, vigilant steady advancement to goals, use of postpyloric and/or continuous feedings in the early postinjury phase;
- Avoidance of overfeeding;
- Consideration of supplementation with antioxidants, glutamine, and ω-3 fatty acids; and
- Customized feeding regimens that are adjusted in response to frequent measures of body weight, CO2, BUN, gut performance, and trends in levels of prealbumin and CRP.

References