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Review

Practical guidelines for nutritional management of burn injury and recovery

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ABSTRACT

Nutrition practice in burn injury requires a multifaceted approach aimed at providing metabolic support during a heightened inflammatory state, while accommodating surgical and medical needs of the patient. Nutritional assessment and determination of nutrient requirements is challenging, particularly given the metabolic disarray that frequently accompanies inflammation. Nutritional therapy requires careful decision making, regarding the safe use of enteral or parenteral nutrition and the aggressiveness of nutrient delivery given the severity of the patient's illness and response to treatment. With the discovery that specific nutrients can actually alter the course of disease, the role of nutrition support in critical illness has shifted from one of preventing malnutrition to one of disease modulation. Today the use of glutamine, arginine, essential fatty acids, and other nutritional factors for their effects on immunity and cell regulation is becoming more common, although the evidence is often lagging. An exciting dichotomy exits, forcing nutrition support specialists to make responsible choices while remaining open to new potential helpful therapeutic options.

Contents

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1. Introduction

Effective nutritional therapy in burn patients involves an understanding of the physiologic and metabolic alterations that accompany traumatic injury. Nutritional support must also accommodate the surgical and medical needs of the patient. The mode of therapy provided, such as route of administration and the aggressiveness of nutrient delivery depends on the severity of the patient's illness and response to treatment. Accordingly, nutritional objectives vary throughout the hospital course as the patient's clinical status changes. The following serves as a guideline for providing nutritional therapy to burned patients throughout the continuum of care. When possible, practice guidelines are evidence-based, however the myriad differences in approaches to burn care and the individual needs of patients preclude a rigid, inflexible approach to nutritional support in this population.

2. Nutritional assessment

2.1. *Determining nutritional status and nutrition risk*

In burn patients, nutritional status is coupled to the stage of injury. Nutritional assessment consequently is a dynamic, ongoing process. At the time of admission, factors related to the patient's pre-burn history (including days post-burn, prior burn care and any complicating injuries), pre-injury height and weight, and clinical appearance serve as the basis for the patient's initial nutritional assessment. Patients who are malnourished (often those patients whose admission is significantly delayed from the time of injury) should be quickly identified since they are at greatest risk for re-feeding syndrome with the initiation of nutrition support [1,2]. They may also benefit from brief intervals of care dedicated to nutritional rehabilitation before further surgical treatment or prior to discharge. In tandem with nutritional status, nutritional risk should be determined. Nutritional risk relates not only to pre-existing nutritional status, but also to factors that can alter the patients' ability to receive and utilize nutrients during their hospital stay such as the severity of burn, age, and complicating conditions such as inhalation injury and organ dysfunction.

As the patient progresses into the acute phase of injury, the physiologic response to trauma deteriorates nutritional status regardless of their initial baseline. Driven by a series of inflammatory mediators, catecholamines, and counter regulatory hormones, this catabolic state triggers whole body protein breakdown, ultimately diminishing the body cell mass (BCM; the metabolically active component of the body), the primary component of which is skeletal muscle [3–5]. Since diminution of the BCM directly and adversely relates to outcome, monitoring and preservation of BCM and more specifically skeletal mass becomes the primary objective of most nutrition support strategies [6].

2.2. *Evaluating nutritional adequacy*

A number of assessment tools serve as proxies for BCM. However, because they rely on assumptions that do not hold true during metabolic stress, they are of limited use in the critically ill burn patient. In fact, most nutritional assessment tools available in a clinical setting are confounded by the physiological elements of the inflammatory response. Even the simplest measures of total body weight or weight change, which are usually reasonable markers of fat and lean tissue status, are obscured by the expansion of extracellular water following acute burn injury [7]. Visceral proteins are better prognostic indicators than parameters of protein status in burn patients during the acute phase response [8,9]. Overestimates of nitrogen intake and underestimates of nitrogen output often invalidate nitrogen balance studies, leading to falsely positive results. In burn injury, the magnitude of error is even further compounded by exudative wound losses and increased ammonia (versus urea) nitrogen excretion that is typical in critical illness [10–12].

Despite their limitations, many of these markers of nutritional status when trended or used collectively can help the clinician in monitoring day to day efficacy of diet therapy. The frequency of their use depends on the phase of care (Table 1). For example, while weights are often confounded by fluid changes, they can be useful when tracked over time and evaluated in the proper context. Recognition that changes in weight during the early acute phase of care may not denote changes in dry weight is important, however once the patient becomes more stable, a new ''baseline'' dry weight value can be used for the purpose of nutrition planning and even medication dosing. With respect to the latter, medications that are titrated to effect (i.e. morphine, fentanyl, midazolam, lorazepam, ketamine, cisatracurium, epinephrine, norepinephrine, dopamine, and dexmedetomidine) or monitored by serum level (i.e. aminoglycosides, vancomycin) should not be changed if a significant weight change occurs [13]. With respect to the former, updating the weight helps reduce undue concern over exaggerated weight loss later in the course of

Table 1 – Monitoring nutritional variables across the continuum of care

Elements of nutritional assessment	Monitoring schedule and salient points		
	Acute[a]	Rehabilitative[a]	Convalescent[a]
Weight	Biweekly Assign a new baseline dry weight following resuscitation Monitor trends to reduce erroneous values due to discrepancies among scale, fluid shifts	Weekly	At scheduled visits
Calorie and protein intakes	Daily	Daily	If nutritional status is a concern, 24 h recall
Albumin	NA	Monthly if necessary	If nutritional status is a concern
Pre-albumin	Biweekly	None	None
C-reactive protein (CRP)	Biweekly	None	None
Urinary urea nitrogen (UUN)	Weekly UUN should diminish over time as catabolic rate wanes Protein goals can be adjusted to accommodate metabolic protein breakdown	None	None
Indirect calorimetry	Weekly	If weight gain cannot be achieved	

[a] Nutritional status/risk.

care. Trended weight information also helps to identify erroneous values that occur with changes in dressing types, splints, and type of scale used.

Interpretation of visceral protein levels also depends on the phase of injury, primarily since this relates to the patient's degree of physiological stress. Defects in both the synthesis and catabolism of albumin as noted by its shortened half-life is following injury make it a poor marker of nutritional status initially [14]. However it can be trended later on in the course of injury, as the acute phase response subsides, or at follow-up visits. Interpreting visceral proteins with high turnover rates in conjunction with measures of acute phase proteins is a good way of assessing nutritional status during the early acute phase of burn injury [15]. When nutritional intake is adequate, a gradual increase in pre-albumin should occur as the acute phase subsides (as represented by a decrease in C-reactive protein, for example). Persistently low pre-albumin levels in the presence of normalizing C-reactive protein may be a sign of protein or calorie deficiency [16]. Likewise, urinary nitrogen excretion can also be used to evaluate the efficacy of nutritional care [17]. While formal nitrogen balance studies can be cumbersome and potentially flawed, serial measures of urinary urea nitrogen levels approximate (albeit imprecisely) the extent of nitrogen breakdown. Table 2 highlights this approach of combining parameters to determine nutritional adequacy during the various phases of injury. Note that part of this approach includes traditional evaluation of actual energy and protein intake in relation to estimated or measured requirement. Setting tolerable levels of intake that will support adequate wound healing and weight loss is a pragmatic, inexpensive outcome-based approach to determining nutritional adequacy [18].

2.3. *Determination of energy and protein requirements*

2.3.1. *Metabolic factors that influence macronutrient utilization*

Like nutritional assessment, inflammation and its effects on metabolism essentially serve as the backdrop for nutrition support planning. Thus, metabolic derangements resulting from stress unfortunately limit the ability to offer optimal nutrition. Following severe injury, increased cellular production of cytokines and other mediators, while a necessary mechanism for survival, puts macronutrient substrate metabolism in disarray [19,20]. Enhanced rates of glucose production, appearance and uptake, accompanied by decreased responsiveness of liver and peripheral tissue to insulin, results in unusually high insulin requirements to achieve normoglycemia. While there is no impairment in the rate of glucose oxidation when compared to normal subjects, a lower percentage of glucose uptake is converted to carbon dioxide [21]. The rest appears to be accounted for by lactate, a possible alternative for further recycling by the liver [22]. This phenomenon is the rationale for capping glucose infusion rates at a maximum of 5 mg/kg minute despite the apparent need by the patient for more calories [23].

Increased cortisol levels stimulate muscle proteolysis, protein breakdown, and protein oxidation [24]. These high rates of protein oxidation account for a large portion of elevated energy expenditure in burn patients [25]. Difficulty replenishing diminished intracellular concentrations of specific amino acids such as glutamine and arginine, due to their increased flux and disposal from protein pools further contributes to muscle protein catabolism [26–28]. In fact, exogenous protein, while capable of enhancing protein synthesis, cannot totally abate muscle protein breakdown despite high nitrogen intakes.

Table 2 – Interpreting trends in biochemical indices in acute burn patients

Cal/Pro intake (% goal)	p-Alb	CRP	UUN	Interpretation	Action
100	↓	↑	↑	Increased inflammation accompanied by increased catabolic rate. Pre-albumin is not reflective of nutritional adequacy	Continue monitoring. Protein intake >1.5 times UUN to cover obligatory losses
<100	↓	↓	↑↓	Inadequate intake based on decreased p-Alb with decreased inflammation	Check weight. Look for obstacles to meeting nutrition plan/revise accordingly
>100	↑	↓	↑↓	Inadequate intake based on goal achievement and increased pre-albumin. Increased UUN may be due to excessive protein intake	Reevaluate protein goal in relation to changing wound and clinical status for potential need to decrease. Check total protein, blood urea nitrogen, creatinine
100	↓	↓	↑	Pre-albumin should trend upwards as inflammatory state subsides. UUN may reflect increased gluconeogenesis	Reevaluate calorie and protein goals, may need to increase. Check weight, energy expenditure, donor site healing

Lastly, enhanced lipolysis combined with impaired fat oxidation results in futile recycling of free fatty acids and triglycerides [20]. In many instances, provision of exogenous fat only exacerbates substrate recycling, and/or restores fatty tissue, making this macronutrient somewhat ineffectual in the context of wound healing and preservation of BCM.

2.3.2. *Clinical factors that influence energy requirement*

The above-described inflammatory-nutrient interactions are part of a well-known, universal phenomenon that, upon activation does not differentiate according to the cause of the initial insult [3,29]. The magnitude of the inflammatory response however is proportional to some degree to the severity of trauma. In addition, various clinical interventions can affect or amplify this metabolic state, further influencing energy requirements. For example, the combined effects of the inflammatory response and evaporative cooling on heat loss (and subsequently metabolic rate), place burn-injured patients among the most hypermetabolic. Conversely early excision and grafting and the use of occlusive dressing are both crucial in minimizing this effect [30,31]. Historically, the extent of open wound area has typically been incorporated into many empirical estimates of energy requirements for burn patients [32,33]. This method of estimating energy needs appears reasonable, however many equations that incorporate wound size overestimate actual measured energy expenditure [34,35]. Furthermore, metabolic rate can remain elevated despite wound closure. The latter may be explained by continued transcutaneous water losses across freshly healed wounds [36], or a prevailing hypermetabolic state, although this requires further study [4].

Clinicians also should be mindful that various aspects of clinical practice, including: environmental measures to minimize heat loss, pain management, sedation, ventilatory support and nutritional therapy all contribute to a patient's overall energy expenditure, often incongruently. While energy expenditure in critically ill seems to have decreased over the past several decades in light of many advances in care, intervening clinical factors specific to each individual patient should be considered when estimating a patient level of stress. Table 3 illustrates a variety of such physiologic conditions/traits and therapeutic interventions that can influence energy expenditure. To the extent that they influence metabolic rate, an awareness of these clinical factors, particularly those that prevail in one's own clinical arena, is important in estimating calorie goals. For example, a patient who has good pain control, is well sedated, and working little towards the effort of breathing while mechanically ventilated may have lower requirements than a patient who is less critically ill, breathing on their own with less sedation and more participation in rehabilitation. In other words, some patients, as they get better may actually have increased daily energy requirements.

Table 3 – Variable effects on energy expenditure in burn patients

	Increase	Decrease	No effect
Physiologic effects			
Age		✓	
Malnutrition		✓	
Wound size	✓		
Sepsis			✓
Protein catabolism	✓		
Pancreatitis	✓		
Pain	✓		
Fever	✓		
Treatment effects			
Mechanical ventilation	✓		
Wound closure			✓
Warm environment		✓	
Surgical procedure			✓
Initiation of nutrition support			✓
Physical therapy	✓		
Medication effects			
Growth hormone			✓
Corticosteroids	✓		
Vasoactive agents	✓		
Neuromuscular blockade		✓	

2.3.3. *Indirect calorimetry*

From the above, it is apparent that energy requirements vary from patient to patient, as well as from one burn unit to another based on standards of burn practice. This makes it difficult and perhaps unwise to generalize energy needs in burn patients. Serial measures of resting energy expenditure by indirect calorimetry, if available, diminish the degree of pure estimate by capturing the stress of disease as well as the effect of many of the clinical factors mentioned in each measurement. This can help avoid over- and under-feeding [37]. Because such measures only reflect a ''brief moment in time'', a factor, which rarely exceeds 30% of the measured metabolic rate, is usually applied to account for activities throughout the day that may contribute to 24-h energy expenditure [38]. The degree of estimation with this method is minimized, and use of serial measures allows energy provision to stay in tune with the change in clinical status. While it is difficult to link indirect calorimetry with improved outcome, overfeeding patients leads to undesirable complications such as fatty liver, hyperglycemia and fluid overload. Moreover, overzealous feeding tends to lead to the accumulation of fat versus lean body mass, therefore of little benefit. Such consequences are likely to be avoided with indirect calorimetry since most formulas overestimate requirements [39–41].

It is our practice to measure energy expenditure whenever clinically feasible. When it is necessary to predict energy requirements, we base energy goals on a patient's estimated resting metabolic rate and apply a factor (usually between 1.0 and 1.75 is used in our unit) that encompasses a combination of clinical and physiologic elements. This factor is evaluated periodically. Either method is preferred to a static estimate that does not account for changes in a patient's clinical status.

2.3.4. *Estimation of protein needs*

Severe burn is characterized by increased amino acid efflux from the skeletal muscle presumably to accommodate amino acid needs for tissue repair, acute-phase protein production, cellular immunity, and gluconeogenesis [4]. Intuitively, inadequate protein intake compromises wound healing, muscle function, and the immune system. Therefore, the objective of protein therapy during after burn is to provide sufficient quantity and quality of amino acids in the diet so as to (1) avert their outflow from skeletal muscle and (2) maximize protein synthesis for optimal wound healing and immune function. Unlike simple balance studies, protein dynamic studies allow us to look beyond the net aspects of protein metabolism by isolating actual rates of both protein synthesis and protein breakdown [5]. This has been helpful in reaching protein goals and establishing realistic outcomes. For example, in adults, protein intakes approaching 1.5 g/kg/day were associated with a net balance between protein synthesis and breakdown. Protein intake greater that 1.5 g protein/kg/day, while stimulating absolute rate of both synthesis and breakdown, did not further benefit net protein synthesis [42], and was not shown to provide any advantage. As previously mentioned, isotopic evidence also shows that protein breakdown cannot be completely abated by exogenous protein following burn [42,43]. Therefore some lean body mass losses can be expected despite adequate protein intake [44]. In fact, it may be that adjunctive anabolic therapy is necessary for optimal preservation of lean body mass [45]. On the other hand, dietary protein alone can improve protein economy, which in turn can enhance increased structural and functional protein synthesis and improve wound healing time [43].

3. Nutrition support strategies

Once energy and protein requirements are established, the mode of nutrient delivery that best meets both the metabolic and clinical needs of the patient is determined. Recognizing the importance of maintaining gut mucosal integrity, most clinicians opt to use enteral nutrition as the preferred mode of therapy [46]. In response, enteral feeding strategies have become increasingly sophisticated and enable considerable flexibility in the initiation, advancement, and composition of enteral nutritional therapy [47]. However the ease in which enteral nutrition can now be provided, should be tempered by sound clinical judgment, in particular to avoid complications of overzealous feeding in the critically ill patient who may be intolerant. So while the debate of enteral versus parenteral nutrition therapy in a general sense seems obsolete, guidelines for practice should ensure that the benefits of enteral nutrition outweigh the potential risks to any given patient are needed.

3.1. *Combined enteral and parenteral nutrition during the early acute phase of injury*

The parenteral route of support has been criticized because it is not physiologic, does not provide adequate nutrition to the gut, and has been associated with a higher rate of complications in critically ill surgical patients [48–51]. However, parenteral nutrition has the advantage of being tolerated by patients who are severely ill and when used properly, is safe in patients who are undergoing frequent surgery [52,53]. Furthermore, it is the lack of enteral as opposed to provision of parenteral nutrition that is most frequently linked with gut barrier failure and infection [54,55]. For several years it has been our practice to use gastric tube feedings combined with supplemental parenteral nutrition, the latter during periods of gastric tube feeding intolerance, hemodynamic instability, septic episodes, or surgery. Retrospective analyses has proven that this practice is safe and effective in our population in terms of adequate calorie and protein intakes, promotion of wound healing, and mortality [18,53,56]. We attribute the success of this approach to three key elements: (1) judicious enteral feeding support according to clinically defined indicators (Table 4); (2) provision of parenteral nutrition based on substrate utilization versus calorie estimate; (3) discriminate use of intravenous lipids. Coincidently, the latter two characteristics result in nutritional therapy that provides a low to moderate calorie intake, which has also been shown to improve outcomes [57].

3.1.1. *Enteral feeding guidelines in early recovery*

Upon admission patients are evaluated for their ability to receive enteral feedings according to their clinical status. Those undergoing aggressive fluid resuscitation are considered at risk for poor intestinal perfusion. Although enteral feedings may actually improve gut perfusion to some degree, the potential

Table 4 – Clinical guidelines for delaying gastric enteral feedings

Delay	Start
Difficult resuscitation or septic onset	Hemodynamically stable
High vasopressor requirement (dopamine: 10–20 μg/kg/min; epinephrine: 0.5 mg/kg/min)	Weaning vasopressor requirement
Apparent abdominal distention	Abdominal girth is at baseline or abdomen is soft, non-distended
Gastric output >200 mL/day	Diminishing gastric output

imbalance between intestinal oxygen demand and perfusion warrants caution during this phase of injury [58]. To date, research has failed to demonstrate strong clinical outcome benefit associated with early enteral feeding [59–62]. Conversely, reports of feeding-induced bowel necrosis in enterally fed, critically ill patients is disconcerting, particularly as clinical indicators to predict this occurrence are lacking [63,64]. Therefore, it is our practice to provide only trophic feeds in patients at risk for diminished gut perfusion. This includes patients who require significant vasopressor requirement [59,65]. Once patients are hemodynamically stable and able to wean from their vasopressor support, their gastric tolerance is assessed. Patients with low GI output (less than 200 mL) and stable abdominal girth (baseline is obtained upon admission) are initiated on gastric feedings at an hourly rate of 0.5–1 mL/kg. They are then quickly advanced unless residuals exceed two times their hourly rate.

3.1.2. *Parenteral nutrition composition*

Because parenteral support has been linked to increased rate of infections and hepatic dysfunction, careful consideration of the composition (Table 5) and rate of administration of solution, as well as proper line care is used when providing this form of nutrition [49,50,66]. In our hospital, the use of one standardized solution has reduced costs, potential for error, and metabolic aberrations that are often attributed to parenteral nutrition. For example, goal volume for parenteral nutrition is determined by the rate of substrate utilization as opposed to a predetermined energy goal (Table 6). This prevents overfeeding of intravenous nutrients that can potentially contribute to hepatic steatosis, fluid edema, and other metabolic derangements. Our findings that glucose infusion rates in excess of 5 μg/kg/min are not oxidized efficiently by adults or children [67] provide the basis for goal infusion rates in all burn patients. This too helps to minimize the incidence of hyperglycemia [68]. Amino acid infusions are targeted to meet 100% of estimated protein requirement. This usually results in a non-protein calorie:nitrogen ratio of 85:1, which is consistent with enhanced wound healing [69,70]. Monitoring guidelines for patients on TPN, according to their level of acuity, are provided in Table 7.

3.1.3. *Discriminate intravenous lipid administration*

Because they may interfere with platelet function, are associated with poor immune function, and may exacerbate lung injury in some situations [71–74], intravenous lipids are avoided unless parenteral support must be provided in excess

Table 5 – Standard parenteral solution for children

Nutrient	Concentration (mequiv./L) (unless specified)	Comments/ rationale
Amino acids (clinisol 15%)	74 g/L	Non-protein calorie:N ratio = 85:1
Dextrose	200 g/L	
Sodium (Na acetate: 2 mequiv.; NaCl: 4 mequiv.)	100	High Na content for to decrease Na supplementation with sodium leaching from wound
Potassium (KPhos: 3 mM; KCl: 2 mequiv.)	50	Enhanced potassium to reduce supplementation requirement
Calcium (Ca Gluc: 10% mequiv.)	9	Maximized
Magnesium ($MgSO_4$: 50% mequiv.)	18	Maximized
Phosphate	15	Maximized
Acetate	120	Maximized to decrease risk of acidosis
Chloride	70.65	
Ascorbic acid	500 mg/L	
Multivitamins[a]	5 mL/L	M.V.I.-12
Trace elements	0.5 mL/L	Micronutrient amounts: Zn = 2500 μg; Cu = 500 μg; selenium = 30 μg

[a] Vitamin K is added to TPN weekly as one weight-based dose: 10 kg, 1 mg; 10–50 kg, 2 mg; >50 kg, 4 mg.

of 3 weeks. Since intravenous lipids have a high propensity for fatty acid-tryglyceride recycling during inflammation and appear to be less protein sparing than glucose, their omission seems inconsequential from a metabolic standpoint [75–77]. Although signs of essential fatty acid deficiency are likely obscured during burn injury, a small amount of intravenous lipids are given if enteral nutrition cannot be started by week 3 of admission. This however is rarely necessary, particularly since many patients advance to full enteral support by then. Patients may also receive essential fatty acids during propofol infusions.

Given the above constraints, it is commonly not possible to deliver all predicted caloric requirements with this regimen. Most of our patients receive an average of 110–130% of their basal metabolic rate. However, when protein is strictly maintained at goal rate, good surgical outcomes can be achieved, with minimal weight loss during these brief periods. Furthermore, parenteral support provided during escalation of tube feedings will lead to more prompt achievement of calorie and protein targets, without complications attributed to the mode of feedings.

3.2. *Enteral nutrition*

Historically, the notion that starvation and protein malnutrition lead to mucosal atrophy served as the impetus for

Table 6 – TPN administration guidelines

Nutrient	Recommended intake	Key elements of care
Total solution	1.75 mL/kg/h for infants and children <20 kg, 1.5 mL/kg/h for >20 kg	TPN can be initiated at goal rate. Adults and older children (>50 kg), may need to begin at 75% goal rate if hyperglycemic prior to initiation
Carbohydrate	5–7 mg/kg CHO/min	Maximum rate of glucose oxidation isotopically determined in younger and older burned children and adults
Protein	2.5–4.0 g/kg IBW	High amino acid content enables protein goal to be met without excessive volume
Fat (20% intralipid)	Initiate at 0.5 g/kg for 12 h. Goal volume: 1.0–1.5 g fat/kg/day. Intralipids are not be administered in doses: >3.6 g/kg/day	Patients on TPN >14 days *not receiving* enteral feedings (*Note*: intralipid may not be indicated in patients receiving propofol). Propofol contains a 10% soybean oil solution and therefore provides essential fatty acids and additional calories (1 kcal/mL). Triglyceride levels are monitored at baseline and weekly. Lipids are held for levels >350 mg/dL

increased reliance on enteral nutrition in hospitalized patients. Knowledge that stress may increase intestinal permeability, a proposed mechanism in bacterial translocation, further advanced the concept of enteral nutrition as being important in immunity [78–80]. While there is little to no direct evidence that enteral nutrition prevents bacterial translocation in humans, the impact of intraluminal nutrition on gastrointestinal tract in immunity appears to be important [81,82]. Moreover, new theories are emerging, linking gut ischemia/reperfusion in the development of sepsis and multiple organ failure following trauma and burn [83–85]. Enteral nutrition therefore is advocated not only to maintain gut integrity, but also to minimize the release of gut-derived mediators that can activate inflammatory cascades that result in free radical damage [86]. Clinically, enteral feedings have a lower risk of infectious complications, are more physiologic and (usually) more cost effective than parenteral support, and are well tolerated in most burn patients.

Table 7 – Biochemical monitoring of patients on TPN

Measurement	Acute	Acute, non-stressed	Non-acute
Electrolytes	Daily	Semi-weekly	Daily for 3 days; weekly
Phos, Mg, iCa	Semi-weekly	Semi-weekly	Weekly
LFT's, Alb, TP	Weekly	Weekly	Biweekly
Pre-albumin, CRP	Weekly	Weekly	Weekly

3.2.1. *Formula selection*

Historically, and to date, enteral supplements have been used to maintain nutritional status and divert negative outcomes associated with malnutrition. In this sense, standard polymeric feedings remain common practice in severe burns and are likely to be sufficient for supporting wound healing and lean body mass when energy and protein intakes are sufficient. Their favorable cost, compared to many specialty products, and the fact that they are well tolerated, makes them a first line of choice in most hospital nutrition formularies. However, in parallel with recognition of the gut as an immune-regulating organ, several key nutrients have been identified, that when given enterally can actually affect physiological processes in response to injury. It follows in theory that formulas containing these nutrients, can actually alter the course of a given disease state. Advances in the technological development of enteral formulations over the past 20–30 years offers clinicians a wide range of such feeding options, some at considerable cost. Here, market availability has actually preceded scientific rationale for use of such products. As research in this area continues to progress however, a paradigm shift in how we view the role of nutrition in burn care management has taken place.

Most specialty formulas that are of interest in burn nutrition have wound healing and/or immune enhancing properties. Among these to be discussed here are two conditionally essential amino acids glutamine and arginine. Glutamine is considered important in many disease states for its numerous properties. With two amine groups, it functions as a nitrogen shuttle, carrying nitrogen for purine and pyrimidine synthesis. Glutamine serves as a primary oxidative fuel source for rapidly dividing cells, including the enterocyte. As a precursor to glutathione, a potent antioxidant, glutamine participates in reducing oxidative damage [86]. Glutamine supplementation in burn injury has shown moderate benefit. We studied the effect of glutamine supplementation (0.6 g/kg) on protein economy and found that a glutamine-enriched diet had a similar effect on protein turnover and breakdown as a mixture of essential amino acids [87]. In another study, glutamine supplementation resulted in decreased muscle protein breakdown (as indicated by 3-methyl-histidine) and improved wound healing when fed enterally. Other clinical benefits of glutamine supplementation in burn patients include reductions in infection rate, length of stay, cost, and mortality [88,89]. Glutamine supplementation is relatively safe, making it a reasonable consideration for practice in this population.

The role of arginine supplementation in burns continues to be explored. Stress-induced depletion of arginine in tissue pools suggests that it too is semi-essential after burn. Increased extrahepatic uptake of arginine contributes to accelerated urea production in burn patients further exacerbating its losses from the body [27]. This is concerning given

arginine's role in wound healing (as a stimulant to growth hormone) and immunity through the nitric oxide pathway [90]. Unfortunately, uncontrolled production of nitric oxide can also be detrimental, and may have contributed to adverse clinical outcomes particularly in patients who are septic [91]. Conversely, the possible benefit of arginine in wound healing can especially be realized in malnourished patients, or patients who are not metabolically stressed, suggesting a role still in the burn population. Further studies are needed to determine safe dosing for the more critically ill patient.

3.2.2. *Small bowel versus gastric feeds*

Controversy continues over the most effective route of gastrointestinal support: intra-gastric tube feedings or small bowel tube feedings. Proponents of small bowel tube feedings suggest that burn patients have slowed gastric emptying and that this mode of delivery will decrease the rate of aspiration pneumonia. The ability, at least in patients in whom the postpyloric location of the tube is certain, to continue enteral feedings during surgery is another major advantage and is used successfully in some burn units. Although postpyloric tubes can be placed blindly with a weighted tube, endoscopically, or using fluoroscopy, duodenal intubation can be technically challenging in many patients. Further, postpyloric tubes can be dislodged into the stomach and approximately 30% of enterally fed patients in the intensive care unit will develop diarrhea.

Gastric tube feedings are tolerated when begun early after injury, obviate the high rate of diarrhea seen in those fed enterally, and can be delivered without a high risk of aspiration. In addition, gastric feeds are more beneficial in ulcer prophylaxis. They have the further advantages of being simple to administer and easy to monitor for tolerance by tube aspiration. When relying on intra-gastric feedings, infusions must be stopped peri-operatively to avoid aspiration. During these intervals, frequent in children with large burns, supplemental parenteral support can be provided (Table 4).

3.3. *Micronutrient supplementation*

Evidence-based practice guidelines are currently unavailable for the assessment and provision of micronutrients in burn patients. Intuitively, diminished gastrointestinal absorption, increased urinary losses, altered distribution, and altered carrier protein concentrations following severe burn will lead to a deficiency in many micronutrients if not supplemented [92–94]. However, caution should be used to avoid toxicities that can result in gastrointestinal tolerance, antagonistic reactions—that can lead to deficiencies of other nutrients, and the potential for other undesirable outcomes, however subtle these may be. Knowledge of the basic properties among the various groups of micronutrients during stress is necessary, as it enables the clinician to apply sound reasoning in practice and in the development of a protocol for micronutrient monitoring and supplementation in the burn patients.

There are a number of characteristics that predominate among micronutrients. Firstly, micronutrients exist in pools that are often in a state of flux. This makes static measures of certain nutrients in the blood not representative of levels in tissue ''pools''. Inter-compartmental fluid shifts, acid–base balance, and recent dietary intake can all affect the presence of a given nutrient within a certain pool. Furthermore, many micronutrients, especially trace elements and fat-soluble vitamins are bound to protein carriers. This is particularly significant, since proteins are highly regulated during the acute phase response. Blood analysis of zinc, copper, selenium and iron can be misleading due to this phenomenon [94]. Even more importantly, hypoproteinemia during malnutrition or acute burn will not confound micronutrient assessment, but it can also impair the nutrient's ability to be transported from its storage form to tissues (where it is needed), making supplementation somewhat futile. This ''functional'' deficiency as in the case of Vitamin A, corrects only when normal protein status returns.

Despite common practice in many burn units, there is little evidence to date for giving pharmacological doses of any micronutrient in burn patients. In our unit, micronutrient supplementation is aimed at correcting a deficiency state. Table 8 is our supplementation protocol for use in children. Worth mentioning is that the majority of patients actually achieve the recommended supplemental amount (above that required under normal conditions) through their standard nutritional therapy. For these patients, supplementation is not necessary. This is a notable advantage to providing adult enteral formulas to children [95].

Table 8 – Nutrient supplementation protocol in children[a]

Micronutrient	Enteral supplementation[b]	Parenteral supplementation
Multivitamin with trace elements[c]	1 tablet/day	1 single dose vial/day
Zinc[d]	25 mg/day	50 μg/kg/day
Copper[d]	2.5 mg/day	20 μg/kg/day
Selenium	50–170 mg/day	2 μg/kg/day
Vitamin C	200 mg/day	200 μg/kg/day

[a] Children greater than 3 years of age.
[b] Children receiving adult or specialty formulas designed for wound healing may not require additional supplementation of individual nutrients.
[c] Vitamins A, E, iron, B complex are provided only as part of multivitamin/trace element preparation.
[d] Addition of a multivitamin supplement with trace elements may be sufficient for meeting requirements.

4. Summary and conclusion

Advances in infection control, early excision and grafting and aggressive nutritional support have greatly improved survival from severe burn injury. Critically ill burn patients are not homogenous. Their needs are complex and often condition specific. Many factors related to the clinical management of these patients, such as surgical needs, mechanical ventilation, and medication use influence nutritional status and the ability to feed a patient. With each change in clinical status, reassessment of nutrient requirement, type and mode of feeding is necessary.

REFERENCES

[1] Sheridan R, Weber J, Prelack K, Petras L, Lydon M, Tompkins R. Early burn center transfer shortens the length of hospitalization and reduces complications in children with serious burn injuries. J Burn Care Rehabil 1999;20:347–50.

[2] Prelack K, Cunningham JJ, Tompkins RG, Sheridan RL. Refeeding of the severely malnourished burn patient. Proc Am Burn Assoc 1996;128:141.

[3] Plank LD, Hill GL. Sequential metabolic changes following induction of systemic inflammatory response in patients with severe sepsis or major blunt trauma. World J Surg 2000;24:630–8.

[4] Hart DW, Wolf SE, Chinkes DL, et al. Determinants of skeletal muscle catabolism after severe burn. Ann Surg 2000;232:455–65.

[5] Kien CL, Young VR, Rohrbaugh DK, Burke JF. Increased rates of whole body protein synthesis and breakdown in children recovering from burns. Ann Surg 1978;187:383–91.

[6] Kotler DP. Nutritional support in AIDS. Am J Gastroenterol 1991;86:539–41.

[7] Prelack K, Sheridan R, Yu YM, et al. Sodium bromide by instrumental neutron activation analysis quantifies change in extracellular water space with wound closure in severely burned children. Surgery 2003;133:396–403.

[8] Carlson DE, Cioffi WG, Mason AD, McManus WF, Pruitt BA. Evaluation of serum visceral protein levels as indicators of nitrogen balance in thermally injured patients. JOEN 1991;15:440–1.

[9] Gottschlich MM, Baumer T, Jenkins M, Khoury J, Warden GD. The prognostic value of nutritional and inflammatory indices in patients with burns. JBCR 1992;13:105–13.

[10] Bell SJ, Molnar JA, Krasker WS, Burke JF. Prediction of total urinary nitrogen from urea nitrogen for burned patients. J Am Diet Assoc 1985;85:1100–4.

[11] Konstantinides FN, Radmer WJ, Becker WK, et al. Inaccuracy of nitrogen balance determinations in thermal injury with calculated total urinary nitrogen. J Burn Care Rehabil 1992;13:254–60.

[12] Waxman K, Rebello T, Pinderski L, et al. Protein loss across burn wounds. J Trauma 1987;27:136–40.

[13] Keaney T. Director of Pharmacy, Shriners Burns Hospital.

[14] Spiess A, Mikalunas V, Carlson S, Zimmer M, Craig RM. Albumin kinetics in hypoalbuminemic patients receiving total parenteral nutrition. J Parenter Enteral Nutr 1996;20:424–8.

[15] Raguso CA, Dupertuis YM, Pichard C. The role of visceral proteins in the nutritional assessment of intensive care unit patients. Curr Opin Clin Nutr Metab Care 2003;6:211–6.

[16] Prelack K, Washek M, Sheridan RL. Pre-albumin and C-reactive protein are predictive of nutritional adequacy in burned children. JBCR 2001;23:s126.

[17] Prelack K, Dwyer J, Yu YM, Sheridan RL, Tompkins RG. Urinary urea nitrogen is imprecise as a predictor of protein balance in burned children. JADA 1997;97:489–95.

[18] Prelack K, Cunningham JJ, Sheridan RL, Tompkins RG. Energy and protein provisions revisited: an outcomes-based approach for determining requirements. JBCR 1997;18:177–81.

[19] Weissman C. The metabolic response to stress: an overview and update. Anesthesiology 1990;73:308–27.

[20] Wolfe RR. Herman award lecture, 1996: relation of metabolic studies to clinical nutrition—the example of burn injury. Am J Clin Nutr 1996;64:800–8.

[21] Wolfe RR, Durkot MJ, Allsop JR, Burke JF. Glucose metabolism in severely burned patients. Metabolism 1979;28:1031–9.

[22] Gore DC, Ferrando A, Barnett J, et al. Influence of glucose kinetics on plasma lactate concentration and energy expenditure in severely burned patients. J Trauma 2000;49:673–7. discussion 677–8.

[23] Burke JF, Wolfe RR, Mullany CJ, Mathews DE, Bier DM. Glucose requirements following burn injury. parameters of optimal glucose infusion and possible hepatic and respiratory abnormalities following excessive glucose intake. Ann Surg 1979;190:274–85.

[24] Bilmazes C, Kien CL, Rohrbaugh DK, Uauy R, Burke JF, Munro HN, et al. Quantitative contribution by skeletal muscle to elevated rates of whole-body protein breakdown in burned children as measured by *N*-methylhistidine output. Metabolism 1978;27:671–6.

[25] Nelson KM, Long CL, Bailey R, Smith RJ, Laws HL, Blakemore WS. Regulation of glucose kinetics in trauma patients by insulin and glucagon. Metabolism 1992;41:68–75.

[26] Biolo G, Fleming RY, Maggi SP, Nguyen TT, Herndon DN, Wolfe RR. Inhibition of muscle glutamine formation in hypercatabolic patients. Clin Sci (Lond) 2000;99:189–94.

[27] Yu YM, Young VR, Castillo L, et al. Plasma arginine and leucine kinetics and urea production rates in burn patients. Metabolism 1995;44:659–66.

[28] Yu YM, Ryan CM, Castillo L, et al. Arginine and ornithine kinetics in severely burned patients: increased rate of arginine disposal. Am J Physiol Endocrinol Metab 2001;280:E509–17.

[29] Monk DN, Plank LD, Franch-Arcas G, Finn PJ, Streat SJ, Hill GL. Sequential changes in the metabolic response in critically injured patients during the first 25 days after blunt trauma. Ann Surg 1996;223:395–405.

[30] Cone JB, Wallace BH, Caldwell Jr FT. The effect of staged burn wound closure on the rates of heat production and heat loss of burned children and young adults. J Trauma 1988;28:968–72.

[31] Caldwell Jr FT, Bowser BH, Crabtree JH. The effect of occlusive dressings on the energy metabolism of severely burned children. Ann Surg 1981;193:579–91.

[32] Curreri PW, Richmond D, Marvin J, Baxter CR. Dietary requirements of patients with major burns. J Am Diet Assoc 1974;65:415–7.

[33] Matsuda T, Clark N, Hariyani GD, Bryant RS, Hanumadass ML, Kagan RJ. The effect of burn wound size on resting energy expenditure. J Trauma 1987;27:115–8.

[34] Ireton-Jones CS, Turner Jr WW, Baxter CR. The effect of burn wound excision on measured energy expenditure and urinary nitrogen excretion. J Trauma 1987;27:217–20.

[35] Turner Jr WW, Ireton CS, Hunt JL, Baxter CR. Predicting energy expenditures in burned patients. J Trauma 1985;25:11–6.

[36] Wallace BH, Cone JB, Caldwell Jr FT. Energy balance studies and plasma catecholamine values for patients with healed burns. J Burn Care Rehabil 1991;12:505–9.

[37] Saffle JR, Medina E, Raymond J, Westenskow D, Kravitz M, Warden GD. Use of indirect calorimetry in the nutritional management of burned patients. J Trauma 1985;25:32–9.

[38] Goran MI, Peters EJ, Herndon DN, Wolfe RR. Total energy expenditure in burned children using the doubly labeled water technique. Am J Physiol 1990;259:E576–85.

[39] Hart DW, Wolf SE, Herndon DN, et al. Energy expenditure and caloric balance after burn: increased feeding leads to fat rather than lean mass accretion. Ann Surg 2002;235:152–61.

[40] Hildreth MA, Herndon DN, Desai MH, Duke MA. Reassessing caloric requirements in pediatric burn patients. J Burn Care Rehabil 1988;9:616–8.

[41] Saffle JR, Larson CM, Sullivan J. A randomized trial of indirect calorimetry-based feedings in thermal injury. J Trauma 1990;30:776–82. discussion 782–3.

[42] Wolfe RR, Goodenough RD, Wolfe MH. Isotopic approaches to the estimation of protein requirements in burn patients. Adv Shock Res 1983;9:81–98.
[43] Patterson BW, Nguyen T, Pierre E, Herndon DN, Wolfe RR. Urea and protein metabolism in burned children: effect of dietary protein intake. Metabolism 1997;46:573–8.
[44] Hart DW, Wolf SE, Mlcak R, et al. Persistence of muscle catabolism after severe burn. Surgery 2000;128:312–9.
[45] Ferrando AA, Sheffield-Moore M, Wolf SE, Herndon DN, Wolfe RR. Testosterone administration in severe burns ameliorates muscle catabolism. Crit Care Med 2001;29:1936–42.
[46] ASPEN Board of Directors and the Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. J Parenter Enteral Nutr 2002;26:1SA–138SA.
[47] Jenkins ME, Gottschlich MM, Warden GD. Enteral feeding during operative procedures in thermal injuries. J Burn Care Rehabil 1994;15:199–205.
[48] Moore FA, Feliciano DV, Andrassy RJ, et al. Early enteral feeding, compared with parenteral, reduces postoperative septic complications. The results of a meta-analysis. Ann Surg 1992;216:172–83.
[49] Sheldon GF, Peterson SR, Sanders R. Hepatic dysfunction during hyperalimentation. Arch Surg 1978;113:504–8.
[50] Rodgers BM, Hollenbeck JI, Donnelly WH, Talbert JL. Intrahepatic cholestasis with parental alimentation. Am J Surg 1976;131:149–55.
[51] Bozzetti F, Braga M, Gianotti L, Gavazzi C, Mariani L. Postoperative enteral versus parenteral nutrition in malnourished patients with gastrointestinal cancer: a randomised multicentre trial. Lancet 2001;358:1487–92.
[52] Datta G, Gnanalingham KK, van Dellen J, O'Neill K. The role of parenteral nutrition as a supplement to enteral nutrition in patients with severe brain injury. Br J Neurosurg 2003;17:432–6.
[53] Sheridan RL, Prelack K, Kadilak P, et al. Supplemental parenteral nutrition does not increase mortality in children. JBCR 2000;21:234S.
[54] Jiang XH, Li N, Li JS. Intestinal permeability in patients after surgical trauma and effect of enteral nutrition versus parenteral nutrition. World J Gastroenterol 2003;9:1878–80.
[55] Kudsk KA, Croce MA, Fabian TC, et al. Enteral versus parenteral feeding. Effects on septic morbidity after blunt and penetrating abdominal trauma. Ann Surg 1992;215:503–11. discussion 511–3.
[56] Cunningham JJ, Lydon MK, Russell WE. Calorie and protein provision for recovery from severe burns in infants and young children. Am J Clin Nutr 1990;51:553–7.
[57] Krishnan JA, Parce PB, Martinez A, Diette GB, Brower RG. Caloric intake in medical ICU patients: consistency of care with guidelines and relationship to clinical outcomes. Chest 2003;124:297–305.
[58] Andel H, Rab M, Andel D, et al. Impact of duodenal feeding on the oxygen balance of the splanchnic region during different phases of severe burn injury. Burns 2002;28:60–4.
[59] Gottschlich MM, Jenkins ME, Mayes T, Khoury J, Kagan RJ, Warden GD. The 2002 clinical research award. An evaluation of the safety of early vs. delayed enteral support and effects on clinical, nutritional, and endocrine outcomes after severe burns. J Burn Care Rehabil 2002;23:401–15.
[60] Braga M, Gianotti L, Gentilini O, Parisi V, Salis C, Di Carlo V. Early postoperative enteral nutrition improves gut oxygenation and reduces costs compared with total parenteral nutrition. Crit Care Med 2001;29:242–8.
[61] Eyer SD, Micon LT, Konstantinides FN, et al. Early enteral feeding does not attenuate metabolic response after blunt trauma. J Trauma 1993;34:639–43. discussion 643–4.
[62] Peter JV, Moran JL, Phillips-Hughes J. A metaanalysis of treatment outcomes of early enteral versus early parenteral nutrition in hospitalized patients. Crit Care Med 2005;33:213–20. discussion 260–1.
[63] Munshi I, Steingrub J, Wolpert L. Small bowel necrosis associated with early postoperative jejunal tube feeding in a trauma patient. J Trauma 2000;49:163–5.
[64] Marvin R, McKinley B, McGuigan M. Non-occlusive bowel necrosis occurring in critically ill trauma patients receiving enteral nutrition manifests no reliable clinical signs for early detection. Am J Surg 2000;179:7–12.
[65] Guerin JP, Levraut J, Samat-Long C, Leverve X, Grimaud D, Ichai C. Effects of dopamine and norepinephrine on systemic and hepatosplanchnic hemodynamics, oxygen exchange, and energy balance in vasoplegic septic patients. Shock 2005;23:18–24.
[66] Sugiura T, Tashiro T, Yamamori H, et al. Effects of total parenteral nutrition on endotoxin translocation and extent of the stress response in burned rats. Nutrition 1999;15:570–5.
[67] Sheridan RL, Yu YM, Prelack K, Young VR, Burke J, Tompkins RG. Maximal parenteral glucose oxidation in hypermetabolic young children: a stable isotope study. J Parenter Enteral Nutr 1998;22:212–6.
[68] Prelack K, Cunningham JJ, Sheridan RL. Glucose tolerance among acutely burned children receiving glucose-based parenteral nutrition. J Parenter Enteral Nutr 1997;21.
[69] Alexander JW, Macmillan BG, Stinnett JD, et al. Beneficial effects of aggressive protein feeding in severely burned children. Ann Surg 1980;192:505–17.
[70] Matsuda T, Kagan RJ, Hanumadass M, Jonasson O. The importance of burn wound size in determining the optimal calorie:nitrogen ratio. Surgery 1983;94:562–8.
[71] Campbell AN, Freedman MH, Pencharz PB, Zlotkin SH. Bleeding disorder from the 'fat overload' syndrome. J Parenter Enteral Nutr 1984;8:447–9.
[72] De La Cruz JP, Paez MV, Carmona JA, De La Cuesta FS. Antiplatelet effect of the anaesthetic drug propofol: influence of red blood cells and leucocytes. Br J Pharmacol 1999;128:1538–44.
[73] Calder PC. Long-chain $n-3$ fatty acids and inflammation: potential application in surgical and trauma patients. Braz J Med Biol Res 2003;36:433–46.
[74] Gottschlich MM, Alexander JW. Fat kinetics and recommended dietary intake in burns. J Parenter Enteral Nutr 1987;11:80–5.
[75] Hart DW, Wolf SE, Zhang XJ, et al. Efficacy of a high-carbohydrate diet in catabolic illness. Crit Care Med 2001;29:1318–24.
[76] Hayashi N, Tashiro T, Yamamori H, et al. Effect of intravenous omega-6 and omega-3 fat emulsions on nitrogen retention and protein kinetics in burned rats. Nutrition 1999;15:135–9.
[77] Long JM, Wilmore DW, Mason AD. Effect of carbohydrate and fat intake on nitrogen excretion during total intravenous feeding. Ann Surg 1977;185:417.
[78] Deitch EA. Intestinal permeability is increased in burn patients shortly after injury. Surgery 1990;107:411–6.
[79] Deitch EA, Morrison J, Berg R, Specian RD. Effect of hemorrhagic shock on bacterial translocation, intestinal morphology, and intestinal permeability in conventional and antibiotic-decontaminated rats. Crit Care Med 1990;18:529–36.
[80] Deitch EA, Winterton J, Berg R. Thermal injury promotes bacterial translocation from the gastrointestinal tract in mice with impaired T-cell-mediated immunity. Arch Surg 1986;121:97–101.
[81] Alverdy J, Chi HS, Sheldon GF. The effect of parenteral nutrition on gastrointestinal immunity. The importance of enteral stimulation. Ann Surg 1985;202:681–4.

[82] Alverdy JC, Chi HS, Selivanov V, Morris J, Sheldon GF. The effect of route of nutrient administration on the secretory immune system. Curr Surg 1985;42:10–3.
[83] Deitch EA, Xu D, Kaise VL. Role of the gut in the development of injury- and shock induced SIRS and MODS: the gut–lymph hypothesis, a review. Front Biosci 2006;11:520–8.
[84] Magnotti LJ, Deitch EA. Burns, bacterial translocation, gut barrier function, and failure. J Burn Care Rehabil 2005;26:383–91.
[85] Ueno C, Fukatsu K, Maeshima Y, et al. Dietary restriction compromises resistance to gut ischemia-reperfusion, despite reduction in circulating leukocyte activation. J Parenter Enteral Nutr 2005;29:345–51. discussion 351–2.
[86] Martindale RG, Cresci GA. Use of immune-enhancing diets in burns. J Parenter Enteral Nutr 2001;25:S24–6.
[87] Sheridan RL, Prelack K, Yu YM, et al. Short-term enteral glutamine does not enhance protein accretion in burned children: a stable isotope study. Surgery 2004;135:671–8.
[88] Garrel D, Patenaude J, Nedelec B, et al. Decreased mortality and infectious morbidity in adult burn patients given enteral glutamine supplements: a prospective, controlled, randomized clinical trial. Crit Care Med 2003;31:2444–9.
[89] Wischmeyer PE, Lynch J, Liedel J, et al. Glutamine administration reduces gram-negative bacteremia in severely burned patients: a prospective, randomized, double-blind trial versus isonitrogenous control. Crit Care Med 2001;29:2075–80.
[90] Castillo L, DeRojas-Walker T, Yu YM, et al. Whole body arginine metabolism and nitric oxide synthesis in newborns with persistent pulmonary hypertension. Pediatr Res 1995;38:17–24.
[91] Dent DL, Heyland DK, Levy H. Immunonutrition may increase mortality in critically ill patients with pneumonia: results of a randomized trial. Crit Care Med 2003;30:17–20.
[92] Berger MM, Cavadini C, Bart A, et al. Cutaneous copper and zinc losses in burns. Burns 1992;18:373–80.
[93] Berger MM, Rothen C, Cavadini C, Chiolero RL. Exudative mineral losses after serious burns: a clue to the alterations of magnesium and phosphate metabolism. Am J Clin Nutr 1997;65:1473–81.
[94] Cunningham JJ, Leffell M, Harmatz P. Burn severity, copper dose, and plasma ceruloplasmin in burned children during total parenteral nutrition. Nutrition 1993;9:329–32.
[95] Prelack K, Sheridan RL. Micronutrient supplementation in the critically ill patient: strategies for clinical practice. J Trauma 2001;51:601–20.