

Nutritional management of the burn patient

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Abstract

The incidence of burn injuries is on the increase in Africa due to migration to urban areas and the development of slum areas, but there is a paucity of such data on the African continent. The South African Medical Research Council has indicated that 3.2% of the South African population is burned annually, with 50% of individuals who suffer burns being younger than 20 years. The Red Cross Children's Hospital admits 650 to 900 children with burn injuries annually.¹

Burn injury, the most severe type of injury from a metabolic point of view, is characterised by the most profound alterations in basal metabolic rate and urinary nitrogen excretion. In addition, requirements for and/or metabolism of macro- and micronutrients are altered or increased. The major improvement in burn survival can be attributed to many factors, one being the development and implementation of improved methods of nutritional support that optimise host defences, enhance wound healing and support the metabolic response to stress.² The greatest threats to survival from burns are still infection/sepsis, with burn wound sepsis and nosocomial pneumonia, including ventilator-associated pneumonia (VAP), being the leading causes of death.^{2,3} Effective medical nutrition therapy in patients with burn injuries requires an understanding of the physiologic and metabolic alterations that accompany the burn injury, alterations in the immune system and the role of reactive oxygen species (ROS).

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Metabolic response

The metabolic response to burn injury is similar to that of any physiological trauma, just more pronounced. When the burn injury exceeds 15 to 20% of the total body surface area (TBSA), it results in systemic disturbances, including a major stress response, impaired immunity and extensive fluid redistribution.^{2,4,5} The loss of circulating volume results in an increase in stress hormones, including catecholamines, glucocorticoids and ACTH, and an increased glucagon to insulin ratio.^{2,4,6,7,8} There is an increased secretion of immune and inflammatory-generated mediators (IL-1 β , IL-6, IL-8, IL-10, TNF- α) initiated by activated platelets and macrophages, prostanoids, oxygen free radicals and their products and acute phase proteins,^{2,6-10} and a decreased secretion of constitutive hepatic proteins.⁸ Other factors implicated in the metabolic response include endotoxin, platelet-activating factor, arachidonic acid metabolites via the cyclo-oxygenase and lipoxygenase pathways, reactive oxygen species (ROS), neutrophil adherence complexes, nitrous oxide and the complement and coagulation cascades.¹¹ In addition, there is a decrease in the normal endogenous activity of anabolic agents, such as human growth hormone and testosterone.⁷ The consequences of these metabolic alterations include increased gluconeogenesis, increased proteolysis, increased ureagenesis, sequestration of micronutrients and altered lipid metabolism.

The magnitude of the response parallels the extent of the burn injury and reaches a maximum of about twice normal when the

burn size exceeds 60% TBSA.^{2,6,11,12} Smoke inhalation and other insults such as sepsis increase the metabolic rate further.⁷ Although the acute phase response is essential for host survival, it becomes auto-destructive if left unchecked. Once the systemic inflammatory response is initiated, it can self-perpetuate, which poses two critical problems: (1) for the cycle to be broken, the initiating focus must be eliminated and the inflammatory response must abate and (2) once the activated mediator factors of the body's macrophage and neutrophil pool have been primed, even a modest second insult can reactivate a mediator release and cause cell destruction.⁷ It should also be borne in mind that the catabolic phase of burns may continue for as long as nine months post-injury.¹⁰ In this regard, two strategies should be considered in reversing the metabolic response: decrease the response by antagonism and/or stimulate anabolism through pharmacological means.⁸ The metabolic response *per se*, as well as the increased physiological demands placed on the cardiac, pulmonary, renal and other organ systems, complicates nutritional support. Patients with major burn injuries also develop immune system impairment, which predisposes them to infection and multi-organ failure (MOF).^{2,13} These changes include alterations in essentially all aspects of specific and non-specific host immune defence systems, and impairment of the gut mucosal barrier.² The severe muscle wasting due to accelerated proteolysis results in muscle weakness that predisposes the patient to pneumonia by limiting the patient's ability to cough and clear secretions.²

Free radicals are formed through various processes after burn injury and overwhelm the inherent, protective free radical-scavenging systems. The acute phase response, with the increase in cytokines and the consequent stimulation of phagocytic cells, results in the formation of oxygen free radicals, leading to lipid peroxidation.¹⁴ Aggressive volume resuscitation results in hydrogen peroxide and superoxide generation through xanthine oxidase.^{15,16} Burn trauma results in the upregulation of inducible nitric oxide synthase (iNOS), with increased production of NO.^{14,15} The generated free radicals subsequently cause peroxidation of membrane phospholipids and enzyme inactivation, and increase capillary permeability and vascular reactivity.¹⁷ These oxygen-derived free radicals are associated with local wound response, the development of burn shock and distant organ injury.^{14,18}

Enhanced free radical production is paralleled by impaired antioxidant capacity (AC). There is a documented decrease in the levels of super oxide dismutase, catalase, glutathione, alpha-tocopherol and ascorbic acid.^{15,16} Smoke inhalation results in a reduction in glutathione, vitamin E and catalase.¹⁹ Furthermore, emerging evidence links gut ischaemia/reperfusion injury to the development of sepsis and MOF.¹⁵

Effect of metabolic response on energy and nutrients

Energy

The metabolic rate is reported to increase proportionally to the increase in burn size up to 50 to 60% TBSA, after which point there is minimal further increase. The mechanism of the metabolic response is multifactorial, with the increase in stress hormones and cytokines playing a central role.^{2,12,16,20} Other factors that play a role include: evaporative water loss from the burn wound, bacterial contamination of the burn wound, bacterial translocation, heat and water loss through the burn wound with the resultant increase in core temperature, reset of temperature set-points in the hypothalamus, smoke inhalation, thermogenesis due to increased nutrient intake, as well as pain and increased protein turnover.^{2,6,8,11,12,15} Burn-related sepsis further contributes to the increase in metabolic rate,¹¹ while early excision and closure reduce the incidence of burn wound sepsis and pain.²¹

Carbohydrates (CHO)

After burn injury there is an increase in the formation of glucose precursors, an increase in the release of amino acids and consequent gluconeogenesis by the liver, altered glucose oxidation, and an increase in plasma clearance of glucose.^{7,8,12} Burn patients also have insulin resistance and an increased glucagon:insulin ratio.^{5,6,8,11,12,21,22} Glucose is the preferred energy substrate for macrophages, leucocytes and fibroblasts in the burned area.² Providing exogenous glucose diminishes endogenous production by only about 50%.⁷ The hyperglycaemia associated with burns is associated with impaired immune function, poor wound healing and exacerbation of protein catabolism.¹¹ Wound-generated lactate returns to the liver, where it is converted back to glucose (Cori-cycle).^{2,6,7,12,21} The increased Cori-cycle has various advantages, which include energy production, lactate-induced bacteriostatic effect due to the alteration in systemic pH, and lactate-induced stimulation of collagen synthesis.

Protein

The catabolic response post-burn is well documented but poorly understood.⁷ The stress hormones and cytokine release (particularly TNF- α) result in the mobilisation of lean body mass.¹¹ Various metabolic pathways are involved in this catabolic response, including the ubiquitin-proteasome pathway, IGF-1/insulin acting through the P13K pathway, and the inhibitory pathway of the NF κ B kinase/NF κ B system.¹¹ The increased cortisol levels also stimulate proteolysis, protein breakdown and protein oxidation.²²

The erosion of lean body mass is proportional to the extent of the injury and may be up to 30 to 40% of the lean body mass in its extreme.⁶ Proteolysis can continue for up to 40 to 90 days post-injury. It is characterised by increased nitrogen excretion and a negative nitrogen balance. Bacteraemia has an added effect on nitrogen excretion. The imbalance of protein synthesis and degradation in favour of the latter,¹¹ together with the resultant muscle weakness, is thought to prolong ventilatory requirements, inhibit cough reflexes and delay the mobilisation of protein-malnourished patients, which significantly increases the risk for pulmonary sepsis.¹¹ In addition, the rate of restoration of lost protein in the burn patient is about one-tenth as rapid as the loss, even with adequate nutrition and progressive exercise. The endogenous anabolic stimulus returns to normal during recovery, but does not exceed normal. It is also believed, but needs to be confirmed, that, since cellular function in this setting is primed for anabolism, the addition of anabolic stimuli, such as growth hormone and testosterone, may enhance protein synthesis.⁷

Lipids

Several aspects of lipid metabolism are significantly altered after burn injury, mainly because of serum changes in epinephrine, glucagons, cortisol and insulin.¹² Burn injury results in increased lipolysis, with the release of free fatty acids (FFA) and triglycerides, mainly induced by catecholamines.^{7,12,23} There is also an increase in fatty acids metabolised via the cyclo-oxygenase enzyme system, with a resultant increase in pro-inflammatory intermediates.¹² Due to the stress response-related drop in albumin there is also a decreased concentration of fatty acids bound to albumin.^{12,23} The free fatty acid turnover is proportional to the burn injury.

Lipid metabolism is also characterised by futile cycles (re-esterification), and decreased ketone production.^{4,6,8,12,22} The increased recycling of lipids appears to be due to the increased catecholamines, and can partially be abolished by beta-blockade.⁶ The decreased ketone production, a primary energy source utilised to decrease protein catabolism, increases the burn patient's reliance on glucose,^{12,23} and the impaired ketogenesis is probably the result of elevated insulin levels. The decreased carnitine levels may result in decreased β -oxidation of long-chain fatty acids and an accumulation of triglycerides, particularly in the liver.²³ The decrease in HDL, which regulates LPL activity,²³ will thus result in an accumulation of triglycerides and a reduction in cholesterol due to the fact that LPL will be reduced, which will affect the turnover from VLDL to LDL.²³

Micronutrients

Marked differences in micronutrient status occur after burn injury as a result of the acute-phase response, losses through the wound, consumption during metabolism and inadequate replacement. Stress

alters the level of trace elements, in particular due to altered intestinal absorption, altered losses and distribution among body proteins, and altered protein concentration. Micronutrient deficiencies are frequent after major burns, but burn patients are particularly prone to acute trace element depletion as a result of extensive exudative losses.²⁴

The acute-phase response is characterised by a decrease in serum iron (Fe), zinc (Zn) and selenium (Se), as well as an increase in serum copper (Cu). This is accompanied by an increase in ferritin and ceruloplasmin.^{25,26} Berger et al found that serum Fe, Se and Zn levels decreased after burn injuries, but, that unexpectedly, serum copper was also severely decreased.²⁶ Large trace element losses in the exudates were noted during the first seven days post-injury.^{27,28} The decrease in serum Fe and Zn is thought to be a protective response, since decreased serum Fe and desaturation of transferrin may restrict the growth of microorganisms, and intravenous Zn supplementation has been associated with increased mortality in animals exposed to endotoxins.²⁶ Because micronutrients play an essential role in metabolism and antioxidant defences, a deficiency state is thought to amplify the already burn-induced metabolic derangements and ongoing catabolism.^{3,7} Common mineral abnormalities include decreased serum calcium, magnesium and phosphate. Magnesium is essential for energy production via ATP reactions. Poor phosphate status is evident early in post-burn injury, due to increased losses and increased use in metabolic pathways.⁷ With regard to the vitamin micronutrients, low levels of serum vitamin C, tocopherol, retinol and vitamin A have been documented after burn injury.^{29–32} With regard to vitamin E levels, a further decline in blood levels has been reported with inhalation injury.³³

Vitamin E supplementation (100 mg/day) has been reported to give rise to an increase in serum vitamin E and a significant decrease in lipid peroxides in burned patients.³⁰ Although decreased vitamin A levels have been linked to the incidence of diarrhoea in burn patients,³⁴ large-dose supplements may result in toxicity because of the decrease in retinol-binding protein during the acute-phase response.³³

Nutrient requirements

Nutrient requirements are markedly increased in the presence of the acute-phase response, and all patients with burns exceeding 20% TBSA should receive nutritional support, as should those with less severe burn wounds but with pre-existing malnutrition and/or diseases such as TB or HIV/AIDS.

Additional factors that may influence the burn patient's requirements include:

- Age – vulnerable groups are children, the elderly and teenagers
- Pregnancy and lactation
- Nutritional status prior to the burn
- Underlying diseases such as TB, HIV/AIDS, diabetes
- Electrolyte disturbances
- Renal failure
- Stress diabetes
- Fever/infection/sepsis

Environmental temperature, humidity, pain and anxiety need to be controlled effectively to avoid a further increase in metabolic rate.^{35,36}

Dickerson asked the very pertinent question: is the determination of the energy and protein requirements of burn patients an art or a science?³⁷ Unfortunately, limitations in estimating nutrient requirements, difficulties in assessing nutritional status and inadequate monitoring in response to feeding more often than not require the integration of “the art of clinical management” with science for maximal patient benefit.³⁷

Goals of nutritional support

The goals of nutritional support include:

- Maintain body mass, particularly lean body mass
- Prevent starvation and specific nutrient deficiencies
- Improve wound healing
- Manage infections
- Restore visceral and somatic protein losses
- Avoid or minimise complications associated with enteral and parenteral nutrition
- Provide the correct amount and mix of nutrients to limit or modulate the stress response and complications

Energy

The variable patient response makes the estimation of energy requirements very challenging for the clinician.³⁷ There are numerous formulae for the calculation of energy requirements, but they all either over- or underestimate patient requirements. An assessment of 46 methods and indirect calorimetry concluded that none of the plethora of such methods was precise.³⁷ In the absence of calorimetry, the methods that have been reported to be the least biased were those of Xie et al³⁸ (Table I) and Milner et al.³⁹ In addition, any such data on requirements must be interpreted by a trained and standardised clinician. It should be realised, for instance, that although indirect calorimetry may accurately reflect energy requirements over a study of 30 minutes, it cannot be extrapolated to a 24-hour period because it does not reflect the increase in energy expenditure during painful procedures, thermogenesis or the effect of exercise in ambulatory patients.² Furthermore, a number of variations of the Harris-Benedict formula (Table II), although not accurate, are often used for practical reasons. In this regard, Deitch suggested that ideal rather than actual body weight should be used in the calculation of requirements, since any equation should more accurately reflect the mass of metabolically active tissue.² These considerations remain important, because excessive energy provision may result in fat mass increase without an increase in muscle mass.⁵

Table I: Formula (Xie et al)³⁸

Energy expenditure (kcal/d) = (1000 kcal × BSA [m²]) + (25 × %BSAB)

BSA: Body surface area

BSAB: Percentage of total body surface area burn

Other factors that are known to influence energy requirements, but are often not taken into consideration in the available equations although they should be attended to, include:

- Malnutrition with or without diseases such as TB and HIV/AIDS
- The ambient temperature – optimal thermoneutral temperature for the burn patient is 30 to 33°C^{2,6,11,21}
- Pain, anxiety and stress increase requirements^{2,6,11,21}

Table II: Estimated nutritional requirements²

Basal energy expenditure (BEE) per Harris-Benedict equation			
Male: $BEE = 66 + (13.7 \times W) + (5 \times H) - (6.8 \times \text{age})$			
Female: $BEE = 655 + (9.6 \times W) + (1.9 \times H) - (4.7 \times \text{age})$			
Adjustments for burn severity			
Extent of burn	BEE	Protein	NPE:N ratio
Healthy individual		1.0 g/kg/d	150:1
Moderate burn (15–30% TBSA)	X 1.5	1.5 g/kg/d	100–120:1
Major burn (15–30% TBSA)	X1.5–1.8	1.5–2 g/kg/d	100:1
Massive burn ($\geq 50\%$)	X1.8–2.1	2–2.3 g/kg/d	100:1

Activity factors: In bed = 1.2 Ambulatory = 1.3 Ventilated = 1.05

- Thermogenesis – do not overfeed
- Ventilation – decreases requirements by up to 20%
- Medication – pentobarbital reduces requirements to 86% of predicted requirements
- Early excision and grafting as well as other procedures/facilities, such as skin grafting or artificial skin, may not always be available in rural areas and may result in higher requirements than those shown by first world indirect calorimetry studies

It is also important to remember that the patient's requirements do change during the course of hospitalisation. Contrary to previous beliefs, wound closure does not immediately decrease requirements, since increased requirements have been shown to persist for nine to 12 months after burn injury.^{2,21,40} It is equally important to remember that a progressive exercise programme should always be combined with adequate nutrition to enhance the restoration of muscle mass and strength.²

CHO

Glucose is important because the burn wound and cellular components of the immune and inflammatory systems are obligate glucose consumers. The administration of CHO is also known to decrease proteolysis.² Thus, about 60 to 70% of energy should be administered as CHO, with care being taken not to exceed the patient's ability to metabolise CHO.² It is particularly important not to exceed 5 to 7 mg/kg/min in parenteral nutrition.^{2,6,22} The metabolic consequences of excessive CHO administration include glucose intolerance, increased carbon dioxide production, increased fat synthesis and the development of fatty infiltration of the liver.^{2,6}

Protein

Protein requirements are increased due to increased muscle catabolism, wound losses and tissue repair. Optimal protein administration is essential, since improved survival has been found with high-protein diets. The NPE:N ratio is also important. Alexander et al found that a ratio of 100:1 improved survival more than the traditional 150:1 to 200:1 ratio.⁴¹ There are many equations for the calculation of protein requirements, but many overestimate requirements and approximately 2 to 2.5 g/kg/day should meet the requirements of most patients with major burns.

Lipids

The adverse effects of lipid administration appear to be dose dependent¹ and, as such, over-supplementation should be avoided. Garrel et al (1995) found that fat supplied at 15% of total energy

reduced infectious morbidity and shortened hospitalisation time compared to 35% of energy requirements being derived from fat.⁴² Fish oils modulate the immune response through enhanced PGE₃ and reduced PGE₁ and PGE₂ formation, as well as by reducing the production of pro-inflammatory cytokines, IL-1, IL6 and TNF.^{4,7,12,23,43} Excessive fish oil supplementation, however, is detrimental due to the consequent inability to regulate TNF production and resultant increased mortality.¹² Medium-chain triglycerides have a theoretical advantage for burn patients, as they are preferentially oxidised with a lesser tendency for deposition in adipose tissue or incorporation in membranes to serve as prostanoid precursors, and they attenuate blockage of the reticulo-endothelial system.⁶ Care must also be taken with parenteral lipids, which must be infused slowly with close monitoring of lipid clearance so as to ensure that triglyceride levels do not rise more than 10 to 20% over baseline values.¹²

The fat intake of burn patients should be less than 20% of total energy requirements.⁷ Other recommendations include 10 to 15% of NPE as fat, with about 5% of NPE from linoleic acid.²³ The optimal $\omega 3:\omega 6$ ratio has not been established.

Nutrient mix

The recommended nutrient distribution of macronutrients should be 50 to 60% carbohydrates, 20 to 25% protein, and 20% or less fat.⁷ Hart et al found that a high-carbohydrate diet, with 3% fat, 82% carbohydrates and 15% protein, stimulated protein synthesis, increased endogenous insulin production and improved lean body mass accretion compared to an isocaloric-isonitrogenous high-fat diet.⁴⁴

Immunonutrition

Arginine

The potential benefit of arginine for the burn patient centres specifically on its effect on wound healing and immunity via the nitric oxide pathway. However, uncontrolled production of nitric oxide can be detrimental. Early enteral L-arginine supplementation (200 to 400 mg/kg/day) for burn patients effectively inhibits the excessive increase in NO level, improves blood supply to the tissues, promotes oxygen transportation and metabolism, and alleviates the occurrence and damage of recessive shock in a dose-dependent manner.⁴⁵ Burned children who received an arginine-supplemented diet (2% of energy, pure arginine salt) had an improved mitogen-stimulated lymphocyte proliferation compared to controls.¹³ The optimal amount needed, timing, administration method and safety of arginine have not been established for the routine use of arginine in the burn patient.

Glutamine

Significant depletion of plasma and muscle glutamine has been documented in acute burn injury and is thought to contribute to muscle wasting, weight loss and infection.⁴⁶ Glutamine is a conditionally essential amino acid for burn patients and has a number of important functions, including functions in metabolism, wound healing, gut integrity, immune function and antioxidant defence.⁷ Glutamine is also an important energy source for immune cells and enterocytes.⁷ Moreover, recent research indicates that glutamine may serve as a vital cell-signalling molecule in states of illness and injury. Glutamine therapy has been shown to enhance heat shock protein (HSP-70)

expression in critically ill patients, and this enhanced HSP-70 expression correlated with decreased length of ICU stay and possible prevention of acute respiratory distress syndrome. Glutamine is also an important precursor of glutathione, a vital antioxidant molecule during ischaemia/reperfusion injury. Recent data also indicate that glutamine can attenuate iNOS expression following ischaemia/reperfusion injury and sepsis.⁴⁷

Garrel et al reported that 26 g enterally-supplied glutamine resulted in a three-fold decrease in the frequency of positive blood cultures.⁴⁸ Supplementation with 0.5 g/kg/day glutamine granules via the enteral route, for 14 days, also significantly increased serum glutamine,^{9,49} plasma pre-albumin and transferrin blood concentration.⁴⁹ Cellular immunity is significantly suppressed after burn injury and glutamine supplementation significantly improved various measures of cellular immunity, but had no effect on humoral immunity.⁹ Hospital stay was significantly reduced in both studies and wound healing was faster.^{7,44} Enterally-fed burn patients who received intravenous supplemented glutamine, 0.57 g/kg/day (continuous infusion over 24 h) had significantly fewer gram-negative bacteremic episodes than the control group, with the glutamine-treated group also having a significant improvement in both pre-albumin and transferrin as well as a decreased C-reactive protein concentration on day 14 post-injury.⁵⁰

The optimal dose, route, administration method and period of glutamine supplementation have not yet been determined. Most trials used enteral doses of 0.35 to 0.57 g/kg/d for seven to 14 days, but it is well known that protein catabolism can last up to 12 months post-injury and glutamine status has not been determined for that period of time. Some practitioners consider it prudent to continue supplementation at least for the ICU period,⁴⁶ despite the modest but consistent documented effects of glutamine supplementation on morbidity and improvements in defined nutritional as well as inflammatory parameters, and the lack of any documented effects of glutamine supplementation on mortality.

Micronutrients

Evidence-based guidelines for micronutrient supplementation are limited. Nevertheless, there is a measure of agreement that the simultaneous presence of micronutrients is required for wound healing and adequate antioxidant defence.²⁴

Vitamin C plays an important role in collagen formation and antioxidant defences in the immune system and is involved in ATP production.³³ High-dose vitamin C supplementation is probably essential during resuscitation after burn injury. Reduction in resuscitation fluid volume, from 4 to 1 ml/kg/%TBSA, has been documented in animal models, as well as in adult burn patients with high-dose vitamin C supplementation during resuscitation.^{51,52} Tanaka et al showed that the administration of 66 mg/kg/h during the first 24 hours, started as soon as possible after admission, significantly reduced resuscitation fluid volume (45.5%), weight gain, wound oedema and the length of mechanical ventilation, and improved early respiratory function.⁵² It is important to note that these studies and recommendations are specific to burn injuries and have not been verified in other critically ill patients. After the resuscitation period, doses of five to 10 times the RDA have been suggested, but there is no data to support this specific recommendation.

Burn patients need at least 100 mg of vitamin E per day, but this recommendation may be too low during the initial two weeks, since Zhang et al found that vitamin E levels only normalised after two weeks of supplementation.³¹ Burn patients are also at risk for vitamin D deficiency due to the hospitalisation and coverage of large parts of the body, and therefore limited ultraviolet exposure and treatment with H₂ antagonists (cimetidine), which are known to inhibit hepatic hydroxylation of vitamin D. It would therefore appear that vitamin D supplementation may be beneficial.³³ Low plasma carotenoid levels have been documented after burn injury,⁵³ and these only increased when supplementation of 30 mg/day was provided via enteral nutrition.²⁹

The best data with regard to trace element supplementation has been published by Dr Berger and colleagues from Switzerland as a result of a series of well-controlled trials.⁵⁴ The intravenous route is preferable for trace element supplementation, because enteral absorption is variable and because of the antagonism between Zn and Cu at mucosal level.²⁶ Supplementation (IV) of copper 2.5 to 3.1 mg/day, selenium 315 to 380 µg/day, and zinc 26.2 to 31.4 mg/day for eight to 21 days resulted in a significant reduction in the number of infections. This was related to a significant reduction of nosocomial and of ventilator-associated pneumonia.³ This is in agreement with the authors' previous data, which showed trace element supplementation to have resulted in a significant reduction in bronchopneumonia infections and consequent shorter hospital stay.⁵⁴ Patients receiving 59 µmol Cu, 4.8 µmol Se and 574 µmol Zn per day intravenously also had a significantly improved clinical course (better graft take, fewer infectious complications), which was reflected by a non-significantly shorter ICU stay. Supplementation was again associated with a significant reduction in infectious complications, especially bronchopneumonia.⁵⁵

Hypomagnesaemia is also common after burn injury due to losses in the exudates and the use of aminoglycoside antibiotics.^{56,57,58} Magnesium should be supplemented according to serum levels, but oral magnesium sulphate must be avoided since it is associated with an increased risk for diarrhoea. For oral supplementation of magnesium, the chloride suspension restores serum levels more effectively than the slow-release tablets. Increased urinary losses, exudate losses, decreased intake or absorption, compartment shifts and increased ATP synthesis contribute to the hypophosphataemia seen after burn injury.⁵⁸ Oral supplementation of a sodium hydrogen phosphate solution effectively restores serum phosphate. A potassium-containing phosphate supplement should be avoided during the acute phase when potassium levels change rapidly. Iron replacement is not indicated in the critically ill burn patient. Reduced serum iron is thought to be the favourable result of the acute-phase response to deter bacterial growth, and supplementation is thought to be associated with an increased risk for infections and increased mortality.²

In patients with burns of lesser severity (< 20% TBSA), one multivitamin tablet a day should meet the micronutrient requirements. Suggested supplementation in the case of more extensive burns (> 20% TBSA) is summarised in Table III.

The experience of the effects of pre-, pro- and synbiotics as well as ornithine- α -ketoglutarate and anabolic agents in burns is primarily experimental, with little or no clinical experience.

Table III: Suggested micronutrients

Nutrient	Amount
Vitamin A (total) Beta-carotene	10 000 IU/d ³³ At least 30 mg/d ²⁹
Vitamin C	66 mg/kg/h during resuscitation ⁵² 5 to 10x RDA thereafter ³³
B vitamins, folic acid	2 to 3x RDA ³³
Vitamin E	At least 100 mg/d ³¹
Trace elements	Copper 2.5 to 3.1 mg/day, selenium 315 to 380 µg/day, and zinc 26.2 to 31.4 mg/day IV for eight to 21 days. No recommendation thereafter, but oral supplementation would probably be appropriate ³
Vitamin D	Unknown, but probably essential as 1,25-dihydroxyvitamin D

Implementation of nutritional support: route and timing

The enteral nutrition route of nutritional support is associated with lesser energy expenditure, reduced bacterial translocation, fewer septic complications, better preservation of immune function and a marked increase in survival when compared to total parenteral nutrition.^{2,7,11} As such, the enteral route is the administration route of choice. Parenteral feeding should be reserved for prolonged ileus or as an adjunct to enteral nutrition to meet energy requirements. Overzealous enteral feeding in a patient on inotrope support can, however, be more detrimental than parenteral nutrition. Two reports of feeding-induced bowel necrosis in trauma patients^{59,60} have been attributed to poor gut perfusion, since enteral nutrition creates a dose- and substrate-dependent increase in intestinal oxygen consumption, while overall organ perfusion is markedly decreased after burn injury.⁶¹

The initiation of enteral nutrition should be immediately post burn injury or at least within 24 to 48 hours. The reluctance of some clinicians to start immediate enteral feeding is related to a fear that it will result in more complications than delayed feeding. This has been shown not to be warranted.⁶² In this regard, early high-energy duodenal feeding is less likely to have any adverse effects on intestinal oxygen balance in the severely burned patient,⁵⁸ especially since frequent periods of fasting for operations reduce nutrient intake and complicate the attainment of set nutrient targets. Jejunostomy feeding throughout the operative and perioperative period has also been shown to be safe and documented to increase nutrient delivery.⁶⁰ Post-burn ileus has been shown to be confined to the stomach and colon, with normal small intestine function, which makes early enteral feeding possible via a jejunostomy or naso-jejunal tube.¹²

Nutrient requirements after burns of lesser severity (< 20% TBSA) are easily met with a regular ward diet. However, if such a patient is also malnourished, a supplementary drink may be required as well as additional micronutrient supplements to correct pre-existing deficiencies. It is also possible to meet the nutrient requirements of patients with large burns who are conscious and cooperative with a high-protein diet and oral supplementary drinks.⁶³ Both Fabiani and Candy⁶⁴ and Jacobs et al⁶⁵ found that patients with extensive burns could be adequately fed and gain weight after the initial

weight loss. The HAM (hyperalimentation per mouth) drinks were made from a combination of commercial and household products and administered at set times throughout the day and night. Such an approach, however, requires dedicated nursing staff who understand the importance of these drinks.

During the implementation of the nutrition care plan, the following factors need to be considered: 1) the volume of food supplied – keep the volume as small as possible by using concentrated supplementary drinks and by adding protein and carbohydrate modules to the food; 2) area burnt – chewing may cause pain in facial burns and if hands have been burnt the patient may have difficulty managing cutlery – consider the consistency of the diet and use cutlery with enlarged grips; 3) psychological state, pain and anxiety may influence appetite and need to be controlled adequately; 4) religious and cultural influences need to be considered to optimise nutrient intake.⁶⁶ The implementation and monitoring of intake rely heavily on the commitment of the burn care team to ensuring optimal delivery of the prescribed nutrients, reporting problems with food intake and assessing the effect of psychological factors on food intake.

Assessment and monitoring

The nutritional assessment of the burn patient should start immediately after injury and should continue for 12 months after recovery. At admission it is important to obtain the patient's pre-burn history, usual weight and height, clinical evaluation for existing signs of nutrient deficiencies (often only a general observation is possible), all relevant biochemical parameters of nutritional status and, if possible, a diet history to determine usual intake. This would help to at least identify those patients who are already malnourished or those with co-morbidities. Implementation of the nutrition care plan should be started with care in malnourished patients to avoid re-feeding syndrome.

Assessing and monitoring the nutritional status and the response to feeding need careful assessment and are often complicated. For instance, traditional markers of nutritional status, such as albumin and transferrin, are influenced by the acute-phase response and therefore are not valid in the burn patient as markers of nutritional status. Daily weights in the acute phase are inaccurate because of dressings, fluid shifts and the removal of eschar. The "gold standard", nitrogen balance studies, is confounded by large amounts of protein lost through the wounds.^{2,37} Anthropometric measurements to determine muscle mass are impractical, often impossible to do and confounded by fluid shifts, and thus are of limited use in the critically ill burn patient. It may also not be possible to use knee-height, arm span or even bed length to determine height in the critically ill patient.

Within these limitations, however, protein losses from the burn wound can be calculated for days one to three post-burn – nitrogen loss = $0.3 \times \text{BSA} \times \% \text{ burn}$, days four to 16 – nitrogen loss = $0.1 \times \text{BSA} (\text{m}^2) \times \% \text{ burn}$ ⁶⁷ or $0.2 \text{ g N/day}/\% \text{ burn}$ during the first week post-injury,⁶⁸ or by the more complicated equation of Bell et al,⁶⁹ which, together with serial measurements of pre-albumin and CRP in addition to albumin, clinical assessment, weight and nitrogen balance, may provide a reasonable indication of response to feeding over time. In conjunction with nutritional support, it should always be borne in mind that progressive resistance exercises in convalescent

burn patients can maintain and improve body mass, augment incorporation of amino acids into muscle proteins, and increase muscle strength and ability to walk longer distances by 50%.^{2,21}

Conclusion

The acute-phase response induced by thermal injury is associated with a severe loss of lean body mass, an imbalance of free radicals in relation to antioxidant defence mechanisms, and impaired immune function. These extensive metabolic alterations mitigate in favour of adequate nutritional support in order to meet the increased energy, protein, fat, carbohydrate and micronutrient requirements. Early enteral nutrition should form the basis of nutritional support in the burn patient. Novel substances, such as glutamine, together with micronutrient supplements may contribute to recovery and the maintenance of lean body mass. In the latter setting, physical exercise is essential to improve muscle mass.

References

- Albertyn R, Bickler SW, Rode H. Paediatric burn injuries in Sub Saharan Africa – an overview. *Burns* 2006;32(5):605–12.
- Deitch EA. Nutritional support of the burn patient. *Critical Care Clinics* 1995;11(3):735–50.
- Berger MM, Eggmann P, Heyland DK, et al. Reduction of nosocomial pneumonia after major burns by trace element supplementation: aggregation of two clinical trials. *Crit Care* 2006;10(6):R153
- De-Souza DA, Green LJ. Pharmacological nutrition after burn injury. *J Nutr* 1998;128:797–803.
- Hart DW, Wolf SE, Herndon DN, et al. Energy expenditure and caloric balance after burn injury. Increased feeding leads to increased fat rather than lean mass accretion. *Ann Surg* 2002;235(1):152–61.
- Treget EE, Yu YM. The metabolic effects of thermal injury. *World J Surg* 1992;16:68–79.
- Demling RH, Seigne P. Metabolic management of patients with severe burns. *World J Surg* 2000;24:673–80.
- Wanek S, Wolf SE. Metabolic response to injury and the role of anabolic hormones. *Current Opinion in Clinical Nutrition and Metabolic Care* 2007;10(3):272–7.
- Peng X, Hong Y, You Z, Wang P, Wang S. Glutamine granule-supplemented enteral nutrition maintains immunological function in severely burned patients. *Burns* 2006;32:589–93.
- Jeschke MG, Barrow RE, Herndon DN. Extended hypermetabolic response of the liver in severely burned pediatric patients. *Arch Surg* 2004;139:641–7.
- Pereira CT, Murphy K, Jeschke M, Herndon DN. Post burn muscle wasting and the effects of treatment. *The International Journal of Biochemistry & Cell Biology* 2005;37:1948–61.
- Waymack JP, Herndon DN. Nutritional support of burned patients. *World J Surg* 1992;16:80–6.
- Marin VB, Rodriguez-Osial L, Schlessinger L, Villegas J, Lopez M, Castillo-Duran C. Controlled study of enteral arginine supplementation in burned children: impact on immunologic and metabolic status. *Nutrition* 2006;22:705–12.
- Latha B, Babu M. The involvement of free radicals in burn injury: a review. *Burns* 2001;27:309–17.
- Horton JW. Free radicals and lipid peroxidation mediated injury in burn trauma: the role of antioxidant therapy. *Toxicology* 2003;189:75–88.
- Filippou D, Papadopoulos VP, Triga A, et al. Nitric oxide, antioxidant capacity, nitric oxide synthase, and xanthine oxidase plasma levels in a cohort of burn patients. *Burns* 2007;33:1001–7.
- Tarber MG, Shimoda K, Murakami K, et al. Burn and smoke inhalation injury in sheep depletes vitamin E: kinetic studies using deuterated tocopherols. *Free Radic Biol Med* 2007;42(9):1421–9.
- Cetikale O, Senel O, Bulan R. The effect of antioxidant therapy on cell-mediated immunity following burn injury. *Burns* 1999;25:113–8.
- Zang Q, Maass DL, White J, Horton JW. Cardiac mitochondrial damage and loss of ROS defense after burn injury: the beneficial effects of antioxidant therapy. *J Appl Physiol* 2007;102:103–12.
- Jeschke MG, Herndon DN, Ebener C, Barrow RE, Jauch J-W. Nutritional intervention high in vitamins, protein, amino acids and -3 fatty acids improves protein metabolism during the hypermetabolic state after thermal injury. *Arch Surg* 2001;136:1301–6.
- Pereira CT, Murphy K, Herndon DN. Altering metabolism. *J Burn Care Rehab* 2005;26(3):194–9.
- Prelack K, Dylewski M, Sheridan RL. Practical guidelines for nutritional management of burn injury and recovery. *Burns* 2007;33:14–24.
- Gottschlich MM, Alexander JW. Fat kinetics and recommended dietary intake in burns. *JPEN* 1987;11(1):80–5.
- Berger MM, Binnert C, Chioloro RL, et al. Trace element supplementation after major burns increases burned skin trace element concentrations and modulates local protein metabolism but not whole-body substrate metabolism. *Am J Clin Nutr* 2007;85:1301–6.
- Kushner I. The phenomenon of the acute phase response. *Ann NY Acad Sci* 1982;389:39.
- Berger MM, Cavadini C, Chioloro R, Guinchar S, Krupp S, Dirren H. Influence of large intakes of trace elements on recovery after major burns. *Nutrition* 1994;10:327–34.
- Berger MM, Cavadini C, Bart A, et al. Cutaneous zinc and copper losses in burns. *Burns* 1992;18:373.
- Berger MM, Cavadini C, Bart A, et al. Selenium losses in 10 burned patients. *Clin Nutr* 1992;11:75.
- Rock CL, Dechert RE, Khilnani R, Parker RS, Rodriguez JL. Carotenoids and antioxidant vitamins in patients after burns. *J Burn Care Rehabil* 1997;18(3):269–78.
- Mingjian Z, Qifang W, Lanxing G, Hong J, Zongyin W. Comparative observation of the changes in serum lipid peroxides influenced by the supplementation of vitamin E in burn patients and healthy controls. *Burns* 1992;18(1):19–21.
- Zhang MJ, Wang QF, Gao LX, Jin H, Wang ZY. Comparative observation of the changes in serum lipid peroxides influenced by the supplementation of vitamin E in burn patients and healthy controls. *Burns* 1992 Feb;18(1):19–21.
- Szebeni A, Nagyesi G, Feuer L. Vitamin A levels in the serum of burned patients. *Burns* 1980;7:313–8.
- Gottschlich MM, Warden GD. Vitamin supplementation in the patient with burns. *J Burn Care Rehabil* 1990;11(3):275–8.
- Gottschlich MM, Warden GD, Michel M, et al. Diarrhea in tube-fed burn patients: incidence, etiology, nutritional impact and prevention. *JPEN* 1988;12:338–45.
- Millar AJW, Smit MJ. Nutrition in the burnt patient. *CME* 1989;7(10):1195–200.
- Prins A. Nutrition support in thermal injury: the ultimate challenge. *Health & Hygiene* 1997;8(1):2–3.
- Dickerson RN. Estimating energy and protein requirements of thermally injured patients: art or science? *Nutrition* 2002;18(5):439–42.
- Xie WG, Li A, Wang SL. Estimation of the calorie requirements of burned Chinese adults. *Burns* 1993 Apr;19(2):146–9.
- Milner EA, Cioffi WG, Mason AD, et al. A longitudinal study of resting energy expenditure in thermally injured patients. *J Trauma* 1999;37:167.
- Wolfe RR, Herndon DN, Jahoor F. Persistence of muscle catabolism after severe burns. *Surgery* 2000;232:455–65.
- Alexander JW, MacMillan BG, Stinett JD, et al. Beneficial effects of aggressive feeding in severely burned children. *Ann Surg* 1980;192:505.
- Garrel DR., Razi M, Lariviere F, Jobin N, Naman N, Emptoz-Bonneton A, Pugeat MM. Improved clinical status and length of care with low-fat nutrition support in burn patients. *J Parenter Enteral Nutr* 1995;19:482–91.
- Alexander JW, Saito H, Ogle CK, Trocki O. The importance of lipid type in the diet after burn injury. *Ann Surg* 1989;204(1):1–8.
- Hart DW, Wolfe SE, Zhang X-J, et al. Efficacy of high-carbohydrate diet in catabolic illness. *Crit Care Med* 2001;29:1318–24.
- Yan H, Peng X, Huang Y, Zhao M, Li F, Wang P. Effects of early enteral arginine supplementation on resuscitation of burn patients. *Burns* 2007;33:179–84.
- Windle EM. Glutamine supplementation in critical illness: evidence, recommendations and implications for clinical practice in burn care. *Journal of Burn Care and Research* 2006;26(6):764–772.
- Wischmeyer PE. The glutamine story: where are we now? *Current Opinion in Critical Care* 2006;12(2):142–8.
- 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.
- Peng X, Hong Y, You Z, Wang P, Wang S. Clinical and protein metabolic efficacy of glutamine granules-supplemented enteral nutrition in severely burned patients. *Burns* 2005;31:342–346.
- 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 Nov;29(11):2075–80.
- Matsuda T, Tanaka H, Schimazaki S, et al. High-dose vitamin C therapy for extensive deep dermal burns. *Burns* 1992;18(2):127–31.
- Tanaka H, Matsuda T, Miyagantani Y, Yukioka T, Matsuda M, Shimazaki S. Reduction of resuscitation fluid volumes in severely burned patients using ascorbic acid administration. *Arch Surg* 2000;135:326–31.
- Rock CL, Rodriguez JL, Khilnani R, Low DA, Parker RS. Carotenoids and antioxidant nutrients following burn injury. *Annals New York Academy of Sciences* 1993 Dec 31;691:274–6.
- Berger MM, Spertini F, Shenkin A, et al. Trace element supplementation modulates pulmonary infection rates after major burns: a double-blind, placebo-controlled trial. *Am J Clin Nutr* 1998;68:365–71.
- Berger MM, Baines M, Raffoul W, et al. Trace element supplementation after major burns modulates antioxidant status and clinical course by way of increased tissue trace element concentrations. *Am J Clin Nutr* 2007;85:1293–300.
- Cunningham JJ, Anbar RD, Crawford, JD. Hypomagnesemia: a multifactorial complication of treatment of patients with severe burn trauma. *JPEN* 1987;11(4):364–7.
- Zaloga GP, Chernow B, Pock A, Wood B, Zaritsky A, Zucker A. Hypomagnesemia is a common complication of aminoglycoside therapy. *Surgery, Gynecology & Obstetrics* 1984;158:561–5.
- Berger MM, Rothen C, Cavadini C, Chiolori 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.
- Munshi I, Steingrub J, Wolpert L. Small bowel necrosis associated with early post-operative jejunal feeding in a trauma patient. *J Trauma* 2000;49:163–5.
- 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.
- Andel H, Rab M, Andel D, et al. Impact of early high caloric duodenal feeding on oxygen balance of the splanchnic region after severe burn injury. *Burns* 2001;27:389–93.
- Hansbrough WB, Hansbrough JF. Success of immediate intragastric feeding with patients with burns. *J Burn Care Rehabil* 1993;14:512–6.
- Jenkins ME, Gottschlich MM, Warden GD. Enteral feeding during operative procedures in thermal injuries. *J Burn Care Rehabil* 1994;15:199.
- Fabiani C, Candy S. Oral hyperalimentation in the nutritional management of burned patients. *SAMT* 1985;67:768–70.
- Jacobs LS, De Kock M, Van der Merwe AE. Oral hyperalimentation and the prevention of severe weight loss in burned patients. *Burns* 1987;13(2):154–8.
- Prins A. Nutrition support in thermal injury: implementation of the nutrition care plan. *Health & Hygiene* 1998;9(5):16–8 & 25.
- Waxman K, Rebello T, Pinderski L, et al. Protein loss across burn wounds. *The Journal of Trauma* 1987;27(2):136–40.
- Soroff HS, Pearson E, Artz CP. An estimation of the nitrogen requirements of equilibrium in burned patients. *Surg Gynecol Obstet* 1961;112:159.
- Bell SJ, Molnar JA, Krasker WS, Burke JF. Prediction of total urinary nitrogen from urea nitrogen for burned patients. *JADA* 1985;85(9):1100–4.