Nutritional Support in Injury and Sepsis

Topic 16

Module 16.1

Nutritional Support in Burns

Metter M. Berger
Rene L. Chiolero

Learning Objectives

- To know historical background of hyperalimentation;
- To know causes of hypermetabolism in major burns and of its change over time;
- To know specific aspects of burn substrate metabolism and electrolyte changes;
- To know specific risks of trace element deficiency.

Contents

Key Messages

- Patients with major burns have increased nutritional requirements;

- Energy requirements vary over time with the largest increases, proportional to the severity of injury, being observed during the first weeks after burning: the return to normal takes up to 6 month;
- Enteral nutrition is the preferred method of feeding, and should be started within the first 24 hours after severe injury;
- Due to large exudative losses, patients with major burns are at risk of acute trace element deficiencies, which can be prevented by early intravenous substitution;
- Nutritional support includes monitoring daily weight changes and energy intakes.

1. Introduction

Although the incidence of burn injury has decreased in Western countries, it still remains a common problem throughout the World. Overall, the metabolic responses of burn patients are qualitatively similar to those of other trauma patients, but often of greater magnitude with an intense acute phase response. Burns also share similar morbidity from shock, acute respiratory distress syndrome, sepsis, and multiple organ dysfunction syndrome, which can all occur in any severely injured patient (1). Burned patients are frequently managed in separate facilities, and have some specific medical characteristics. Their resuscitation requires massive quantities of sodium containing fluids(2). They suffer cutaneous exudative losses of fluids containing large quantities proteins, minerals and micronutrients, causing acute deficiency syndromes; (3) venous access is more difficult due to the destruction of the skin at the puncture sites (higher risk of catheter related infection), (4) the surface needing repair is extensive and explains the requirement for prolonged nutritional support, which is rare in other trauma; and (5) burn patients require much longer treatment in intensive care units (ICU) compared with other trauma cases, and require more prolonged nutritional support (2).

2. Pathophysiology

2.1 Fluid Alterations

2.1.1 Increased Permeability

In the early phase of burns involving > 20% of body surface (BSA), there is a transient massive increase in capillary permeability, with an obligatory plasma loss from the intravascular space into the extravascular compartment. In the absence of fluid resuscitation, these extensive capillary fluid losses cause shock and organ failure. The most frequent formula used in the fluid resuscitation of burned patients is the Parkland formula, which is based on lactated Ringer's solution:
Fluid requirement (ml) = 4 x body weight (kg) x total burn BSA (%)
One half of this fluid is administered as crystalloid over the first 8 hours after injury and the rest over the next 16 hours: this calculated volume is only indicative. Fluid resuscitation of major burns, though vital, also has also deleterious effects which start with the creation of generalised oedema, and it's consequences, eg respiratory failure, abdominal compartment syndrome, and, the most visible, oedema of the skin which may compromise its perfusion and lead to "extension" of the skin necrosis caused by the original burn injury. The permeability changes last for about 24 hours, being maximal during the first 12 hours and are responsible for the extensive fluid requirements. Over the second 24 hours, fluid requirements decrease by about 50%. From the third day the oedema fluid is progressively reabsorbed into the intravascular compartment, at which time the fluid requirements decrease further.

2.1.2 Exudates and Evaporation

Until surgical closure, the burn wounds lose about 1 litre of fluid per 10% BSA per day. In addition there are evaporative water losses, which are increased by fever and worsened by the use of fluidized beds.

2.1.3 Fluid Resuscitation

All resuscitation formulae deliver roughly 0.5 mmol sodium /kg body weight/%burned area, creating a large positive sodium balance. Colloids may be started after about 12 hours when capillary leakage is

beginning to lessen, allowing a greater proportion of the infused colloid to be retained within the intravascular space. Albumin should only be considered with major burns > 40% BSA, and when albuminemia is < 18 g/L. Fluid shifts are extensive, and require the patients to be weighed every day, since weighing is the only accurate way of measuring water balance (large exudative and evaporative losses).
After initial resuscitation, free water requirements may remain high for many days, especially when patients are nursed on fluidised beds. Water losses may be sufficient to cause hypernatraemia, unless matched by intake.

3. Metabolic Response

The metabolic response to trauma is essentially biphasic, and is followed by a late recovery phase 1.

3.1 Ebb Phase

Immediately after injury, there is a period of hemodynamic instability with reduced tissue perfusion, and release of high levels of catecholamines. This has classically been called the «ebb phase». Its is characterized by lowered total oxygen consumption (VO2), and low metabolic rate. Depending on the severity of injury and on the success of the hemodynamic resuscitation, it may be extremely short-lived and last a few hours, or persist for a few days depending on the severity of injury and the quality of resuscitation.

3.2 Flow Phase

This first phase is progressively replaced by the « flow phase », characterized by high VO2, elevated resting energy expenditure (REE), elevated substrate flows and accelerated potassium and nitrogen losses. Visceral blood flow and splanchnic O2 consumption increase with total cardiac output and total VO2 3. During this phase, the body's temperature is generally increased and central thermoregulation is shifted upward, especially in severe burns.
The literature of the 70-ies reported increases in energy expenditure of 150-200% of REE, proportional to the severity and extent of the burn. Modern management has reduced this greatly, decreasing the need for very high energy intakes. The largest increase is during the first weeks, the duration of this change depending on the burns size (4), and reverting slowly to normal during the following months whatever the age of the patient (5).
Extensive protein losses occur from the skin surface until wound closure. Skeletal muscle protein catabolism is markedly increased and synthesis may be impaired well into the convalescence or anabolic phase of the illness. The synthesis of acute phase reactants and some visceral proteins is increased. Net nitrogen balance is therefore negative. These changes may be ameliorated but not suppressed by good overall management and by nutritional support.

3.3 Recovery

This phase starts when the flow phase declines, the burned surface is covered, and the patient starts to mobilise. It requires high levels of energy with hypermetabolism lasting up to a year postinjury, to restore lost tissue, to fuel physical rehabilitation, and to complete the process of wound healing. After major burns, this phase may last up till 2 years.

4. Energy and Substrate Requirements

4.1 Energy Requirements

The concept of hyperalimentation was developed for burn patients in the 70ties after observing their muscle wasting. Many formulas were designed during that period to estimate the energy and protein requirements: the most frequently cited Curreri equation is a typical example. Since then, resuscitation and surgical techniques have progressed and contributed to reducing energy expenditure.
Resting energy expenditure can be influenced by other factors, including:
Nursing in a thermoneutral environment using radiant heat (28-31 °C)
Early escar excision, debridement and grafting

Management of fluids
Stress caused by pain and anxiety
Early enteral feeding
Infections
Catecholamine release caused by stress: administration of beta-blocking agents is one of the most successful in reducing REE, and carries limited risks. A recent trial carried out in severely burned children has shown that ß-blockers may prove a safe way to reduce energy expenditure and protein catabolism 7. Hypermetabolism is partly reversed.
Low growth hormone and IGF1 especially in children (substitution) (8)
Low testosterone and thyroid hormones (oxandrolone supplements) (9)
Taking care of these variables constitutes the non nutritional management of burns.
As both underfeeding and overfeeding have deleterious consequences, accurate assessment of REE is desirable to adjust the individual caloric intake, particularly in patients with a prolonged and complicated clinical course: in severely burned patients, access to indirect calorimetric determination or REE is recommended.
The Curreri formula should not be used anymore as it promotes hyperalimentation in all patients and is worst in the most common patients, i.e. those with burns 20-60% BSA (Figure 1).

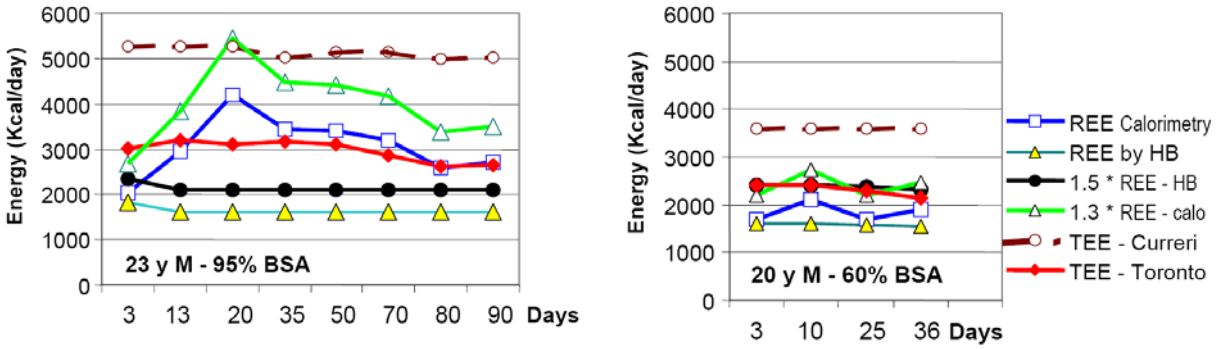

Figure 1 Comparison of energy requirements in 2 patients with major bunrs: A: 20 years-old male, 60 kg, 170 cm, burned 60%BSA, B: 21 years-old male, 73 kg, 180 cm, 95% BSA. Total energy requirements (TEE) were set at 1.3 * REE determined by indirect calorimetry in both cases, and compared to 1.5 times the REE calculated by the Harris-Benedict (HB) equation, or TEE by the Toronto equation, or by the outdated Curreri equation.

Hyperalimentation, particularly with carbohydrate, not only further increases energy expenditure through diet induced thermogenesis but, by raising the respiratory quotient, increases CO2 production and hence the gas exchange load on lungs. It also increases catecholamines production, increasing energy expenditure, and favours de novo lipogenesis. On the other hand an inadequate intake allows unnecessary loss of tissue, particularly lean mass. Measurements of REE by indirect calorimetry, confirm lower total energy requirements than those derived from the historical Curreri formula. The Harris-Benedict equation adjusted for activity and stress has long remained the recommended tool, multiplying the calculated REE by 1.5 to 2. Nevertheless, this equation does not take either fever or size of burn into account, nor the time elapsed since injury. Indeed REE changes over time, with a peak lasting 2-6 weeks depending on burn severity and complications (4, 6). The modern Toronto equation 6 is the only one to integrate all the factors which affect requirements such as sex, weight, height, burned BSA, fever, previous days' caloric intake and time elapsed since injury (Table 1): it is the most precise, being closest to calorimetry determinations especially in burns up to 60% BSA.

Table 1 Equations to estimate energy requirements in burns

Equation	Equation
Toronto [6]	TEE = -4343 + (10.5 x %BSA burn) + (0.23 x CI) + (0.84 x EREE) + (114 x T°C) - (4.5 x days post injury)
Harris & Benedict	TEE = EREE x activity factor x stress factor * where EREE = M: = 66.5 + (13.8 x weight) + (5.0 x height) - (6.8 x age) F: = 655.1 + (9.6 x weight) + (1.8 x height) - (4.7 x age) *: major surgery: 1.0-1.2, skeletal trauma: 1.2-1.5, major burn: 1.4-1.8

TEE = total energy expenditure, EREE = Harris Benedict estimated REE, BSA = burned body surface area, CI = caloric intake during the previous day

During the first few days, and in the absence of an indirect calorimeter, a rough estimation of energy requirements can be used, by giving 30-35 kcal/kg per day for burns < 40% BSA, and 35-50 kcal/kg per day for burns ≥ 40% BSA. Thereafter the Toronto equation should be used. Nevertheless, in the largest burns, indirect calorimetry remains the optimal tool for ensuring that intake is adapted accurately to changing metabolic requirements.

Short term changes in weight from day to day reflect fluid balance, although long term changes, particularly in the recovery phase, are useful measures of tissue gain or loss in response to nutritional intake.

Figure 1 shows two young patients' energy requirements determined by either Harris-Benedict, Toronto equations or by indirect calorimetry: the Toronto equation is closest to the calorimetric determinations.

4.2 Proteins

Persistent muscle protein catabolism is a major problem in severely injured patients. The net result is devastating. Over the first 21 days after injury, critically ill trauma patients lose up to 16% of their total body protein content despite full nutritional support 10. During the first 10 days, close to two thirds of this protein loss come from skeletal muscle, coming also from viscera thereafter.

Accurate nitrogen balances in burned patients are difficult because of the wound losses, which approximate 10 g nitrogen per 10% burned BSA during the first week (11). They are so large in major burns,that nutrition cannot compensate for them. Measurements of urinary nitrogen or urea nitrogen give a useful reflection of prevailing net catabolism. Nitrogen excretion may be as high as 30 g per day in severely burned patients compared to 2 g/day in fasted normal subjects. In a series of burned and injured patients, described by Larsson et al. in 1984, given 45-50 kcal/kg/day energy intake (high by modern standards), nitrogen balance improved up to a protein intake of 0.2 g /kg/day (≈ to 1.25 g/kg/day), i.e. 2-3 times the minimum requirement for normal subjects. Further increases in nitrogen intake produced no further improvement in nitrogen balance. In practice we may give less energy and slightly more nitrogen than in this study.

In Europe, current practice is to give 1.3-1.5 g protein/kg/day (0.2-0.25 g N/kg/day), although higher doses have been advocated in the USA. Higher intakes are usually oxidised, contributing to the increased urea production rate rather than being used for anabolic purposes. As in health, nitrogen balance depends not only on the nitrogen or protein but also on the energy supply.

Plasma albumin levels decrease during the acute-phase response, although the fractional synthesis is increased. During the early phase after injury, serum concentrations are frequently below 20 g/L, due to increased capillary permeability fluid dilution, redistribution, and increased catabolism. Serum albumin remains between 20 and 30 g/L for many weeks, which is well tolerated. There is no rationale for providing albumin to burned patients on a systematic basis within these ranges. Outcome studies carried out in severely burned children have shown no benefit of supplementation 12. Administration of albumin 20% for oncotic purpose when plasma values are below 18 g/l is common practice but not evidence based.

Net muscle catabolism with net burned skin anabolism has recently been shown in an isotopic trial in 10 patients, using a sophisticated 5 compartment model 13, and has confirmed the theory that muscle protein breakdown supplies the required precursors for protein synthesis within the healing wound.
Glutamine and arginine: Both amino acids are conditionally essential. They improve the function of gut mucosa and immune function, which may play a role in reducing septic complications in burned patients. Up to 30 g/day of glutamine and of arginine have been recommended. But there are yet no conclusive data in burns, although there seems to be reasonable evidence that glutamine reduces infectious complications. A series of trials using a precursor of glutamine, ornithine ¤-ketoglutarate (OKG) have shown promising results in both animal and human settings, in terms of improved wound healing, and improved immunity 14.

4.3 Lipids

Increased lipolysis occurs as part of the metabolic response to injury giving high free fatty acid levels for oxidation and increasing glycerol release for gluconeogenesis. This increase results from elevated counterregulatory hormone levels (catecholamine and glucagon), along with decreased insulin sensitivity. It is recommended that fat supply should not exceed 30% of energy. A prospective randomised trial strongly suggests that a normal fat supply may favour infectious complications, and that lower proportions of fat (15% of total calories) may lower infection rates 15.
The type of fatty acid appears unimportant, although the ω-3 PUFA are potential immuno-modulatory and anti-inflammatory agents in a dose of up to 3-5 g/day. There is some data to show that they may improve outcome in other conditions, but there are no specific burns trials. The role of other fatty acids remains to be established.

4.4 Carbohydrates

Injury initiates a strong increase in endogenous glucose production and turnover 16 combined with glucose intolerance of such a degree that it was long called the pseudo-diabetes of burns – a term which is no longer in use. Glucose serves preferentially as cellular fuel for healing wounds and inflammatory tissues. Glucose oxidation rates increase to 130% above those of control subjects after trauma, but administration of glucose, even in large amounts, fails to suppress endogenous glucose production, gluconeogenesis, and protein breakdown.
The fatty liver infiltration resulting from increased de novo lipogenesis is commonly observed in major burns. It probably results from the hypercaloric feeding with excessive amounts of carbohydrate 17, 18. Above administration rates of 6mg/kg/min, CO2 production rates also rise steeply in burned patients (see above) with no other useful metabolic effect. It also becomes increasingly difficult to control hyperglycemia,. Based on these considerations and the above mentioned maximal oxidising capacity for glucose, it seems reasonable to avoid a glucose intake exceeding 5 g/kg per day (using lipids as alternative energy substrate and exceeding 30% of energy intakes is debatable considering the lower infection rates observed with low lipid intakes – see §3.3.) 15 19. This has become even more important since the recent demonstration that tight control of glycaemia < 7 mmol/l, using insulin, reduces mortality and morbidity in critically ill surgical patients 20. Optimal glycaemia has yet to be determined in burns: considering the high risk of hypoglycaemia and the high glucose tissue requirements, it seems a reasonable compromise to aim at keeping glycemia < 8 mmol/l.

5. Micronutrient Requirements

During the hypermetabolic phase, the metabolism of micronutrients is increased in parallel with that of glucose, protein and fat, and there are increased losses from the burn area. In addition, some of the micronutrients have antioxidant functions, which are of utmost importance to burned patients in order to counteract the increase in free radical production observed in burns. These nutrients include selenium and zinc, and the vitamins B, C, E and β-carotene. Supplementation has been assessed in various conditions with beneficial clinical results. The precise requirements of trace elements and vitamins have yet to be determined for burned patients, but all recent data are in agreement with increased requirements (21). To achieve antioxidant effects, the supplements should be provided early on, starting during the first hours after injury.

5.1 Trace Elements and Minerals

Burned patients suffer significant trace element deficiencies involving predominantly copper, iron, selenium and zinc. The patients loose biological fluids through cutaneous wound exudates, drains, and haemorrhage, which cause negative balances during the first week after injury 11, 22. The exudative wound losses in burns >20% BSA are so important that a trace element depletion of body stores must be anticipated by early substitution. The alterations in trace element metabolism are reflected by low plasma concentrations, which persist for many weeks after injury. The interpretation of the low plasma levels is complicated by the acute-phase response, characterised by decreased plasma levels of iron, selenium and zinc, and increased copper. Supplementation with quantities of trace elements matched to balance the exudative losses, restores serum concentrations to some extent 23, 24. Selenium stores can also be assessed by measuring the enzymatic activity of plasma glutathione peroxidase.

Copper is of special importance in burns as collagen is dependent on it for maturation: the losses through exudate reach 20-40% of body content during the first week after injury 11, 25. Copper deficiency has been associated with fatal arrhythmias. Selenium is essential for glutathione peroxidase activity and zinc for immunity and cell replication 26. Iron requires a word of caution during the acute phase response, free iron being prooxidant. Intravenous supplements are associated with a worsening of the oxidative stress, an increased risk of renal failure 27, and an increased risk of infection as it is preferentially taken up by gram negative bacteria 28.

Magnesium and phosphorus losses through exudates are extensive and explain, to a large extent, the increased requirements in burns 29.

Sodium requirements vary: while intake is necessarily high during the resuscitation phase (up to 150 g sodium in 48 hours in burns > 50% BSA), requirements decrease thereafter. Hypernatremia is frequently observed during the remobilisation of edema between days 5 and 15, as well as during severe sepsis and should be managed is by increasing free water intakes either by the enteral route (preferred) or intravenously (glucose 5%).

5.2 Vitamins

A series of vitamins have are of major importance in major burns:

- The water-soluble vitamins of the B complex are not stored in appreciable amounts and are rapidly be depleted. Their requirements are greatly increased, being important cofactors for carbohydrate metabolism (vit. B1) ;
- Vitamins A and E have antioxidant function and are involved in tissue repair;
- Vitamin C is crucial in collagen synthesis in addition to its antioxidant effect. Therefore, a total daily intake of 1-2 g is highly recommended. According to recent studies, this quantity may be insufficient during the early phase after burns, since the use of mega-doses might achieve a capillary leak stabilising effect 30.

The fat-soluble vitamins D, and K are stored in fat deposits and are slowly depleted during prolonged diseases: there are reports of late deficiencies of vitamin D after major burns 31. The deficiency is probably multifactorial: loss of the skin's capacity to synthesise Vitamin D in burned areas, and limited exposure to sun.

6. Route of Feeding

The benefits of enteral nutrition are high in burned patients. Although the fluid shifts that occur in the shock-phase following severe burn cause significant oedema in the gut wall, and favour gastrointestinal paresis; using the gastric route during the first 24 hours after injury, even in patients with major burns, is associated with a high success rate 32. The practice in Lausanne is to use early enteral feeding, except when temporarily contraindicated by abdominal problems (abdominal trauma, electrical injury or bowel ischemia).

Oral feeding is only used in minor burns or in the recovery period: early on, it exposes the patient to the risk of underfeeding.

6.1 Enteral Nutrition

Enteral nutrition is preferred in burns as in other critically ill patients. Early enteral administration of nutrients can improve splanchnic perfusion (animal trials), blunt the hypermetabolic response,

stimulate intestinal IgA production, and maintain intestinal mucosal integrity as well as gut motility. By the end of the first week after injury most of the patient's energy requirements should be supplied enterally 33. Nevertheless a recent randomised trial did not confirm the benefit of early feeding in burns 34.
The feeding solutions should be polymeric, and fiber containing.
Delayed gastric emptying is sometimes observed in burned patients, in connection with the heavy analgesia and sedation which these patients require. In severely burned patients, postpyloric feeding solves this problem: nutrition may even be continued during long surgical procedures in those patients who remain intubated, to avoid repeated interruptions to nutritional intake with resultant underfeeding 35. Careful monitoring is required to prevent pulmonary aspiration. Slow constant gastric or postpyloric infusion is better tolerated than bolus administration. Gastric suction can be continued with simultaneous nasojejunal feeding.
Diarrhoea is a frequent complication observed during tube feeding. The causes of this complication are several, but antibiotic therapy is the most frequent, followed by excessive rate of administration (>200 ml/hour), or hyperosmolar feeds. Alternatively, centres using high doses of opioids for sedation observe severe constipation: our practice is to include the use of emolients from the 2nd day of injury in the feeding routine, and to use fibre containing diets.
There is one major risk to enteral feeding: because of the limits imposed by gastrointestinal tolerance the delivery of the large volumes required to meet the energy requirements may not be achieve, which may result in malnutrition. Insisting on using EN alone if the gut churns may therefore result in insufficient energy delivery for long periods, and put the patient at risk of malnutrition. Many patients also require repeated surgical sessions, with the nutritional consequences of repeated fasting, and shorter periods available for nutrient delivery. Compromise has to be found between the anaesthesia fasting rules and the nutritional requirements. Supplementary parenteral feeding may be required in such condition. The two techniques are complementary.
Finally non ischaemic bowel necrosis is a rare complication that has been described mainly in trauma and burn patients benefiting from early enteral feeding and occurring during the second week after injury.

6.2 Enteral Access

The techniques people are used to, work best in their hands. But the different options for intestinal accesses should be kept in mind in difficult cases. A study, performed in 106 burned patients, showed that gastric feeding initiated within 6 hours of injury was adequate in a large proportion of patients, although energy intake was significantly lower in the most severely burned patients >60% BSA 33. Nasogastric feeding tubes are the simplest to place, but also the easiest to pull out. Nasojejunal tubes are generally well tolerated, and enable feeding round the clock, reducing the durations of fasting required by the frequent interventions. Finally, with severe burns to the face, it may be very difficult for surgical reasons to leave a tube through the nostrils, and percutaneous endoscopic gastro- or jejunal feeding tubes (PEG or PEJ) may be an appropriate alternative. This technique carries its own risks, but has been used successfully in our unit in our most severely burned patients.

6.3 Immunomodulating Diets (IMD)

Their use is controversial in critically ill patients 36, 37. Patients suffering major burns belong to this category, and are frequently septic. There may be a role for these diets which combine glutamine, arginine with other micronutrients, but conclusive trials are lacking. In our unit, IMD may be used as starting diet for a maximum of 7-10 days, and at a maximal volume of 1000 ml/day, in combination with other fibre containing and high nitrogen polymeric diets .

6.4 Parenteral Route

Parenteral nutrition (PN) is a second choice for nutritional support in burns, but may prove life saving to prevent or correct malnutrition in cases of insufficient energy delivery by the enteral route or of gastrointestinal complications. Central venous access, however, carries the risk of infection and sepsis. There is no place for peripheral nutrition in the burned patient. Excessive caloric and carbohydrate intakes, easily achieved with PN and rarely with EN, should be avoided. Therefore, the daily monitoring of energy delivery is particularly important during PN.

The intravenous route is the only way to deliver the large amounts of micronutrients that are required during the first 2 weeks after injury 1. Nevertheless, this supplementation is only considered in burns > 20% BSA requiring central venous lines for other purpose.

7. Summary

Patients with major burns have increased nutritional requirements and are at particular high risk of malnutrition. Hypermetabolism is the rule, protein catabolism exceeding anabolism until closure of the wounds. The consequent loss of lean body mass cannot be counteracted by nutrition alone, emphasising the need to reduce metabolic requirements by non-nutritional means, eg nursing in a warm environment, control of infection, early debridement and grafting etc,. Energy requirements vary over time, with the largest increases being observed during the first weeks after injury: the return to normal takes up to 6 month. Enteral nutrition is the optimal feeding route, and should be started within the first 24 hours after injury to avoid installation of intestinal paresis. Additional pharmacological tools in adults include beta-blocking agents to decrease the catecholamine induced hypermetabolism and net protein catabolism, and oxandrolone to stimulate protein anabolism. In children, rh-growth hormone may be considered.
Oxidative stress is intense after major burns and is worsened by acute micronutrient deficiencies. Due to large exudative losses, patients with major burns are exposed to acute trace element deficiencies, which can be prevented by early intravenous substitution. If unsubstituted, trace element deficiencies contribute to increasing infectious complications and to delayed wound healing and recovery: early intravenous supplementation prevents such complications. Nutritional management includes monitoring daily weight changes, mainly to measure fluid balance, and energy requirements and intakes.

8. References

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