Introduction

Burn injuries are followed by a profound hypermetabolic response, which is characterised by circulatory, physiological, catabolic and immune system changes. This response can persist for up to 24 months post burn. It is mediated by a 50-fold elevation in plasma catecholamines, cortisol and inflammatory cells. This leads to whole body catabolism, significantly elevated resting energy expenditure (REE) and multi-organ dysfunction. These patients have a number of metabolic derangements, including increased REE, increased cardiac work, increased myocardial oxygen consumption, marked tachycardia, severe lipolysis, liver dysfunction, severe muscle catabolism, increased protein degradation, insulin resistance and growth retardation. Early excision and grafting is the cornerstone of management. No treatment modality supersedes early wound coverage. Early enteral nutrition, thermoregulation and resistance training are other components of care. Basic management should be correctly executed before pharmacological agents are employed.

Resting energy expenditure

The metabolic rate in burn patients approaches 180% of the predicted rate using the Harris-Benedict equation. There is a curvilinear increase in the resting metabolic rate of patients from close to normal predicted values in burns less than 10% total body surface area (TBSA), to twice that of normal predicted values in patients with burns greater than 40% TBSA. On admission, the resting metabolic rate for severely burnt patients at thermal neutral temperatures (30°C) is 140% of the predicted basal rate. It drops to 130% once the wounds are fully healed, and then to 120% at six months after the injury. The REE for burn patients is as high as 110-120% of the predicted basal rate, even as long as one year post burn. Increased catabolism results in loss of total body protein, weakened immune defenses and delayed wound healing.

Multi-organ dysfunction

Multi-organ dysfunction is a hallmark of the acute phase response post burn. Immediately post burn, the patient may experience low cardiac output and decreased cardiac contractility. This is characteristic of early shock. However, cardiac output and the heart rate increase by more than 50% compared to that in non-burnt patients 3-4 days post injury. The liver enlarges in size by two weeks post burn, and may be as large as 200% its normal size by discharge.

Whole body catabolism

Muscle protein degrades much faster than it is synthesised in post-burn patients. Decreased strength and failure to rehabilitate are just two of the consequences of the net protein loss which leads to loss of lean body mass and severe muscle wasting in these patients. Ten per cent loss of total body mass is associated with immune dysfunction, 20% loss with decreased wound healing and 30% with an increased risk of pneumonia, while a 40% loss of total body mass may lead to death.

Severely burnt, catabolic patients may lose up to 25% of their total body mass after acute burn injury. Protein degradation persists for up
to nine months post burn. This protein catabolism leads to significant growth retardation for up to 24 months post burn.

Sepsis

Patients who develop sepsis of their burn wounds experience increased REE and protein catabolism up to 40% more than those with like-size burns and no sepsis. Burn patients are more susceptible to sepsis as a result of the altered immune responses found in catabolic patients. The sepsis results in further muscle and protein catabolism which propagates the vicious cycle.

Modulation of the hypermetabolic response

Early excision and grafting have revolutionised burn care by attenuating the hypermetabolic response. A 40% reduction in the metabolic rate results in patients who have been totally excised and grafted within three days of the burn, and for burns which are more than 50% TBSA, when compared to patients with like-size burns excised and covered one week after injury. Early excision and grafting prevents further net protein loss and catabolism.

In one study, sepsis rates were also influenced by early excision and grafting. When the only difference was time to excision, the incidence of sepsis in the early excision group was 20%, and climbed to 50% in the late group. Early excision and grafting is the single most important available modality with which to modulate the hypermetabolic response, and also reduces the incidence of sepsis, while further decreasing REE. Other modalities can be used as an adjunct to this. However, if wound coverage is not achieved, the other modalities will be ineffective.

Thermoregulation

Core and skin temperature is raised 2° above normal in a burned patient. This results in profound water and heat loss. Water loss can be as extreme as 4 litres per metre squared of burn area per day. When patients do not mount this response, they are either septic or have exhausted their physiological capability to maintain the required body temperature. It has been shown in some studies that the hypermetabolic response can be attenuated by increasing the ambient temperature to 33°. At this temperature, the energy required for vapourisation is derived from the environment, rather than from the patient. Increasing the ambient temperature in the operating theatre and patient’s room is a simple intervention that can be used to decrease the metabolic rate.

Nutrition

Aggressive, early enteral feeding in severely burnt patients mitigates the degree and extent of the hypermetabolic response and improves outcomes. Patients with burns of 40% TBSA lose 25% of their preadmission weight by 21 days with oral alimentation alone. Enteral nutrition is preferable to parenteral nutrition (PN). The advantages of enteral nutrition are reduced bacterial translocation, maintenance of gut motility and the preservation of “first pass” nutrient delivery to the liver. PN alone, or in combination with enteral nutrition, is associated with overfeeding, liver failure, an impaired immune response, increased septic complications and increased mortality. PN should only be considered in patients with enteral feeding intolerance or prolonged ileus. There is some evidence that increased protein replacement, with the aim of maintaining or even increasing lean body mass, may be beneficial. Nutritional needs are profound owing to increased protein and muscle catabolism, a paucity of glycogen stores and an increased metabolic rate. Dramatic improvements in survival have resulted from improving the net protein balance and metabolic rate.

Exercise

Growth retardation continues long into the rehabilitative phase in the paediatric burn population. Exercise training is an essential component of the administered metabolic treatment. It not only helps to reduce functional limitations as the patient progresses through the rehabilitative phase, but also increases the lean body mass, and improves strength, the ability to walk distances and overall cardiopulmonary capacity.

Pharmacology

Pharmacological agents which block or reverse mediators of the hypermetabolic response are one of the management strategies. Blocking beta-adrenergic receptors and negating the effects of elevated levels of circulating catecholamines after a severe burn reduces the cardiac work, tachycardia, metabolic rate and thermogenesis. The result is a reduced rate of cardiac complications and decreased mortality. Propranolol has also been shown to increase lean body mass and decrease skeletal muscle wasting. Propranolol effectively increased the efficiency of muscle protein synthesis at a dose of 0.5-4.0 mg/kg/day. Enhanced glycogenolysis and protein breakdown, in both the liver and skeletal muscle, results in an increase in triglycerides, and urea and glucose production, which, in turn, leads to hyperglycaemia. This contributes to muscle protein catabolism, complications of reduced graft take and increased morbidity and mortality. Improved donor site healing was demonstrated with continuous insulin infusion, titrated to keep the patient euglycaemic for seven days. Intensive insulin therapy also stimulates muscle protein synthesis and increases lean body mass without increasing hepatic triglyceride production.

Hypoandrogenaemia is another devastating consequence of severe burn injury. Prolonged and persistent reduction in testicular steroid production occurs in severely burnt males. The subsequent loss of lean body mass is a consequence of the decreased levels of testosterone, coupled with elevated levels of cortisol. The administration of testosterone ameliorates muscle protein loss. However, despite its efficacy, the long-term administration of testosterone is fraught with both expense and difficulties with compliance. It was demonstrated in research carried out on oxandrolone, a synthetic analogue, that it is safe in both genders because it results in only 5% of the masculinising effects of testosterone. It improves net muscle protein synthesis and protein metabolism in severely burnt patients when administered at a dose of 0.1 mg/kg twice daily.
Oxandrolone increases lean body mass and bone mineral content, and increases muscle strength during the acute phase post burn and up to one year of treatment. The 1% risk of hirsutism and hepatic dysfunction in patients receiving oxandrolone is outweighed by the significant improvement in lean body mass, protein synthesis and overall growth.

Other modalities which have been used include recombinant human growth hormone, insulin-like growth factor 1, insulin-like growth factor-binding protein-3, fenofibrate (peroxisome proliferator-activated receptor agonist), exenatide (glucagon-like peptide-1) and ketoconazole.

**Conclusion**

The hypermetabolic response to a burn injury is profound. If left untreated, that state results in physiological exhaustion and the burn injury may be fatal. Numerous modalities attenuate the hypermetabolic response. However, early excision and grafting is the cornerstone of management. No modality supersedes early wound coverage. Early enteral nutrition, thermoregulation and resistance training are other simple modalities which can be implemented in burn patients with significant burn injuries. Basic management should be correctly executed before pharmacological agents are employed. In fact, pharmacological agents which attenuate the hypermetabolic response should be reserved for specialised burn units with documented favourable outcomes for large burns. Managing burns through early excision and grafting is a fundamental principle to which general surgeons should aspire.

**Bibliography**