The Hypermetabolic Response to Burn Injury and Interventions to Modify this Response

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KEYWORDS

• Hypermetabolism • Burns • β-blockade
• Catabolism • Catecholamines • Wasting

Severe thermal injury, defined as burns encompassing over 40% of a patient's total body surface area (TBSA), is followed by a pronounced hypermetabolic response that persists for up to 1 to 2 years postburn (**Fig. 1**).[1,2] The response is characterized by increased metabolic rates, multiorgan dysfunction, muscle protein degradation, blunted growth, insulin resistance, and increased risk for infection.[1–5]

The initial stress response to severe injury, as originally described by Cuthbertson, features an ''ebbed'' phase with a decrease in tissue perfusion and a decrease in metabolic rate. In severe burns, this response lasts for the first 2 to 3 days postburn. The subsequent ''flow'' phase is characterized by an increase in metabolism and hyperdynamic circulation. When left untreated, physiologic exhaustion ensues, and the injury becomes fatal.[6–9]

Major progress has been made since the recognition of the hypermetabolic response. This article describes the magnitude of the metabolic and catabolic responses to major burn injury and discusses the effects of various interventions to mitigate the hypermetabolic response. Numerous therapeutic strategies to modify this response have arisen in the past half century and include early excision and grafting, thermoregulation, early continuous enteral feeding with a high-carbohydrate high-protein diet, the use of anabolic agents growth hormone, insulin-like growth factor-1 (IGF-1), insulin-like growth factor binding protein-3 (IGFBP-3), insulin, oxandrolone, propranolol, and the use of therapeutic exercise. This article outlines the destructive properties of the hypermetabolic response and the many strategies that have been implemented over the last decade to alter this response to improve burn care, quality of life, and survival in burned patients.

THE HYPERMETABOLIC RESPONSE IN SEVERE BURNS

Mediators of the Hypermetabolic Response

Catecholamines and corticosteroids are the primary mediators of the hypermetabolic response following burns greater than 40% TBSA.[10] There is a 10- to 50-fold surge of plasma catecholamine and corticosteroid levels that last up to 9 months postburn.[11,12] Burn patients have increased resting energy expenditures, increased cardiac work, increased myocardial oxygen consumption, marked tachycardia, severe lipolysis, liver dysfunction, severe muscle catabolism, increased

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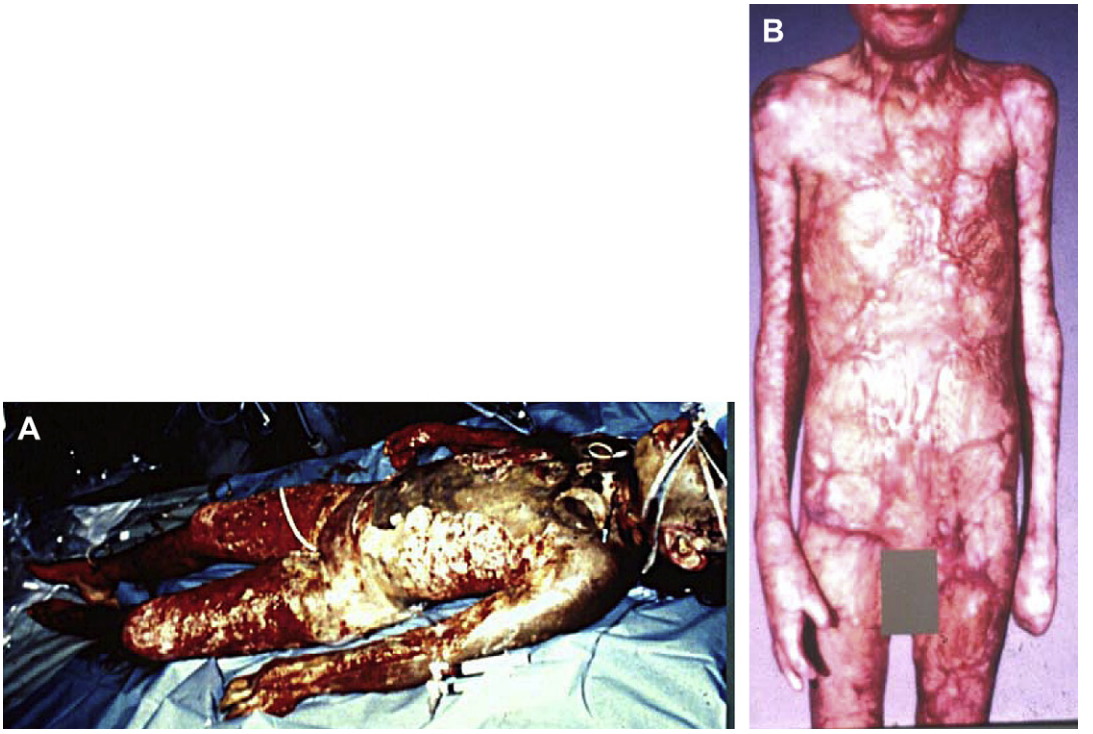

Fig. 1. Adolescent burn patient with a 90% TBSA flame burn at admission (*A*) and at 1 year (*B*).

protein degradation, insulin resistance, and growth retardation.[13–16]

Acute Phase Proteins (Cytokines and Hormonal Changes)

Cytokine levels peak immediately after burn, approaching normal levels only at 3 to 6 months postburn.[11] Serum hormones, constitutive and acute phase proteins, are abnormal throughout acute hospital stay. Serum IGF-1, IGFBP-3, parathyroid hormone, and osteocalcin drop immediately after the injury and remain decreased until 2 months postburn compared with normal levels.[11] Sex hormones and endogenous growth hormone levels decrease around 3 weeks postburn and remain low.[11] Larger burn injuries are characterized by more pronounced and persistent inflammatory responses indicated by higher concentrations of proinflammatory cytokines that promote more severe catabolism.[17]

Changes in Resting Energy Expenditures

Past studies showed metabolic rates of burn patients approaching 180% of that of predicted based on the Harris-Benedict equation.[18] The resting metabolic rate of patients with large burns increases in a curvilinear fashion from close to normal predicted levels for TBSA less than 10% to twice that of normal predicted levels at 40% TBSA and above. For severely burned patients, the resting metabolic rate at thermal neutral temperature (30°C) tops 140% of predicted basal rate on admission, reduces to 130% once the wounds are fully healed, and then to 120% at 6 months after injury (**Fig. 2**).[11] Even 12 months postburn, the resting energy expenditures for burn patients are 110% to 120% of predicted,

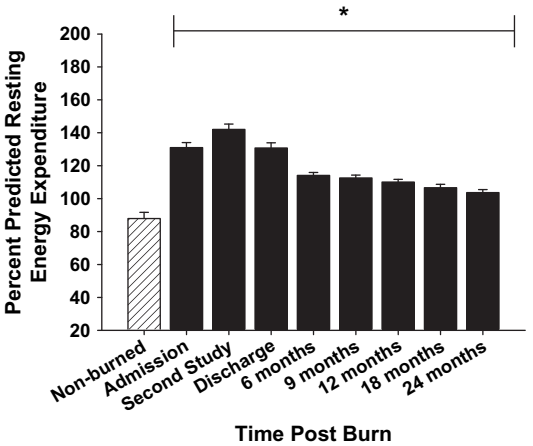

Fig. 2. Metabolic rates of severely burned (≥40% TBSA) compared with normal nonburned children. *Significance at a $P<.05$.