cellular metabolic events:
(i) HSPs - synthesised in response to a variety of stress
- have protective roles in sepsis and ischaemia-reperfusion
(ii) leukocyte activation
- leads to oxidative burst, production of free radicals, proteases and arachidonic acid metabolites
(iii) apoptosis
- TNF alpha, IL-10, cortisol and NO have all been implicated in this process

intermediary metabolism
(i) protein metabolism
- IL-1, TNF-alpha & other cytokine and hormonal responses lead to extreme protein catabolism.
- glutamine, alanine and other amino acids are mobilised from skeletal muscle & taken up by hepatocytes and gut mucosa; glutamine depletion may occur
- fraction of energy derived from glucose is reduced while that derived from
- oxygen consumption and myocardial work
- redistribution away from gut may result in bacterial translocation to the blood stream
- high catecholamine levels are arrhythmogenic
- systemic inflammation can result in tissue destruction
- hyperglycaemia

systemic protein system responses
(i) acute phase response
- a systemic response to injury characterised by redirection of hepatic protein synthesis and haematoalogical alterations
- production of protein involved in defence is increased (eg fibrinogen, CRP, haptoglobin, complement C3) while synthesis of serum transport & binding molecules is reduced (albumin, transferrin)
(ii) complement cascade
- triggers production of chemoattractants (C3a, C5a), vasoactive anaphylactoids (C4a, C5a), opsonins (C3b), stimulation of neutrophil & monocyte burst (C3b)
- neutrophil adherence to endothelium (C5a)

energy balance and oxygen delivery
- hypermetabolism increases oxygen demand and consumption; however, aerobic glycolysis rather than anaerobic glycolysis is characteristic of the metabolic response to stress in usual circumstances

surgical techniques
- minimally invasive surgical techniques are associated with reduced cytokine release
- starvation & nutrition
- starvation alone produces adaptive hypometabolism while critical illness is associated with prominent protein catabolism; malnourishment in combination with critical illness is associated with increased morbidity & mortality
- drugs
- steroids are associated with critical illness myoneuropathy
- catecholamines, theophylline, calcium channel blockers and antibiotics all have immunomodulatory effects

Cytokines:
- soluble, non-antibody, regulatory proteins responsible primarily for the inflammatory response
- the following are the major cytokines involved in the response to stress
(i) TNF-alpha
- an early mediator after exposure to endotoxin
- TNF-alpha administration reproduces all features of septic shock including hypermetabolism, fever, anorexia, hyperglycaemia, protein catabolism & lactic acidosis
(ii) Interleukins
- IL-1 is a potent inducer of the HPA axis as well as noradrenergic neurons
- IL-6 is the main mediator of the acute phase response
- IL-8 induces neutrophil adhesion, chemotaxis and enzyme release
- IL-4 and IL-10 are anti-inflammatory cytokines
(iii) colony stimulating factors
- stimulate the proliferation of haematopoetic cells, superoxide and cytokine production by neutrophils & macrophages
(iv) interferon gamma
- participates in acquired cell-mediated immunity

neuroendocrine mediators
- afferent neuronal impulses and cytokine release from the site of injury or infection activate the sympathetic nervous system and the HPA axis
(i) catecholamines
- are increased
(ii) HPA axis
- activation results in gluconeogenesis, protestysis & lipolysis
(iii) insulin and glucagon levels
- are increased but the insulin levels are inappropriately low for the level of hyperglycaemia
(iv) growth hormone
- levels increase transiently but IGF-1 is depressed
(v) thyroid hormone
- T4 levels are usually low-normal
(vi) ADH, renin, angiotensin, aldosterone & prolactin levels increase

- magnitude of the response is proportional to extent of injury
- other factors impacting on the response include:
(i) ischaemia and reperfusion
(ii) nutritional status
(iii) surgical procedures
(iv) drugs
(v) genetic polymorphisms
- some components of the response are destructive & modulation represents a potential therapeutic target