Body's response to injury & surgery

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Basic concepts in homeostasis

- **Homeostasis refers to the co-ordinated physiological processes which maintains steady states of the body;**
  - **it requires several body systems (eg CNS, CVS) to work together.**

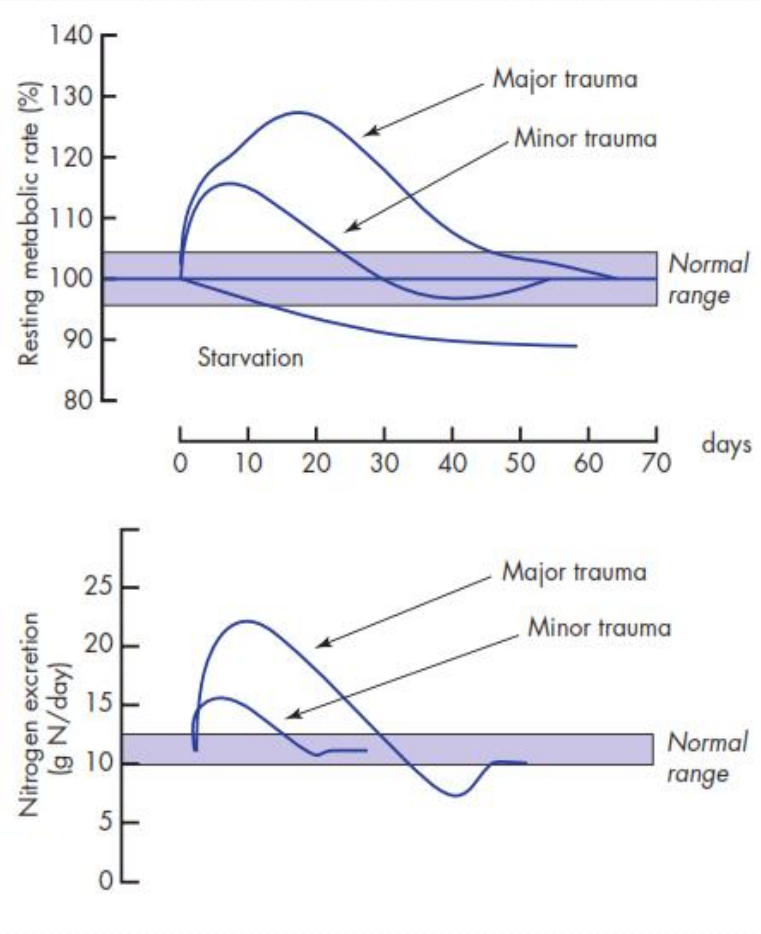
- **These responses are, in general, beneficial to the host and allow healing/survival.**

Basic concepts in homeostasis

- **With the better understanding of the metabolic injury response, elective surgery aims to reduce the need for a homeostatic response by minimising the primary insult (minimal access surgery and 'stress-free' perioperative care).**
- **In emergency surgery, with trauma, sepsis or hypovolaemia, compounding the primary problem, there is a requirement**
  - **to augment homeostatic responses (resuscitation),**
  - **to resolve the primary insult (operation) and**
  - **to provide organ support (critical care).**

The graded nature of the injury response

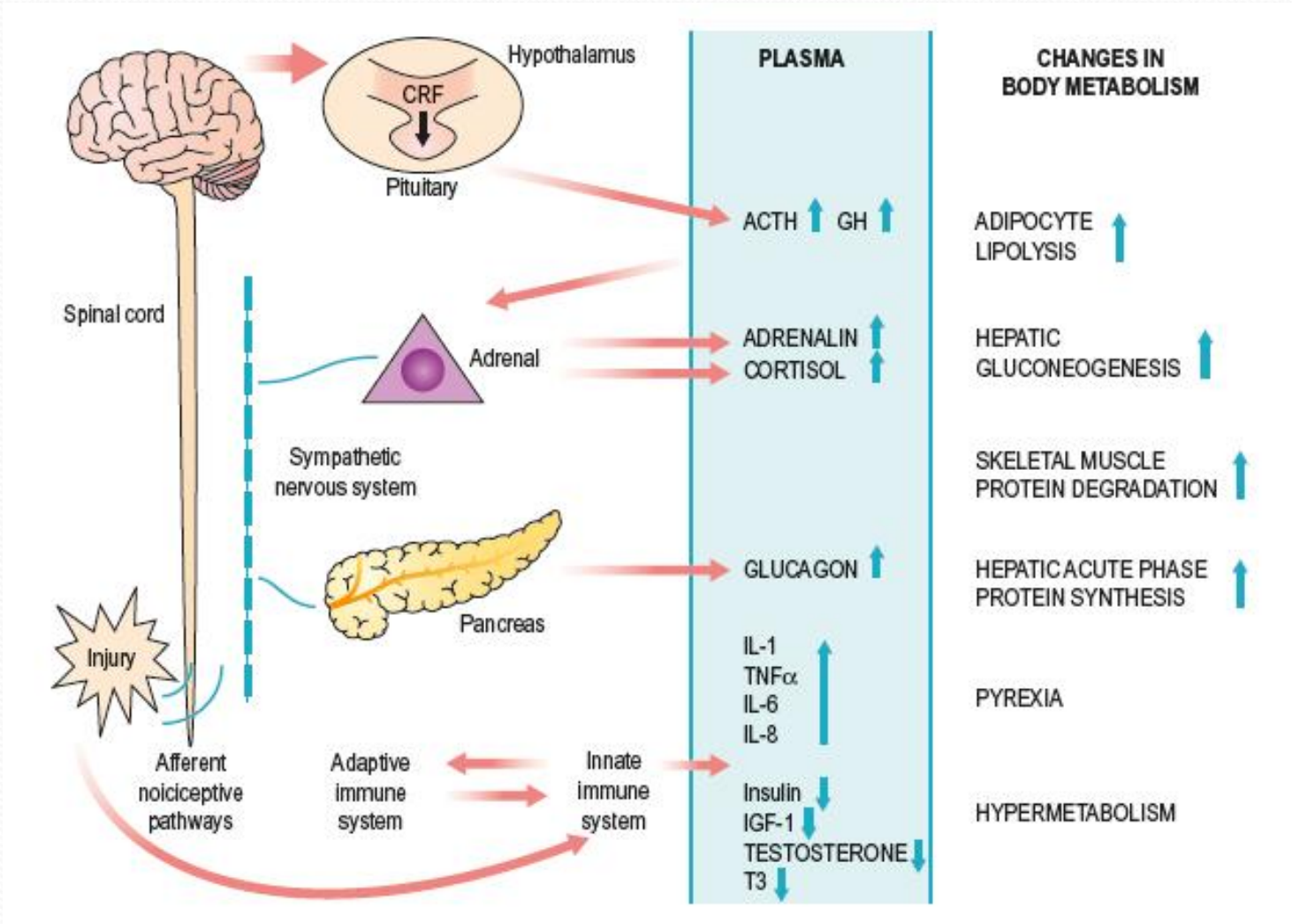
- **The response to injury is graded, ie the more severe the injury, the greater the response (Figure).**
  - **This includes both physiological/ metabolic changes, as well as immunological changes.**
- **Thus, following elective surgery of intermediate severity, there may be a transient and modest rise in temp, HR, RR, energy expenditure and WBC count.**
- **Following major trauma/sepsis, these changes are accentuated, resulting in SIRS, hypermetabolism, marked catabolism, shock and even MODS.**



Biphasic neuroendocrine response to injury/critical illness

- **Acute phase** characterised by an actively secreting **pituitary** and elevated counter-regulatory hormones (**cortisol, glucagon, adrenaline**).
  - These changes are **beneficial** for short-term survival
- **Chronic phase** associated with **hypothalamic suppression** and low serum levels of the respective target organ hormones.
  - These changes contribute to **chronic wasting**.

The integrated response to surgical injury (first 24–48 hours): neuroendocrine stress response and proinflammatory cytokine response .



Systemic inflammatory response syndrome following major injury

- **Is driven initially by proinflammatory cytokines (e.g. IL-1, IL-6 and TNFa)**
- **Is followed rapidly by increased plasma levels of cytokine antagonists and soluble receptors (e.g. IL-1Ra, TNF-sR)**
- **If prolonged or excessive may evolve into a counter inflammatory response syndrome**

- **Intravenous infusion of a cocktail of 'counter-regulatory' hormones (glucagon, glucocorticoids and catecholamines) reproduces many aspects of the metabolic response to injury.**

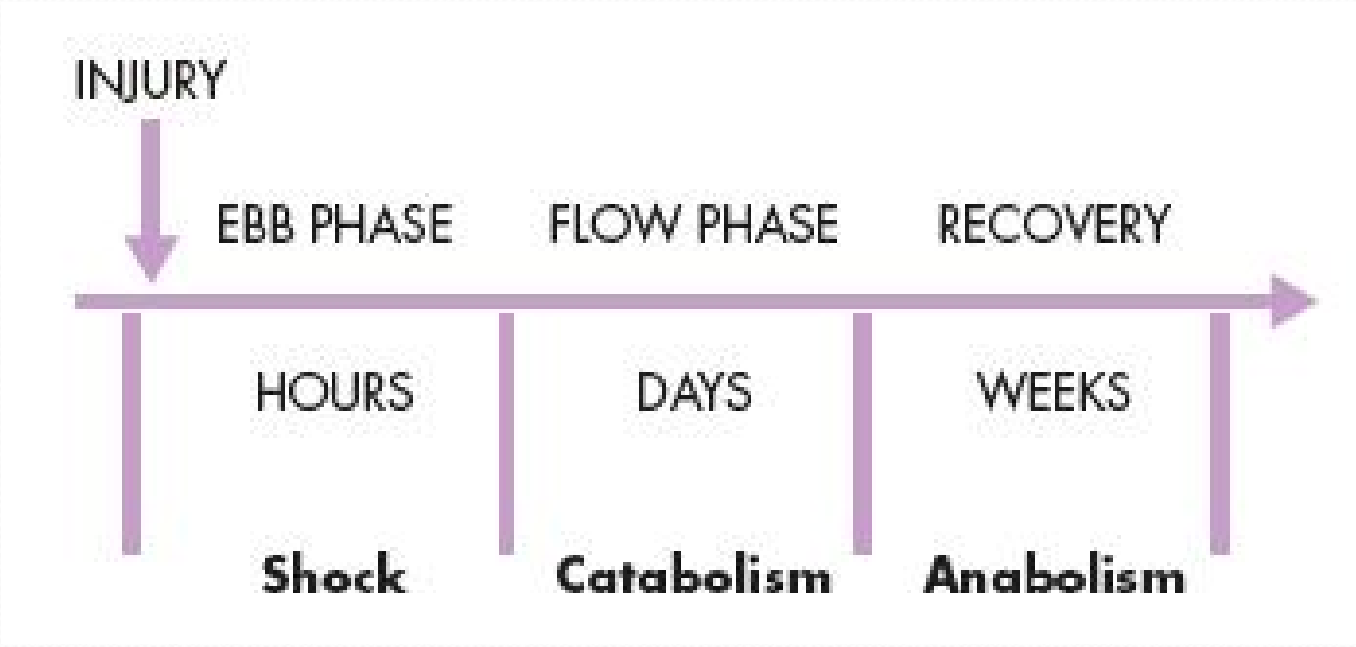
Physiological response to injury

The natural response to injury includes:

- **Immobility/rest**
- **Anorexia**
- **Catabolism**

The changes are designed to aid survival of moderate injury in the absence of medical intervention.

Phases of the physiological response to injury.



The metabolic stress response to surgery and trauma: the 'ebb and flow' model

- **The ebb phase begins at the time of injury and lasts for approximately 24–48 hours.**
  - **may be attenuated by proper resuscitation, but not completely abolished.**
  - **characterised by hypovolaemia, dec. BMR, reduced cardiac output, hypothermia and lactic acidosis.**
  - **predominant hormones are catecholamines, cortisol and aldosterone (following activation of the renin–angiotensin system).**
  - **magnitude of response depends on the degree of blood loss and the stimulation of somatic afferent nerves at the site of injury.**
  - **main physiological role is to conserve both circulating volume and energy stores for recovery and repair.**

- **Following resuscitation, the ebb phase evolves into a hypermetabolic flow phase;**
  - **involves mobilisation of body energy stores for recovery and repair, and the subsequent replacement of lost or damaged tissue.**
  - **characterised by tissue oedema, increased BMR, increased cardiac output, raised temp, leukocytosis, inc. oxygen consumption and inc. gluconeogenesis.**
  - **subdivided into;**
    - **an initial catabolic phase, lasting about 3–10 days, followed by**
    - **an anabolic phase, which may last for weeks if extensive recovery and repair are required following serious injury.**

- **During the catabolic phase, the increased production of counter-regulatory hormones (catecholamines, cortisol, insulin and glucagon) and inflammatory cytokines (e.g. IL-1, IL-6 and TNFa) results in significant fat and protein mobilisation, leading to significant weight loss and increased urinary nitrogen excretion.**
  - **increased production of insulin is associated with significant insulin resistance.**

- **The combination of prolonged catabolism & insulin resistance, predisposes complications, esp. infectious and cardiovascular.**
  - **The complications will further aggravate the neuroendocrine and inflammatory stress responses, thus creating a vicious catabolic cycle.**

Purpose of neuroendocrine changes following injury

- **To provide essential substrates for survival**
- **To postpone anabolism**
- **To optimise host defence**

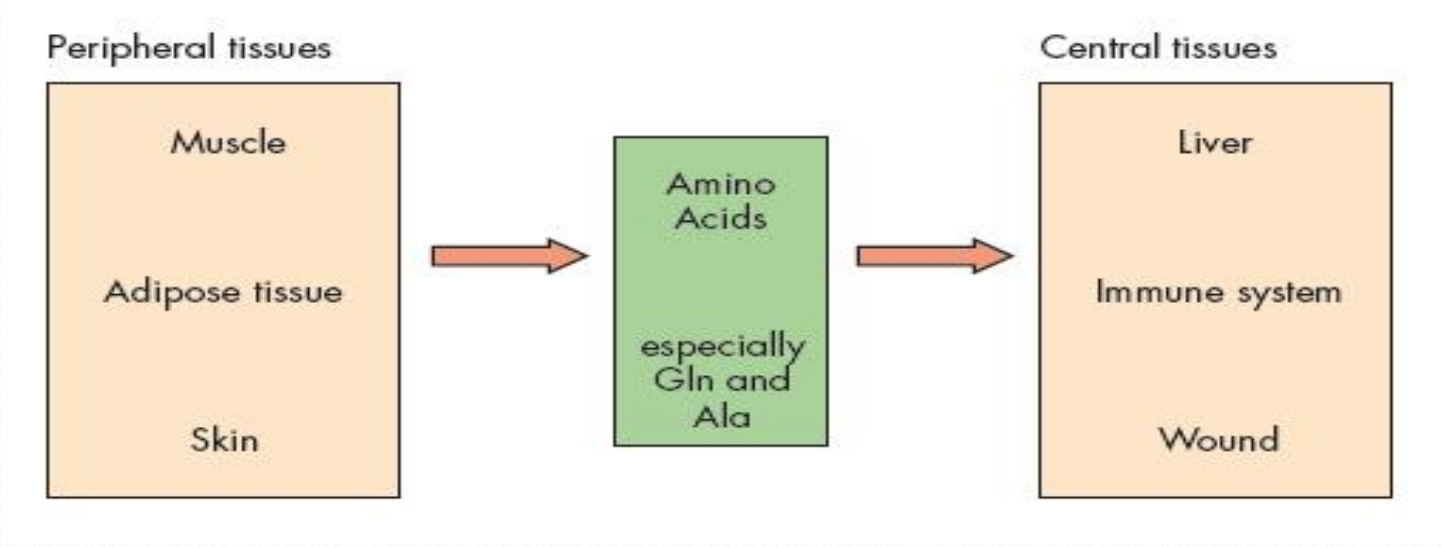
- **These changes may be helpful in the short term, but may be harmful in the long term, especially to the severely injured patient who would not survived without medical intervention.**

Key catabolic elements of the flow phase

- **These elements determine the extent of catabolism and thus govern the metabolic and nutritional care of the surgical patient.**
  - **Remember, during the injury response, not all tissues are catabolic.**
  - **Indeed, the coordinated response allow the body to reprioritise limited resources away from peripheral tissues (muscle, adipose tissue, skin) and towards key viscera (liver, immune system) and the wound.**

Hypermetabolism

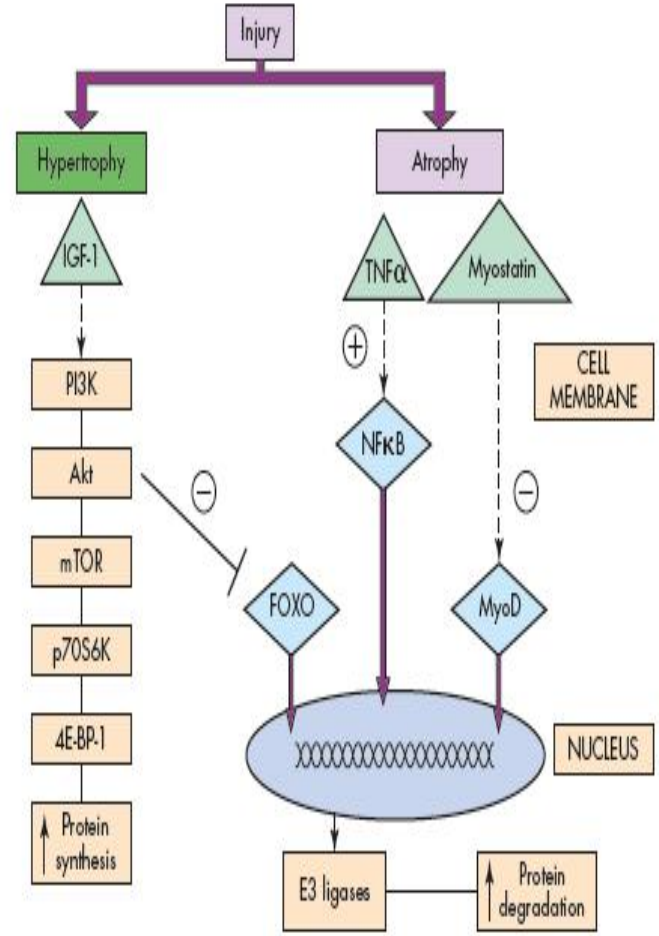
- **Is mainly caused by an acceleration of energy-dependent metabolic cycles**
- **Is limited in modern practice due to routine critical care**



During the metabolic response, the body reprioritises protein metabolism away from peripheral tissues and towards key central tissues.

Skeletal muscle wasting

- **Provides amino acids for the metabolic support of central organs**
- **Is mediated at a molecular level mainly by activation of the ubiquitin–proteasome pathway**
- **Can result in immobility and contribute to hypostatic pneumonia and death if prolonged and excessive**



The major catabolic and anabolic signaling pathways involved in skeletal muscle homeostasis.

Hepatic acute phase response

It represents a reprioritization of body protein metabolism towards the liver and is characterized by:

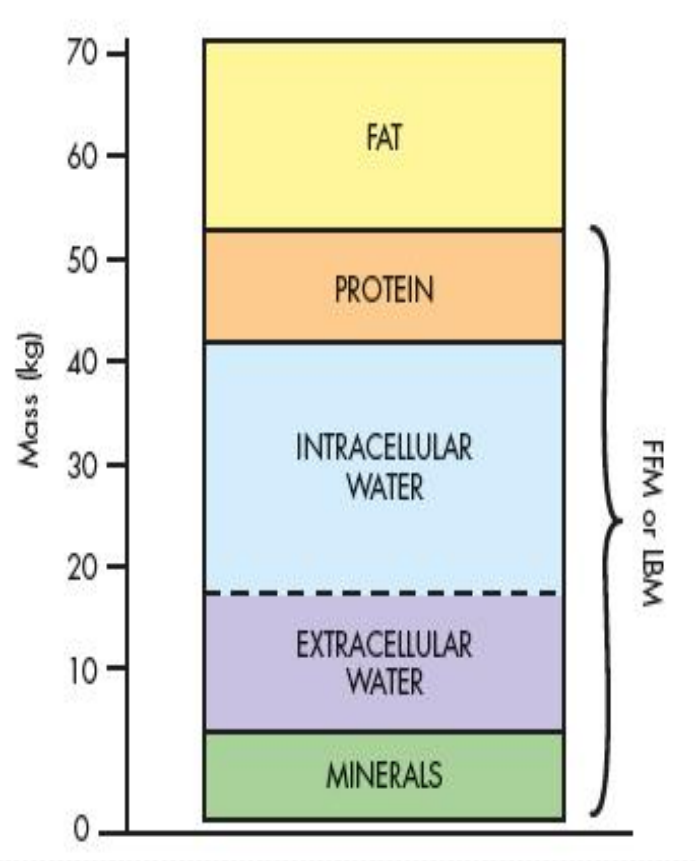
- **Positive reactants (e.g. CRP): plasma concentration ↑**
- **Negative reactants (e.g. albumin): plasma concentration ↓.**

Insulin resistance

- **Following surgery or trauma, postoperative hyperglycaemia occur, due to;**
  - **increased glucose production**
  - **decreased glucose uptake in peripheral tissues.**
- **Decreased glucose uptake is due to insulin resistance which is transiently induced within the stressed patient.**
  - **Probably due to proinflammatory cytokines and decreased responsiveness of insulin-regulated glucose transporter proteins.**
  - **degree of insulin resistance is proportional to the magnitude of injury.**
  - **Following routine upper abdominal surgery, insulin resistance may persist for about 2 weeks.**
  - **The patients behave like type II diabetes mellitus.**
- **The mainstay of management is intravenous insulin infusion (eg intensive approach using sliding scales, or a conservative approach).**

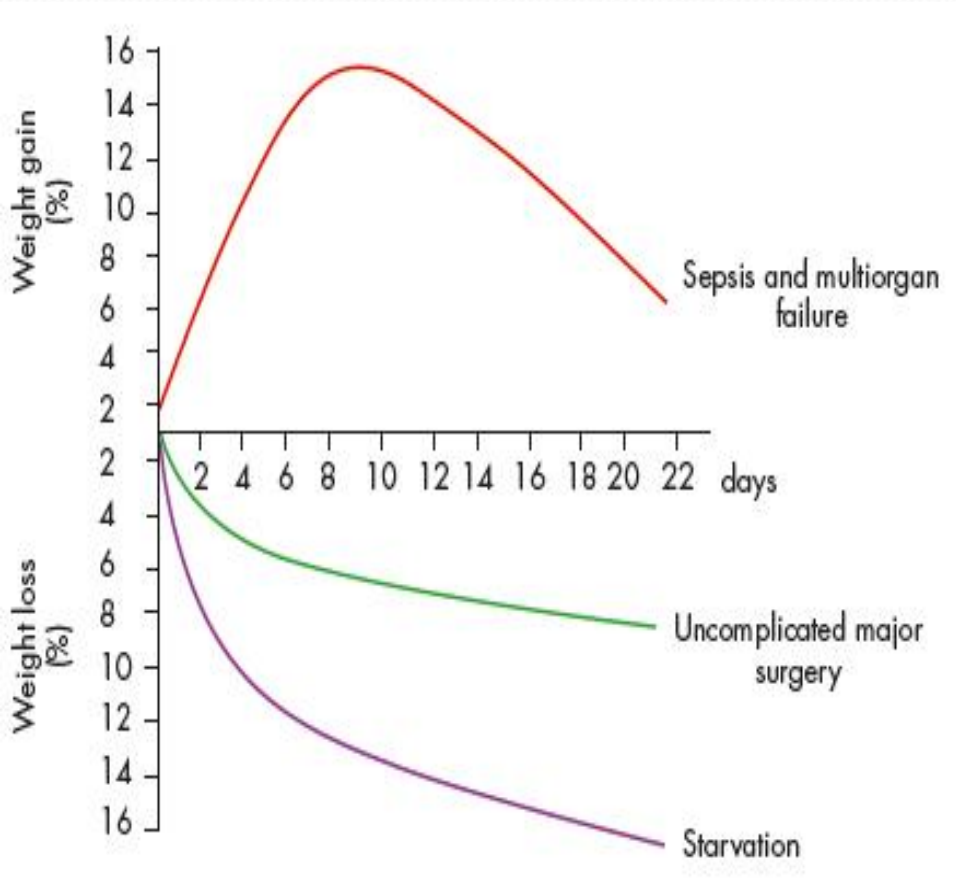
Changes in body composition following injury

- The main labile energy reserve in the body is fat, and the main labile protein reserve is skeletal muscle.
  - fat mass can be reduced without any effect on function,
  - loss of protein mass results not only in skeletal muscle wasting, but also depletion of visceral protein status.
- Within lean issue, each 1 g of nitrogen is contained within 6.25 g of protein, which is contained in 36 g of wet weight tissue.
  - Thus, the loss of 1 g of nitrogen in urine is equivalent to the breakdown of 36 g of wet weight lean tissue.
  - Protein turnover in the whole body is about 150–200 g / day.



The chemical body composition of a normal 70-kg male.

Changes in body weight that occur in serious sepsis, after uncomplicated surgery and in total starvation.



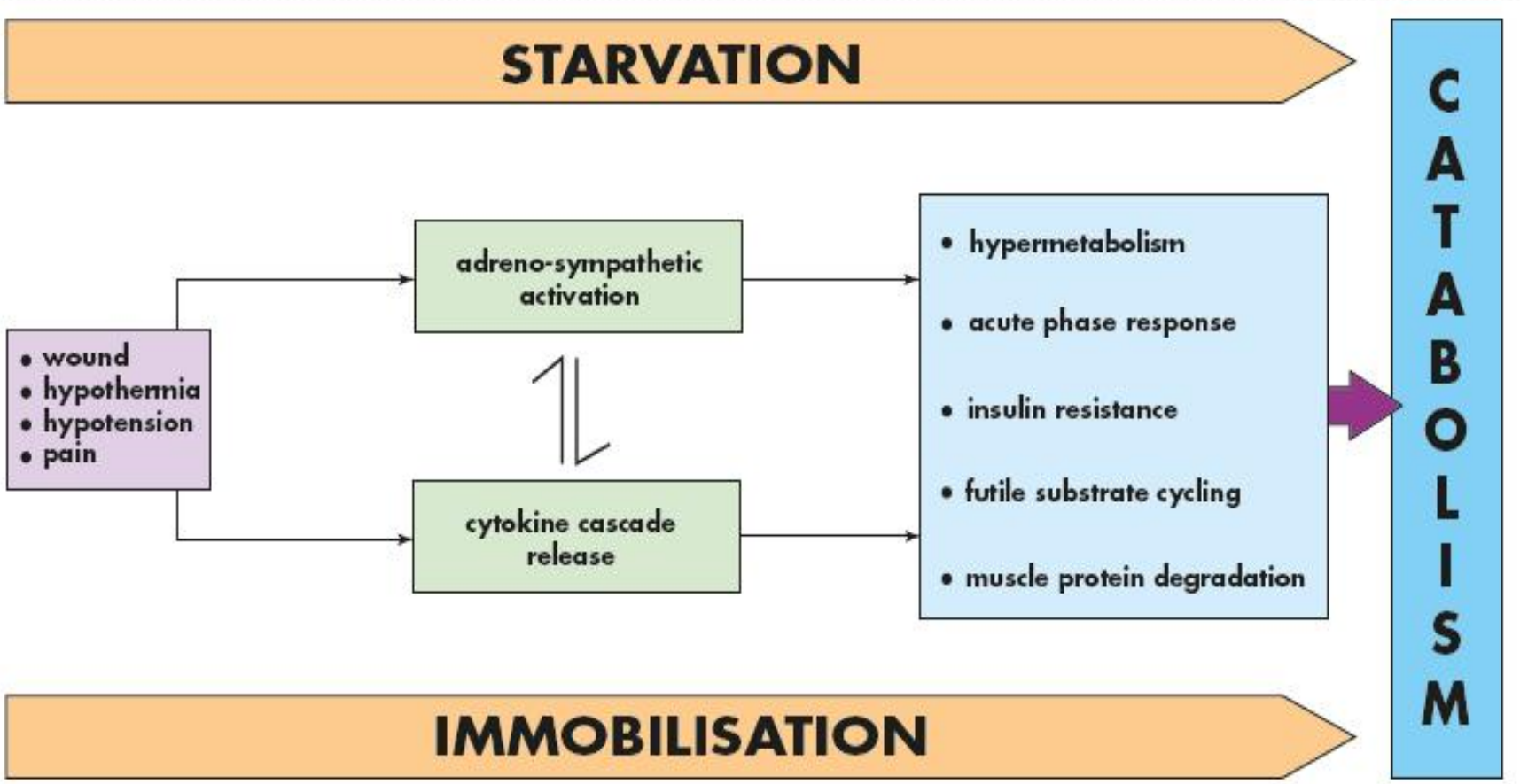
- **Body weight increases immediately on resuscitation with an expansion of extracellular water by 6–10 litres within 24 hours.**
- **Thereafter, even with optimal metabolic care and nutritional support, total body protein will diminish by 15% in the next 10 days, and body weight will reach negative balance as the expansion of the extracellular space resolves.**

- **It is now possible to maintain body weight and nitrogen balance following major elective surgery.**
  - **by blocking the neuroendocrine stress response with epidural analgesia and providing early enteral feeding.**
  - **early fluid retention phase can be avoided by careful intraoperative fluid balance, with avoidance of excessive intravenous saline.**

Avoidable factors that compound the response to injury

- Continuing haemorrhage
- Hypothermia
- Tissue oedema
- Tissue underperfusion
- Starvation
- Immobility

Factors that exacerbate the metabolic response to surgical injury



Concepts behind optimal perioperative care

- There is now a strong scientific rationale for avoiding;
  - unmodulated exposure to stress,
  - prolonged fasting and
  - excessive administration of intravenous (saline) fluids.

- minimal access surgery can reduce the magnitude of surgical injury and enhances homeostasis and recovery.

- Modulating the stress/inflammatory response at the time of surgery may have long-term sequelae.
  - ß-blockers and statins improve long-term survival after major surgery, may be due to suppression of innate immunity.
  - Epidural analgesia used to reduce pain, block the cortisol stress response and attenuate postoperative insulin resistance.

The End!