The metabolic response to injury

LEARNING OBJECTIVES

• Classical concepts of homeostasis
• Mediators of the metabolic response to injury
• Physiochemical and biochemical changes that occur during injury and recovery
• Changes in body composition that accompany surgical injury
• Avoidable factors that compound the metabolic response to injury
• Concepts behind optimal perioperative care

Basic concepts

• Homeostasis is the foundation of normal physiology
• ‘Stress-free’ perioperative care helps to restore homeostasis following elective surgery
• Resuscitation, surgical intervention and critical care can return the severely injured patient to a situation in which homeostasis becomes possible once again

BASIC CONCEPTS IN HOMEOSTASIS

• ‘Homeostasis: the co-ordinated physiological process which maintains most of the steady states of the organism.’ (Walter Cannon)
• Responses to injury are, in general, beneficial to the host and allow healing/survival. (John Hunter).
• It is important to recognise that the response to injury is graded, the more severe the injury, the greater the response.
• This concept not only applies to physiological/metabolic changes but also to immunological changes/sequelae.
THE METABOLIC STRESS RESPONSE TO SURGERY AND TRAUMA:

The physiological 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.

The neuroendocrine response to severe injury/critical illness is biphasic:

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

![The metabolic stress response to surgery and trauma: the ‘ebb and flow’ model](image)
Systemic inflammatory response syndrome (SIRS) following major injury:

- Is driven initially by pro-inflammatory cytokines (e.g. IL-1, IL-6 and TNFα)
- 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 counterinflammatory response syndrome (CARS)

In 1930, Sir David Cuthbertson divided the metabolic response to injury in humans into ‘ebb’ and ‘flow’ phases:

- **Ebb phase** begins at the time of injury and lasts for approximately 24–48 hours. It may be attenuated by proper resuscitation, but not completely abolished.
- The ebb phase is characterised by: hypovolaemia, decreased basal metabolic rate, reduced cardiac output, hypothermia and lactic acidosis.
- The predominant hormones regulating the ebb phase are: catecholamines, cortisol and aldosterone (following activation of the renin–angiotensin system).

The flow phase may be subdivided into an initial catabolic phase, lasting approximately 3–10 days, followed by an anabolic phase, which may last for weeks if extensive recovery and repair are required following serious injury.

**Purpose of neuroendocrine changes following injury is to:**

- Provide essential substrates for survival
- Postpone anabolism
- 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 otherwise not have survived without medical intervention.
KEY CATABOLIC ELEMENTS OF THE FLOW PHASE OF THE METABOLIC STRESS RESPONSE

Hypermetabolism following injury:
- Is mainly caused by an acceleration of futile metabolic cycles
- Is limited in modern practice by elements of routine critical care

During the metabolic response to injury, the body reprioritises protein metabolism away from peripheral tissues and towards key central tissues such as the liver, immune system and wound.

Changes in body composition following major surgery/critical illness
- Catabolism leads to a decrease in fat mass and skeletal muscle mass
- Body weight may paradoxically increase because of increase in the extracellular fluid space

Alterations in hepatic protein metabolism:
the acute phase protein response (APPR)

The hepatic acute phase response represents a reprioritisation of body protein metabolism towards the liver and is characterised by:
- Positive reactants (e.g. CRP): plasma concentration
- Negative reactants (e.g. albumin): plasma concentration
Insulin resistance

*Following surgery or trauma, postoperative hyperglycaemia develops as a result of increased glucose production combined with decreased glucose uptake in peripheral tissues.

*Decreased glucose uptake is a result of insulin resistance which is transiently induced within the stressed patient.

Suggested mechanisms for this phenomenon include the action of pro-inflammatory cytokines and the decreased responsiveness of insulin-regulated glucose transporter proteins. The degree of insulin resistance is proportional to the magnitude of the injurious process. Following routine upper abdominal surgery, insulin resistance may persist for approximately 2 weeks.

Avoidable factors that compound the response to Injury

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

A proactive approach to prevent unnecessary aspects of the surgical stress response:

- Minimal access techniques
- Blockade of afferent painful stimuli (e.g. epidural analgesia)
- Minimal periods of starvation
- Early mobilisation
Body response to trauma

Trauma in general initiate a series of biochemical and physiological reactions created by secretion of hormones and mediators (neuro - endocrine) as an adaptive mechanism for restoration of hemostasis and promote tissue healing.

The intensity of the reaction is proportional to the severity of the injury.

It is also affected by the age, pre trauma health state and accompanied disease.

The main stimulus of the neuro endocrine reaction are

1- Changes in the effective circulatory volume like hemorrhage, burn, diarrhea or vomiting.
2- Changes in the concentration of Oxygen or Carbon dioxide like in asphyxia, chest trauma or head injury.
3- Pain and noxious stimuli.
4- Sepsis like sever infection, peritonitis.

The neuro-endocrine response characterized by secretion of hormones that control and maintain the reaction These Hormones called the stress hormones which include:

1- catcholamin.
2- corticosteroid.
3- glucagons.
4- renin - angiotonsen
5- aldosteron
6- vasopressin
7- growth hormone

Caticholamine:  

Secreted from the adrenal medulla in form of adrenalin and nor adrenalin, there actions are:

1- Increase sympathetic tone result in vasoconstriction and increase cardiac rate and contractility.
2- Glycogenolysis, gluconeogenesis, (hyperglyseemia)
3- ketolysis (break down of protein into AA)
4- lipolysis (break down of lipid into FA)

**Corticosteroid:**

Secreted from the adrenal cortex its actions are:

1- glycogenolysis, gluconeogenesis,
2- ketolysis.
3- lipolysis.
4- stabilize cell membrane and lysosoms.
5- Anti inflammatory action.
6- increase intravascular volume.
7- permissive effect to catecholamine

**Renin angiotensin system:**

Secreted from the distal convoluted tubule its actions are:

1- Vasoconstriction
2- Increase cardiac rate and contractility
3- Increase vascular permeability.
4- Stimulate aldosteron and vassopressin secretion.

**Glucagon:**

Secreted from the pancreas its actions are:

1- glycogenolysis, gluconeogenesis
2- lipolysis
3- ketogenesis.
4- inhibit insulin secretion
5- increase cardiac rate and contractility

**Aldosteron:**

from adrenal cortex, it increase water and sodium retention from the kidney.

**Vassopressin:**

from posterior pituitary gland its actions are:
1-Vasoconstriction  
2-Increase cardiac rate and contractility.

**Growth hormone:**  
from anterior pituitary gland its actions are:  
1-Glycogenolysis, gluconeogenesis  
2-Lipolysis  
3-Ketogenesis  
4-Promote action of catecholamine.

**The aim of the neuro endocrine response are:**  
1- Hyper glycemia.  
2- Production of amino acid(AA).  
3- Production of fatty acid (FA).  
4- Restore fluid and electrolyte.  
5- Support cardiac function.  
6- Maintain vascular resistance.

**The body response pass into 3 phases**  

*1- The ebb phase:*  
it’s the first 24 to 48 hours after injury the aim is to restore circulation and prepare fuel for the next phase. The metabolic changes are:  
1- Glycogenolysis  
2- Gluconeogenesis  
3- Increase secretion of stress hormones.  
4- Decrease secretion of insulin  
The result of these changes are:  
Hyperglycemia, water and sodium retention, increase vascular resistance, decrease urine output and elevation of blood pressure.
2- *The flow (catabolic) phase:*

It’s started after 48 hours and may last several weeks depending on the severity of the injury.

The metabolic changes are:

1. Increase in resting energy expenditure which is due to catecholamine, this results in hypermetabolic state.
2. Increase oxygen consumption by tissue.
3. Increase secretion of stress hormones.
4. Hyperglycemia: which is needed for
   - A- CNS metabolism.
   - B- WBC and RBC nutrition.
   - C- Wound healing
   - D- Immune system function.
5. Ketolysis (protein break down) to AA which is used for
   - A- intermediates to gluconeogensis
   - B- provide AA for the syntheses of leukocytes and cellular proliferation.
6. Lypolysis: degradation of fat to FA which is used for:
   - A- intermediates to gluconeogensis
   - B- energy substrate for muscles specially of respiration, heart and kidneys (non glucose depended tissue)

3- *anabolic phase:*

It’s the last phase started after abolishing of infection and disappearance of pain and subsiding of inflammation.

The body start to build its self again and return the functional capacity of the organ, it needs along time to restore body protein and fat.

Its characterized by

1. Increase body Wight
2. Stabilization of cardiac output
3. Returne of blood sugar to normal.
In summary the response to injury result in

1- Hyper metabolism
2- Hyperglycemia.
3- Hyper catabolism

The aim is to provide high circulating substrate (glucose, AA, FA)

*but*

On the expense of body tissue stores.

If the body support fail to meet the body requirement during the hyper metabolic phase, the cellular energy level well decrease and result in

MULTIPLE ORGAN DYSFUNCTION SYNDROMAND MULTIPLE ORGAN FAILURE