Systemic Response to Injury and Metabolic Support

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Topics

- Definition of Homeostasis
- Nature of the injury response
- Mediators of the metabolic response
- The Ebb and Flow model
- Changes in body composition following injury
- Avoidable factors that compound to the response of injury
- Minimizing Surgical Stress Response

Homeostasis

- Homeostasis, any self-regulating process by which biological systems tend to maintain stability while adjusting to conditions that are optimal for survival.
- It is a coordinated physiological process, which maintains most of steady states of the organism.

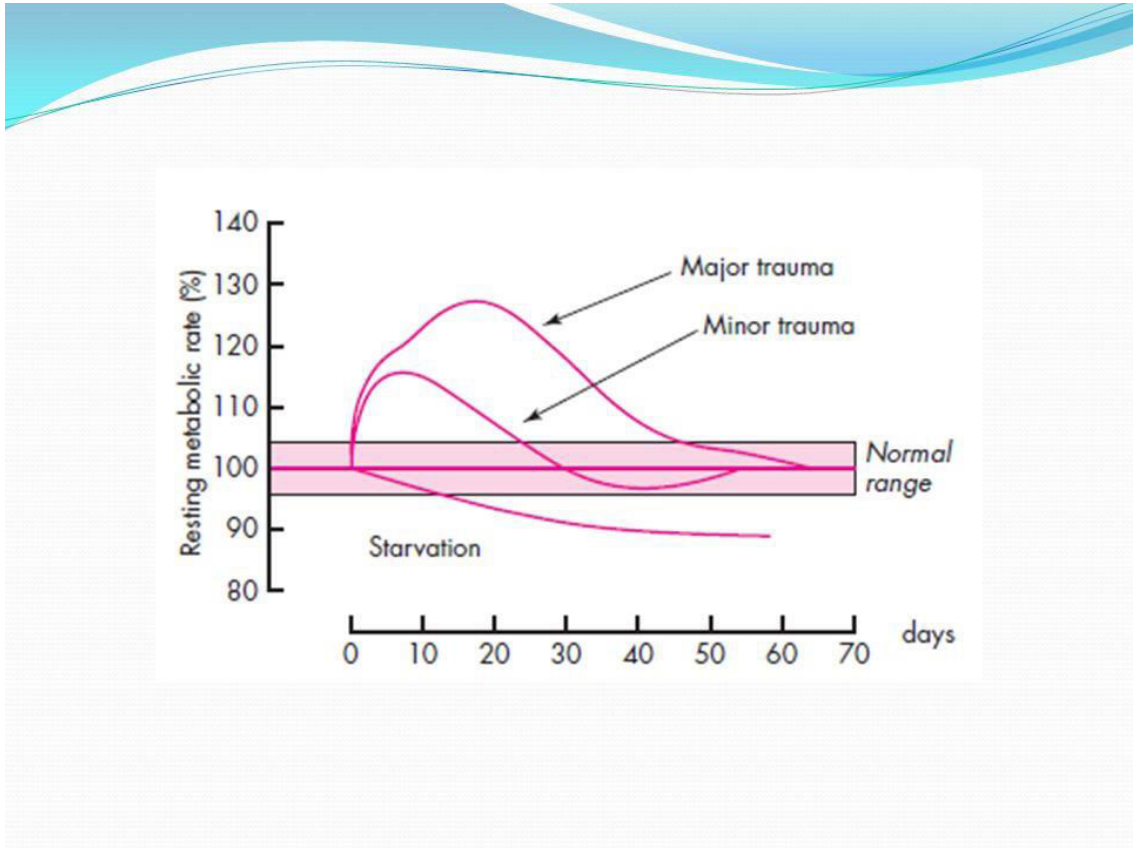
Homeostasis

- Homeostasis is the foundation of normal physiology
- Stress free peri-operative care helps 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
- Elective surgery practice seeks to reduce the need for homeostatic response by minimizing the primary insult (as in Minimal Access Surgery)

Nature of the injury response

- It is graded

*** THE MORE SEVERE THE INJURY, THE GREATER THE RESPONSE ***



Response to Elective Surgery

1- Transient rise in temperature

2- Rise in HR & RR

3- Increase in peripheral WBCs

Response to Major trauma/sepsis

1- SIRS

2- Hypermetabolism

3- Marked Catabolism

4- Shock → MODS

SIRS CRITERIA (ANY TWO)

- TEMP > 100.4 OR <95.0
- RR > 20 OR PACO2 <32MMHG
- HR >90 /MIN
- WBC >12,000 OR <4,000

SEPSIS (16% MORTALITY)

SIRS WITH A MICROBIAL SOURCE

SEVERE SEPSIS (20%)

SEPSIS WITH > ONE ORGAN SYSTEM DYSFUNCTION. (HYPOTENSION, AMS, ACISODIS, OLIGUIRA, ARDS, ETC.)

SEPTIC SHOCK (69%)

SEVERE SEPSIS WITH HYPOTENSION UNRESPONSIVE TO FLUID RESUSCITATION

MODS

> ONE ORGAN SYSTEM REQUIRING INTERVENTIONAL HOMEOSTASIS

ROSENS 6TH EDITION

Mediators of the Metabolic Response to Injury

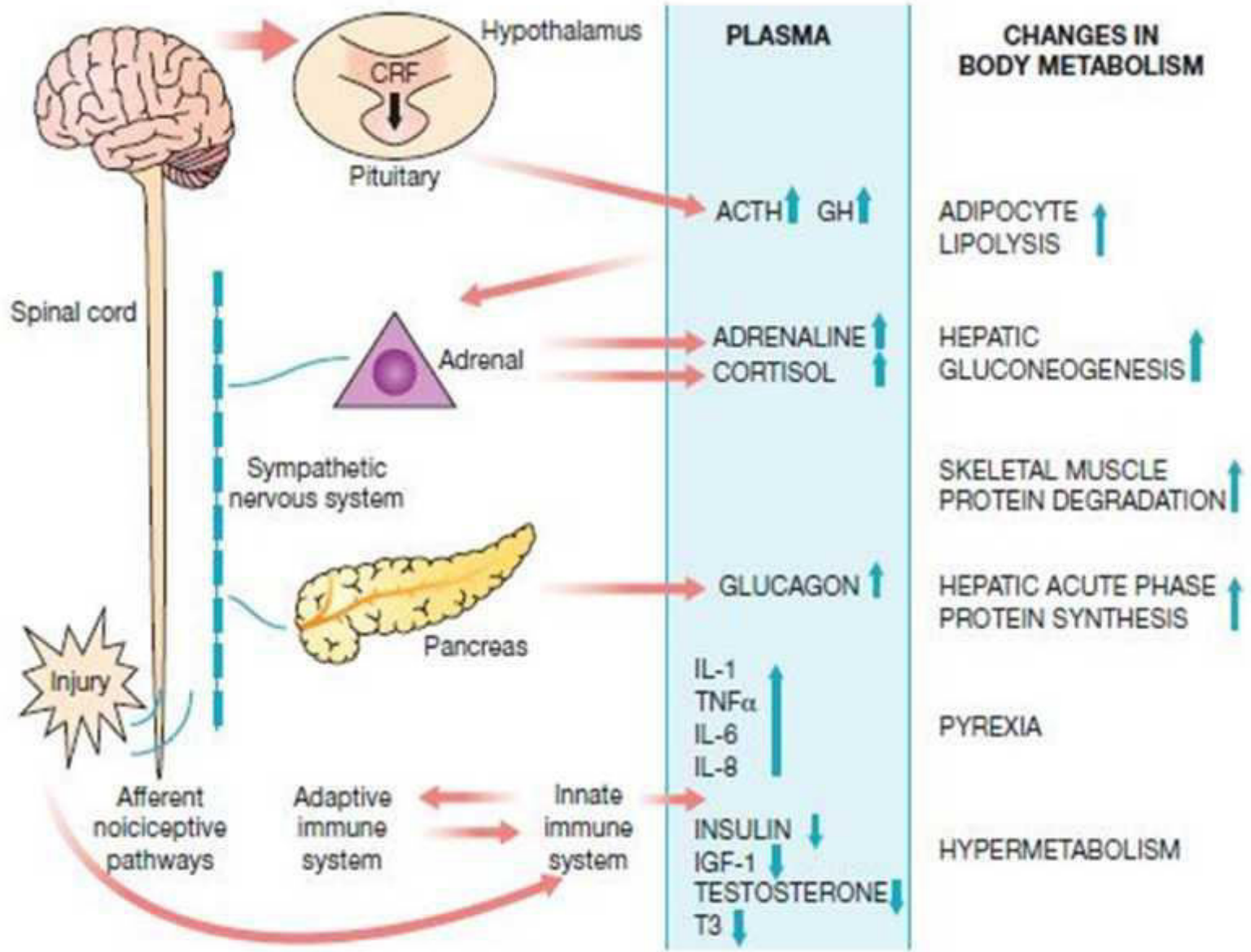


Figure 1.2 The integrated response to surgical injury (first 24–48 hours): there is a complex interplay between the neuroendocrine stress response and the proinflammatory cytokine response of the innate immune system.

Mediators of the Metabolic Response to Injury

1- Neuroendocrine Response:

- The neuroendocrine response to sever injury/critical illness is biphasic.

1- Acute Phase: it is characterized by an actively secreting pituitary and elevated counter regulatory hormones (cortisol, glucagon, adrenaline). Changes are thought to be beneficial for short term survival.

2- Chronic Phase: it is associated with hypothalamic suppression and low serum levels of the respective target organ hormones. Changes contribute to chronic wasting.

Purpose of neuroendocrine changes following injury

1- Provides essential substrates for survival

2- Postpone anabolism

3- Optimize host response

Mediators of the Metabolic Response to Injury

2- Immunological Response:

- Proinflammatory cytokines:

A) Interleukin 1

B) TNF-alpha

C) Interleukin 6 (promotes the hepatic acute phase response) and 8

D) Nitric oxide

E) Prostanoids (via COX 2)

F) Endothelin 1

Mediators of the Metabolic Response to Injury

2- Immunological Response:

- Anti-inflammatory mediators:

A) IL 1 RA

B) TNF soluble receptors

C) IL 4,5,9,13

D) TGF- Beta

Counter Anti-inflammatory Response Syndrome (CARS)

- Specialized Proresolving Mediators:

A) Essential fatty acid-derived lipoxins

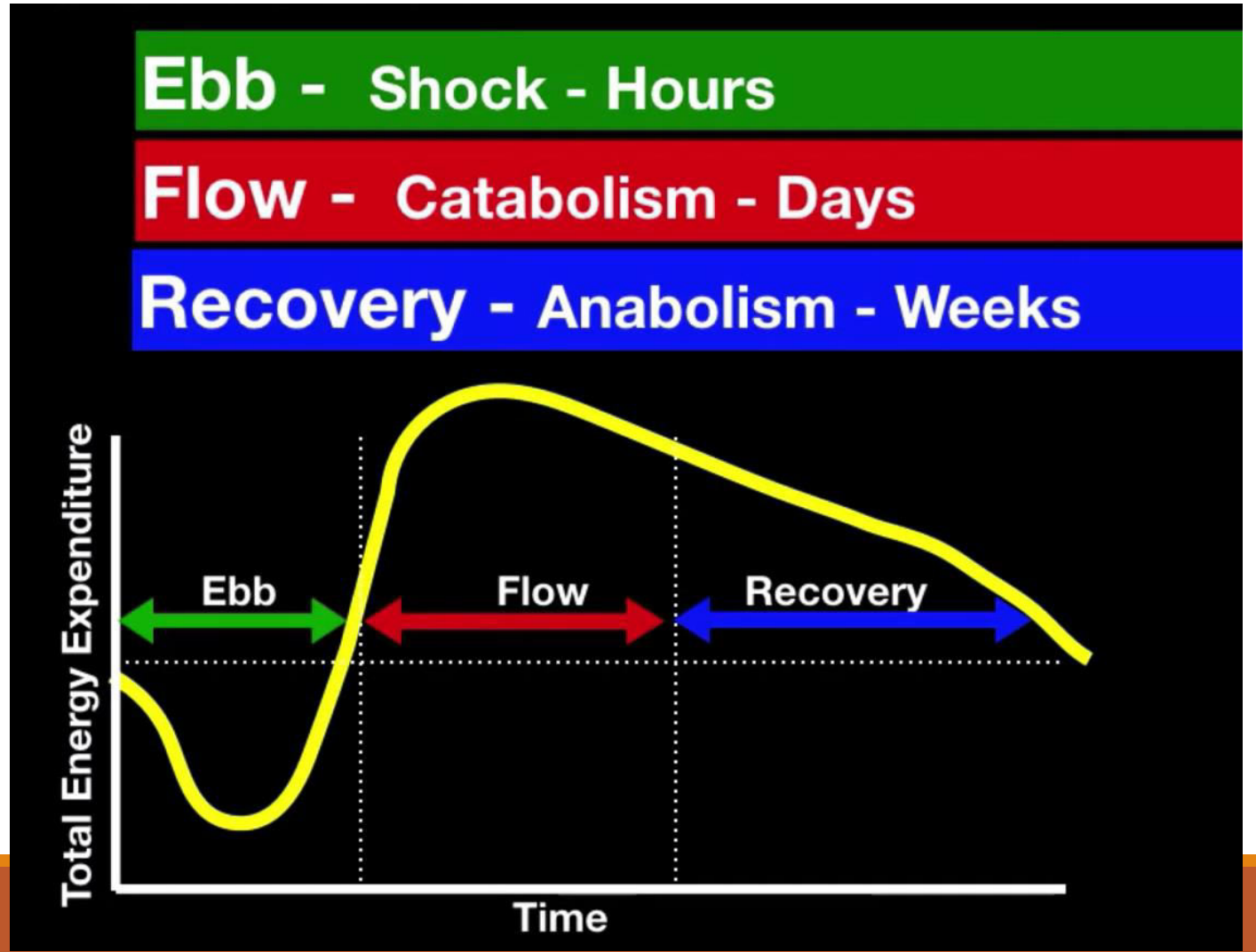
B) Resolvins

C) Protectins

D) Maresins

These limit and resolve the inflammation

The Ebb and Flow Model



Ebb Phase

- **Characterised by:**

Hypovolemia

Decreased BMR

Reduced CO

Hypothermia

Decreased oxygen consumption

Increased fatty acids and glycerol

Increased cortisol

Decreased Insulin

Hyperglycemia

Lactic acidosis

Ebb Phase

- **Hormones regulating:**

  Catecholamine

  Cortisol

  Aldosterone

- **Main physiological role:**

  Conserve Energy

Flow Phase

- **Characterised by:**

Tissue edema

Increased BMR

Increased CO

Raised body temperature

Leukocytosis

Proteinolysis

Lipolysis

Hepatic acute phase response

Increased oxygen consumption

Increased gluconeogenesis

Recovery Phase

Occurs 3-8 days after elective surgery

Weeks to months after major trauma or sepsis

Corticoid withdrawal phase

Restoration of body protein and fat stores

Catabolic Phase (flow phase)

1- Protein Catabolism → Muscle Degradation:

Protein serves as the greatest precursor for glucose for gluconeogenesis

Surgical stress leads to increased protein breakdown and this proteolysis leads to increased nitrogen excretion in the urine

This response is proportional to injury where the amount of protein breakdown can be up to 30 grams of nitrogen a day excreted in the urine which is equivalent to 1.5% loss of lean body mass a day which is up to 1 kilogram of skeletal muscle broken down everyday

So proteolysis leads to Skeletal Muscle Atrophy to provide amino acids which act as precursors for gluconeogenesis

Muscle protein recovery can be regained in the anabolic period along with exercise and nutritional support

Catabolic Phase (flow phase)

2- Lipid Metabolism:

Lipids provide the primary fuel after trauma injury

Hormones and inflammatory mediators will lead to increase in lipolysis

Lipolysis will lead to breaking down of triglycerides and an increase in fatty acids that are circulating throughout the body

Free fatty acid oxidation may provide more energy than needed

Catabolic Phase (flow phase)

3- Carbohydrates:

The metabolic response to injury is to increase glucose

Severity of trauma and injury parallels hyperglycemia

Excessive glucose (if given in form of dextrose in TPN) can lead to excess carbon dioxide production and suboptimal pulmonary function as well as hepatic steatosis

Catabolic Phase (flow phase)

4- Insulin Resistance:

Insulin in normal conditions:

1- Leads to quick uptake of glucose and storage as glycogen in liver, muscle and adipose tissue

2- Reduce muscle protein degradation

3- Stimulate lipogenesis and prevents lipolysis

Cont.

4- Insulin Resistance:

Insulin under stress:

Glucagon, catecholamines, cortisol, growth hormone and cytokines lead to increased release in amino acids, free fatty acids and glucose in the bloodstream and a suppressed insulin secretion

This eventually creates insulin resistance, and this resultant hyperglycemia leads to pro-inflammatory response

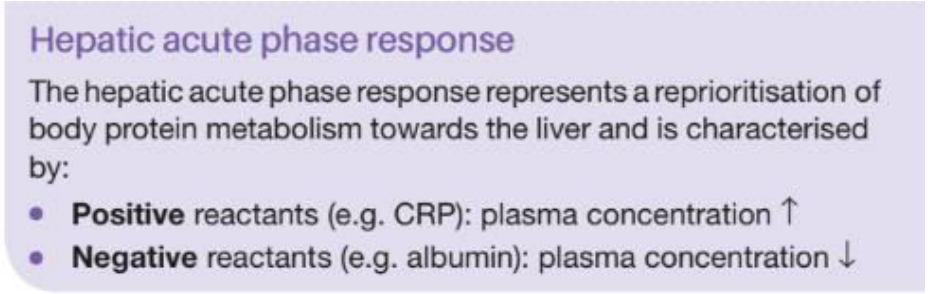
That’s why it is important to take exogenous insulin to normalize glucose levels

Catabolic Phase (flow phase)

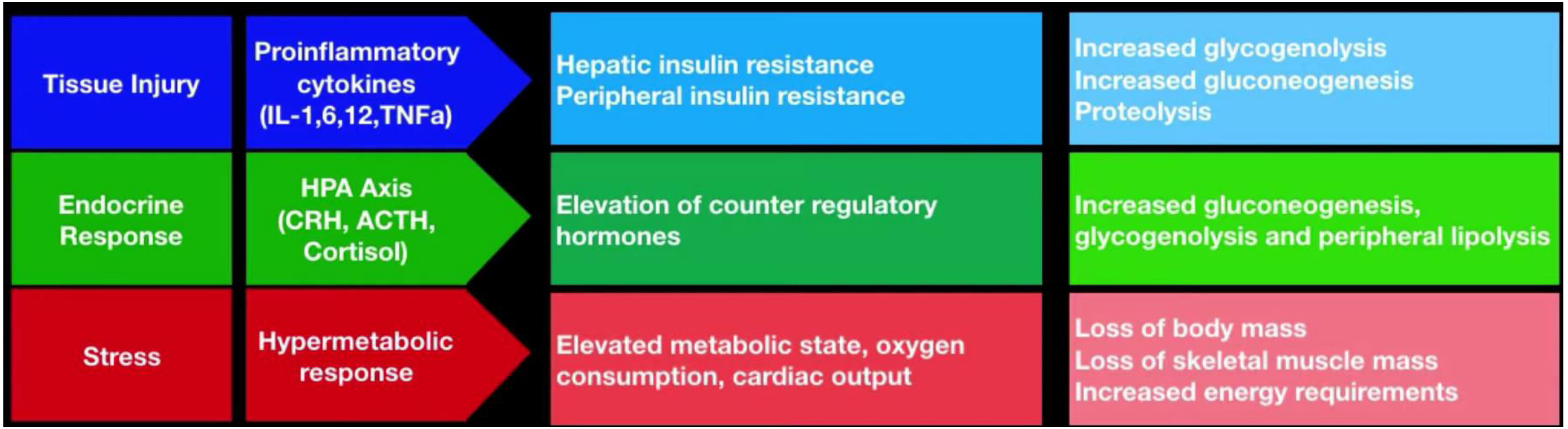
5- Hepatic protein metabolism (Acute phase protein response)

In response to inflammatory conditions, including surgery, trauma, sepsis, cancer or autoimmune conditions, circulating peripheral blood mononuclear cells secrete a range of proinflammatory cytokines, including IL-1, IL-6 and TNFα.

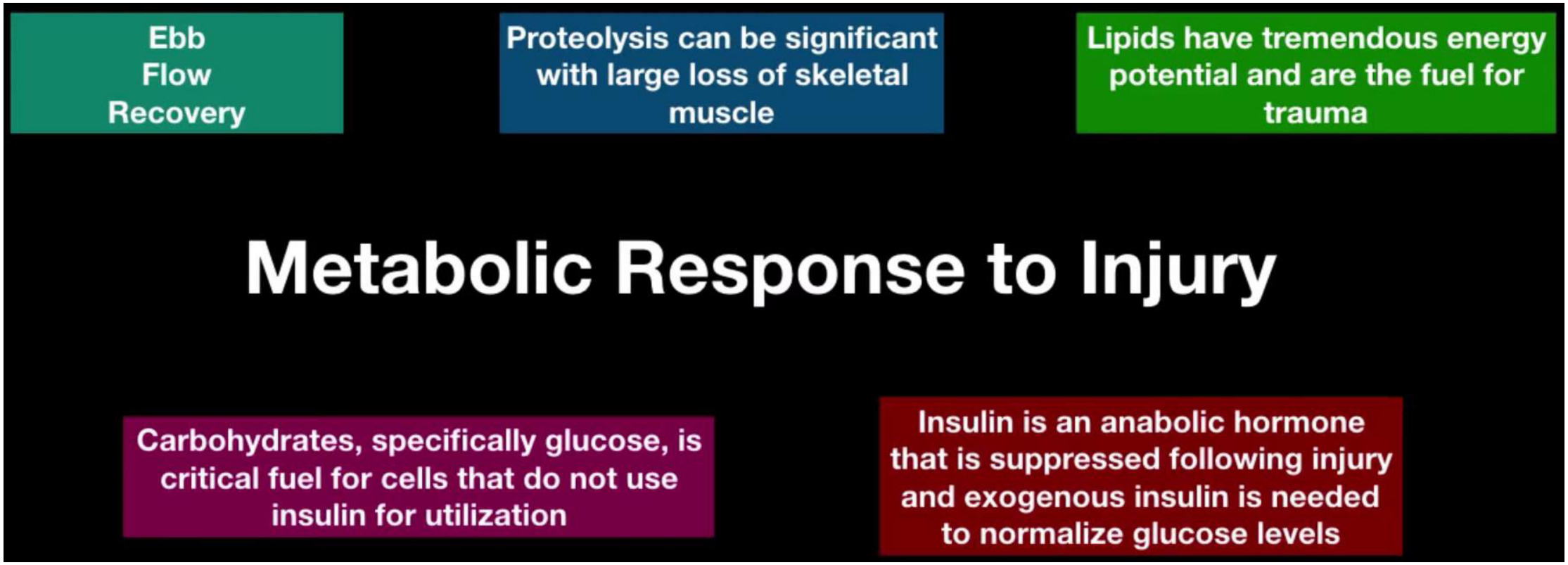
These cytokines, in particular IL-6, promote the hepatic synthesis of positive acute phase proteins, e.g. fibrinogen and C-reactive protein (CRP).



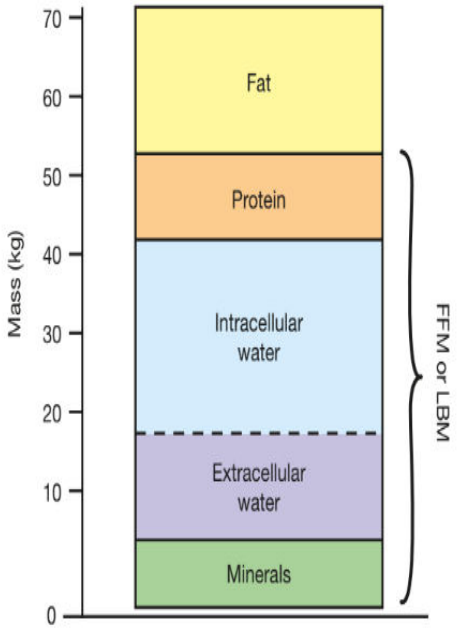
Summary


Tissue Injury
Proinflammatory cytokines (IL-1,6,12,TNFa)
Hepatic insulin resistance
Peripheral insulin resistance
Increased glycogenolysis
Increased gluconeogenesis
Proteolysis
Endocrine Response
HPA Axis (CRH, ACTH, Cortisol)
Elevation of counter regulatory hormones
Increased gluconeogenesis, glycogenolysis and peripheral lipolysis
Stress
Hypermetabolic response
Elevated metabolic state, oxygen consumption, cardiac output
Loss of body mass
Loss of skeletal muscle mass
Increased energy requirements

Summary


Ebb
Flow
Recovery
Proteolysis can be significant with large loss of skeletal muscle
Lipids have tremendous energy potential and are the fuel for trauma
Metabolic Response to Injury
Carbohydrates, specifically glucose, is critical fuel for cells that do not use insulin for utilization
Insulin is an anabolic hormone that is suppressed following injury and exogenous insulin is needed to normalize glucose levels

Changes in body composition following injury



- The average 70-kg male can be considered to consist of fat (13 kg) and fat-free mass (or lean body mass: 57 kg). In such an individual, the lean tissue is composed primarily of protein (12 kg), water (42 kg) and minerals (3 kg).
- The protein mass can be considered as two basic compartments, skeletal muscle (4 kg) and non-skeletal muscle (8 kg), which includes the visceral protein mass.
- The main labile energy reserve in the body is fat whilst the main labile protein reserve in the body is skeletal muscle.
- fat mass can be reduced without major detriment to function, loss of protein mass results not only in skeletal muscle wasting, but also in depletion of visceral protein status.

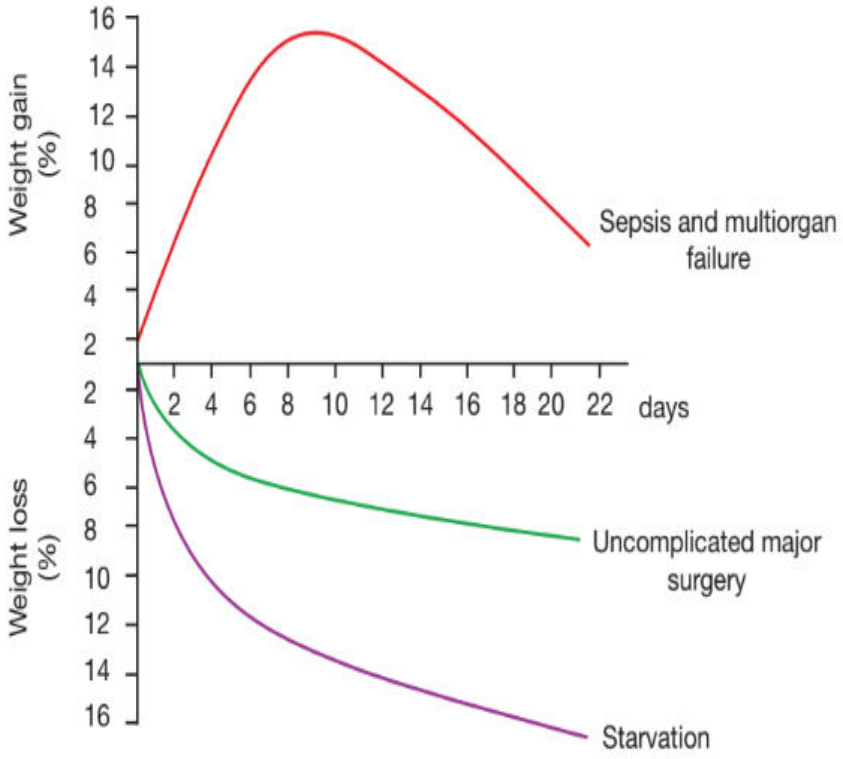
Changes in body composition following major surgery/ critical illness

- Catabolism leads to a **decrease** in fat mass and skeletal muscle mass
- Body weight may paradoxically **increase** because of expansion of extracellular fluid space

Changes in body composition following injury

Within lean issue, each 1 g of nitrogen is contained within 6.25 g of protein, which is contained in approximately 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 of the order of 150–200 g per day.

In major injury there is auto-catabolism which leads to urinary loss of nitrogen of 10-20 grams/day. This in turn results in a loss of 500 grams of wet weight lean tissue per day.
In severe sepsis or major blunt trauma, there is an increase in body weight at first as a result of an expansion of extracellular fluid space.



Avoidable factors that compound the response to injury

1. Continuing hemorrhage: Due to volume loss, both aldosterone and ADH are released, this leads to salt and water retention, which in turn causes visceral edema, careful intra-operative fluid balance must be maintained.
2. Hypothermia: Hypothermia results in increased elaboration of adrenal steroids and catecholamines. If uncontrolled, it results in in 2-3 folds increase of post-operative cardiac arrhythmias and increased catabolism.
3. Tissue edema: Increased capillary leak is mediated by a wide variety of mediators including cytokines, prostanoids, bradykinin and nitric oxide. Vasodilatation implies that intravascular volume decreases, which induces shock if inadequate resuscitation is not undertaken.
4. Tissue underperfusion: Compromised microcirculation and subsequent cellular hypoxia will lead to organ failure.
5. Starvation
6. Immobility: Immobility has been recognized as a potent stimulus for inducing muscle wasting. Early mobilization is an essential measure to avoid muscle wasting.

Starvation

During starvation, the body is faced with an obligate need to generate glucose to sustain cerebral energy metabolism (100g per day).

This is achieved in the first 24 hours by mobilizing glycogen stores and thereafter by hepatic gluconeogenesis from amino acid, glycerol and lactate

The energy metabolism of other tissues is sustained by mobilizing fat from adipose tissue

Such fat metabolization is mainly dependent on a fall in circulating insulin levels

The liver converting free fatty acids into ketone bodies which can serve as substitute for glucose for cerebral energy metabolism

Starvation

Provision of 2L of IV 5% dextrose as IV fluid for surgical patients who are fasted provides 100g of glucose per day and has a significant protein sparing effect

Modern guidelines on fasting prior to anesthesia allow intake of clear fluids up to 2 hours before surgery

Minimizing Surgical Stress Response

1. Early oral/enteral feeding (to reduce catabolism of the body)
2. Maintenance of proper fluid balance (to avoid mismatch in the extracellular and intracellular fluid balance)
3. Minimal access techniques
4. Blockade of afferent painful stimuli (by epidural anesthesia)
5. Minimal periods of starvation
6. Early mobilization

Thank You!