Metabolic Response to Injury and Sepsis

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4.1 Metabolic Response to Surgery

It can be subdivided into an early response phase and a late response phase. It is triggered in a region located near the hypothalamus—the paraventricular nucleus and the locus coeruleus[1] and driven by a hypothalamic-pituitary axis and the sympathetic nervous system.

- The **early response** phase is subdivided into:
  - **The Ebb phase**[2] occurs soon after the injury and lasts **24–48 h**. It is characterized by ↓metabolism. It is largely driven by cytokine release and hormones. Lipolysis occurs with the release of free fatty acids.
    ↓insulin secretion and ↑ catecholamines leading to hyperglycemia.
  - **Flow phase** may last from a **few days to several weeks,** depending on the nature and extent of the injury. It is characterized by increased metabolism. It is largely driven by catecholamines.
    Proteolysis occurs with the release of amino acids.
- **Late chronic phase**
  - Characterized by efforts at recovery, repair, and restoration.

[1] *Coeruleus* (Latin) dark or even sky blue. Nucleus in the pons which secretes noradrenaline.

[2] David Cuthbertson (1900–89)—British physiologist, introduced this concept in 1942.

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4.1.1 Factors Responsible for the Early Phase Response Include

- **Antidiuretic hormone** (ADH)
  - It is produced by the hypothalamus, stored, and released by the posterior pituitary gland.
  - Acts on distal convoluted tubules and collecting ducts in the kidneys to increase water reabsorption, thus conserving water and maintaining blood pressure. In high concentrations, it causes peripheral vasoconstriction, again helping to raise the blood pressure.
- **Renin-angiotensin-aldosterone system**
  - Activation causes salt and water retention in the kidneys, peripheral vasoconstriction and causes the sensation of thirst.
- **Catecholamine release**
  - From adrenal medulla leads to glycogenolysis, proteolysis, and lipolysis.
- **Glucocorticoids**
  - From adrenal cortex causes ↑ glucose levels and ↑ glycogenolysis, lipolysis and proteolysis.
- **Acute phase reactants**
  - Such as C-reactive protein, fibrinogen, and haptoglobin from the liver also contribute to the inflammatory response.
- **Leucocyte response**
  - ↑ neutrophil leukocytes ↑lymphocytes.

4.1.2 Factors Responsible for the Late Response Phase Include

- Insulin
- Growth hormones
- 17 keto steroids

4.1.3 Tissue Response to Injury

The tissues in which the injury occurs also have an innate reaction and response initiated and orchestrated by a variety of cytokines released from monocytes, macrophages, and T cells. They provoke local paracrine and wider systemic effects.

The cytokines are divided into:

- Pro-inflammatory cytokines
  - TNF-α causing ↑ temperature and tachycardia
  - Interleukins: IL-1β; IL-2; IL-6 (regulating liver production of acute-phase reactant proteins); IL-8
  - Interferon-γ
- Anti-inflammatory cytokines
  - Interleukins: IL-1ra, IL-4, IL-10, IL-12, IL-13
  - TGF-β

4.2 Systemic Inflammatory Response Syndrome (SIRS)

Localized inflammation is a physiological protective response that is generally tightly controlled by the body at the site of injury.

Loss of this local control or an overly activated response results in an exaggerated systemic response which is clinically identified as systemic inflammatory response syndrome (SIRS).

SIRS can be diagnosed (in adults/older children when two or more of the following are present:

- **Heart rate**
  - >90 **b**eats/min
- **Temperature**
  - <36 or >38 °C (>38.5 °C in children)
- **Tachypnea**
  - >20 bpm or, on blood gas, a $PaCO_2$ < 4.3 kPa (32 mmHg)
- **White blood cell count**
  - <4 or >12 × 10^9/L

Various modifications have been made with reference to pediatric age groups (Table 4.1).

4.3 Multiple Organ Dysfunction Syndrome (MODS)

- Definition
  - "altered organ function (>2 systems) in acute illness such that intervention is needed."

It is hypothesized by Deitch to be caused by increased intestinal mucosal permeability to the intestinal Gram-negative organisms (mucosal barrier breakdown) secondary to splanchnic hypoperfusion. Additional liver dysfunction leads to the escape of toxins into the circulation, activating widespread immune reactions in tissues resulting in tissue damages and organ dysfunctions.

Table 4.1 Pediatric definitions of SRS

Age	Heart rate		Respiratory rate (bpm)	WBC (×10^9/L)	BP (systolic)
	Brady	Tachy			
0–1 week	<100	>180	>50	>34	<65
1 week to 1 month	<100	>180	>40	>19 <5	<75
1 month to 1 year	<90	>180	>34	>17 <5	<100
2–5 years	–	>140	>22	>15 <6	<94
6–12 years	–	>130	>18	>13 <4	<104
13–18 years	–	>110	>14	>11 <4	<117

Differences with Age

There are differences in neonates, although much less study has been performed. In principle, the above sequence holds, although in neonates, there is a small increase in oxygen consumption and resting energy expenditure immediately after surgery with a return to normal levels by 12–24 h. Higher endogenous opioids may blunt this response to injury.

Critical illness leading to multiorgan dysfunction syndrome (MODS) and associated acute renal failure is less common in children compared to adult patients.

Further Reading

1. Deitch EA. Multiple organ failure. Pathophysiology and potential future therapy. Ann Surg. 1992;216:117–34.
2. Pierro A. Metabolism and nutrition in the surgical neonate. J Pediatr Surg. 2002;37:811–22.
3. Goldstein B, Giroir BM, Randolph A. International pediatric consensus conference: definitions for sepsis and organ dysfunction in children. Pediatr Crit Care Med. 2005;6:2–8.
4. McHoney M, Eaton S, Pierro A. Metabolic response to surgery in infants and children. Eur J Pediatr Surg. 2009;19:275–85.