sepsis

lecture 24

Sepsis is a serious condition resulting from the presence of harmful microorganism (infection) in the blood or even in the tissue, and the body's response against them leads to dysfunction of various organs, shock & death.
Septic shock is a sepsis with hypotension, which require to maintain the mean arterial blood pressure> 65mmhg & serum lactate concentration > 2mmol

Sepsis is described in three phases:

1. Sustained extensive inflammation
2. Immune suppression
3. Failure to return to normal homeostasis

Sepsis mortality is often related to :

1. Suboptimal quality of care
2. Inadequate health infrastructure
3. Poor infection prevention measures in place.
4. late diagnosis
5. Inappropriate clinical mangement

❁ *Antimicrobial resistance microorganisms farther complicate sepsis management, particularly for immunocompromised patients.*
❁ *Different pathogens will have the same immune reaction (strong activation of the innate immune system) even if the infection is not pathogenesis (non-infectious).*

Sepsis/extensive inflammation through:

Complement activation

- *there is uncontrolled activation of complement component leads to tissue damage & organ failure, all complement pathways are activated.*
- *blockage of C5a signaling pathway shows an improvement of sepsis outcome in several animal model.*

Coagulation, endothelial cell activation & vascular leakage

Strong activation of the coagulation system result in disseminated intravascular coagulation; which is clinically associated with hemorrhage (due to consumption of clotting factors& platelets)& thrombosis.

- **Tissue factor** is the main driver of coagulation activation in sepsis.
- Inhibition of tissue factor leads to prevention of organ failure.
- there is **barrier incompetency(عَجْز)**due to exaggerated inflammation which highly increase leukocytes & platelets migration.

Loss of barrier integrity causes leakage of intravascular proteins & plasma into extravascular space (tissue edema, reduced microvascular perfusion).

Neutrophils extracellular traps.

patients with sepsis have increased NETosis level in their circulation, this feature associated with **organ dysfunction.**

Role of platelets

cause direct cell toxic effects mediated by platelet derived microorganism.

Innate response activator B cell

- important in bacteria eradication.
- it produces IL-3 which increase inflammation & the production of myeloid monocular cells.

Sepsis/ immune suppression

characterized by:

1. lymphocyte exhaustion. (strong depletion of CD4+T-cells & CD8+ T-cells, B cells, DC by apoptosis)
2. reprogramming of APC. (reduce expression of HLA-DR)
3. diminished the capacity of macrophages & granulocyte cells to produce pro-inflammatory cytokines.
4. increase the risk of secondary infection.

Methods to treat sepsis

1. Immune suppression ⇒ inhibit complements or coagulation.

2. Blood purification technique ⇒ removing PAMPs & inflammatory mediators from the circulation, MBPC is a device that removes pathogens & toxins from the blood.
3. Immune stimulation⇒ using INF-γ, IL-7, IL-15.