Sepsis and Septic Shock

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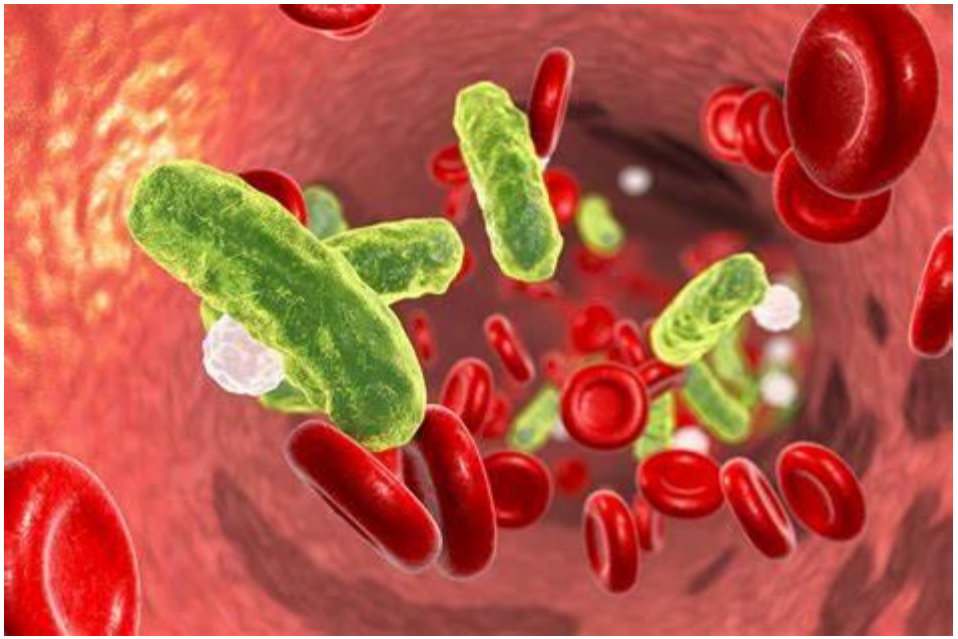

Definition

- **Sepsis** is defined as life-threatening **organ dysfunction** caused by a **dysregulated host response** to infection.

- Organ dysfunction is defined using the Sequential Organ Failure Assessment **score (SOFA)**

- Organ dysfunction is operationalised by an **acute increase in SOFA score of ≥2 from the patient's baseline level**.

- **Mortality** has been estimated to be ≥10 percent with Sepsis and ≥40 percent when shock is present .

Sepsis: *SIRS Criteria*

Temperature	<36°C or >38°C
Heart Rate	>90 beats per minute
Tachypnea	>20 breathes per minute or $PaCO_2$ <32 mm Hg
White Blood Cell Count	WBC <4,000/mm³ or WBC >12,000/mm³ or >10% immature (band) forms

Systemic Inflammatory Response Syndrome

≥2 criteria

Sepsis

SIRS *plus*
confirmed or presumed infection

Severe Sepsis

Sepsis *plus*
organ dysfunction

Septic Shock

Severe sepsis *plus*
refractory hypotension

Multiple Organ Dysfunction Syndrome

Evidence of ≥ 2 organs failing

Changes in new Definition of Sepsis

- The term SIRS has been removed due to poor specificity of many of SIRS criteria

- Previous categories of **sepsis, severe sepsis, and septic shock** have now been changed to **infection**, **sepsis**, and **septic shock**.

- SOFA score has been included to indicate organ dysfunction.

SOFA Score	0	1	2	3	4
Respiratory System (PaO2/FiO2)	Normal	<400	<300	<200	<100
Platelets (10^5 /µl)	>150	<150	<100	<50	<20
Bilirubin (mg/dl)	<1.2	1.2-2.0	2.0-6.0	6.0-12.0	>12
CVS	MAP>70mmHg	<70mmHg	Dopamine <5µg/kg /min or Dobutamine any dosage used	Dopamine 5-15µg/kg/min or epinephrine <0.1µg/kg/min or norepinephrine <0.1µg/kg/min	Dopamine >15µg/kg/min or epinephrine >0.1µg/kg/min or norepinephrine > 0.1µg/kg/min
CNS (GCS)	15	13-14	10-12	6-9	<6
Renal system	Creat ; normal	1.2-1.9	2-3.4	3.5-4.9 Urine output - <500ml/day	>5 <200ml/day

Quick SOFA variable (qSOFA)

- Rapid (~1 min) **assessment of an infected patient likely to have sepsis.**

- It indicates either prolonged hospital stay or high risk for mortality in patients with infection.

- Includes :
  - Altered mental state
  - SBP<100mmHg
  - RR >22/min

2 out of 3 indicates Poor prognosis

High specificity but poor sensitivity.

qSOFA

HYPOTENSION
≤100mmHg

AMS
GCS ≤13

TACHYPNEA
RR ≥ 22 bpm

Pathophysiology

- Infection (Pathogen Associated Molecular Patterns, PAMPs) enters body.

- Recognised by Pattern Recognition receptors, PRRs within Innate sysytem

- PRRs also recognises host cell contents such as DNA and mitochondria released in response to damage to cells known as ‘Damage Associated Molecular Patterns’ (DAMPs)

- Activation of **PRRs** by PAMPs and DAMPs triggers the increased production of a range of pro- and **anti-inflammatory mediators** such as TNF-α and interleukins, such as IL-1, IL-6 and IL-10.

- Generally **pro and anti inflammatory mediators** work in balance and end result is normal tissue repair and healing.

- In sepsis there is exaggerated Inflammatory response. The cause of which is still uncertain.

Biologic effects of proinflammatory cytokines such as TNF and IL-1

- Fever
- Hypotension
- Acute phase protein response
- Coagulation activation
- Fibrinolytic activation
- Leukocytosis
- Neutrophil degranulation and augmented antigen expression (TNF)
- Increased endothelial permeability (TNF)
- Stress hormone response
- Enhanced gluconeogenesis (TNF)
- Enhanced lipolysis (TNF)

Aetiology

- 80% is due to **community acquired**
- **MC site involved** - Lungs(65%) >abdomen(20%) >bloodstream(15%)
- SOAP study revealed almost **equal prevalance of both Gram positive cocci and Gram negative bacillus**
- **Commom organism** involved : Staph.aureus /E.coli and Pseudomonas
- 2012 Intensive Care Over Nations study, showed More prevalance of GNB when compared to GPCs.

General Risk factors

- Extremes of age
- Immunosupressed patients

Risk factors for bloodstream infections

- Indwelling catheters
- Parenteral nutrition

Risk factors for Chest infection

- Extremes of age
- Immunosuppression
- Aspiration pneumonia
- COPD
- Prolonged Intubation
- Thoracic surgeries

Risk factor for UTI

- Indwelling catheters
- Females
- Poor mobility

Diagnosis

- **Leukocytosis** (white blood cell [WBC] count >12,000 microL^{-1}) or **leukopenia** (WBC count <4000 microL^{-1})
- Normal WBC count with **greater than 10 percent immature forms**.
- **Hyperglycemia** (plasma glucose >140 mg/dL or 7.7 mmol/L) in the absence of diabetes.
- **Plasma C-reactive protein** more than two standard deviations above the normal value.
- **Arterial hypoxemia** (arterial oxygen tension [PaO_2]/fraction of inspired oxygen [FiO_2] <300).

- **Acute oliguria** (urine output <0.5 mL/kg/hour for at least two hours despite adequate fluid resuscitation).
- **Creatinine** increase >0.5 mg/dL or 44.2 micromol/L.
- **Coagulation abnormalities** (international normalized ratio [INR] >1.5 or activated partial thromboplastin time [aPTT] >60 seconds).
- **Thrombocytopenia** (platelet count <100,000 microL^{-1}).
- **Hyperbilirubinemia** (plasma total bilirubin >4 mg/dL or 70 micromol/L).
- **Adrenal insufficiency** (eg, hyponatremia, hyperkalemia), and the euthyroid sick syndrome can also be found in sepsis.

Blood Lactate

- **Hyperlactatemia** is not specific for tissue hypoperfusion.
- An elevated serum lactate (eg, >2 mmol/L) can be a manifestation of organ hypoperfusion
- **A serum lactate level ≥4 mmol/L is consistent** with, but not diagnostic of, septic shock.
- It remains of **prognostic importance** in patient with sepsis.
- **Reduction in lactate levels is known to have good prognosis.**
- Therefore it is important **to repeat the measurements of blood lactate** to monitor its kinetics and inform further management.

- **Radiological evaluation :** based on symptoms

- **Plasma procalcitonin**
  - More than two standard deviations above the normal value. Elevated serum procalcitonin levels are associated with **bacterial infection and sepsis**

Management

Fluid resuscitation

- Indicated in **hemodynamically instable patient** as indicated by
  - Hypotension (systolic **blood pressure <90 mm Hg**,
  - mean arterial pressure **<70 mm Hg**, or a decrease in
  - systolic blood pressure of >40 mm Hg from baseline) or
  - elevated lactate concentration **(≥2 mmol/L)**

- Recommends rapid administration of **30 mL/kg crystalloid** fluids, which should be initiated within the first hour.

Fluid resuscitation

- Mutiple studies have showed no difference between crystalloid and colloids

- **Colloids** are more expensive and nephrotoxic (except Albumin) . So in case colloids are to be used , then **Albumin** is preferred.

- Among crystalloids, few studies have showed balanced solutions (Chloride deficit) to be better then Normal saline

- **Balanced solutions** : Ringer Lactate, Hartmann solutions

Source control

- Source control is the removal of infected tissue, drainage of an abscess, or removal of an infected device.

- **Considered best practice in the management of sepsis.**

- Observational data showed that inadequate early source control was associated with an increase in 28-day mortality from 26 • 7% to 42 • 9%.

Antibiotics

7% increase in risk of death for every hour of delay

- Should be started **within 1hr of sepsis** diagnosis
- The results of cultures are unlikely to be known at the time of recognition of sepsis,
- So the choice of antimicrobial therapy is largely **empirical.**
- If any pathogen is detected, antimicrobial should be directed towards it
- **De-escalation of antimicrobials** should be considered daily and at the earliest stage when the clinical situation permits.

Vasoactive agents

- A **mean arterial pressure of 65 mm Hg** is an appropriate initial target for most patients with septic shock .

- A study showed that a higher mean blood-pressure target (80–85 mm Hg) was not associated with better survival compared with a lower target (65–70 mm Hg).

- Patients with a **history of chronic hypertension** were less likely to develop **acute kidney injury** if managed with the higher blood-pressure target, but were also more likely to develop **arrhythmias**.

- **Norepinephrine is the preferred first-line vasopressor** because of its increased potency and reduced risk of arrhythmias compared with dopamine

Cardiac dysfunction

- Sepsis is frequently associated with **(reversible) myocardial dysfunction**.

- The classic understanding of septic shock as a purely distributive shock with intact cardiac function has changed, and it is now established that **cardiac dysfunction (systolic and diastolic) can be present even during the early stages of the disease.**

- **Inotropic agents might be considered for patients with suspected cardiac dysfunction** in association with inadequate cardiac output.

- Using inotropic agents routinely as an adjunct to standard haemodynamic therapy should be discouraged, especially in the absence of evident cardiac dysfunction.

- A trial published in 2016 showed that **routine administration of levosimendan was not superior to placebo** for improving organ dysfunction in patients with septic shock, and might be associated with harm.

Glycaemic control

- The current consensus is to control glycaemia, maintaining it at **less than 180 mg/dL**, but to avoid tight glycaemic control.

Nuritional support

- Trials published in 2016 and 2018 failed to show benefits of either the enteral or the parenteral

- One study showed that early **enteral feeding, compared with the parenteral route, in ventilated patients with shock was associated with a greater risk of gastrointestinal complications (including gut ischaemia**).

Steroids

- Use is **controversial**
- European Society of Intensive Care Medicine and the Society of Critical Care Medicine suggest **some benefit of using corticosteroids in sepsis only if shock is present**.
- There is some evidence that steroids are associated with ICU-acquired weakness,and thus it is still not clear whether the clinical benefit outweighs the sideeffects.
- **ADRENAL multicentre study** (3800 patients), was negative for its primary outcome (mortality), but showed **shorter durations of shock and ICU stay in the glucocorticoid group** compared with the placebo group.
- In the second, another large multicentre trial (1241 patients), a combination of hydrocortisone and fludrocortisone was associated with **a lower all-causes 90-day mortality compared with the placebo**

Hemoglobin target

- > 7gm/dl in absence of Ischaemic Heart Disease.

Arterial oxygen saturation

- A single centre trial published in 2016 showed **worse survival rates for patients managed with a high arterial oxygen saturation target (97–100%) compared with those managed with a lower target (94–98%)**.

- An FiO2 of 1 (hyperoxia) was associated with a higher mortality compared with an FiO2 aiming at an oxygen saturation of 88–95% (normoxia).

Take Home message

- "Measure **lactate level**. Re-measure if initial lactate is >2 mmol/L"
- "Obtain **blood cultures** prior to administration of Antibiotics"
- "Administer **broad-spectrum antibiotics**"
- "Rapidly administer 30 mL/kg crystalloid for hypotension or lactate ≥4 mmol/L" .
- "Apply **vasopressors** if patient is hypotensive during or after fluid resuscitation to maintain **MAP ≥65 mm Hg.**
- Maintain **sugars at less than 180 mg/dL**, but to avoid tight glycaemic control

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