

سُبْحَانَكَ اللَّهُمَّ











# Sepsis and Septic Shock

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- **Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection** (proinflammatory and antiinflammatory reactions)
  - **Pneumonia**, **peritonitis**, **urinary tract infections**, **soft tissue infections**
  - **Organ failure** is the hallmark sign of sepsis and most frequently occurs in
    - respiratory
    - cardiovascular systems
    - renal
    - central nervous system
    - hematologic
    - hepatic


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- Sepsis is most often caused by bacteria, but fungal and viral infections can also instigate sepsis
  - gram-negative bacteria : 38% to 62%
  - gram-positive bacteria : 40% to 52%
  - fungi : 5% to 19%
  - Viral infections : 1% to 7%

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- Women who are **black, smoke**, and are **older the 35 years** may be more likely to be **at risk of maternal sepsis**
  - The reported **maternal mortality** rate ranges from **20 to 28 percent** in **pregnant patients with septic shock and multiple organ failure**.

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- The etiologies of infection during pregnancy are different in the **antenatal** and **postnatal** period



## Antenatal infections

- The most common severe infections are **septic abortion**,
  - intraamniotic infection (**chorioamnionitis**), complicated **pyelonephritis**, and **pneumonias caused by Streptococcus**
  - **pneumoniae and influenza**
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## Post-natal infections

- The most common postpartum infection is **endometritis**.
- It is usually due to **mixed flora**, including anaerobic, gram negative, and gram positive organisms
- Others : **wound infections**, **necrotizing fasciitis**, **toxic shock syndrome**, **pelvic abscess**, **gas gangrene of the myometrium** (usually due to clostridial species that colonize the GI tract and vagina), **septic pelvic thrombophlebitis**, **pyogenic sacroiliitis** , and **clostridium difficile colitis**





# DIAGNOSIS

- SIRS
  - SOFA criteria
  - qSOFA
  - NEWS
  - MEWS
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ORGAN SYSTEM	SCORE
Respiration	
Pao <sub>2</sub> /Fio <sub>2</sub> , mm Hg (kPa)	
<400 (53.3)	1
<300 (40)	2
<200 (26.7) with respiratory support	3
<100 (13.3) with respiratory support	4
Central nervous system	
GCS score	
13–14	1
10–12	2
6–9	3
<6	4
Cardiovascular	
MAP or use vasopressors (μg/kg/min)	
MAP <70 mm Hg	1
Dopamine <5 or dobutamine (any dose) <sup>a</sup>	2
Dopamine 5.1–15 or epinephrine ≤0.1 or norepinephrine ≤0.1	3
Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1	4
Liver	
Bilirubin, mg/dL (μmol/L)	
1.2–1.9 (20–32)	1
2.0–5.9 (33–101)	2
6.0–11.9 (102–204)	3
>12.0 (204)	4
Coagulation	
Platelets, × 10 <sup>3</sup> /μL	
<150	1
<100	2
<50	3
<20	4
Renal	
Creatinine, mg/dL (μmol/L) or urine output, mL/day	
1.2–1.9 (110–170)	1
2.0–3.4 (171–299)	2
3.5–4.9 (300–440) or <500	3
>5.0 (440) or <200	4

# SOFA Score

## Hematologic and Biochemical Evaluation

- ▶ **leukocytosis** (white blood cell count,  $>12,000/\text{mm}^3$ ), **leukopenia** (white blood cell count,  $<4000/\text{mm}^3$ ), normal white blood cell count with  $>10\%$  **immature forms**,
- ▶ an elevated plasma **C-reactive protein**, and elevated plasma **procalcitonin**
- ▶ First signs of **AKI** are an increase in **creatinine** with or without acute oliguria (urine output  $<0.5\text{ mL/kg/h}$  for at least 2 hours despite adequate fluid resuscitation).
- ▶ **Marked hyperbilirubinemia** (T bilirubin  $>4\text{ mg/dL}$ ) indicate **liver dysfunction**.
- ▶ **Renal and liver tests should be monitored during the course of sepsis**



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- **Thrombocytopenia** (platelet <100,000) is seen in up to 50% of patients
  - Low platelet counts can suggest **DIC** (INR>1.5 or PTT >60, low fibrinogen levels, and elevated markers of FDP or D-dimer levels).
  - **Lactate** levels can be elevated (>1 mmol/L or >9 mg/dL, or twice these values in septic shock) and signal poor tissue perfusion. **High levels are associated with poor outcome.**
  - **Arterial blood gas** analysis often shows a metabolic acidosis with compensatory respiratory alkalosis; **acidosis and hypoxia are markers of severe disease.**
  - **hyperglycemia** (plasma glucose >140 mg/dL) in the absence of diabetes
  - **low albumin levels** due to **capillary leakage, altered hepatic metabolism, or poor nutrition.**



## Pathogen Detection

- **Routine microbiologic cultures** (**blood, urine, sputum, wound, CSF, joint fluid**) should be obtained before starting antimicrobial therapy in patients with suspected sepsis or septic shock.
- **Two sets of blood cultures** (aerobic and anaerobic) should always be included.
- In patients with an **intravascular catheter** (in place >48 hours), at least one blood culture set should be obtained from the catheter (along with simultaneous peripheral blood cultures) to assist in the diagnosis of a potential catheter-related bloodstream infection.



## Diagnostic Imaging



- ▶ chest radiography for the evaluation of pneumonia,
- ▶ standard computed tomography can be helpful to assess infection in the sinuses, lungs, liver, and abdomen.
- ▶ Ultrasonography may be useful for evaluating gallbladder and kidney dysfunction.





# THERAPY

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- ▶ **Although there are no prospective studies of early goal-directed therapy during pregnancy, the management of sepsis should be similar to that of the nonpregnant patient and use the same targets.**

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- ▶ **Sepsis and septic shock are medical emergencies**, and treatment and resuscitation should begin immediately.
  - ▶ **Routine microbiologic cultures**
    - ❖ Patients with **hypoperfusion** should receive at least **30 mL/kg of IV crystalloid within 3 hours** and should be reassessed frequently.
    - ❖ **Intravenous antimicrobials**
  - ▶ using **albumin** in patients who received large volumes of crystalloids
  - Starches, gelatin



## Vasoactive Agent Management



Use norepinephrine as first-line vasopressor

*For patients with septic shock on vasopressor*



Target a MAP of 65mm Hg



Consider invasive monitoring of arterial blood pressure

*If central access is not yet available*



Consider initiating vasopressors peripherally\*

*If MAP is inadequate despite low-to-moderate-dose norepinephrine*







Consider adding vasopressin

*If cardiac dysfunction with persistent hypoperfusion is present despite adequate volume status and blood pressure*





Consider adding dobutamine or switching to epinephrine

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- **Norepinephrine** is the **first choice** for patients who need vasopressors. **Vasopressin or (epinephrine) can be added.**
  - In settings where norepinephrine is not available, epinephrine or dopamine can be used as an alternative (risk for arrhythmias )
  - **IV hydrocortisone (200 mg/day)**: given as 50 mg intravenously every 6 h or as a continuous infusion at a dose of norepinephrine or epinephrine  $\geq 0.25$  mcg/kg/min at least 4 h
  - **Inotropes**
    - For adults with septic shock and **cardiac dysfunction** with persistent hypoperfusion despite adequate volume status and arterial blood pressure, **suggest** either **adding dobutamine to norepinephrine or using epinephrine alone**
    - levosimendan

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- **Blood transfusion** should be reserved for patients with **HB <7.0 g/dL** except in special circumstances such as **severe hypoxemia, hemorrhage and myocardial ischemia**.
  - **Platelets** should be given if the PLT is **<10,000/mm<sup>3</sup> or <20,000/mm<sup>3</sup> with bleeding**.
  - **Prone ventilation**
  - **Mechanical ventilation** in adult patients with **sepsis-induced ARDS** :
    - with a target **tidal volume of 6 mL/kg**
    - An upper limit goal for **plateau pressures of 30 cm H<sub>2</sub>O**
    - **Higher PEEP** in patients with sepsis-induced moderate-to-severe ARDS.
  - **ECMO**
  - **Neuromuscular blocking agents**
  - **blood glucose management** in ICU patients with sepsis : initiating insulin dosing when **BS >180 mg/dL**.
    - 144–180 mg/dL



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- **renal replacement therapy** :AKI who require renal replacement therapy
  - **Sodium bicarbonate**
    - hypoperfusion-induced lactic acidemia: **suggest against** using sodium bicarbonate therapy to improve haemodynamics or to reduce vasopressor requirements
    - For adults with septic shock, severe metabolic acidemia ( $\text{pH} \leq 7.2$ ) and AKI
  - Pharmacologic **prophylaxis against venous thromboembolism** using low molecular weight heparin (**LMWH**) **over** unfractionated heparin (**UFH**) in the absence of contraindications for these agents.
  - **Stress ulcer prophylaxis** should be given to patients with sepsis or septic shock **who have risk factors for gastrointestinal bleeding**.
  - **Vitamin C**
  - **Immunoglobulins**
  - Administration of **early parenteral nutrition** alone or parenteral nutrition in combination with enteral feedings is **not recommended** in critically ill patients who can be fed enterally. The administration of parenteral nutrition is **not recommended over the first 7 days** in critically ill patients with sepsis or septic shock for whom early enteral feeding is not feasible.



# Antimicrobial Therapy

## Antibiotic Timing

Shock is present

Shock is absent

Sepsis is definite  
or probable



Administer antimicrobials **immediately**, ideally within 1 hour of recognition

Sepsis is possible



Administer antimicrobials **immediately**, ideally within 1 hour of recognition



Rapid assessment\* of infectious vs noninfectious causes of acute illness



Administer antimicrobials **within 3 hours** if concern for infection persists



➤ **Intravenous antimicrobials**

➤ **Empirical broad-spectrum therapy** is recommended with **one or more AB**

➤ **combination therapy**

❑ In patients at high risk for **MDR organisms** : using **two gram negative** agents for empiric treatment

➤ **proven** infection or colonisation with antibiotic-resistant organisms within the preceding **year**

➤ **healthcare** associated

➤ **broad-spectrum AB** use within the preceding **90** days

➤ concurrent use **selective digestive decontamination**

➤ **travel** to a highly endemic country within the preceding 90 days and hospitalisation abroad within the preceding 90 days




# MRSA

- prior **history** of MRSA infection or colonization
- recent **IV** antibiotics
- history of recurrent **skin infections** or chronic wounds
- presence of **invasive devices**
- **Haemodialysis**
- recent **hospital admissions** and severity of illness






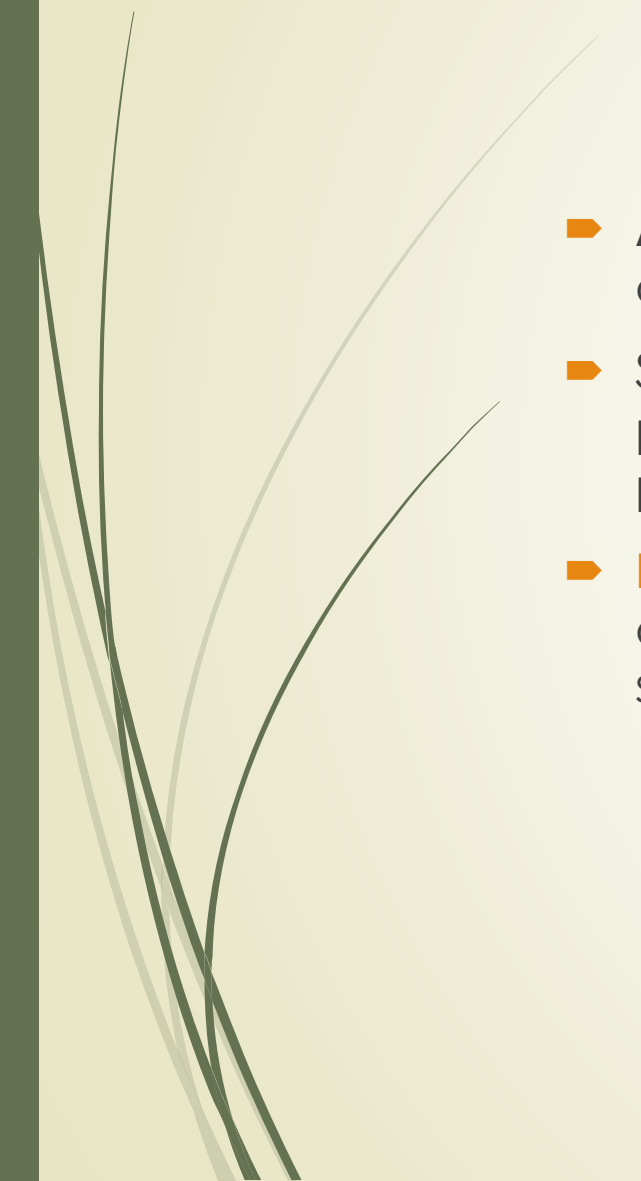
## Antifungal therapy



- ▶ Candida colonisation at multiple sites
  - ▶ Surrogate markers such as Serum Beta-D-Glucan assay
  - ▶ Neutropenia
  - ▶ Immunosuppression
  - ▶ Severity of illness (High APACHE score)
  - ▶ Longer ICU length of stay
  - ▶ Central venous catheters and other intravascular devices
  - ▶ IVDU
  - ▶ TPN
  - ▶ Broad spectrum AB
  - ▶ Gastrointestinal tract perforations and anastomotic leaks
  - ▶ Emergency gastrointestinal or hepatobiliary surgery
  - ▶ Acute renal failure and haemodialysis
  - ▶ Severe thermal injury
  - ▶ Prior surgery
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## Antiviral therapy

- Influenza
- COVID 19
- **Immunocompromised patients**
  - including patients with neutropenia, HIV, haematological malignancies, HSCT and solid organ transplants
  - **HSV,EBV,CMV** ,and respiratory viruses such as **adenoviruses**
  - **Dengue, Ebola, Lassa, Marburg, Sin Nombre** and **Chikungunya virus**

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- **Antimicrobial therapy should be narrowed** **once pathogen identification** and sensitivities are established or adequate clinical improvement is noted.
  - Sustained systemic **antimicrobial prophylaxis** is **not recommended** in patients with severe inflammatory states of noninfectious origin (e.g., severe pancreatitis, burn injury).
  - **Dosing strategies of antimicrobials** should be optimized based on accepted **PK/PD** principles and specific drug properties in patients with sepsis or septic shock.

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- **Antimicrobial treatment duration** of **7–10 days** is adequate for most serious infections associated with sepsis and septic shock. (host, microbe, drug, and anatomical site)
  - **Longer courses** are appropriate in patients who have a **slow clinical response, undrainable foci of infection, bacteremia with *Staphylococcus aureus*, some fungal and viral infections, or immunologic deficiencies** including neutropenia.
  - **Shorter courses** are appropriate in some patients, particularly patients with **rapid clinical resolution** following effective source control of **intraabdominal or urinary sepsis** and patients with **anatomically uncomplicated pyelonephritis**.
  - **Daily assessment for deescalation** of antimicrobial therapy
  - Measurement of **procalcitonin** levels
    - to support **shortening** the duration of AB
    - to support **discontinuation** of empirical AB



## Source Control

- ▶ **A specific anatomic diagnosis of infection** requiring emergent source control should be identified or excluded as rapidly as possible in any patient with sepsis.
- ▶ drainage of an abscess, debriding infected necrotic tissue, removal of a potentially infected device
- ▶ intra-abdominal abscesses, gastrointestinal perforation, ischaemic bowel or volvulus, cholangitis, cholecystitis, pyelonephritis associated with obstruction or abscess, necrotizing soft tissue infection, other deep space infection (e.g., empyema or septic arthritis), and implanted device infections
- ▶ **Required source control interventions** should be implemented as soon as medically and logistically possible
- ▶ **Prompt removal of intravascular access devices** that are a possible source of sepsis or septic shock is recommended after other vascular access has been established



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