Sepsis - Dr. Abdulwahid

How to manage?

- 54yr male
- 24 hr Fever and delirium
- Initial Obs
    - HR 162, RR 30,O2 sats 95% , BP 116/82, GCS 13/15
- History
    - Migratory abdominal pain and fever 1/7
- Past History
    - Left ureteric stone, 6mm

Differential Diagnosis

- Pancreatitis
- Ischeamic Gut
- Hypovolaemic shock
    - GI bleed / AAA rupture / ectopic / dehydration
- Cardiogenic shock
    - AMI / Myocarditis / Tamponade
- PE
- Toxic Shock
- Addisonian crisis (note relative adrenocorticoid insufficiency in many septic patients)
- Thyroid Storm

Consensus Definitions

- **Colonization:** microbiological event (presence of bacteria, viruses, fungi...) with no host response
- **Infection:** microbiological event (caused by bacteria, viruses, fungi,...) inducing some host response or the presence of these microorganisms in a normally sterile tissue (cerebrospinal fluid, peritoneum...)
- **Sepsis:** host response to a microbiological event (induced by the presence of bacteria, viruses, fungi...)
- **Severe sepsis:** sepsis associated with organ dysfunction, such as coagulation abnormalities, altered mental status, or oliguria
- **Septic shock:** sepsis with hypotension (requiring the administration of vasopressor agents), associated with signs of altered tissue perfusion (such as oliguria or altered mental status), and hyperlactatemia

Infection

- Either:
    - **Bacteraemia** (or viraemia/fungaemia/protozoan): is the presence of bacteria within the bloodstream
    - **Septic focus** (abscess / cavity / tissue mass)

SIRS

- **2/4** of;
    - **Temp** >38 or <36
    - **HR** >90
    - **Respiratory Rate** >20 or PaCO2 <32 (4.3kPa)
    - **WCC** >12 or <4 or >10% **bands** (immature forms)

Sepsis

- Is the systemic response to infection

Sepsis

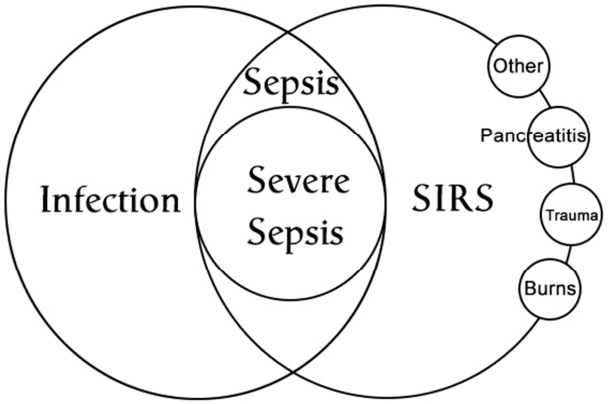
- - SIRS
- + Infection

Severe Sepsis

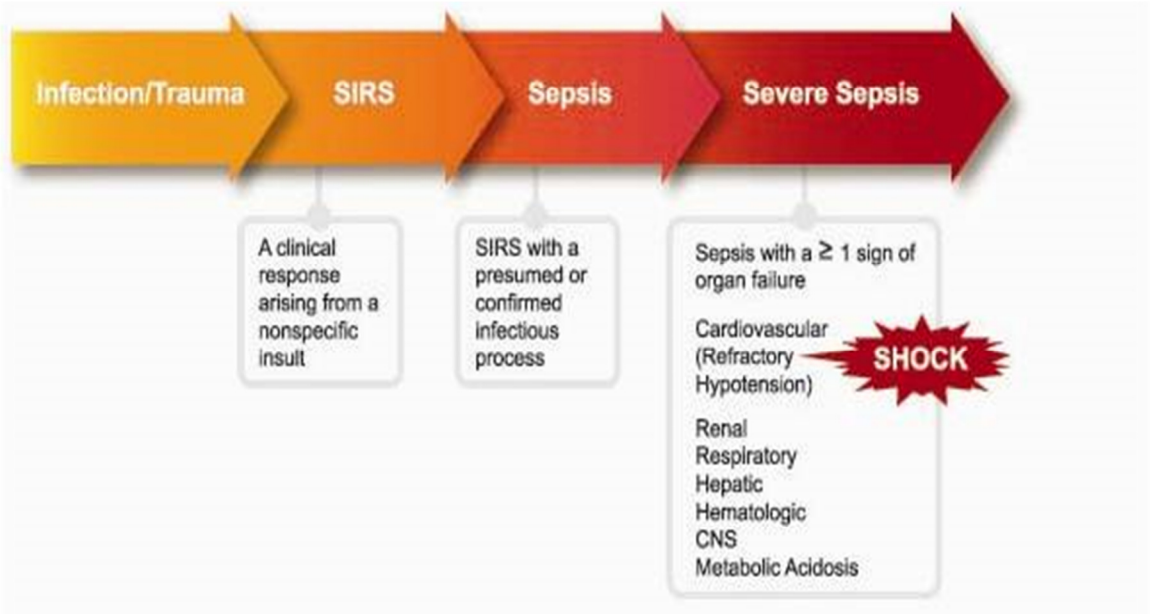
- - Sepsis
- + Organ dysfunction

Septic shock

- - Sepsis
- + Hypotension despite fluid resuscitation



SEPSIS: Defining a Disease Continuum



Complications

Organ System Involvement

- Circulation
  - Hypotension,
  - increases in microvascular permeability
  - Shock
- Lung
  - Pulmonary Edema,
  - hypoxemia,
  - ARDS
- Hematologic
  - DIC, coagulopathy
  - (DVT)
- GI tract
  - stress ulcer
  - Translocation of bacteria,
  - Liver Failure,
  - Gastroparesis and ileus,
  - Cholestasis
- Kidney
  - Acute tubular necrosis,
  - Renal Failure
- Nervous System
  - Encephalopathy
- Skeletal Muscle
  - Rhabdomyolysis
- Endocrine
  - Adrenal insufficiency

Sources of Sepsis: The International Cohort Study

	Severe Sepsis	Septic Shock
Respiratory	66	53
Abdomen	9	20
Bacteremia	14	16
Urinary	11	11
Multiple	-	-

Pathophysiology

- Excessive **anti-inflammatory** response
- Sepsis: **auto-destructive** process allowing normal responses to infection/injury to involve normal tissues

Severe Sepsis: The Final Common Pathway

Endothelial Dysfunction and Microvascular Thrombosis → Hypoperfusion/Ischemia → Acute Organ Dysfunction (Severe Sepsis) → Death

High Risk Patients For Sepsis and Dying

- Middle-aged, **elderly**
- **Post op** / post trauma
- Post **splenectomy**
- **Transplant**
- **Immune** suppressed
- **Alcoholic** / Malnourished
- Genetic predisposition
- **Delayed** appropriate antibiotics
- **Comorbidities** : AIDS, renal or liver failure, neoplasms

Identification of septic focus

- history
- physical examination
- imaging
- cultures
    - Blood cultures, urine culture, sputum culture, abscess culture.

Investigations

Basic	Specific? Source
• WBC • Platelets • Coags • Renal function • Glucose • Albumin • LFT • ABG	• Urine • CxR • Blood Cultures • Biopsy
May all be normal early on!	

Differentiate sepsis from noninfectious SIRS

- Procalcitonin
- C-reactive protein (CRP)
- IL-6
- protein complement C3a
- Leptin
    - test is **not yet** readily available for clinical practice

Treatment of Sepsis

- Antibiotics
- Early aggressive fluid resuscitation
- Inotropes for BP support (Dopamine, vasopressin, norepinephrine)
- Source control
- Steroid therapy (adrenal insufficiency)
- Activated protein C
- Ventilatory Strategies
- Glycemic control
- Newer therapies.

I.V. antibiotics

- Initiated as soon as cultures are drawn.
- Severe sepsis should receive **broad spectrum** antibiotic.
- Empiric antifungal drug; Neutropenic patients, DM, chronic steroids.

Antibiotics

> ***Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock.***

- Abx within 1 hr hypotension: 79.9% survival
- Survival decreased 7.6% with each hour of delay
- Mortality increased by 2nd hour post hypotension
- Time to initiation of Antibiotics was the single strongest predictor of outcome

Antibiotics dosing

- Dosage for intravenous administration (normal renal function).
- Imipenem-cilastin 0.5g q 6h
- Meropenem 1.0g q 8h
- Piperacillin-tazobactam 3.375gq 4h or 4.5 g q 6h
- Cefepime1-2 q 8hr
- Gatifloxacin 400mg iv q d
- Ceftriaxone 2.0g q 24hr
- Levofloxacin500mg q d

Source control

- Early recognition of the Sepsis syndrome.
- Surgical intervention when indicated.
- Aggressive supportive care in intensive care units.

Surgery

- Get the **pus out of abscesses** or foci of infection should be drained
- **Early definitive care ;** e.g.; ruptured appendix, cholecystitis

Supportive

- Oxygenate / Ventilate
- Volume
- Electrolyte homeostasis
- Inotropes
- (DVT) and stress ulcer prophylaxis

ARDS causes respiratory failure

- in patients with severe Sepsis
- Assess the airway, respiration, and perfusion
- Supplemental oxygenation,
- Ventilator for respiratory failure

Sepsis-induced hypotension

- systolic less than 90 mm Hg
- or a reduction of more than 40 mm Hg from baseline in the absence of other causes of hypotension."

1. A loss of plasma volume into the interstitial space,
2. Decreases in vascular tone,
3. Myocardial depression.

Treatment of Hypotension

- Intravenous fluids: Crystalloids vs. Colloids.
- need more than 'maintenance' + replace losses

Fluid Therapy

- No mortality difference between;
    - colloid vs. crystalloid

Goals for initial resuscitation

- Central venous pressure 8 to 12 mmHg.
- Mean arterial pressure 65 mmHg.
- Urine output 0.5 mL per kg per hr.
- Pulmonary capillary wedge pressure exceeds 18 mmHg

Drugs commonly used for circulatory support

Drug	Pharmacologic Role	Clinical Effect	Usual Dose Range
Epinephrine	Alpha- and beta-adrenergic agonist	Chronotropism, inotropism, vasoconstriction	5 to 20 µg/min
Norepinephrine	Alpha- and beta-adrenergic agonist *	Chronotropism, inotropism, vasoconstriction	5 to 20 µg/min
Dopamine	Dopamine and beta-adrenergic agonist, progressive alpha-adrenergic effect with increasing doses	Chronotropism, inotropism, vasoconstriction	2 to 20 µg/kg of body weight/min
Dobutamine	Beta-adrenergic agonist	Chronotropism, inotropism, vasodilation	5 to 15 µg/kg/min
Phenylephrine	Alpha-adrenergic agonist	Vasoconstriction	2 to 20 µg/min
* The alpha-adrenergic effect is greater than the beta-adrenergic effect			

Steroids

For Non-responders;

- Improved refractory hypotension
- Reduced mortality 10%
- 50mg of hydrocortisone iv q 6hrs
- With fludrocortisone 50mcg ngt for 7 days

Stress hyperglycemia

In critically ill patients Due to;

1. A decreased release of insulin
2. increased release of hormones with effects countering insulin
3. increased insulin resistance
4. Hyperglycemia diminishes the ability of neutrophils and macrophages to combat infections.

Tight Glycemic control

- Continuous **insulin infusion**
- Maintaining serum glucose levels between **80 and 110 mg/dl**
- Decreased **mortality** development of **renal failure**

Failed therapies

- **Corticosteroids**— high dose methylprednisolone
- **Anti-endotoxin antibodies**
- **TNF antagonists**—soluble TNF receptor
- **Ibuprofen**

Mortality

- Sepsis:
    - 30% - 50%
- Septic Shock:
    - 50% - 60%