Sepsis and Septic Shock
Sepsis and Septic Shock Definitions

- Sepsis
- Septicemia
- SIRS
- Severe Sepsis
- Septic Shock
- MODS
- ARDS
- CARS
Septic Shock

Most common cause of death
- Human SMICU
- Large animal NICU

Fatality rate
- Human medicine 20-80%
- NBC NICU - 137 cases
  Sepsis without shock - 17%
  Septic shock - 90%

Fatalities
- Refractory hypotension
- ARDS
- MODS
Sepsis and Septic Shock
Etiology

Infectious causes

- Bacterial infections
  - Gram negative pathogens – 60%
  - Gram positive pathogens – 40%
- Viral pathogens
- Fungal pathogens

Bacteremia detected in neonate

- Sepsis < 30%
- Septic Shock > 70%

Localized infections
May never isolate causative agent

Noninfectious causes
Septic shock

Inflammatory response (SIRS)

Immunosuppression (CARS)
Concept of Sepsis

Initiators

Bacteria
  → Bacterial toxins
    → Tissue damage

Endotoxin
  → Direct tissue damage
    → Endotoxemia Shock

Initiators
  → SIRS
    → MODS Shock
      → Balanced Cure
        → Disharmony Shock Death

Innate Immunity
  → SIRS CARS

Disharmony
  → Shock
    → Death
Initiation of Inflammatory Reactions

- Gram-positive Bacteria
- Gram-negative Bacteria
- Viral agents
- Fungal agents
- Hypoxia ischemia
- Trauma/burns

Innate Immunity

Inflammatory activators (TNF, IL-1, IL-6)

CARS ↔ SIRS
Septic Shock

**Initiators of mediator response**

**Gram negative pathogens**
- Endotoxin
- Formyl peptides
- Exotoxins
- Proteases

**Gram positive pathogens**
- Exotoxins
- Enterotoxins
- Hemolysins
- Peptidoglycans
- Lipoteichoic acid
Septic Shock

Pathogenesis - Cardiovascular effects

- Heart rate increases
- Cardiac output increases
- Systemic vascular resistance low
  - Arteriolar tone is decreases - hypotension
  - Venous tone decreased - venous pooling
- Pulmonary vascular resistance is high
  - Right-to-left shunt
- Despite increase cardiac output
  - Tissue hypoperfusion - malperfusion
  - Increased lactate
  - Decreased oxygen utilization
Septic Shock

Pathogenesis - Cardiovascular effects

- Decreased sensitivity to catecholamines
  - Circulating vasodilator substances
  - Adrenergic receptor down-regulation
- Loss of microvascular autoregulatory mechanisms
  - Microvascular damage
- Distributive shock
  - Maldistribution of blood flow
  - Dilation of most vascular beds
  - Constriction of some
Sepsis and Septic Shock
Portals of Entry

- GIT - Translocation
- Respiratory tract - Aspiration
- Placenta - in utero
- Umbilicus
Sepsis and Septic Shock
Predisposing factors

- Placentitis – may be protective
- Prematurity
- Hypoxic-Ischemic disease
- Hypothermia
- FPT
- Stress
- Poor nutrition
- Poor husbandry
Sepsis and Septic Shock
Localized Infections

- Pneumonia
- Enteritis
- Arthritis
- Osteomyelitis
- Meningitis
- Omphalitis
- Uveitis
Sepsis and Septic Shock

Signs of Sepsis

- Fever/hypothermia
- Loss of suckle, lethargy, weakness
- Tachycardia, tachypnea
- Injection, Icterus – oral, scleral
- Petechia - oral, scleral, aural
- Hyperemic coronary bands
- Linear dermal necrosis
- Increased/decreased CRT
- Shock
SIRS damage
MODS

GI tract
  • Breach of the intestinal barrier
  • Translocation of bacteria

Lungs
  • Acute Respiratory Distress Syndrome (ARDS)

CNS
  • Breakdown blood brain barrier
  • Inflammatory mediators
  • Neurosteroid balance

Renal failure
  • Decreased renal blood flow – vascular damage
  • Acute tubular necrosis
Recognition of SIRS
Release of inflammatory mediators

- Fever
- Tachycardia
- Tachypnea
- Vasodilatation (warm skin)
- Mild controlled infection or systemic responses
Recognition of SIRS/Septic Shock

Bounding pulses
- Widen pulse pressure
- Increased cardiac output
- Increased systemic vascular resistance

Hypoperfusion
- Somnolence
- Fall asleep on feet
- Decreased urine output

Before endothelial damage/dysfunction
- Intervention is most dramatic
Recognition of SIRS/Septic Shock

Shock progresses

Other signs of decreased perfusion

- Cool extremities
  
  Secondary to increase vasomotor tone

  Normal or high BP

  Cold progressing to ice cold legs
Recognition of SIRS/Septic Shock

- Homeostatic mechanisms fail
  Hypotension occurs
  Pulse pressure narrows
- Legs cold
- Tachycardia
- Tachypnea
- Recumbent and nonresponsive
- Decreased cardiac output
- Hypoxia and metabolic acidosis
Sepsis and Septic Shock
Therapeutic interventions

Key interventions

- Treat underlying infection
- Provide hemodynamic support
- Support during MODS and metabolic crisis
- Block proinflammatory mediators
Sepsis and Septic Shock
Therapeutic interventions

• Treat underlying infection

• Anticipate bacteria infection
  Antimicrobial therapy

• Viral infections
  Acyclovir

• Hyperimmune plasma transfusion
Sepsis and Septic Shock
Antimicrobials

- Penicillin
- Amikacin
- Cephalosporins
- Ticarcillin/clavulanic acid
- Imipenem
Septic Shock

Hemodynamic support

Goals

• Clear blood lactate
• Normalize perfusion
• Optimize cardiac output
• Increase systemic oxygen delivery
Septic Shock

Hemodynamic support - Fluid therapy

Crystalloids or colloids?

Crystalloid push
  - Bolus 20 ml/kg over 10-20 minutes
  - Reassess patient after every push
    - Blood pressure
    - Leg temperature
    - Peripheral pulse - arterial fill
    - Urine production
    - Mental status

Transfusions
  - Plasma
  - Whole blood

Don’t overhydrate
Septic Shock
Pressors/Inotropes

- Therapeutic goal
  Increase perfusion
  Not “get good BP numbers”
- Inotropic effect most important
  Increase cardiac output
- Pressor effect
  Can negate inotropic effect
  Hopefully will correct malperfusion
- Use a mix of inotropes and pressors
- Each patient - pharmacokinetic experiment
- Arrhythmias - tachycardia
Septic Shock
Pressors/Inotropes

- Dopamine
- Dobutamine
- Norepinephrine
- Epinephrine
- Vasopressin
Optimize O2 availability
Internasal O2 as soon as shock recognized
  High flows 8-10 lpm
  Utilize even if Pao2 appears adequate
Ventilate early
  Decrease work of breathing
    25% of O2 consumption to support respiration
  Cardiovascular function improves
  Make respiratory failure easier to manage
Modest PEEP
  Decrease work of breathing, pulmonary resistance
  Decrease hypoxia, need for high FIO2
Improve gas exchange with inhaled NO
Sepsis and Septic Shock
Nutritional Support

Sepsis is associated with
- Hypermetabolism
- Catabolism

Hyperglycemia
- Catecholamine stimulated glycolysis
- Catecholamine mediated insulin resistance
- Insulin therapy
  - Strict glucose control

Hypoglycemia
- Often profound, refractory hypoglycemia
- Monitor blood glucose levels frequently
- IV glucose therapy
Sepsis and Septic Shock
Inhibiting Toxic Mediators

Antitoxins - Antiendotoxin
Anti-interleukin-1 receptor
Antibradykinin, AntiPAF
AntiTNF, TNF antagonists, NSAIDs
Steroids, Interleukin-1 antagonists
Bradykinin antagonists, Modulate NO
Antiadhesion factors

Large clinical trials in man
- Not show improvement of survival
- Activated protein C (Xigris)
SIRS/Septic Shock
Inhibiting toxic mediators

Why the failures?

Interactions are very complex
Compensatory anti-inflammatory response syndrome (CARS)
Genetic variations in mediators
Timing – interactions
Effective therapy for septic shock await

- Understanding the interaction and balance
- Understanding the timing
Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

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Crit Care Med 2008; 36:296–327