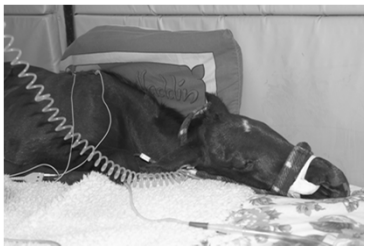
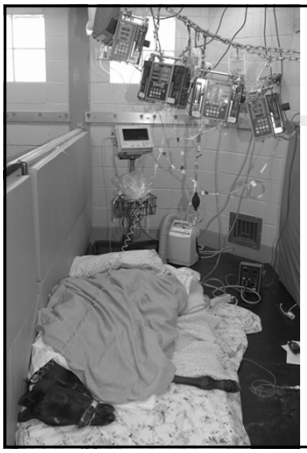
Sepsis and Septic Shock

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

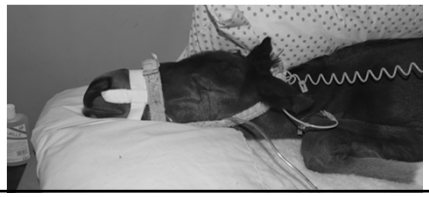
Noninfectious causes

Septic Shock Pathogenesis

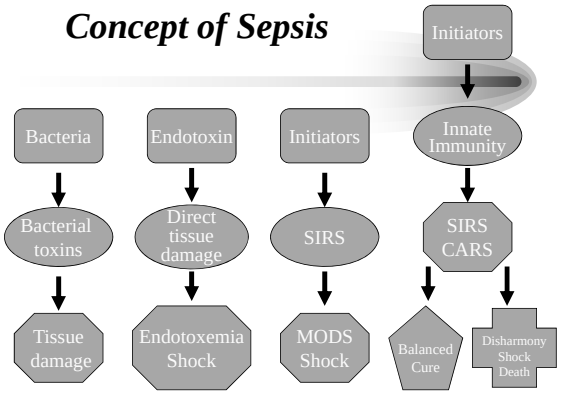
Septic shock

Inflammatory response (SIRS)

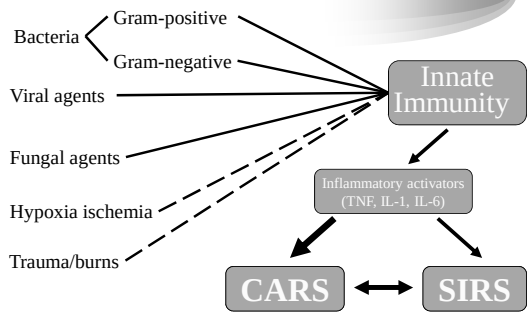
Immunosuppression (CARS)



Concept of Sepsis



Initiation of Inflammatory Reactions

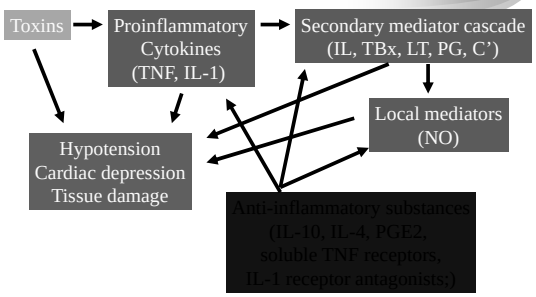


Septic Shock Initiators of mediator response

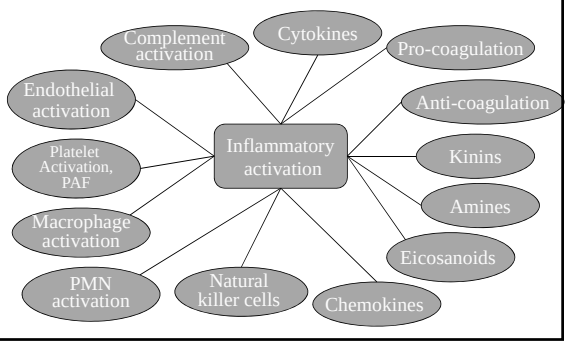
Gram negative pathogens
- Endotoxin
- Formyl peptides
- Exotoxins
- Proteases

Gram positive pathogens
- Exotoxins
- Enterotoxins
- Hemolysins
- Peptidoglycans
- Lipoteichoic acid

Septic Shock Mediator response



Inflammatory Cascade



Septic Shock
Pathogenesis - Cardiovascular effects

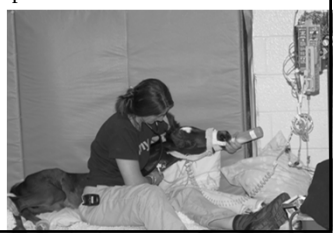
- Heart rate increases
- Cardiac output increases
- Systemic vascular resistance low
  - Arteriolar tone is decreases - hypotension
  - Venus tone decreased - venous pooling
- Pulmonary vascular resistance is high
  - Right-to-left shunt
- Despite increase cardiac output
  - Tissue hypoperfusion - malperfusion
  - 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

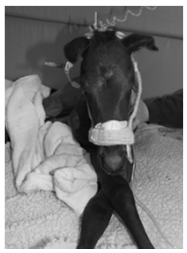
Sepsis and Septic Shock Portals of Entry

- GIt - Translocation
- Respiratory tract - Aspiration
- Placenta - *in utero*
- Umbilicus

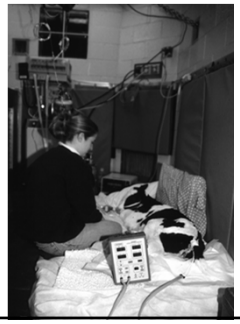


Sepsis and Septic Shock Predisposing factors

- Placentitis – may be protective
- Prematurity
- Hypoxic-Ischemic disease
- Hypothermia
- FPT
- Stress
- Poor nutrition
- Poor husbandry



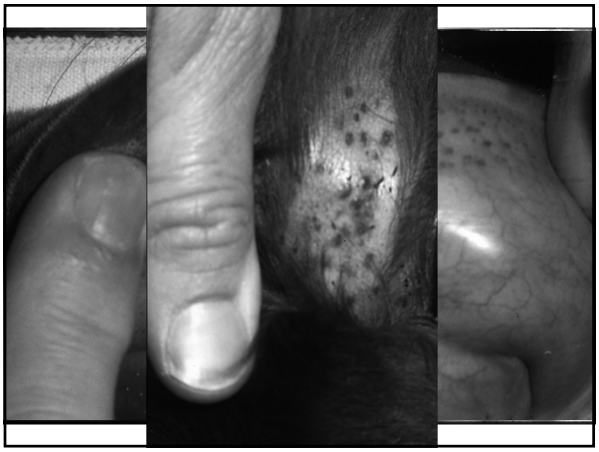
Sepsis and Septic Shock Localized Infections

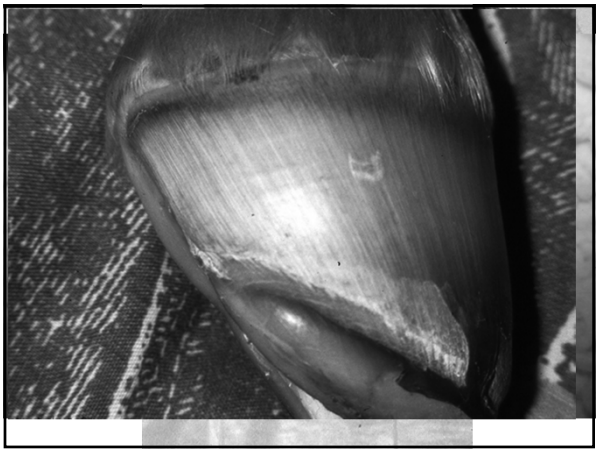


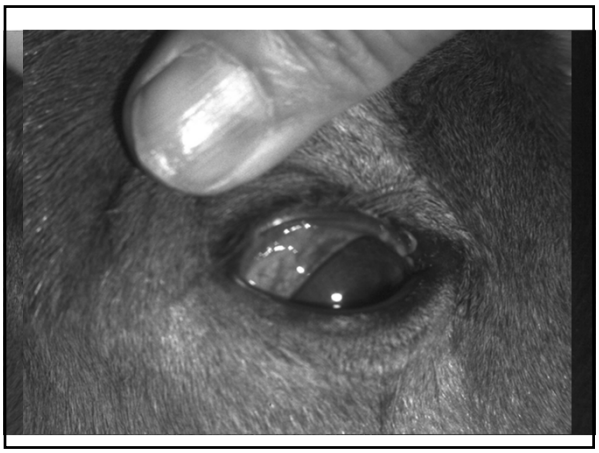
- Pneumonia
- Enteritis
- Arthritis
- Osteomyelitis
- Meningitis
- Omphalitis
- Uveitis

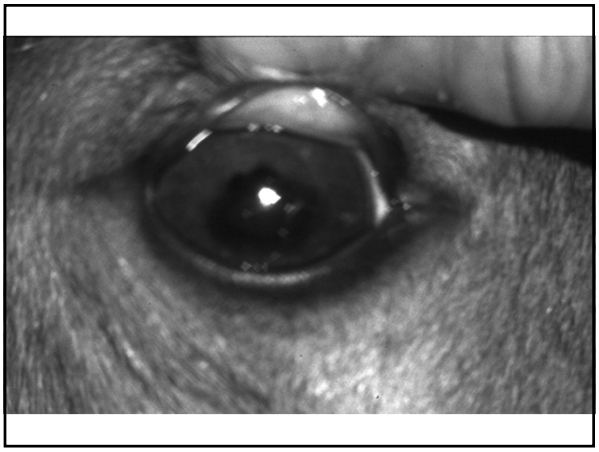
Sepsis and Septic Shock
Signs of Sepsis

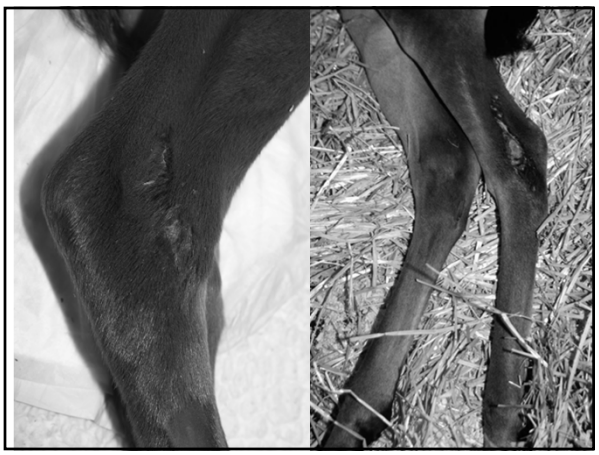
- Fever/hypothermia
- Loss of suckle, lethargy, weakness
- Tachycardia, tachypnea
- Injection, Icterus – oral, scleral
- Petechia - oral, scleral, aural
- Hyperemic coronary bands
- Linear dermal necrosis
- Increased/decreased CRT
- Shock











*Systemic Inflammatory Response Syndrome **SIRS***

- Over activation of the inflammatory response
- Constellation of signs
  - Fever or hypothermia
  - Leukopnea
  - Tachycardia, Tachypnea
- Septic Shock

SIRS** damage **MODS

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

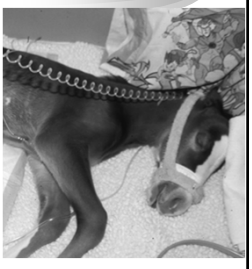
Lungs
- Acute Respiratory Distress Syndrome (ARDS)

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
- Imipenim

Septic Shock
Hemodynamic support

Goals

- Clear blood lactate
- Normalize perfusion
- Optimize cardiac output
- Increase systemic oxygen delivery

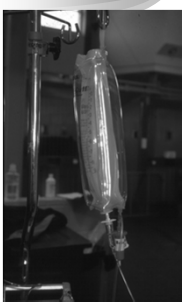
Septic Shock
Hemodynamic support - Fluid therapy

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

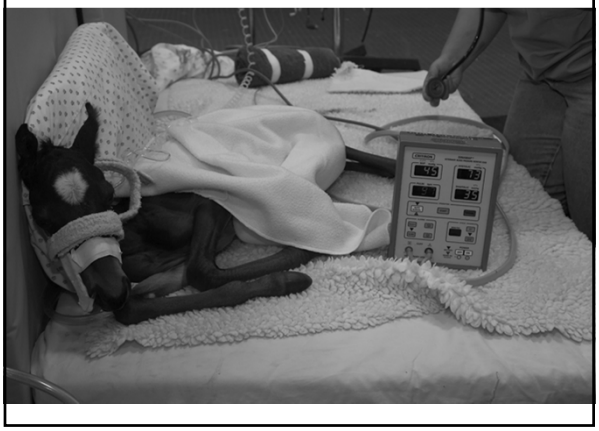
Transfusions
- Plasma
- Whole blood

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

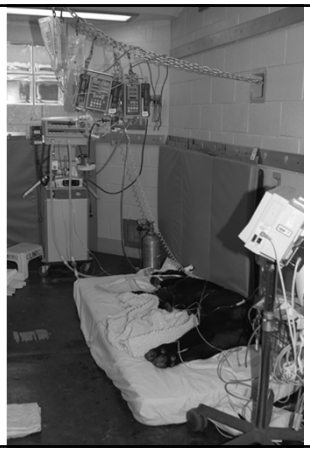
- Dopamine
- Dobutamine
- Norepinephrine
- Epinephrine
- Vasopressin

Septic Shock
Oxygen therapy

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

SIRS/Septic Shock
SIRS – CARS Balance

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

R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Jean M. Carlet, MD; Julian Bion, MD; Margaret M. Parker, MD; Roman Jaeschke, MD; Konrad Reinhart, MD; Derek C. Angus, MD, MPH; Christian Brun-Buisson, MD; Richard Beale, MD; Thierry Calandra, MD, PhD; Jean-Francois Dhainaut, MD; Herwig Gerlach, MD; Maurene Harvey, RN; John J. Marini, MD; John Marshall, MD; Marco Ranieri, MD; Graham Ramsay, MD; Jonathan Sevransky, MD; B. Taylor Thompson, MD; Sean Townsend, MD; Jeffrey S. Vender, MD; Janice L. Zimmerman, MD; Jean-Louis Vincent, MD, PhD; for the International Surviving Sepsis Campaign Guidelines Committee

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