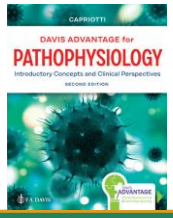

Chapter 46

SIRS, Sepsis, Shock, MODS, and Death

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Overview

- Severe illnesses may develop the following:
  - Systemic inflammatory response syndrome (SIRS)
  - Sepsis, septic shock
  - MODS
    - Multiple organ dysfunction syndrome

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SIRS

- Overwhelming inflammatory reaction
- Develops significant damage to body
- Diagnosis (two of the following)
  - Tachycardia (HR greater than 90/min)
  - Tachypnea (RR greater than 20/min)
  - Hyperthermia or hypothermia (higher than 38°C or lower than 36°C)
  - Leukocytosis (greater than 12,000/mm^3), leukopenia (lower than 4,000/mm^3) or greater than 10% immature forms

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SIRS (continued)

- All major systems compensate for significant injury/insult
- Sympathetic NS and endocrine response similar to alarm stage of stress response
  - HR, cardiac output, and RR increase
  - GI activity and urine output decrease
  - Increased catecholamines, glucocorticoids, mineralocorticoids, antidiuretic hormone (ADH), angiotensin II

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CARS: Immunosuppression After SIRS

- CARS
  - Compensatory anti-inflammatory response syndrome (CARS)
  - Common after SIRS
  - Leads to increased infection risk (i.e., sepsis)
  - Patient susceptible to hospital-acquired infections

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Possible Progression

- SIRS can lead to CARS
- CARS may lead to development of sepsis
- Septic shock may develop
- MODS may develop
- Death

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Sepsis

- Body-wide infection
  - AKA: "bloodstream infection"
- Overwhelms immune system
  - Bacterial sepsis is most common form
- Risks
  - Immunosuppression
  - Older age (urosepsis may develop)
  - Severe sepsis: sepsis complicated by end-organ dysfunction
    - Renal failure, hypotension, disseminated intravascular coagulation (DIC)

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Manifestations of Sepsis

- Alteration in mental state
- Hypoxemia
  - Arterial oxygen less 72 mm Hg
- Elevated plasma lactate level
- Oliguria

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Septic Shock

- Severe sepsis with persistent life-threatening hypotension
- Medical emergency
- Hypotension does not respond to fluid replacement and vasopressors
- Virulent microbe: *Clostridia*, *S. aureus*, *Streptococci A*
- Immunocompromised are most at risk

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Septic Shock (continued_1)

- Microbial exotoxins or endotoxins
  - Potent vasodilation
  - Capillary permeability
  - Lead to hypotension
  - Decreased organ perfusion
- Toxins also alter coagulation
  - Activation (microthrombi formed) OR
  - Decreased coagulation

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Septic Shock (continued_2)

- Epinephrine and cortisol increase in sepsis
  - Decreased insulin sensitivity, increase glycogenolysis
    - Elevates blood sugar
      - Decreases WBC function
  - Control of blood sugar levels is very difficult
- "Warm shock" may develop
  - Skin is warm and pink despite failing circulatory system

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Multiple Organ Dysfunction Syndrome (MODS)

- Progressive and potentially reversible dysfunction of two or more organs
- Variety of causes, sepsis most common
- MODS is leading cause of death in ICU

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Theories of MODS

- Hypoxia-microvascular theory
  - Microvascular injury prevents oxygen delivery
- Gut theory
  - Decreased blood flow to GI tract, increases permeability
  - GI contents released
- Endotoxin theory
  - Endotoxins release from Gram-negative bacteria cause widespread inflammation and circulatory collapse

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Four Clinical Phases of MODS

- Stage 1
  - Increased volume requirements and mild respiratory alkalosis
  - Oliguria, hyperglycemia, and increased insulin requirements
- Stage 2
  - Tachypneic, hypocapnic, and hypoxemic
  - Moderate liver dysfunction
- Stage 3
  - Shock with azotemia and acid-base disturbances, significant coagulation abnormalities
- Stage 4
  - Vasopressor dependent, oliguric or anuric
  - Ischemic colitis, lactic acidosis

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Shock

- Inability of the heart and lungs to satisfy needs of peripheral tissues
- SBP less than 90 mm Hg or drops 40 mm Hg below the patient's normal BP
  - Severe hypotension results in inadequate perfusion
- BP does NOT define shock
- Several forms of shock

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Types of Shock

1. Cardiogenic shock
2. Hypovolemic shock
3. Septic shock
4. Anaphylactic shock
5. Neurogenic shock

- All types converge to same physiological pathway, leading to cellular hypoxia and compensatory mechanisms

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Three Stages of Shock

1. Initial
2. Progressive
3. Irreversible

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Initial Stage of Shock

- Sudden drop in tissue perfusion
- Activation of SNS
- Activation of RAAS
- Patient appears with increased HR, anxious, increased RR, pale
- Goal
  - Compensate to maintain perfusion

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Progressive Stage of Shock

- Decreased perfusion of lungs, kidneys, gut, pancreas, and liver
- As perfusion decreases, further manifestations develop
- Decreased GFR, increased toxins, GI decreased peristalsis
- Goal
  - Conserve blood for heart and brain

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Irreversible Stage of Shock

- Perfusion no longer maintained to heart and brain
- Myocardial and cerebral ischemia
- Widespread cellular hypoxia
- Anaerobic metabolism
- Loss of cellular function in various tissues
  - Organelles fail, cell dies, and release lysosomal enzymes

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Inflammatory Response to Shock

- Immune system stimulated by cellular breakdown
- Intestinal barrier breaks down with hypoxia, stimulating immune response further
- Massive cytokine release leading to capillary permeability increase, compromising perfusion further

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Lactic Acidosis in Shock

- Result of anaerobic metabolism due to inadequate oxygen
- Lactic acid levels build up
- Cardiac, respiratory, neurological, and brain function are adversely affected by lactic acid
- Adverse effects progressively worsen with increasing lactic acid levels

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GI Consequences in Shock

- Decreased perfusion of GI tract enable intestinal contents to enter blood
- Induce systemic inflammatory response
- Pancreas function decreases
- Intestinal edema ensues due to loss of capillary integrity
  - AKA: “intestinal third space fluid loss”
  - Sequestration of many liters of fluid

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Hormone Release During Shock

- Epinephrine and cortisol
  - Inhibit insulin activity
  - Increased glucose levels
- Decreased WBC activity with hyperglycemia

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Coagulation During Shock

- Increased clot formation
- Endothelium
  - Secretion of thromboxane A2 and thromboplastin
  - Activation of the coagulation cascade
- Inhibition of activated protein C and other fibrinolytic pathways
  - Clots may form that the body is unable to lyse
    - Can lead to tissue ischemia

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Types of Shock Based on Etiology

- Cardiogenic
  - Failure of the heart
- Hypovolemic
  - Large depletion of blood or fluids
- Anaphylactic
  - Severe allergic reaction
- Neurogenic shock
  - Injury to spinal cord or brain
- Septic
  - Infection

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Cardiogenic Shock

- Severe hypotension less than 90 mm Hg SBP for 30 minutes, despite adequate fluid
- Most common cause is myocardial infarction
  - Arrhythmias
  - Cardiac tamponade
    - Fluid build up around the heart that restricts the heart action
- Heart unable to maintain pressure to perfuse tissues
- Low urine output, cyanosis, altered mental status, elevated heart rate

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Cardiac Tamponade: Pulsus Paradoxus

- Under normal conditions, inspiration causes jugular vein pressure to decrease
- Pulsus paradoxus
  - Jugular vein pressure increases during inspiration
  - Pressure on heart causes fluid back up in jugular veins
- Beck's triad
  - May occur in cardiac tamponade: distant heart sounds, low BP, high jugular vein pressure

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Hypovolemic Shock

- Low blood volume: Loss of 20% or more of before signs of hypovolemic shock
  - Hemorrhage
  - Severe dehydration: diarrhea (especially in children), vomiting, ascites, or severe burns
  - Decreased venous return
- May induce coronary ischemia, renal tubular necrosis
- RAAS and SNS activated
  - Vasoconstriction and fluid retention

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Anaphylactic Shock

- Due to overwhelming immune response to allergen
- Urticaria, bronchospasm, angioedema
- Swelling of throat, bronchoconstriction, vasodilation, increased capillary permeability

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Neurogenic Shock

- SNS is disrupted
- Spinal cord injury, brain injury, or during anesthesia
- Widespread vasodilation reduces venous return to the heart
- Hypotension occurs, without normal SNS compensations

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Assessment of Critically Ill Patient

- Tachycardia or bradycardia
- Tachypnea
- Cyanosis
- Metabolic acidosis
- Changes in mentation or consciousness
- Low urine output
- Blood pressure is usually low, but not necessarily
- Electrocardiographic changes
- Cardiac output, either reduced or increased
- Central venous pressure, either high or low
- Total peripheral resistance, either markedly increased or reduced

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Diagnosis

- APACHE II (Acute Physiology And Chronic Health Evaluation system)
  - Assesses probability of survival of an ICU patient
- Glasgow Coma Scale (GCS) score
- Simplified Acute Physiology Score (SAPS II)
- Sepsis-related Organ Function Assessment score (SOFA)
- Multiple Organ Dysfunction Score

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Treatment of Cardiogenic Shock

- Cardiogenic shock most commonly caused by extensive MI
  - Treatment involves maintaining ventricular function
- Beta blockers may be used (can be contraindicated in severe shock)
- Aspirin
- Dobutamine and dopamine

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Treatment of Cardiogenic Shock (continued_1)

- Surgery
  - Cardiac tamponade, acute mitral insufficiency, acute ventricular septal defect, or acute ventricular perforation
- Intra-aortic balloon pump (IABP)
- IABP counterpulsation
  - Enhances coronary blood flow, reduces afterload, and decreases LV work
  - Balloon inflates in aorta to maintain flow to coronary arteries

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Treatment of Cardiogenic Shock (continued_2)

- Percutaneous left- and right-ventricular mechanical circulatory support (MCS) devices
  - Changing the management of cardiogenic shock and severe heart failure
  - *Example:* left ventricular assist device (LVAD)
    - LVAD may be temporary treatment while patient awaits transplant
    - "Bridge therapy"

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Treatment of Hypovolemic Shock

- Stop fluid loss
- Rapid, adequate fluid replacement
- Volume expanders used first
- Blood transfusion may be necessary
- Use urine output to gauge replacement amount

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Treatment of Septic Shock

- Very complex course of treatment
- Broad-spectrum antibiotics
- Fluid maintenance
- Cardiac support agents
- Vasoconstrictors (some may be ineffective)
- Dialysis and/or intubation may be necessary
- IV insulin to control blood sugar

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Treatment of Anaphylactic Shock

- Epinephrine: intramuscular or IV
- Antihistamines and glucocorticoids
- IV saline to accommodate fluid shifts
- Intubation may be necessary

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Treatment of Neurogenic Shock

- IV vasoconstrictors
- Angiotensin II recommended to maintain vasoconstriction
- Fluid administration
- Atropine: anticholinergic agent
  - Counteract parasympathetic bradycardia
- Treat underlying central nervous system injury

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Adult Respiratory Distress Syndrome (ARDS)

- Widespread injury of alveoli
  - Severe hypoxemia, acute dyspnea
  - ALI: acute lung injury, most severe form
- Injury to lungs causes secretion of cytokines
  - Type I and type II epithelial cells affected
  - Decreased surfactant
- Decreased oxygen exchange
  - Carbon dioxide exchange less affected, as carbon dioxide more soluble

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ARDS Risk Factors

- Aspiration
- Bacteremia
- Fractures
- Massive transfusion
- Near drowning
- Pneumonia
- Trauma

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ARDS Diagnosis

- Must differentiate from heart failure
  - Echocardiogram, BNP levels
- Chest x-ray
  - Must differentiate from pulmonary edema
- Arterial blood gases
  - Initially hypoxemia drives ventilation and reduces carbon dioxide
  - Over time, carbon dioxide levels may elevate as oxygen levels fall

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ARDS Treatment

- Mechanical ventilation
- Medically induced coma
- Numerous medications have proven to be ineffective
- Treatment of etiology is most important

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Acute Kidney Injury (AKI)

- Renal ischemia and renal toxicity
- Urine output needs to be at least 400 mL/day
  - Oliguria less than 400 mL/day
  - Anuria less than 100 mL/day
- Nephrons very sensitive to hypoperfusion
- Comorbidities increase risk for AKI

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Acute Kidney Injury (AKI) (continued)

- Diagnosis
  - Serum BUN and Cr
  - Brown casts in urinalysis indicate tubular necrosis
  - Urinalysis
- Treatment
  - AKI in ICU patients increases risk of death
  - Dialysis

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Abdominal Compartment Syndrome (ACS)

- Pressure within the abdominal cavity increases to greater than perfusion pressure
- Ischemia of abdominal tissues
- Normal intra-abdominal pressure (IAP) is 0 to 5 mm Hg
- Intra-abdominal hypertension (IAH): pressure greater than 8 mm Hg

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Abdominal Compartment Syndrome (ACS) (continued_1)

- Cause of ACS is increased capillary permeability of intestines
- Third space edema in abdomen develops
- As IAP increases:
  - Decreased venous return to heart
  - Decreased renal perfusion
  - Diaphragm compression
  - Breakdown of GI barrier

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Abdominal Compartment Syndrome (ACS) (continued_2)

- Patient presents:
  - Abdominal pain, increased abdominal girth, decreased urine output, syncope, nausea
- Diagnosis
  - Monitor IAP and abdominal perfusion pressure
- Treatment
  - Hourly monitoring of IAP
  - Restrict fluid resuscitation, nasogastric tube suction, colloid infusion

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Hepatic Failure

- Failure as a result of decreased perfusion
  - Decreased cardiac output
  - Increased IAP
  - Prolonged TPN (total parenteral nutrition)
  - Bacterial infection of liver can occur if GI barrier broken down
- Jaundice, abdominal distension
- Treatment
  - IV fluids, nutrition maintenance

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Disseminated Intravascular Coagulation (DIC)

- Impairment of coagulation cascade
- Alternating episodes of bleeding and clot formation
- Uncontrolled bleeding may result
  - Bleeding from three diverse sites may indicate DIC
  - Petechiae and ecchymosis may be present
- Diagnosis
  - Prolonged clotting times, thrombocytopenia, elevated D-dimer

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Determination of Death

- Before exam, rule out other morbid conditions (severe electrolyte imbalances, hypotension, drug intoxication)
- Brain death: neurological exam
  - Two exams performed
  - Interval between exams determined by patient's age

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Brain Death

- Presence of coma
- Absence of motor responses
- Absence of pupillary responses to light and pupils at midposition with respect to dilation (4 to 6 mm)
- Absence of corneal reflexes
- Absence of caloric responses
  - Absence of vestibulo-ocular/oculo-cephalic reflexes
- Absence of gag reflex
- Absence of coughing in response to tracheal suctioning
- Absence of sucking and rooting reflexes
- Absence of respiratory drive at a $PaCO_2$ that is 60 mm Hg or 20 mm Hg above normal baseline values

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Assessment of Coma and Brainstem Reflexes

- Presence of coma determined first
- Depth of coma
  - Motor responses to painful stimuli
- Glasgow Coma Scale (GSC)
- Brainstem reflexes
  - Caloric stimulation
  - Eye reflexes
  - Lack of independent respiratory drive

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Confirmatory Tests for Brain Death

- Cerebral angiography
- Electroencephalography
- Transcranial Doppler ultrasonography
- Nuclear imaging

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Postmortem Changes

- Putrefaction and autolysis
- Rigor mortis
  - Postmortem stiffening
- Livor mortis
  - Discoloration on dependent portions
- Tardieu spots
  - Petechiae
- Algor mortis
  - Cooling process
- Purge fluid

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