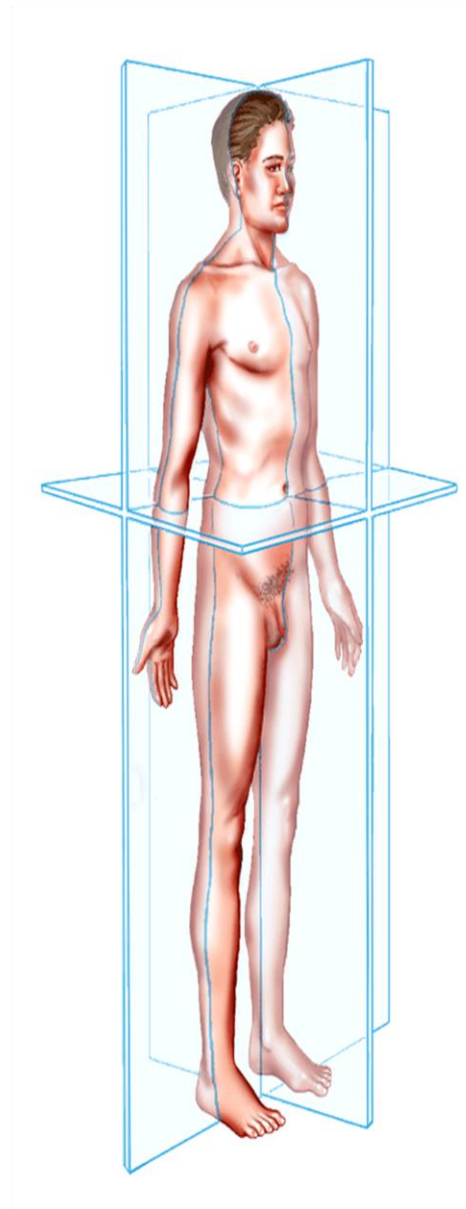
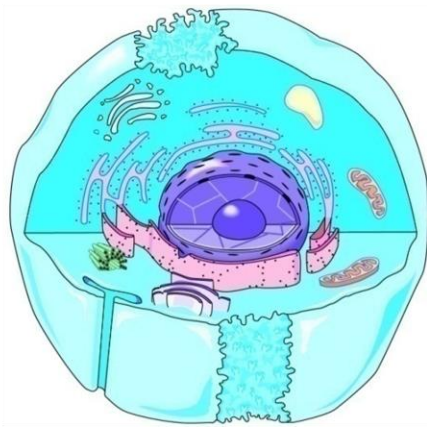
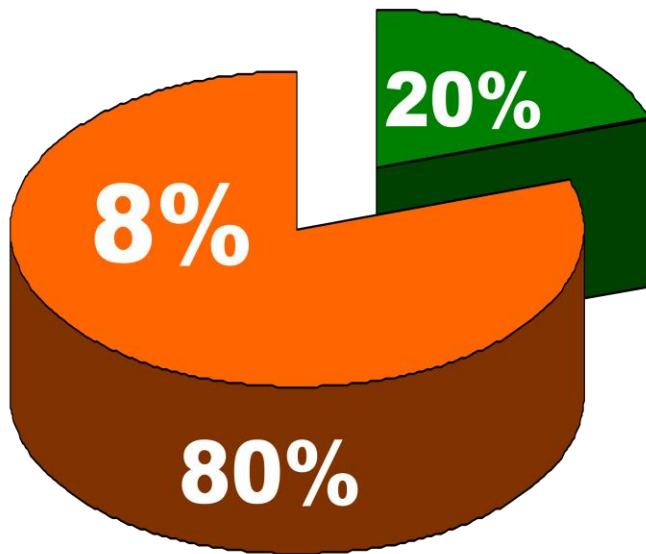


Multisystem



MULTISYSTEM

I. Introduction

- A. AACN CCRN/CCRN-E Blueprint 8%**
- ✓ Asphyxia
 - ✓ Distributive Shock (e.g. anaphylaxis)
 - ✓ Multi-Organ Dysfunction Syndrome (MODS)
 - ✓ Multisystem Trauma
 - ✓ Septic Shock/Septic Shock
 - ✓ System Inflammatory Response Syndrome (SIRS)
 - ✓ Toxic Ingestions/Inhalations (e.g., drug/alcohol overdose)
 - ✓ Toxin/Drug Exposure

II. Toxic Exposure (Ingestions/Inhalations)

A. Pathophysiology

- ✓ Absorption
- ✓ Distribution
- ✓ Metabolism
- ✓ Elimination

B. Assessment

- ✓ ABCs ...ALWAYS....ALWAYS....ALWAYS
- ✓ DE and Poison Control
- ✓ Secondary Survey (full assessment)
 - Vital Signs
 - LOC
 - Heart Rate and Rhythm
 - Temperature:
 - Hyperthermia - Salicylates & Cocaine
 - Hypothermia - Barbiturates & Opiates
 - Respiratory Rate
 - Blood Pressure
 - Full System Assessment
- ✓ History
- ✓ Environment/Bystanders
- ✓ AMPLE: Allergies, Medications, Past Illnesses, Last Meal, Events

Primary Survey A airway B breathing C circulation D deficit – Neuro E exposure

- ✍ SAMPLE: Signs/Symptoms, Allergies, Medications, Past Illnesses, Last Meal, Events
- ✍ Diagnostic Work
 - Toxicology Screens: Blood, Urine, Gastric Aspirate
 - CBC, Chemistry, LFTs, Coags, ABG
 - Chest X-Ray, ECG
 - Abd X-Ray (body packing/stuffing)
 - Pregnancy Test

B. Treatment Options

- ✍ Rapid Response: Unknown Substance, Unconscious Victim
 - Ampule D50 IV: Hypoglycemia
 - Thiamine 100mg IV: Prevent Wernicke-Korakoff's Syndrome
 - Naloxone 2mg IV, IM or ET: Narcotic Antagonist
- ✍ Antidote When Known and Available (see below)
- ✍ Prevent Absorption & Enhance Elimination
 - Oralgastric Lavage
 - Emetics (not recommended)
 - Activated Charcoal
 - Diuresis
 - Whole Bowel Irrigation
 - Hemodialysis
- ✍ Don't Negate Psycho/Social and Family Indications

C. Common Toxins (Review Complete Toxicology Table in Patho Book or AACN Core Curriculum)

Toxin	Problem/ Presentation	Antidote	Assessment & Treatment
Acetaminophen	Liver Failure	N-Acetylcysteine (NAC) (Mucomyst) PO, IV	N/V, Right UQ Pain, Bleeding Elevating LFTs NAC, Gastric Lavage, Charcoal
Alcohol	Respiratory Depression Seizures Liver Failure (chronic)	No Direct IV Fluids Helpful	Altered LOC, ETOH on Breath, Hx Protect Airway, NTG – Lavage (within 1hr)

			ABGs, IV Fluids, Seizure Precautions, Monitor and Tx Electrolyte Imbalance
Carbon Monoxide	Hypoxia Replaces O ₂ on Hgb	Removal From Exposure Oxygen Admin	Altered LOC, Headache, Seizures, Coma, Flu-Like Complaints 100% Oxygen Hyperbaric Oxygen
Cocaine	Stimulates Sympathetic System HTN, CP, ECG Δs, Headache, Stroke, Seizures, Hyperthermia	None	OD Levels Look Like Hypoxia, Stroke, Head Injuries, MI, Hyperthermia Treat the Physical Presenting Problem (MI, Stroke etc.) Protect Airway – Admin O ₂ Benzodiazepines: Sedation Vasodilators: HTN ACS Tx: see Cardiac Section Provide Cooling Seizure Tx and/or Prophylactic
Cyclic Antidepressants	CNS: Seizure, Coma CV: Rhythm Disturbance Anticholinergic: Decreased Gastric Emptying, Urinary Retention	Sodium Bicarbonate Physostigmine (Antilirium) (Reverses CNS effects)	ECG Δs: Tachy, Vent Dysrhythmias, Heart Blocks, Wide QRS Hypotension Altered LOC: Confusion, Agitation, Hallucinations, Seizures, Coma Admin NaBicarb, GI Evacuation: Lavage and Charcoal Monitor ECG and Tx PRN
Opiates	Cardiac and Respiratory Depression	Naloxane (Narcan)	Decreased HR, BP, RR Administer Naloxane
Salicylate (aspirin, pepto bismal, cough/cold preps)	Acute: Central Stimulation of Respiratory System (hyperventilation) Metabolic: Met Acidosis, Hyperthermia, Hypoglycemia, Platelet Dysfunction (bleeding) Chronic: Bleeding	No Direct Sodium Bicarbonate for Met Acidosis	Hyperventilation, Resp Alk & Met Acidosis, Dehydration, N&V, Hyperpyrexia, Bleeding ABG, Get Blood Levels, Chemistry, Platelet Ct, Coags Gastric Lavage, Charcoal, IV Fluids Tx Metabolic Derangements Cool Temp, Seizure Precautions Hemodialysis

III. Toxic Exposures (External)

Chemical Exposure

- ✦ Identify if Possible
- ✦ Antidote if Possible
- ✦ Remove Chemical
- ✦ Brush if Powder
- ✦ Flush if Liquid- large volumes of NS or H₂O
- ✦ Cover w Sterile Damp Dressing
- ✦ Never Rub Area

IV. Asphyxia

Severe oxygen deprivation (hypoxia) secondary to decreased air flow

- ✦ Drop in PaO₂
- ✦ Rise PaCO₂
- ✦ Decreased Level of Consciousness
- ✦ MODS → Death

Common Causes

- ✦ Physical Suffocation/Hanging
- ✦ Foreign Body/Obstruction in Upper Airway
- ✦ Drowning
- ✦ Electrical Shock
- ✦ Gastric Aspiration
- ✦ Smoke or Toxic Gas Inhalation

Treatment Priorities

- ✦ Open Airway
- ✦ Oxygenate and Ventilate
- ✦ Monitor
- ✦ Lactate Level
- ✦ Consider Therapeutic Hypothermia
- ✦ Organ Support & Surgery if Required

V. Shock

A. Definitions

“A manifestation of the rude unhinging of the machinery of life.” Gross, 1872

“A momentary pause in the act of Death.”
John Collins Warren, 1895

Clinical Definition for Shock

The inability of the circulatory system to supply oxygen and nutrients to the cells of the body.

The oxygen demands are greater than the supply.

B. CLASSIFICATIONS OF SHOCK

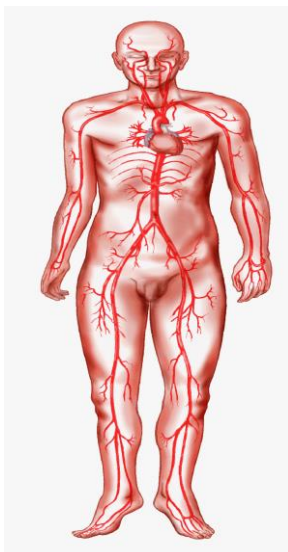
Hypovolemic Shock:

1. Definition:

Hypovolemic Shock is the most common type of shock. It also is the easiest to treat if identified early. Shock develops when blood volume is insufficient to fill the intravascular space causing a preload deficit and ultimately a decreased cardiac output.

2. Cause:

Absolute/Direct or Relative/Indirect Loss of Volume



Absolute/Direct Losses

External Hemorrhage

Gastrointestinal Volume Losses

- ☛ Diarrhea
- ☛ Vomited
- ☛ Gastric Suction
- ☛ Ostomies

Renal Volume Losses

- ☛ Massive Diuresis

<ul style="list-style-type: none"> ☼ Hyperglycemic Osmotic Diuresis ☼ Diabetes Insipidus
Plasma Losses <ul style="list-style-type: none"> ☼ Burns ☼ Skin Lesions ☼ Fistulas ☼ Excessive Sweating ☼ High Fever

Relative/Indirect Losses
Sequestration of Fluid <ul style="list-style-type: none"> ☼ Cirrhosis ☼ Intestinal Obstruction ☼ Ileus ☼ Peritonitis
Internal Hemorrhage/Volume Losses <ul style="list-style-type: none"> ☼ Hemothorax ☼ Hemorrhagic Pancreatitis ☼ Ruptured Spleen ☼ Long Bone or Pelvic Fx ☼ Arterial Dissection ☼ Hemoperitoneum ☼ Ascites ☼ Extra Uterine Pregnancy
Vasodilation <ul style="list-style-type: none"> ☼ Sepsis ☼ Anaphylaxis ☼ Spinal Shock
Salt Depletion
Addisonian Crisis
Hypopituitarism

Adapted with Additions from Rauen & Munro (1998). Shock. In Kinney, M., et al. *AACN Clinical Reference for Critical Care Nursing*. Mosby: Philadelphia

3. Clinical Presentation:

Patient presentation will depend

1. Percent volume loss
2. Duration of hypovolemia
3. Activation and response of compensatory mechanisms

4. Therapeutic Goal:

Restore adequate intravascular volume as quickly as possible and stop losses. The fluid options and crystalloid vs colloid controversy will be addressed in the management section of this seminar.

Neurogenic Shock

1. Definition:

A loss of vasomotor tone secondary to inhibition of neural output. The loss of sympathetic tone allows the parasympathetic nervous system to dominate, which causes a drop in systemic vascular resistance (massive vasodilation) and bradycardia. Cardiac output drops because of the lack of preload and slow heart rate.

2. Causes:

The most common cause of neurogenic shock is spinal cord injury at or above the T6 level. This injury can be complete or incomplete and the shock state typically occurs quickly after the injury and maybe self limiting or transient. The shock state may last up to three weeks.

- ☛ Spinal Cord Injury
- ☛ Deep General Anesthesia
- ☛ Spinal Anesthesia
- ☛ Damage to the Basal Regions of the Brain
- ☛ Prolonged Medullary Ischemia
- ☛ Central Nervous System Problems

3. Clinical Presentation:

Parasympathetic dominance is the hallmark of spinal shock. Vasodilation and bradycardia are the classic clinical presentation. During the shock state the patient will typically have no motor or sensory function below the level of the lesion. Long term disability/function cannot be determined until the shock state has subsided.

4. Therapeutic Goal:

Stop the initiating cause and stabilize the spine as soon as possible. During the shock state therapies revolve around administering volume (fill the tank), beta stimulation (increase heart rate), alpha stimulation (vasoconstriction).



Anaphylactic Shock

1. Definition:

Massive vasodilation occurs because of an antigen-antibody reaction which activates mast cells and basophils triggering the release of vasoactive mediators (histamine, serotonin, bradykinin, eosinophil chemotactic factor, prostaglandins, heparin, leukotrienes, platelet-activating factors, adenosine and various proteolytic enzymes) which stimulates a systemic response. This results in tremendous vasodilation and increased capillary permeability, with loss of fluid into the interstitial space and resultant hypotension from the relative hypovolemia.

2. Cause:

The initial activating response can be immunoglobulin E (IgE) or non-IgE mediated. Anaphylaxis is IgE mediated and is typically the result of a specific antigen exposure. An anaphylatoid response is mediated by a non-IgE reaction. There is direct activation of the mediators listed above (not antigen-antibody) from a source. A wide range of agents can cause this response: anti-inflammatory drugs, contrast media, opiates, polysaccharide volume expanders and anesthetics.

COMMON CAUSES

Foods ☛ Eggs ☛ Milk ☛ Nuts ☛ Legumes	Antibiotics ☛ Penicillins ☛ Cephalosporins ☛ Tetracyclines ☛ Erythromycin	Chemotherapy ☛ Cisplatin ☛ Cyclophosphamide ☛ Daunorubicin ☛ Methotrexate	Other Drugs ☛ Protamine ☛ Thiazides ☛ Chlorpropamide
Venoms ☛ Bees ☛ Wasps ☛ Snakes ☛ Spiders	NSADs ☛ Salicylates ☛ Ibuprofen ☛ Indomethacin	Insulin ☛ Pork ☛ Beef ☛ Human	Diagnostic Agents ☛ Iodinated Radiocontrast Agents
Blood Products	Local Anesthetics	General Anesthetics	Narcotics

3. Clinical Presentation:

The release of the vasoactive mediators cause an array of systemic effects which lead to decreased oxygen delivery and shock.

- ☛ Hypotension
- ☛ Generalized Edema (increased capillary permeability)

- ☛ Laryngeal Edema
- ☛ Severe Bronchoconstriction
- ☛ Difficulty Breathing
- ☛ Coronary Vasoconstriction
- ☛ Urticaria
- ☛ Angioedema
- ☛ Itching
- ☛ Fever
- ☛ Flushed or Warm Skin
- ☛ Anxiety

4. Therapeutic Goal:

Identify and stop the exposure to the causative agent. Block the effects of the vasoactive mediators. Treatment options are typically anti-histamines, vasoconstrictors, bronchodilators, and fluid resuscitation.

Septic Shock

1. Definition:

1992 ACCP/SCCM Definitions Bone, R. et al (1992) Chest, 101, pg 1644-1655

⇒ **Sepsis**: the systemic response to infection, manifested by two or more of the following conditions as a result of infection:

- ✓ Temperature > 38° C or < 36°C
- ✓ Heart Rate > 90 beats per minute
- ✓ Respiratory Rate > 20 bpm or PaCO₂ < 32mmHg
- ✓ WBC > 12,000 or < 4,000, or > 10% immature (bands) forms

⇒ **Systemic Inflammatory Response Syndrome (SIRS)**: The systemic inflammatory response to a variety of severe clinical insults. The response is manifested by two or more of the following conditions:

- ✓ Temperature > 38° C or < 36°C
- ✓ Heart Rate > 90 beats per minute
- ✓ Respiratory Rate > 20 bpm or PaCO₂ < 32mmHg
- ✓ WBC > 12,000 or < 4,000, or > 10% immature (bands) forms

⇒ **Severe Sepsis**: Sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may include, but are not limited to

- ✓ Lactic acidosis
- ✓ Oliguria
- ✓ Acute alteration in mental status

⇒ **Septic Shock**: Sepsis-induced with hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but are not limited to:

- ✓ Lactic Acidosis
- ✓ Oliguria
- ✓ Acute alteration in mental status

Pt who is receiving inotropic or vaspressor agents may not be hypotensive at the time that perfusion abnormalities are measured.

2001 SCCM/ESICM/ACCP/ATS/SIS

International Sepsis Definitions Conference

Levy, M., et al. (2003). 2001 SCCM/ESICM/ATS/SIS International sepsis definitions conference. CCM 31(4), 1250-1256.

⇒ **Approved and supported 1992 definitions. Offered S&S for sepsis and staging system (lacks evidence at this time).**

⇒ **General Variables:**

- ✓ Fever (core $>38.3^{\circ}\text{C}$)
- ✓ Hypothermia (core $<36^{\circ}\text{C}$)
- ✓ Heart Rate $>90\text{min}$ or >2 SD above the normal value for age
- ✓ Tachypnea
- ✓ Altered mental status
- ✓ Significant edema or positive fluid balance (20ml/kg over 24 hr)
- ✓ Hyperglycemia (plasma glucose >120) in absence of DM

⇒ **Inflammatory Variables:**

- ✓ Leukocytosis (WBC $>12,000$)
- ✓ Leukopenia (WBC $<4,000$)
- ✓ Normal WBC with $>10\%$ immature forms (bands)

- ✓ Plasma C-Reactive Protein > 2 SD above normal value
- ✓ Plasma Procalcitonin > 2 SD above normal value (IL-6)

⇒ **Hemodynamic Variable:**

- ✓ Arterial Hypotension (SBP < 90mmHg, MAP < 70, or SBP decreased >40mmHg in adults or < 2SD below normal for age)
- ✓ SvO₂ > 70%
- ✓ CI > 3.5L/min

⇒ **Organ Dysfunction Variables:**

- ✓ Arterial Hypoxemia (PaO₂/FiO₂ <300)
- ✓ Acute Oliguria (UO < 0.5mL/kg/hr)
- ✓ Creatinine Increase > 0.5mg/dL
- ✓ Coagulation Abnormalities (INR > 1.5 or APT > 60sec)
- ✓ Ileus (absent bowel sounds)
- ✓ Thrombocytopenia (platelet count < 100,000)
- ✓ Hyperbilirubinemia (plasma total bilirubin > 4mg/dL)

⇒ **Tissue Perfusion Variables:**

- ✓ Hyperlactatemia (>1mmol/L)
- ✓ Decreased capillary refill or mottling

2. Causes: Infection is the cause of sepsis. The infective agent can be a bacteria (gram positive or negative), virus or fungi. Once the infection moves from a local to a systemic problem, sepsis and septic shock can result.

3. Clinical Presentation:

Although initiated by a localized infection, once the patient is septic they present with a systemic inflammatory response. This response is a systemic reaction to the release of endotoxin and biochemical mediators stimulated by inflammation and inadequate oxygen delivery. The patient will present with a relative hypovolemia secondary to massive vasodilation.

- ☛ Relative Hypovolemia and Hypoperfusion
- ☛ Increased Capillary Permeability and Edema
- ☛ Myocardial Depression
- ☛ Lactic Acidosis

- ☛ Pulmonary Capillary Leak Leading to ALI
- ☛ Activation of Complement System Leading to Microthrombi
- ☛ Platelet Abnormalities
- ☛ Gluconeogenesis and Insulin Resistance

4. Therapeutic Goal:

Identify and stop the causative agent. Block the effects of the inflammatory mediators. Treatment options typically include

1. Antibiotics
2. Fluid Resuscitation
3. Vasopressors
4. Ventilation and Oxygenation
5. Restore Hemopoietic Balance.

.....

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD₁; Mitchell M. Levy, MD₂; Andrew Rhodes, MB BS₃ et al
Critical Care Medicine **February 2013** • Volume 41 • Number 2

Recommendations: Initial Resuscitation and Infection Issues (Table 5)

A. Initial Resuscitation

1. Protocolized, quantitative resuscitation of patients with sepsis- induced tissue hypoperfusion (defined in this document as hypotension persisting after initial fluid challenge or blood lactate concentration ≥ 4 mmol/L). Goals during the first 6 hrs of resuscitation:

- a) Central venous pressure 8–12 mm Hg
- b) Mean arterial pressure (MAP) ≥ 65 mm Hg
- c) Urine output ≥ 0.5 mL/kg/hr
- d) Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively (grade 1C).

2. In patients with elevated lactate levels targeting resuscitation to normalize lactate (grade 2C).

B. Screening for Sepsis and Performance Improvement

1. Routine screening of potentially infected seriously ill patients for severe sepsis to allow earlier implementation of therapy (grade 1C).

2. Hospital-based performance improvement efforts in severe sepsis (UG).

C. Diagnosis

1. Cultures as clinically appropriate before antimicrobial therapy if no significant delay (> 45 mins) in the start of antimicrobial(s) (grade 1C). At least 2 sets of blood cultures (both aerobic and anaerobic bottles) be obtained before antimicrobial therapy with at least 1 drawn percutaneously and 1 drawn through each vascular access device, unless the device was recently (<48 hrs) inserted (grade 1C).
2. Use of the 1,3 beta-D-glucan assay (grade 2B), mannan and anti-mannan antibody assays (2C), if available and invasive candidiasis is in differential diagnosis of cause of infection.
3. Imaging studies performed promptly to confirm a potential source of infection (UG).

D. Antimicrobial Therapy

1. Administration of effective intravenous antimicrobials within the first hour of recognition of septic shock (grade 1B) and severe sepsis without septic shock (grade 1C) as the goal of therapy.
 - 2a. Initial empiric anti-infective therapy of one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into tissues presumed to be the source of sepsis (grade 1B).
 - 2b. Antimicrobial regimen should be reassessed daily for potential deescalation (grade 1B).
3. Use of low procalcitonin levels or similar biomarkers to assist the clinician in the discontinuation of empiric antibiotics in patients who initially appeared septic, but have no subsequent evidence of infection (grade 2C).
- 4a. Combination empirical therapy for neutropenic patients with severe sepsis (grade 2B) and for patients with difficult-to-treat, multidrug-resistant bacterial pathogens such as *Acinetobacter* and *Pseudomonas* spp. (grade 2B). For patients with severe infections associated with respiratory failure and septic shock, combination therapy with an extended spectrum beta-lactam and either an aminoglycoside or a fluoroquinolone is for *P. aeruginosa* bacteremia (grade 2B). A combination of beta-lactam and macrolide for patients with septic shock from bacteremic *Streptococcus pneumoniae* infections (grade 2B).
- 4b. Empiric combination therapy should not be administered for more than 3–5 days. De-escalation to the most appropriate single therapy should be performed as soon as the susceptibility profile is known (grade 2B).
5. Duration of therapy typically 7–10 days; longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteremia with *S. aureus*; some fungal and viral infections or immunologic deficiencies, including neutropenia (grade 2C).

6. Antiviral therapy initiated as early as possible in patients with severe sepsis or septic shock of viral origin (grade 2C).

7. Antimicrobial agents should not be used in patients with severe inflammatory states determined to be of noninfectious cause (UG).

E. Source Control

1. A specific anatomical diagnosis of infection requiring consideration for emergent source control be sought and diagnosed or excluded as rapidly as possible, and intervention be undertaken for source control within the first 12 hr after the diagnosis is made, if feasible (grade 1C).

2. When infected peripancreatic necrosis is identified as a potential source of infection, definitive intervention is best delayed until adequate demarcation of viable and nonviable tissues has occurred (grade 2B).

3. When source control in a severely septic patient is required, the effective intervention associated with the least physiologic insult should be used (eg, percutaneous rather than surgical drainage of an abscess) (UG).

4. If intravascular access devices are a possible source of severe sepsis or septic shock, they should be removed promptly after other vascular access has been established (UG).

F. Infection Prevention

1a. Selective oral decontamination and selective digestive decontamination should be introduced and investigated as a method to reduce the incidence of ventilator-associated pneumonia; This infection control measure can then be instituted in health care settings and regions where this methodology is found to be effective (grade 2B).

1b. Oral chlorhexidine gluconate be used as a form of oropharyngeal decontamination to reduce the risk of ventilator-associated pneumonia in ICU patients with severe sepsis (grade 2B).

Recommendations: Hemodynamic Support and Adjunctive Therapy (Table 6)

G. Fluid Therapy of Severe Sepsis

1. Crystalloids as the initial fluid of choice in the resuscitation of severe sepsis and septic shock (grade 1B).

2. Against the use of hydroxyethyl starches for fluid resuscitation of severe sepsis and septic shock (grade 1B).

3. Albumin in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids (grade 2C).

4. Initial fluid challenge in patients with sepsis-induced tissue hypoperfusion with suspicion of hypovolemia to achieve a minimum of 30 mL/kg of crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid may be needed in some patients (grade 1C).

5. Fluid challenge technique be applied wherein fluid administration is continued as long as there is hemodynamic improvement either based on dynamic (eg, change in pulse pressure, stroke volume variation) or static (eg, arterial pressure, heart rate) variables (UG).

H. Vasopressors

1. Vasopressor therapy initially to target a mean arterial pressure (MAP) of 65 mm Hg (grade 1C).

2. Norepinephrine as the first choice vasopressor (grade 1B).

3. Epinephrine (added to and potentially substituted for norepinephrine) when an additional agent is needed to maintain adequate blood pressure (grade 2B).

4. Vasopressin 0.03 units/minute can be added to norepinephrine (NE) with intent of either raising MAP or decreasing NE dosage (UG).

5. Low dose vasopressin is not recommended as the single initial vasopressor for treatment of sepsis-induced hypotension and vasopressin doses higher than 0.03-0.04 units/minute should be reserved for salvage therapy (failure to achieve adequate MAP with other vasopressor agents) (UG).

6. Dopamine as an alternative vasopressor agent to norepinephrine only in highly selected patients (eg, patients with low risk of tachyarrhythmias and absolute or relative bradycardia) (grade 2C).

7. Phenylephrine is not recommended in the treatment of septic shock except in circumstances where (a) norepinephrine is associated with serious arrhythmias, (b) cardiac output is known to be high and blood pressure persistently low or (c) as salvage therapy when combined inotrope/vasopressor drugs and low dose vasopressin have failed to achieve MAP target (grade 1C).

8. Low-dose dopamine should not be used for renal protection (grade 1A).

9. All patients requiring vasopressors have an arterial catheter placed as soon as practical if resources are available (UG).

I. Inotropic Therapy

1. A trial of dobutamine infusion up to 20 micrograms/kg/min be administered or added to vasopressor (if in use) in the presence of (a) myocardial dysfunction as suggested by elevated cardiac filling pressures and low cardiac output, or (b) ongoing signs of

hypoperfusion, despite achieving adequate intravascular volume and adequate MAP (grade 1C).

2. Not using a strategy to increase cardiac index to predetermined supranormal levels (grade 1B).

J. Corticosteroids

1. Not using intravenous hydrocortisone to treat adult septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (see goals for Initial Resuscitation). In case this is not achievable, we suggest intravenous hydrocortisone alone at a dose of 200 mg per day (grade 2C).

2. Not using the ACTH stimulation test to identify adults with septic shock who should receive hydrocortisone (grade 2B).

3. In treated patients hydrocortisone tapered when vasopressors are no longer required (grade 2D).

4. Corticosteroids not be administered for the treatment of sepsis in the absence of shock (grade 1D).

5. When hydrocortisone is given, use continuous flow (grade 2D).

Recommendations: Other Supportive Tx of Severe Sepsis (Table 7)

K. Blood Product Administration

1. Once tissue hypoperfusion has resolved and in the absence of extenuating circumstances, such as myocardial ischemia, severe hypoxemia, acute hemorrhage, or ischemic heart disease, we recommend that red blood cell transfusion occur only when hemoglobin concentration decreases to <7.0 g/dL to target a hemoglobin concentration of 7.0–9.0 g/dL in adults (grade 1B).

2. Not using erythropoietin as a specific treatment of anemia associated with severe sepsis (grade 1B).

3. Fresh frozen plasma not be used to correct laboratory clotting abnormalities in the absence of bleeding or planned invasive procedures (grade 2D).

4. Not using antithrombin for the treatment of severe sepsis and septic shock (grade 1B).

5. In patients with severe sepsis, administer platelets prophylactically when counts are <10,000/mm³ (10 x 10⁹/L) in the absence of apparent bleeding. We suggest prophylactic platelet transfusion when counts are < 20,000/mm³ (20 x 10⁹/L) if the patient has a significant risk of bleeding. Higher platelet counts (≥50,000/mm³ [50 x 10⁹/L]) are advised for active bleeding, surgery, or invasive procedures (grade 2D).

L. Immunoglobulins

1. Not using intravenous immunoglobulins in adult patients with severe sepsis or septic shock (grade 2B).

M. Selenium

1. Not using intravenous selenium for the treatment of severe sepsis (grade 2C).

N. History of Recommendations Regarding Use of Recombinant Activated Protein C (rhAPC)

A history of the evolution of SSC recommendations as to rhAPC (no longer available) is provided.

O. Mechanical Ventilation of Sepsis-Induced Acute Respiratory Distress Syndrome (ARDS)

1. Target a tidal volume of 6 mL/kg predicted body weight in patients with sepsis-induced ARDS (grade 1A vs. 12 mL/kg).
2. Plateau pressures be measured in patients with ARDS and initial upper limit goal for plateau pressures in a passively inflated lung be ≤ 30 cm H₂O (grade 1B).
3. Positive end-expiratory pressure (PEEP) be applied to avoid alveolar collapse at end expiration (atelectotrauma) (grade 1B).
4. Strategies based on higher rather than lower levels of PEEP be used for patients with sepsis-induced moderate or severe ARDS (grade 2C).
5. Recruitment maneuvers be used in sepsis patients with severe refractory hypoxemia (grade 2C).
6. Prone positioning be used in sepsis-induced ARDS patients with a Pao₂/Fio₂ ratio ≤ 100 mm Hg in facilities that have experience with such practices (grade 2B).
7. That mechanically ventilated sepsis patients be maintained with the head of the bed elevated to 30-45 degrees to limit aspiration risk and to prevent the development of ventilator-associated pneumonia (grade 1B).
8. That noninvasive mask ventilation (NIV) be used in that minority of sepsis-induced ARDS patients in whom the benefits of NIV have been carefully considered and are thought to outweigh the risks (grade 2B).
9. That a weaning protocol be in place and that mechanically ventilated patients with severe sepsis undergo spontaneous breathing trials regularly to evaluate the ability to discontinue mechanical ventilation when they satisfy the following criteria: a) arousable; b) hemodynamically stable (without vasopressor agents); c) no new potentially serious conditions; d) low ventilatory

and end-expiratory pressure requirements; and e) low Fio₂ requirements which can be met safely delivered with a face mask or nasal cannula. If the spontaneous breathing trial is successful, consideration should be given for extubation (grade 1A).

10. Against the routine use of the pulmonary artery catheter for patients with sepsis-induced ARDS (grade 1A).

11. A conservative rather than liberal fluid strategy for patients with established sepsis-induced ARDS who do not have evidence of tissue hypoperfusion (grade 1C).

12. In the absence of specific indications such as bronchospasm, not using beta 2-agonists for treatment of sepsis-induced ARDS (grade 1B).

P. Sedation, Analgesia, and Neuromuscular Blockade in Sepsis

1. Continuous or intermittent sedation be minimized in mechanically ventilated sepsis patients, targeting specific titration endpoints (grade 1B).

2. Neuromuscular blocking agents (NMBAs) be avoided if possible in the septic patient *without* ARDS due to the risk of prolonged neuromuscular blockade following discontinuation. If NMBAs must be maintained, either intermittent bolus as required or continuous infusion with train-of-four monitoring of the depth of blockade should be used (grade 1C).

3. A short course of NMBA of not greater than 48 hours for patients *with* early sepsis-induced ARDS and a Pao₂/Fio₂ < 150 mm Hg (grade 2C).

Q. Glucose Control

1. A protocolized approach to blood glucose management in ICU patients with severe sepsis commencing insulin dosing when

2 consecutive blood glucose levels are >180 mg/dL. This protocolized approach should target an upper blood glucose ≤180 mg/dL rather than an upper target blood glucose ≤110 mg/dL (grade 1A).

2. Blood glucose values be monitored every 1–2 hrs until glucose values and insulin infusion rates are stable and then every 4 hrs thereafter (grade 1C).

3. Glucose levels obtained with point-of-care testing of capillary blood be interpreted with caution, as such measurements may not accurately estimate arterial blood or plasma glucose values (UG).

R. Renal Replacement Therapy

1. Continuous renal replacement therapies and intermittent hemodialysis are equivalent in patients with severe sepsis and acute renal failure (grade 2B).

2. Use continuous therapies to facilitate management of fluid balance in hemodynamically unstable septic patients (grade 2D).

S. Bicarbonate Therapy

1. Not using sodium bicarbonate therapy for the purpose of improving hemodynamics or reducing vasopressor requirements in patients with hypoperfusion-induced lactic acidemia with pH ≥ 7.15 (grade 2B).

T. Deep Vein Thrombosis Prophylaxis

1. Patients with severe sepsis receive daily pharmacoprophylaxis against venous thromboembolism (VTE) (grade 1B). This should be accomplished with daily subcutaneous low-molecular weight heparin (LMWH) (grade 1B versus twice daily UFH, grade 2C

versus three times daily UFH). If creatinine clearance is <30 mL/min, use dalteparin (grade 1A) or another form of LMWH that has a low degree of renal metabolism (grade 2C) or UFH (grade 1A).

2. Patients with severe sepsis be treated with a combination of pharmacologic therapy and intermittent pneumatic compression devices whenever possible (grade 2C).

3. Septic patients who have a contraindication for heparin use (eg, thrombocytopenia, severe coagulopathy, active bleeding, recent intracerebral hemorrhage) not receive pharmacoprophylaxis (grade 1B), but receive mechanical prophylactic treatment, such as graduated compression stockings or intermittent compression devices (grade 2C), unless contraindicated. When the risk decreases start pharmacoprophylaxis (grade 2C).

U. Stress Ulcer Prophylaxis

1. Stress ulcer prophylaxis using H2 blocker or proton pump inhibitor be given to patients with severe sepsis/septic shock who have bleeding risk factors (grade 1B).

2. When stress ulcer prophylaxis is used, proton pump inhibitors rather than H2RA (grade 2D)

3. Patients without risk factors do not receive prophylaxis (grade 2B).

V. Nutrition

1. Administer oral or enteral (if necessary) feedings, as tolerated, rather than either complete fasting or provision of only intravenous glucose within the first 48 hours after a diagnosis of severe sepsis/septic shock (grade 2C).

2. Avoid mandatory full caloric feeding in the first week but rather suggest low dose feeding (eg, up to 500 calories per day), advancing only as tolerated (grade 2B).

3. Use intravenous glucose and enteral nutrition rather than total parenteral nutrition (TPN) alone or parenteral nutrition in conjunction with enteral feeding in the first 7 days after a diagnosis of severe sepsis/septic shock (grade 2B).

4. Use nutrition with no specific immunomodulating supplementation rather than nutrition providing specific immunomodulating supplementation in patients with severe sepsis (grade 2C).

W. Setting Goals of Care

1. Discuss goals of care and prognosis with patients and families (grade 1B).
2. Incorporate goals of care into treatment and end-of-life care planning, utilizing palliative care principles where appropriate (grade 1B).
3. Address goals of care as early as feasible, but no later than within 72 hours of ICU admission (grade 2C).

Distributive Shock

Neurogenic, anaphylactic and septic shock are also known as distributive shock because of the relative hypovolemia that occurs in each due to massive vasodilation.

Signs & Symptoms Of Distributive Shock

Signs & Symptoms	Septic	Neurogenic	Anaphylactic
Blood Pressure	Low	Low	Low
Heart Rate	High	Low	High
Cardiac Output	High/Low	Low	Low
Temperature	High	Normal	High
Skin	Warm/Cold	Warm	Warm
Respiratory Rate	High	High	High
WBC	High	Normal	High
Sympathetic NS	Stimulated	Blocked	Stimulated
Edema	Present	Absent	Present
Bronchospasm	Absent	Absent	Present

Rauen, C., Munro, N. (1998). Shock. In Kinney, M. *AACN Clinical Reference for Critical Care Nursing*. Pg 1157

Initial Hemodynamic Parameters in Shock States

Shock State	HR	BP	CO	PAPs	CVP	PAOP	SVR
Hypovolemic	High	Low	Low	Low	Low	Low	High
Cardiogenic	High	Low	Low	High	High	High	High
Neurogenic		Low	Low	Low	Low	Low	Low

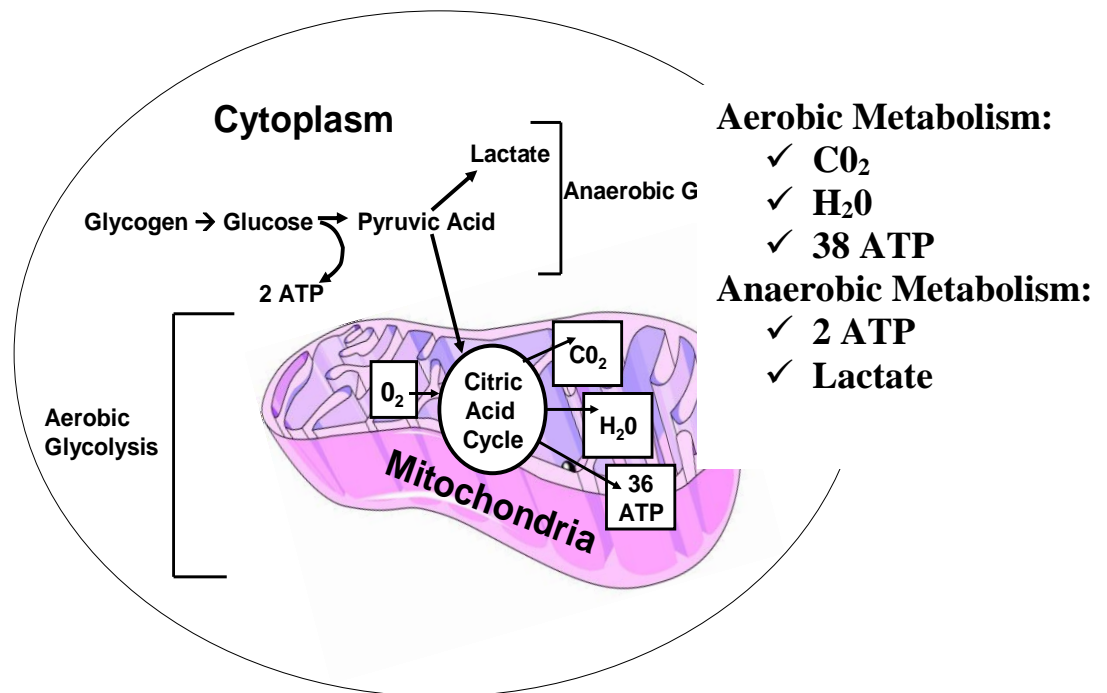
Anaphylactic	High	Low	High/ Low	Low	Low	Low	Low
Septic	High	Low	High/ Low	Low	Low	Low	Low

C. STAGES OF SHOCK

All of the shock states cause hypoperfusion. There is inadequate oxygen supply to the tissue resulting from hypoperfusion, decreased blood pressure, and inadequate cardiac output. A supply/demand imbalance develops and the patient moves into anaerobic metabolism and lactic acidosis. Many physiologic mechanisms in the body delay this occurrence by compensating for the perfusion deficit.

Rauen & Munro, 1998

1. Aerobic vs Anaerobic Metabolism



2. Stage 1 – Compensatory Stage

As inadequate perfusion persists and significant numbers of cells are affected, an imbalance of oxygen supply and demand occurs. Hypoxemia, hypotension, and acidosis activate the body's compensatory mechanisms. The physiological goal of

compensation is to supply or improve oxygenation and perfusion to the cells.

- ✓ Neural Response
- ✓ Hormonal Response
- ✓ Chemical Response

Goal

Improve Cardiac Output and Oxygen Delivery

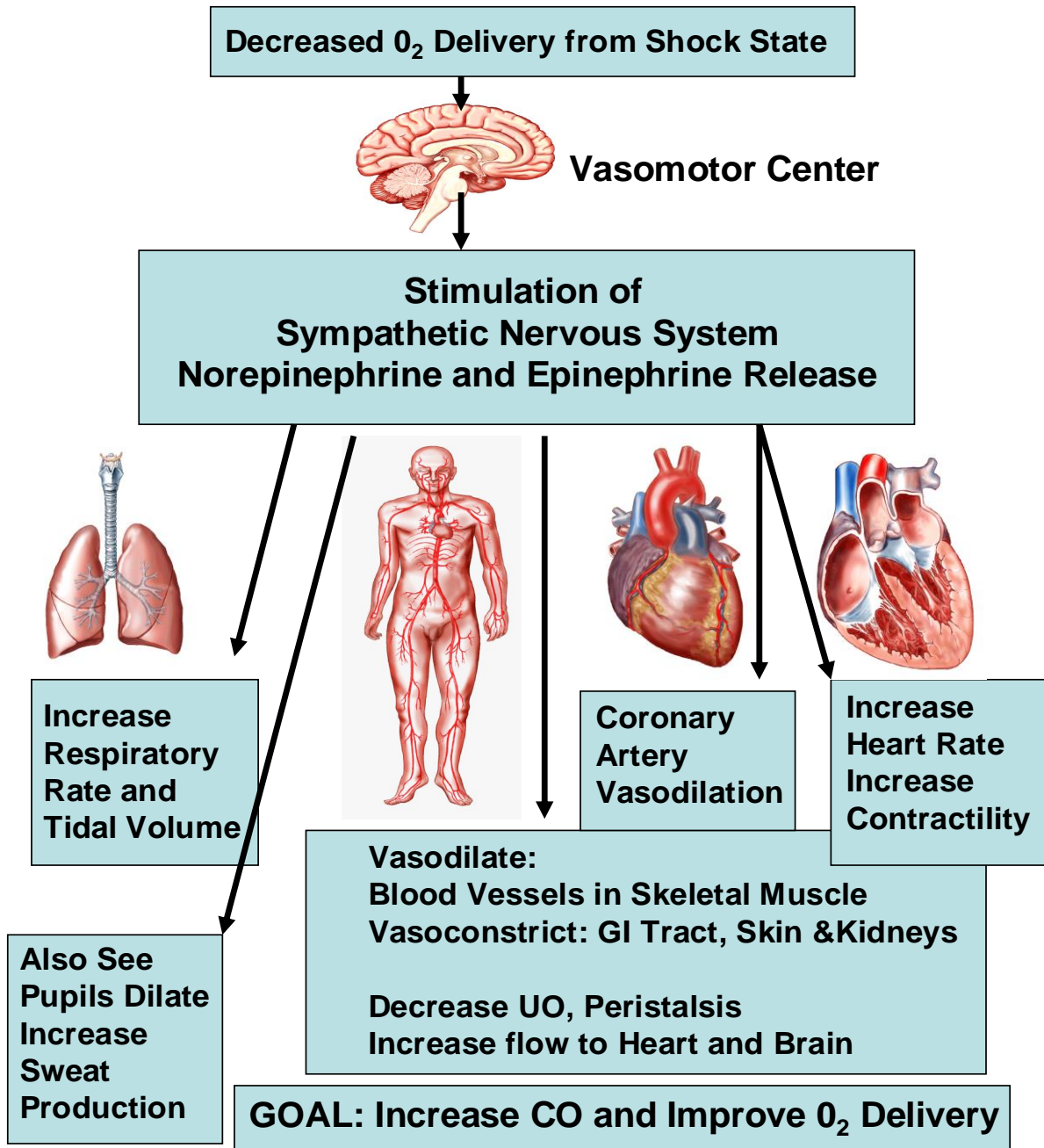
Mechanisms

Activated Sympathetic Nervous System

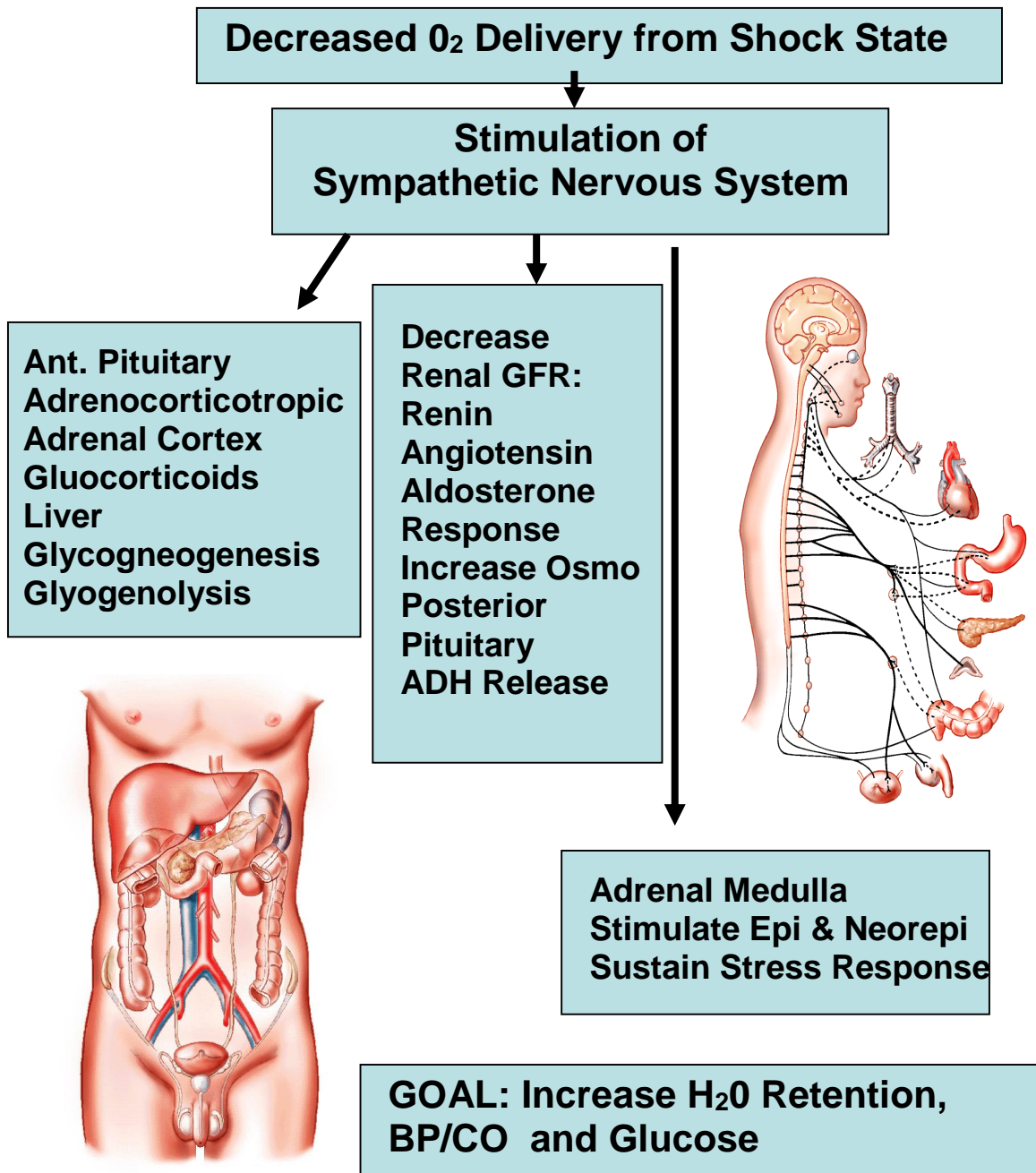
Renin/Angiotensin/Aldosterone System

Chemoreceptor Stimulated Respiratory Alkalosis

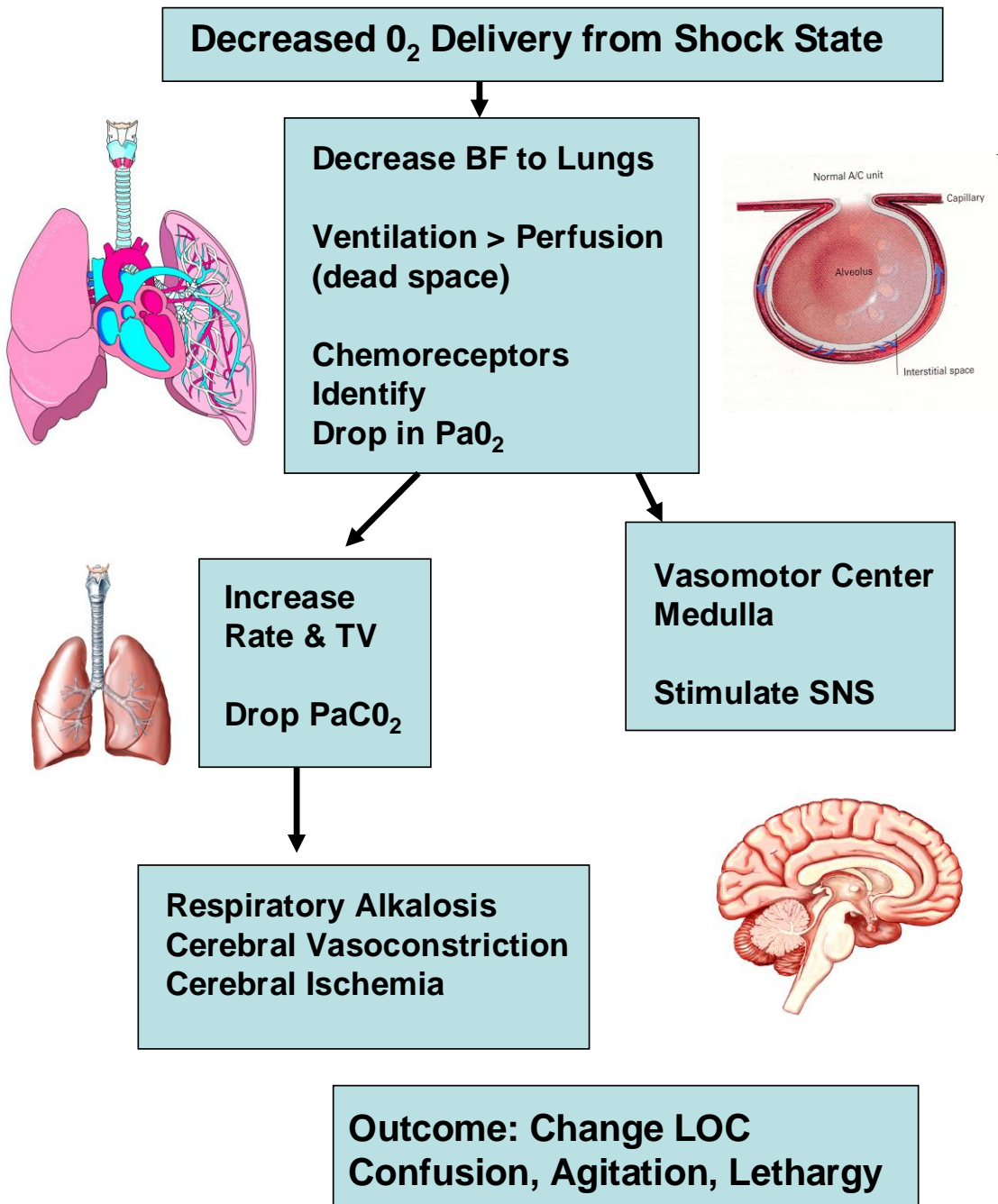
Stage 1
Compensation
Neural Compensation



Stage 1
Compensation
Hormonal Compensation



Stage 1
Compensation
Chemical Compensation



3. **Stage 2 – Decompensatory Stage**

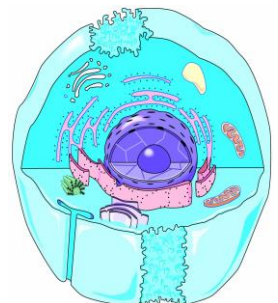
As shock progresses, the compensatory mechanisms begin to fail. The progression of shock is evident at the cellular, organ, and system levels; and extensive physiological dysfunctions occur. The arteriolar and precapillary sphincters require sufficient energy in the form of adenosine triphosphate (ATP) to maintain a vasoconstrictive state. As energy dissipates with the progression of shock, the sphincters relax, allowing blood to flow into organs and sequester. Sludging of the blood in these capillary beds occurs, and the microcirculation becomes blocked. Metabolic waste products, microaggregates of platelets, white blood cells, and clots accumulate, further enhancing sludging and contributing to the development of metabolic acidosis. In response to these events chemical mediators are released that are harmful to the microcirculation and general system function. This will be reviewed in more detail in the cellular response to shock section.

4. **Stage 3 – Irreversible Stage**

This is the final stage of shock. It is also referred to as the refractory phase because the body systems are no longer responsive to treatment. As each organ system decompensates and requires more and more support, they reach a point where therapeutic measures are no longer effective in maintaining function. The term irreversible is appropriate because it is at this point when several, if not all, of the systems cross the line from organ dysfunction to organ failure.

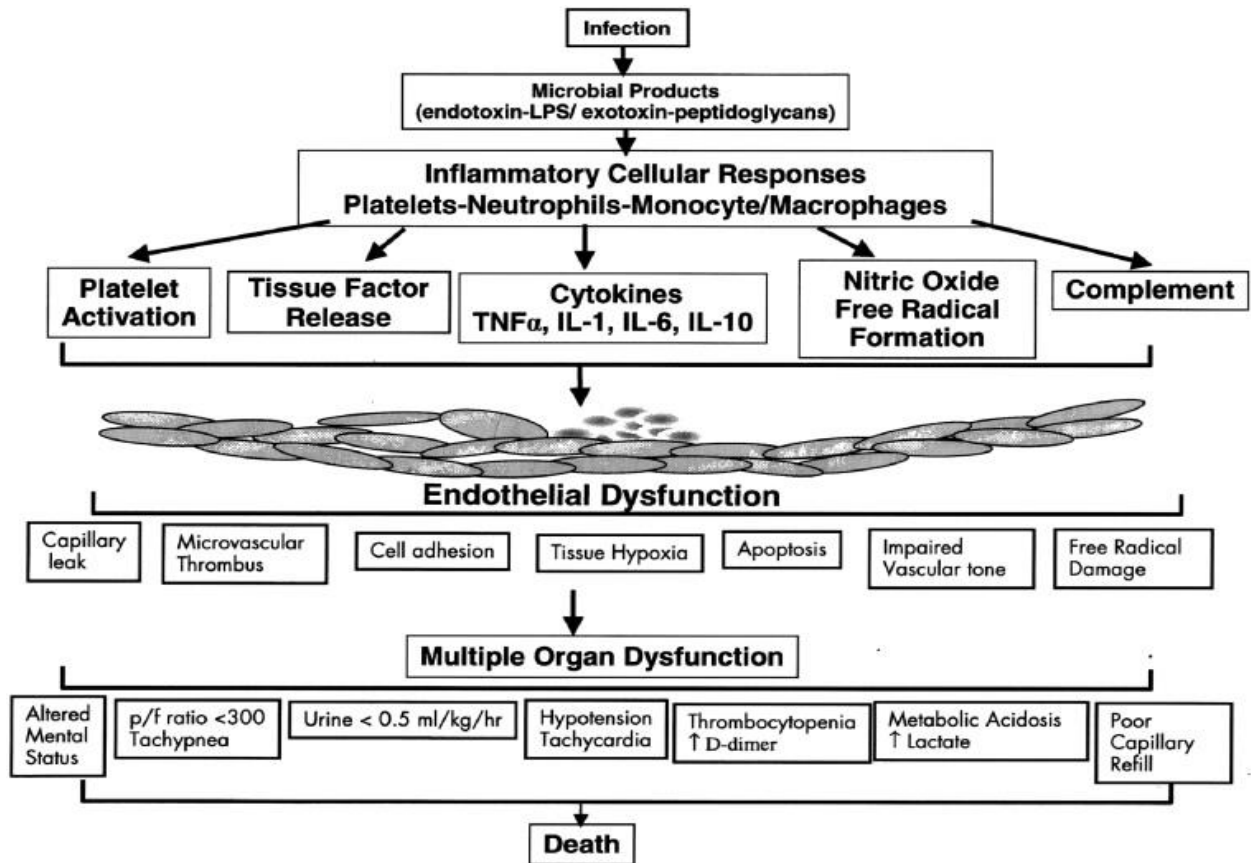
D. Cellular Response to Shock

By definition shock is an imbalance between oxygen supply and demand. The resultant hypoxia and/or ischemia initiate a cascade of tissue, organ and cellular responses/reactions. These reactions are intended to assist with shock compensation and healing but when left unregulated actually become the source of further chaos.



MECHANISM OF CELLULAR INJURY

Overview

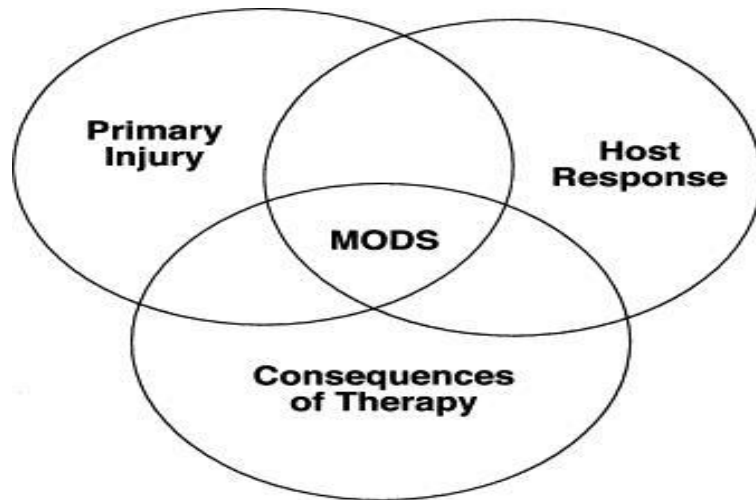


Summary of sepsis pathology. Reprinted with permission of Eli Lilly and Company; Copyright 2003.

VI. MODS

MODS: Multiple Organ Dysfunction Syndrome: the presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention.

1. Risk Factors & Common Causes



Khadaroo, R., Marshall, J. (2002). ARDS and the multiple organ dysfunction syndrome. *Crit Care Clinics*, 18(1).

Primary Injury Factors

- ⇒ Hypovolemic Shock – Hemorrhage
- ⇒ Trauma – Penetrating Abd Trauma
- ⇒ ARDS
- ⇒ Infection
- ⇒ Prolonged Intestinal Ischemia
- ⇒ Hypoperfusion States – Perfusion Deficit
- ⇒ Sepsis
- ⇒ Pregnancy – Prolonged Membrane Rupture

Host Related Factors

- ⇒ Extremes of Age
- ⇒ Malnutrition
- ⇒ Chronic Disease – CRF, DM, COPD
- ⇒ Debilitated States
- ⇒ Stress
- ⇒ IV Drug or ETOH Abuse
- ⇒ Vascular Insufficiency
- ⇒ Splenectomy

Consequences of Therapy

- ⇒ Massive Fluid or Blood Therapy

- ⇒ Immunosuppressive Therapy
- ⇒ Antibiotic Therapy
- ⇒ Prolonged ICU Course
- ⇒ Intubated Longer Than 2 Days
- ⇒ Invasive lines, Catheters, Devices
- ⇒ Surgery or Anesthesia

2. **Sequential Organ Dysfunction**

** Indicates parameter from 2001 SCCM/ESCM/ACCP/ATS/SIS
International Sepsis Definitions Conference

PULMONARY SYSTEM Day 2.3

** Arterial Hypoxemia ($\text{PaO}_2/\text{FiO}_2 < 300$)

THEORY
Respiratory Rate $5 \leq \text{bpm}$ or ≥ 49
$\text{PaO}_2 < 60\text{mmHg}$ on $\text{FiO}_2 > 50\%$
Serum pH ≤ 7.24 with $\text{PaCO}_2 \geq 49$ torr
Five or more days on the ventilator
Progressive ARDS <ul style="list-style-type: none"> ✓ PEEP $> 10\text{cmH}_2\text{O}$ ✓ $\text{FiO}_2 > 50\%$ ✓ Diffuse Infiltrates on Chest X-ray

HEPATIC SYSTEM Day 5.9

**Hyperbilirubinemia (plasma total Bilirubin $> 4\text{mg/dL}$)

THEORY
Bilirubin $> 2.0\text{mg/dL}$
With any of the following
Clinical Jaundice
Elevated Liver enzymes
Elevated Blood Ammonia
Albumin $< 2.8\text{gm/dL}$
Refractory Hyperglycemia

HEMATOLOGIC SYSTEM Day 5

**** Coagulation Abnormalities (INR > 1.5 or APT > 60sec)**

**** Thrombocytopenia (platelet ct < 100,000)**

THEORY
Prolonged Bleeding
Thrombocytopenia
Disseminated Intravascular Coagulation

GASTROINTESTINAL SYSTEM Day 9.5

**** Ileus (absent bowel sounds)**

THEORY
Stress Ulcer
Pancreatitis
Ileus w NG output > 600cc/24 hr (one of the above three with the below)
Inability to Tolerate TF Despite no intestinal obstruction
Gastric Bleeding
Bacterial Growth in Stool Culture

RENAL SYSTEM Day 11.6

**** Acute Oliguria (UO < 0.5ml/kg/hr)**

**** Creatinine Increased > 0.5mg/dL**

THEORY
BUN \geq 100mg/dL
Creatinine \geq 3.5 mg/dL or double admission
Urine Output \leq 20cc/hr or 500cc/24 hr
Creatinine Clearance < 30 ml/min
Requiring Dialysis

NEUROLOGIC SYSTEM

THEORY
Glasgow Coma Score \leq 6
Decreased Level of Consciousness
Confusion is an early marker, followed by progressive obtundation advancing to coma

CARDIOVASCULAR SYSTEM

THEORY
Heart Rate ≤ 54 bpm
SBP < 90 mmHg > 1 hr
MAP ≤ 49 mmHg
CI < 1.5 L/min/m ²
PAOP > 20 mmHg
Intractable Dysrhythmias
Inotropic Support for Tissue Perfusion
Capillary Leak Syndrome

Mortality Prediction

Organ Failure Mortality

# FAILED ORGANS	MORTALITY RATE
Single Organ Failure	10-40%
Two Organ Failure	41-67%
Three Organ Failure	60-100%
Four Organ Failure	100%

VII. SUMMARY