Hemodynamic Disorders V

SHOCK

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Disseminated Intravascular Coagulation (DIC)

+ Widespread thrombosis within microcirculation that may be of sudden (acute) or insidious onset.

+ Life threatening disorder (Death is coming!)

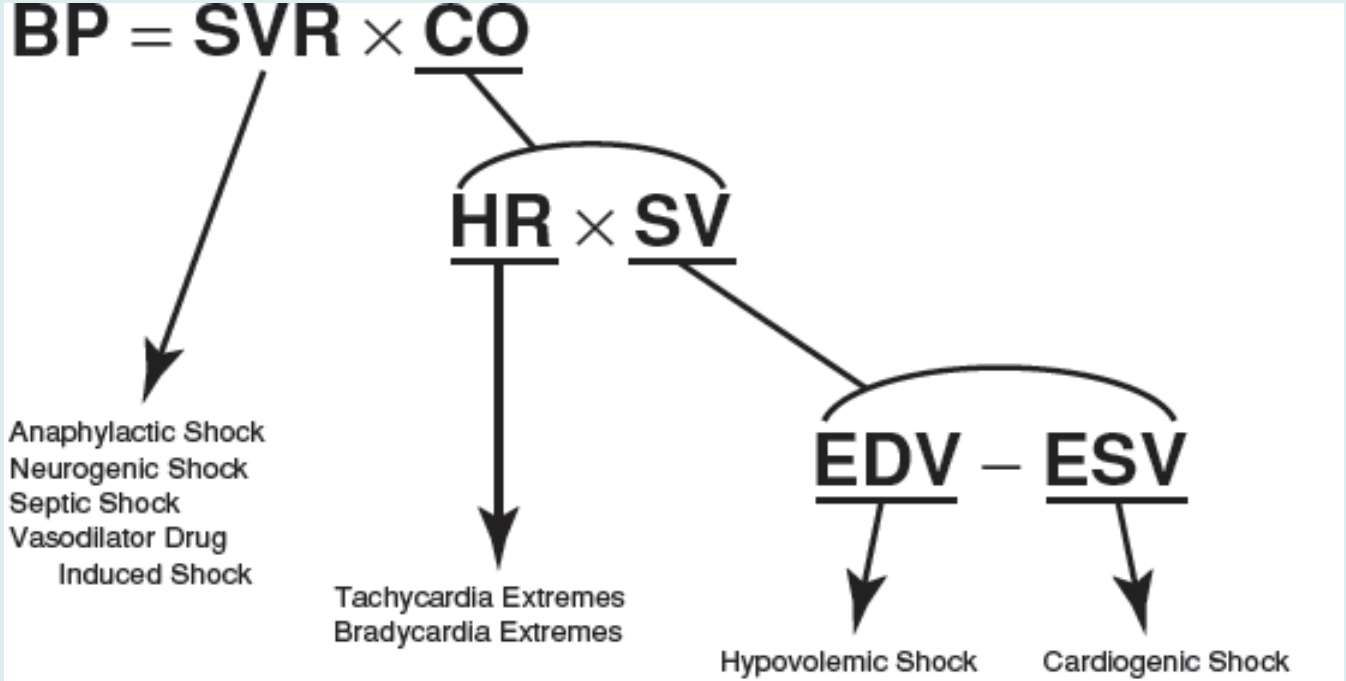
+ Seen as a complication in many settings starting from obstetric complications to advanced malignancy.

+ The widespread microvascular thrombosis consumes platelets and coagulation proteins (hence the synonym consumptive coagulopathy), also, fibrinolytic mechanisms are activated.

+ The net result is that excessive clotting and bleeding may co-exist in the same patient.

SHOCK!

- Commonly misused “psychogenic”
- A state in which diminished cardiac output or reduced effective circulating blood volume impairs tissue perfusion and leads to cellular hypoxia.



BP = blood pressure, SVR = systemic vascular resistance, HR = heart rate, SV = stroke volume, EDV = end diastolic volume (i.e. preload), ESV = end systolic volume (i.e. contractility)

Source: Stone CK, Humphries RL: *Current Diagnosis & Treatment: Emergency Medicine, 7th Edition:* www.accessmedicine.com

Shock fall into three general categories:

Cardiogenic shock

Low cardiac output (myocardial pump failure).

Caused by myocardial damage (infarction), ventricular arrhythmias, extrinsic compression (cardiac tamponade), or outflow obstruction (PE).

Hypovolemic shock

Low cardiac output due to loss of blood or plasma volume (hemorrhage or fluid loss from severe burns)

Septic shock

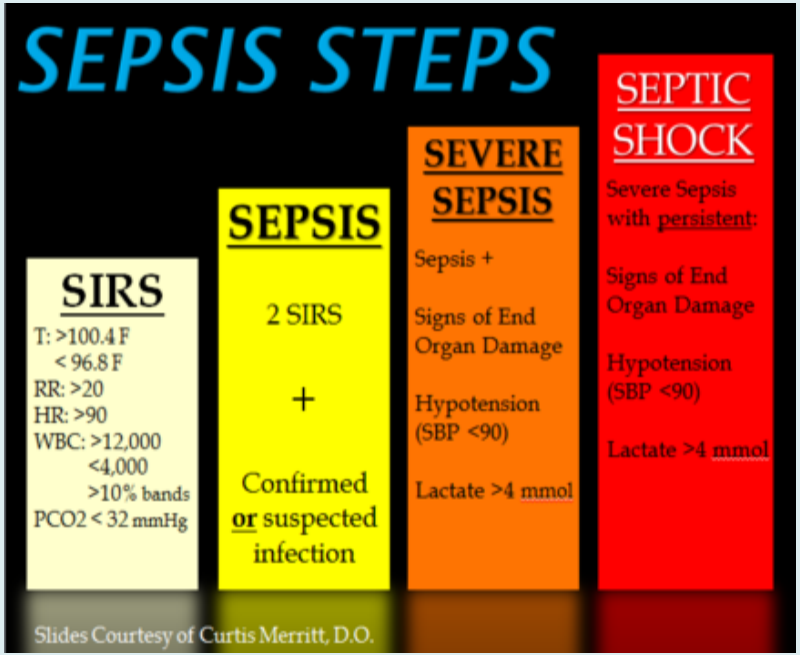
Triggered by microbial infections.

associated with severe systemic inflammatory response syndrome (SIRS).

Type of Shock	Clinical Examples	Principal Pathogenic Mechanisms
Cardiogenic	Myocardial infarction Ventricular rupture Arrhythmia Cardiac tamponade Pulmonary embolism	Failure of myocardial pump resulting from intrinsic myocardial damage, extrinsic pressure, or obstruction to outflow
Hypovolemic	Hemorrhage Fluid loss (e.g., vomiting, diarrhea, burns, trauma)	Inadequate blood or plasma volume
Septic	Overwhelming microbial infections Gram-negative sepsis Gram-positive septicemia Fungal sepsis Superantigens (e.g., toxic shock syndrome)	Peripheral vasodilation and pooling of blood; endothelial activation/injury; leukocyte-induced damage; disseminated intravascular coagulation; activation of cytokine cascades

- At the start, cellular injury is reversible, but **prolonged shock eventually leads to irreversible tissue injury** and is often fatal
- Less commonly, shock can result from a loss of vascular tone associated with anesthesia or secondary to a spinal cord injury *(***neurogenic shock***)*. **Anaphylactic shock** results from systemic vasodilation and increased vascular permeability that is triggered by an immunoglobulin E–mediated hypersensitivity reaction

Septic shock



- US: 2% of all admissions (half of ICU)
- Septic shock incidence is increasing with time due to
  (1) Ironically, improvements in life support for critically ill patients.
  (2) Growing ranks of immunocompromised hosts (chemotherapy, immunosuppression, advanced age, or human immunodeficiency virus infection).
  (3) Increasing prevalence of multi-drug resistant organisms in the hospital setting

- Septic shock is most frequently triggered by gram positive bacterial infections, followed by gram-negative “endotoxic shock”.
- Microorganisms can cause septic shock because a variety of microbial constituents can trigger the process.
- Macrophages, neutrophils, dendritic cells, endothelial cells, and soluble components of the innate immune system (e.g., complement) recognize and are activated by several substances derived from microorganisms.
- These cells initiate a number of inflammatory responses that interact in a complex fashion to produce septic shock and multiorgan dysfunction.

Pathogenesis of Septic Shock

Inflammatory responses

Microbial cell wall constituents engage receptors on cells of the innate immune system:

(1) Toll-like receptors (TLRs) recognize substances containing “pathogen-associated molecular patterns” (PAMPs).

(2) G-protein–coupled receptors: detect bacterial peptides.

(3) C-type lectin receptors (e.g.,Dectins).

.. Inflammatory responses

- Activated immune cells produce numerous cytokines (TNF, IL-1, IFN-γ, IL-12, and IL-18,), inflammatory mediators (high-mobility group box 1 protein (HMGB1)).
- These molecules induce endothelial and other cells to upregulate adhesion molecule expression and further stimulate cytokine and chemokine production.
- The complement cascade is also activated by microbial components; anaphylotoxins (C3a, C5a), chemotactic fragments (C5a), and opsonins (C3b).

Counterinflammatory responses.

- Hyperinflammatory state triggers counterregulatory immunosuppressive mechanisms.
- Patients may oscillate between hyperinflammatory and immunosuppressed states during their clinical course.
- Counterregulatory mechanisms can result to immune suppression renders patients susceptible to superinfections.

.. Counterinflammatory responses.

(1) a shift from proinflammatory (TH1) to anti-inflammatory (TH2) cytokines.
(2) anti-inflammatory mediators (soluble TNF receptor, IL-1 receptor antagonist, and IL-10)
(3) lymphocyte apoptosis.
(4) Induction of cellular anergy (Lack of reaction).

Endothelial activation and injury

- Inflammatory cytokines loosen endothelial cells tight junctions → vessels leak → accumulation of protein-rich fluid throughout the body.
- This impedes tissue perfusion → hinders nutrient delivery & waste removal (this is exacerbated by Tx with intravenous fluids).
- Activated endothelium upregulates production of nitric oxide (NO), vasoactive mediators (C3a, C5a, and PAF), → contribute to vascular smooth muscle relaxation →systemic hypotension.

Induction of a procoagulant state

- Sepsis alters the expression of factors to favor coagulation.
- Proinflammatory cytokines increase tissue factor production & decrease the production of endothelial anti-coagulant factors. They also Dampen fibrinolysis (increasing plasminogen activator inhibitor-1)
- Vascular leak & edema decrease blood flow→ stasis → diminished washout of activated coagulation factors.
- *Produce DIC* in up to half of septic patients.

Metabolic abnormalities

- Hyperglycemia; cytokines (TNF & IL-1) stress-induced hormones (glucagon, growth hormone, and glucocorticoids), and catecholamines all drive gluconeogenesis.
- Insulin resistance; proinflammatory cytokines suppress insulin release & promot insulin resistance in liver and other tissues.
- Hyperglycemia decreases neutrophil bactericidal function & increased adhesion molecule on endothelial cells.

Metabolic abnormalities

- In sepsis, initially, an acute surge in glucocorticoid production happened, but it maybe followed by adrenal insufficiency:

(1) A functional deficit of glucocorticoids (depression of the synthetic capacity)

(2) Adrenal necrosis from DIC (*Waterhouse-Friderichsen syndrome*)

- Cellular hypoxia → diminished oxidative phosphorylation → increased lactate production & lactic acidosis (anaerobic glycolysis)

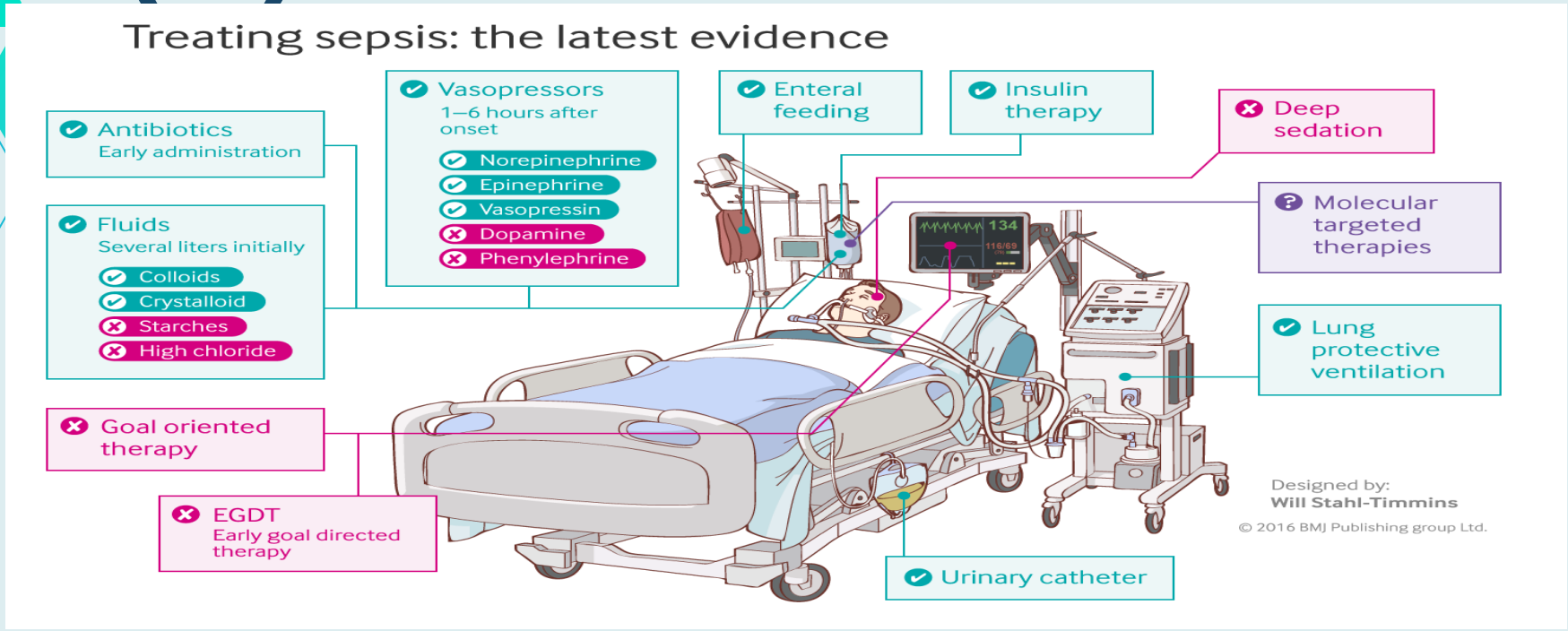
Organ dysfunction

- Systemic hypotension, interstitial edema, & small vessel thrombosis → decrease the delivery of oxygen & nutrients → cellular hypoxia.
- Mitochondrial damage from oxidative stress impairs oxygen use.
- Cytokines & secondary mediators diminish myocardial contractility & cardiac output.
- Vascular permeability & endothelial injury → *acute respiratory distress syndrome*
- All these factors cause multiple organs failure (kidneys, liver, lungs, and heart) → Death.

Severity and outcome of septic shock depends on:

- The extent and virulence of the infection,
- The immune status of the host,
- The presence of other comorbid conditions,
- Pattern and level of mediator production.

The multiplicity of factors & their complexity explain why attempts to intervene therapeutically with antagonists of specific mediators have not been effective & may had harmful effects in some cases.



Management

- Intravenous fluids, vasopressors, and supplemental oxygen to maintain blood pressure and limit tissue hypoxia.
- even in the best of clinical centers, septic shock remains an obstinate clinical challenge.

Stages of shock

- Shock is a progressive disorder that leads to death if the underlying problems are not corrected.
- Unless the insult is massive and rapidly, shock tends to evolve through three general stages. (documented most clearly in hypovolemic shock but are common to other forms as well)

An initial nonprogressive stage. Reflex compensatory mechanisms are activated and vital organ perfusion is maintained.

A progressive stage. Tissue hypoperfusion & onset of worsening circulatory & metabolic derangement, including acidosis.

An irreversible stage. Cellular & tissue injury is so severe that even if the hemodynamic defects are corrected, survival is not possible.

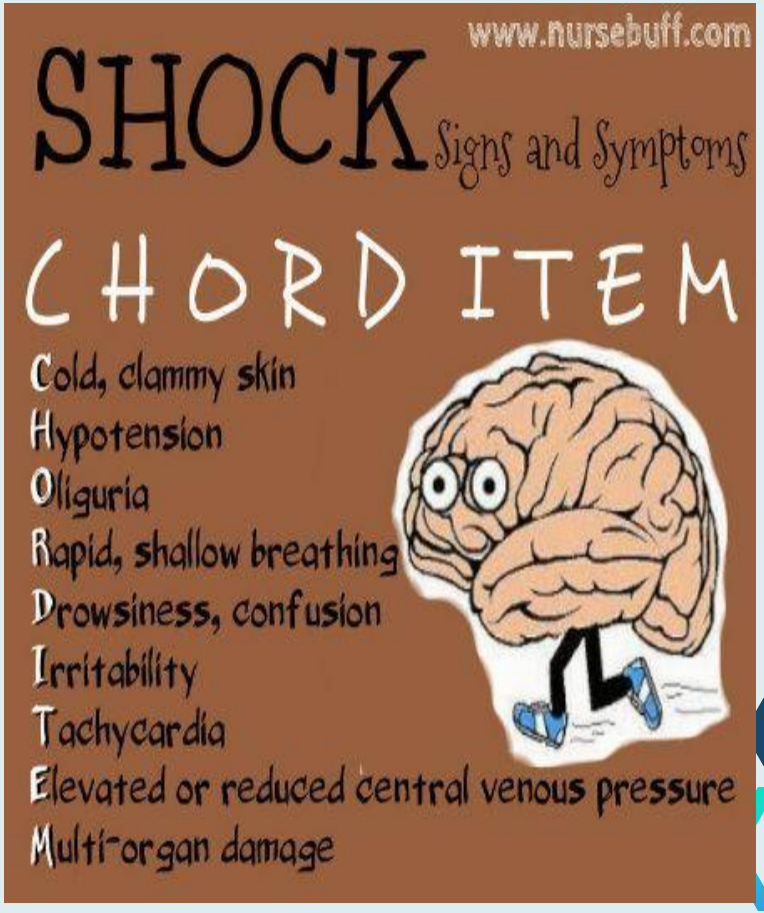
Neurohumoral mechanisms maintain cardiac output and blood pressure:

- Baroreceptor reflexes
- Release of catecholamines
- Anti-diuretic hormone.
- Activation of the renin-angiotensin-aldosterone axis.
- Generalized sympathetic stimulation.

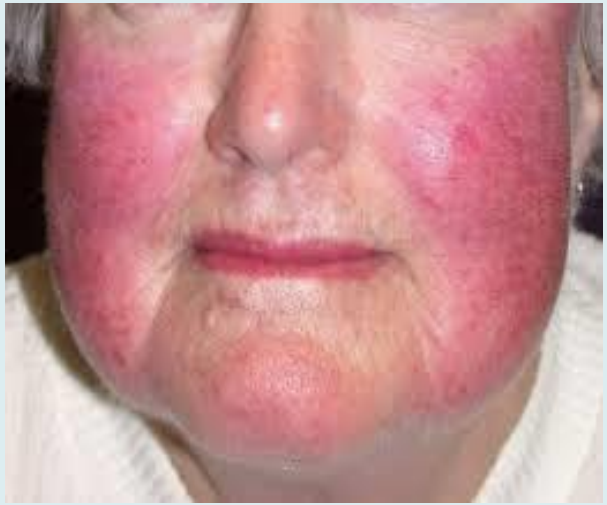
Net effect : tachycardia, peripheral vasoconstriction, & renal fluid conservation.
Coronary & cerebral vessels are less sensitive to sympathetic signals → maintain relatively normal caliber, blood flow, & oxygen delivery. Thus, blood is shunted away from the skin to the vital organs such as the heart & brain.

Prognosis varies with the origin of shock and its duration.

- More than 90% of young, otherwise healthy patients with hypovolemic shock survive with appropriate management.
- Septic & cardiogenic shock are associated with worse outcomes, even with state-of-the-art care.

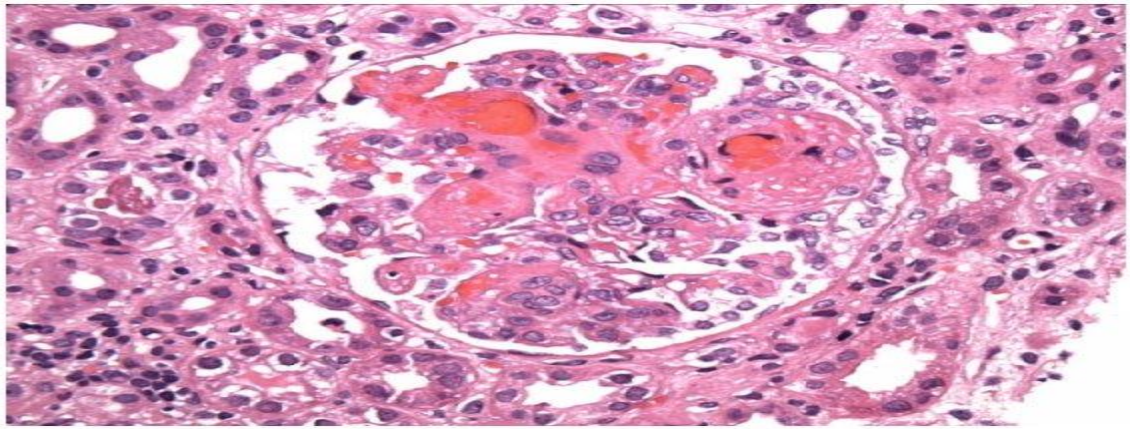


Cutaneous vasoconstriction causes the characteristic “shocky” skin coolness and pallor. Septic shock can initially cause cutaneous vasodilation, so the patient may present with warm, flushed skin.

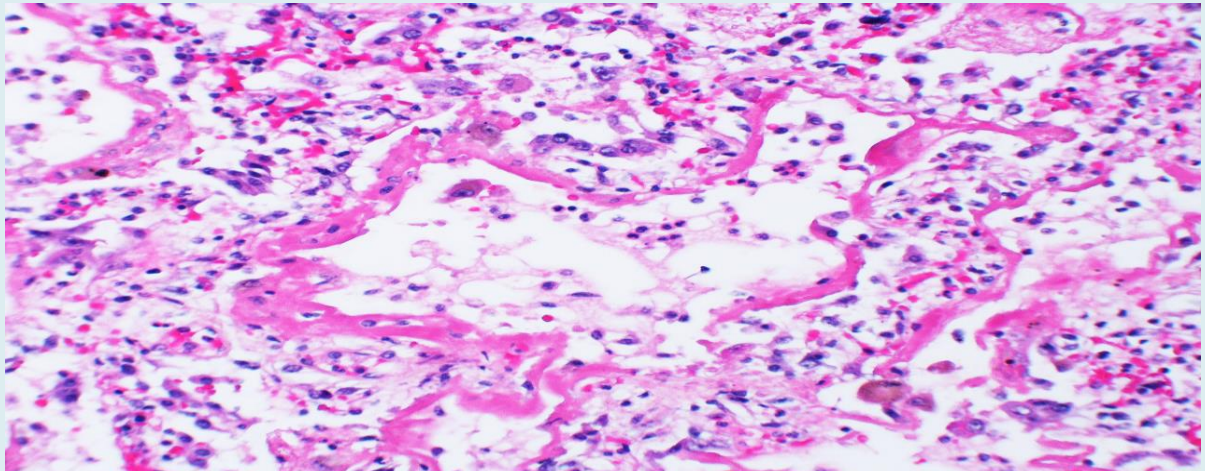


Morphology

- The cellular and tissue effects of shock are essentially those of hypoxic injury (combination of hypoperfusion & microvascular thrombosis)
- Any organ can be affected; the brain, heart, kidneys, adrenals, & gastrointestinal tract are most commonly involved.
- Fibrin thrombi can form in any tissue but typically are most readily visualized in kidney glomeruli.



- **Adrenal cortical cell lipid depletion** reflects increased use of stored lipids for steroid synthesis.
- **lungs are resistant to hypoxic injury in hypovolemic shock (e.g.; hemorrhage)**, but sepsis or trauma can precipitate diffuse alveolar damage
- Except for neuronal and myocyte ischemic loss, affected tissues can recover completely if the patient survives.



Thanks!

Any questions?