HAEMODYNAMIC DISORDERS, THROMBOEMBOLIC DISEASE, and SHOCK

TOPIC 5
SHOCK

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HOD, Pathology
MCWH

References:

- Robbins & Cotran Pathologic Basis of Disease- 9th edition
- Davidson's Principles and Practice of Medicine-23rd edition
- IMAGES- Above mentioned books & internet

CONTENTS

- Definition
- Types of shock
- Pathogenesis of different types of shock
- Stages of shock
- Morphology in different organs
- Clinical course
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Shock

SHOCK - Dutch word 'schokken'- to jolt / jerk suddenly

Potentially a life threatening condition that requires immediate attention

Shock- Definition

Shock is a state in which **diminished cardiac output** or **reduced effective circulating blood volume** impairs tissue perfusion and leads to **cellular hypoxia**

Shock

↓ Blood volume / ↓ CO /Redistribution of blood

↓

Inadequate effective circulating volume

↓

Widespread hypoperfusion of tissues

↓

Tissue hypoxia

↓

SHOCK

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TYPES OF SHOCK

Major types of shock

CARDIOGENIC

HYPOVOLEMIC

SHOCK ASSOCIATED WITH SYSTEMIC INFLAMMATION

Less common / rare types of shock

- Neurogenic shock
- Anaphylactic shock

Cardiogenic shock

Clinical Example	*Principal mechanisms*
▪Myocardial infarction ▪Ventricular rupture ▪Arrhythmia	Myocardial pump failure due to intrinsic damage
▪Cardiac tamponade	Extrinsic compression
▪Pulmonary embolism	Obstruction to outflow

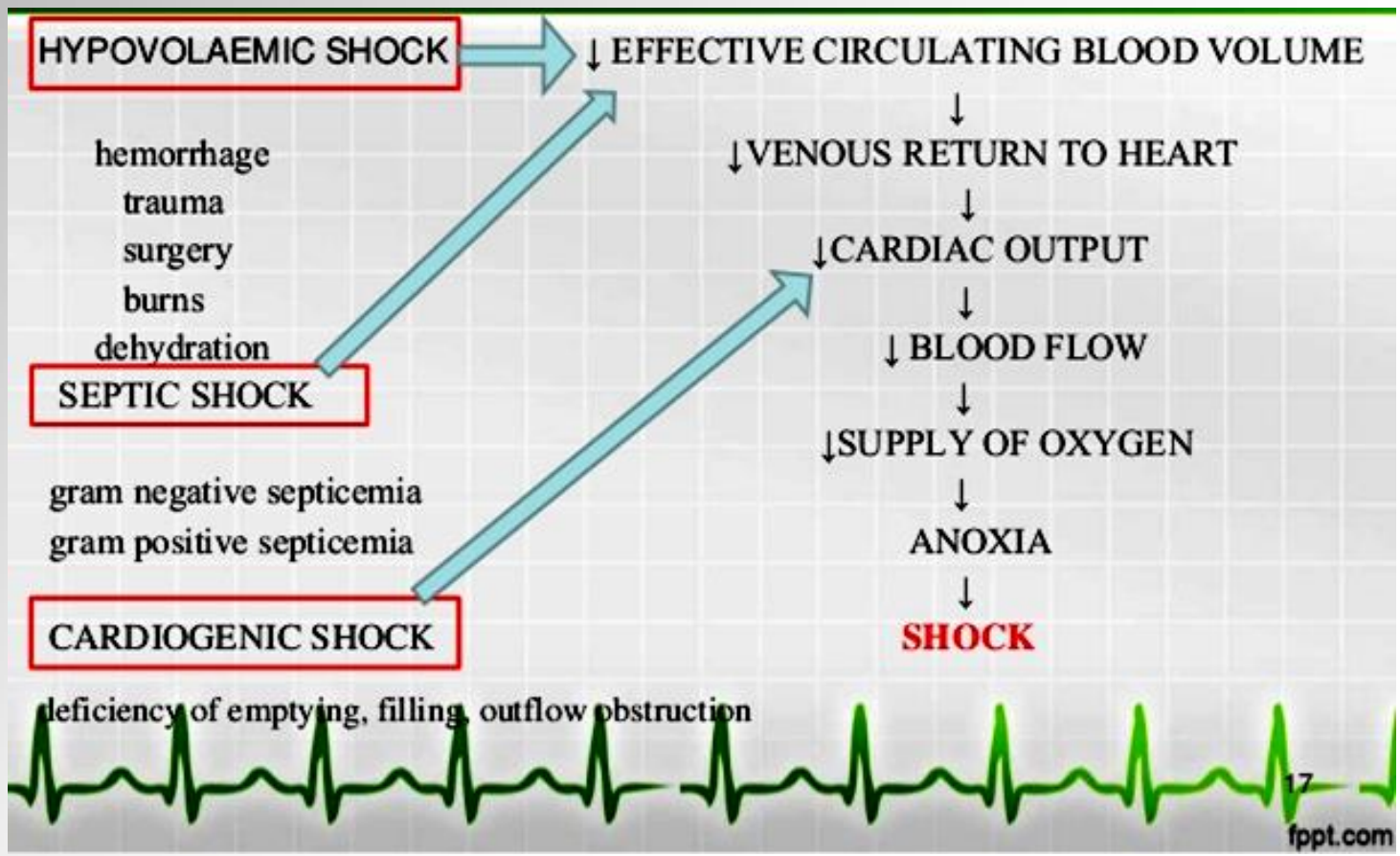
Hypovolemic shock

Clinical Example	*Principal mechanisms*
▪Fluid loss- Haemorrhage, diarrhea, vomiting, burn, trauma	Inadequate blood or plasma volume

Shock associated with systemic inflammation

Clinical Example	*Principal mechanisms*
▪Overwhelming microbial infection (bacterial/ fungal) (SEPTIC SHOCK) ▪Superantigens ▪Trauma, burn, pancreatitis	▪Cytokine cascade activation ▪Peripheral vasodilatation and pooling of blood, ▪Endothelial injury/ activation, ▪Leukocyte induced damage, ▪DIC

PATHOPHYSIOLOGY



Shock associated with systemic inflammation

Microbial & non microbial

- Release of **inflammatory mediators**
- Arterial **vasodilation**
- Vascular leakage- **edema**
- **Venous pooling of blood-** insufficient blood supply to tissues

Shock associated with systemic inflammation

All these leads to

- **Tissue hypoperfusion**
- **Cellular hypoxia**
- **Metabolic derangements**
- **Organ dysfunction**
- If persistent – **organ failure and death**

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME

Septic shock

Shock caused by microbial infection is called

Septic Shock

Pathogenesis of Septic shock

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Septic shock

Mortality rate is more than 20% and ranks first among the causes of death in ICU in the US

Increasing incidence of septic shock is attributable to

- **Improved *life support* for high risk patients**
- **An increase in *invasive procedures***
- **Growing number of *immunocompromomised hosts* (secondary to chemotherapy, immunosuppression, or infection with human immunodeficiency virus)**
- **Increasing prevalence of *multidrug resistant organisms* in the hospital setting**

Septic Shock

Septic shock most frequently triggered by

- **Gram-positive bacterial infection**

Followed by

- **Gram negative bacteria** and
- **Fungi**

Septic Shock

- Hence an older synonym "**endotoxic shock**" is **no longer appropriate**

Pathogenesis of Septic Shock

- Microbial cell wall constituents/ products contain **Pathogen Associated Molecular Patterns (PAMPs)** are detected by receptors on cells of the immune system **Toll like receptors (TLRs)** present on the surfaces of various cells of the immune system
- This **triggers the pro-inflammatory** signaling pathways

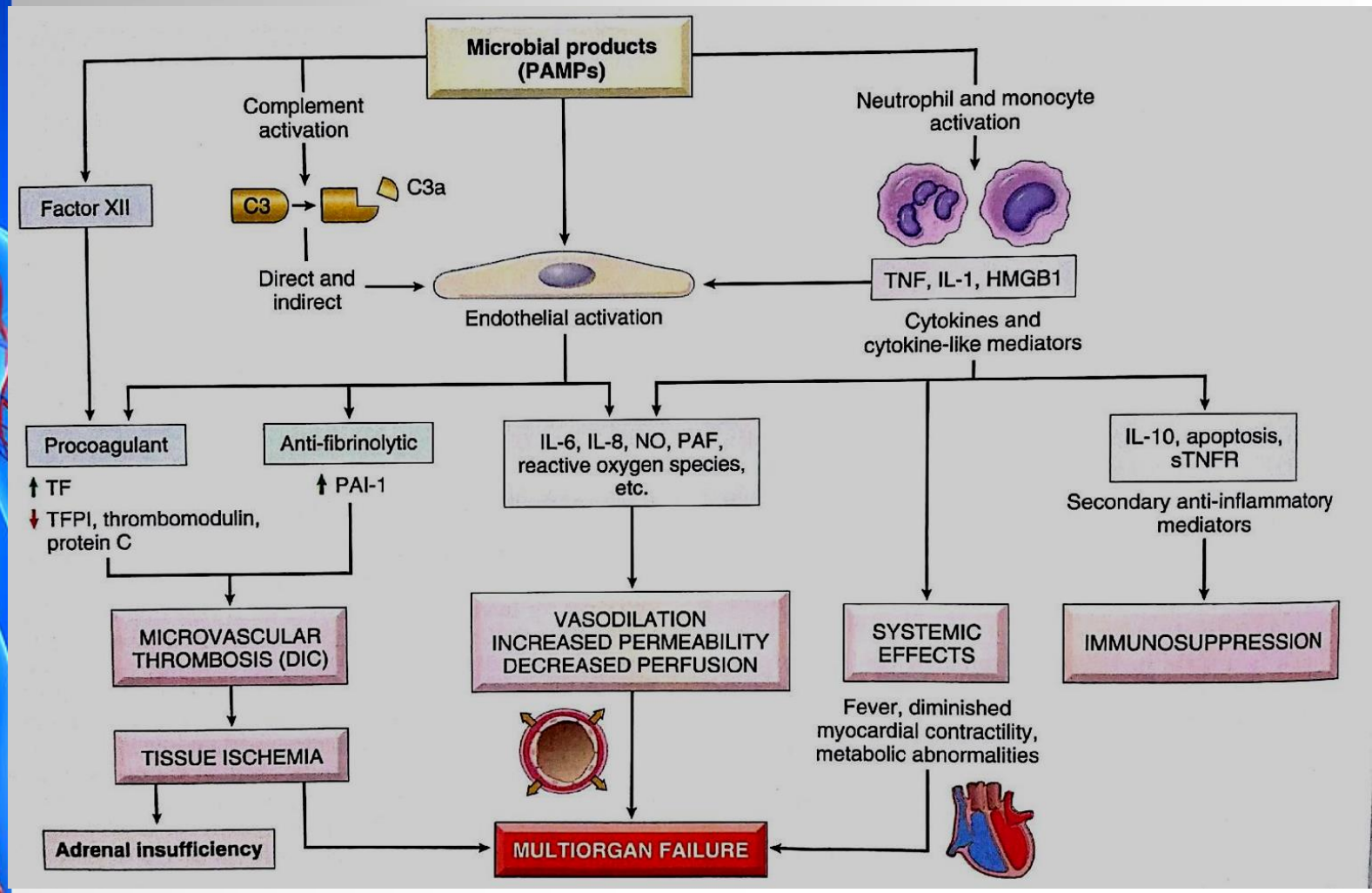
Pathogenesis of Septic Shock

This binding results in the followings:

- **Direct activation of endothelial cells**
- **There is activation of neutrophils and monocytes**
- **Activation of complement cascade**
- **Activation of the coagulation cascade directly through factor XII and indirectly through endothelial cells**

* **PLEASE FOLLOW THE FLOW CHART IN NEXT SLIDE**

Major pathogenic pathways in septic shock



***Detail is in the following slides**

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Pathogenesis of Septic Shock

- All these result in : **(Follow the flow chart in previous slide**)

1. **<u>Endothelial cell activation and injury-</u>** results in production of IL6, IL8, NO, PAF, ROS which leads to vasodilation, increased vascular permeability, edema and decreased tissue perfusion

2. **<u>Induction of a procoagulant state-</u>** Tissue factor production is increased and there is decrease in anticoagulant factors (TFPI, Thrombomodulin, Protein C.

This leads to microvascular thrombosis (DIC) and tissue ischaemia

Pathogenesis of Septic Shock

3. **Activation of the complement system-** with production of C3a, C5a, c3b- all of which contribute to a proinflammatory state

4. **Activation of inflammatory cells-** release of cytokines (TNF, IL1 etc) causes systemic effects such as fever, diminished myocardial contractility

5. **Immunosuppression**- at the same time there is release of some anti inflammatory mediators (IL10, TNF receptors, and apoptosis) by the inflammatory cells. This leads to a state of immunosuppression

Pathogenesis of Septic Shock

6. **Metabolic abnormalities-** insulin resistance and hyperglycemia develops

7. **Organ dysfunction-** systemic hypotension, interstitial edema, microvascular thrombosis all decrease the delivery of oxygen and nutrients to the tissues. High level of cytokines and mediators diminish cardiac contractility and cardiac output

Pathogenesis of Septic Shock

Ultimately all these lead to multiorgan failure (particularly the kidneys, liver, lungs and heart) leading to **death**

Septic Shock- severity & outcome

- Extent and virulence of the infection
- The immune status of the host
- The presence of other co-morbid conditions
- The pattern and level of mediator production

Co morbid relating to a medical condition that co occurs with another

Rare types of shock

- Neurogenic
- Anaphylactic

Neurogenic Shock

- Neurogenic shock occurs in
- **Anesthetic accidents**
- **Spinal cord injury**
- There is of loss of sympathetic nerve activity
- Massive peripheral vasodilatation
- Decrease in peripheral vascular resistance
- This leads to a reduction in venous return to the heart, resulting in a decrease in cardiac output, with hypotension rapidly following.

Anaphylactic shock

- This type of shock is a severe allergic reaction in which an antigen-antibody reaction occurs
- **Initiated by generalized type I IgE mediated hypersensitivity reaction**
- **CAUSES:**

➢ **Drugs**

➢ **Transfusion of incorrectly cross-matched blood**

➢ **Foods**

➢ **Insect bites**

STAGES OF SHOCK

Shock is a ***progressive disorder*** if uncorrected leads to death

Evolves through 3 stages

- **Initial Non progressive phase**
- **Progressive stage**
- **Irreversible stage**

STAGES OF SHOCK

Nonprogressive phase

Neurohumoral mechanisms come into play to maintain CO & BP

- **Baroreceptor Reflexes**
- **Release of Catecholamines**
- **Activation of Renin - Angiotensin axis**
- **ADH release**
- **Gen Sympathetic Stimulation**

STAGES OF SHOCK

Nonprogressive phase

The net effect is

- *Tachycardia*
- *Peripheral vasoconstriction*
- *Renal conservation of fluid*

Coronary and **cerebral** vessels are less sensitive to the systemic response thus maintains normal caliber, blood flow and oxygen delivery

STAGES OF SHOCK

Progressive Stage

Vital organs begin to experience significant hypoxia

↓

Impairment of intracellular aerobic respiration

↓

Anaerobic glycolysis

↓

Lactic acidosis → pH lowered

↓ vasomotor response → arterioles dilate

peripheral pooling of blood

Cardiac output ↓

anoxic injury to endothelial cell → DIC

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STAGES OF SHOCK

Irreversible stage

- Widespread cell injury
- Leakage of lysosomal enzymes
- Myocardial contractile function worsens (due to cytokines and mediators)
- Ischemic bowel allows intestinal for to enter the circulation
- Anuria develops due to ATN and renal failure - complete renal shutdown

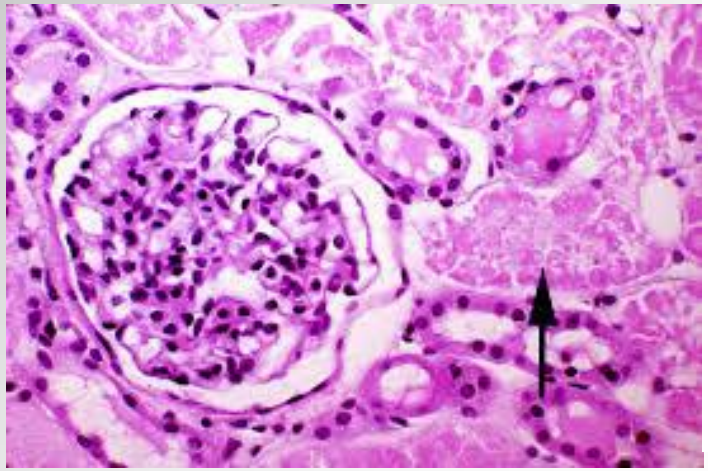
Morphology of Shock

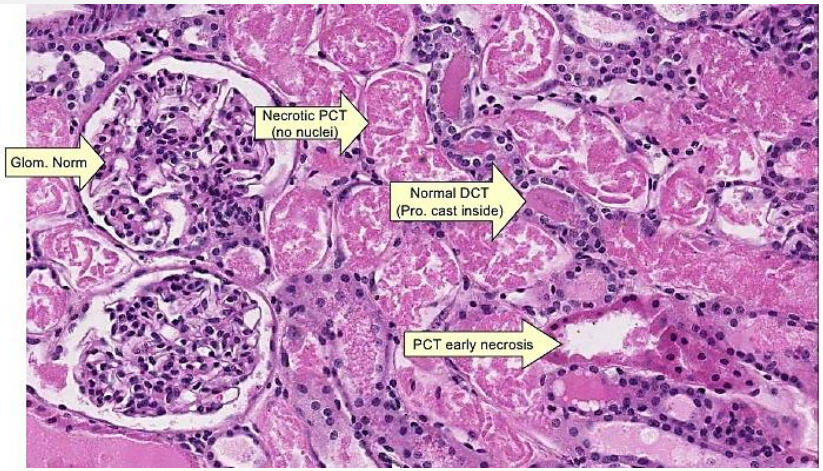
- The cellular and tissue changes induced by cardiogenic and hypovolemic shock are essentially those of hypoxic injury
- Any tissue can manifest
- Particularly evident in brain, heart, lungs , kidney, GIT and adrenals

Morphology of Shock

- **Adrenals**: cortical lipid cell depletion
- **Kidneys**: acute tubular necrosis
- **Lungs**: diffuse alveolar damage
- **Heart**: subendocardial contraction bands
- **GIT**: haemorrhagic enteropathy
- **Brain**: ischaemic encephalopathy

Acute Tubular Necrosis in Kidney





Shock - Clinical Course

Manifestations depend on the precipitating insult

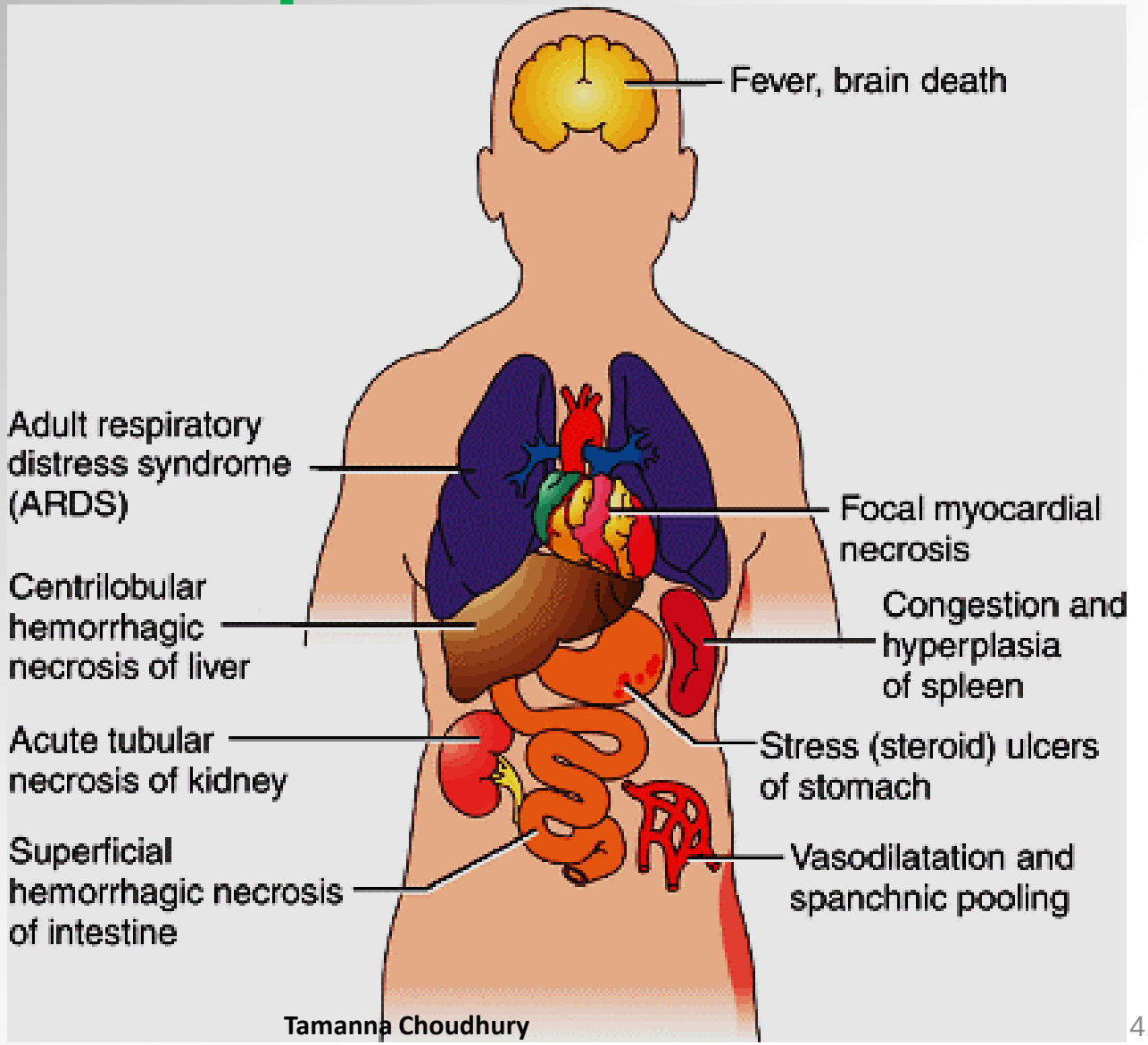
Hypovolemic & Cardiogenic shock

Hypotension
tachypnea
weak, rapid pulse
cool, clammy, cyanotic skin

Septic shock

Warm, flushed skin

Complications of shock



Shock - PROGNOSIS

Varies with the origin & duration of shock

Hypovolemic shock	90% survives
Cardiogenic & Septic shock	Mortality rate is high

Practice questions

- Define shock.
- What are the different types of shock?
- What are the causes and principal mechanism of hypovolemic shock?
- What are the causes and principal mechanism of cardiogenic shock?
- Discuss the pathogenesis of septic shock.
- What are the stages of shock?
- What are the morphological changes in different organs in hypovolemic/ cardiogenic shock?
- What is anaphylactic shock?
- What is neurogenic shock?

MCQ

In shock

a) Tissue hypoperfusion begins in the progressive phase

b) Lactic acidosis occurs in nonprogressive phase

c) Baroreceptor reflex is active in nonprogressive phase

d) Aerobic respiration persists in progressive phase

e) Initially there is vasodilatation

MCQ

In shock

a) Tissue hypoperfusion begins in the progressive phase **T**

b) Lactic acidosis occurs in nonprogressive phase **F**

c) Baroreceptor reflex is active in nonprogressive phase **T**

d) Aerobic respiration persists in progressive phase **F**

e) Initially there is vasodilatation **T**

Thank You