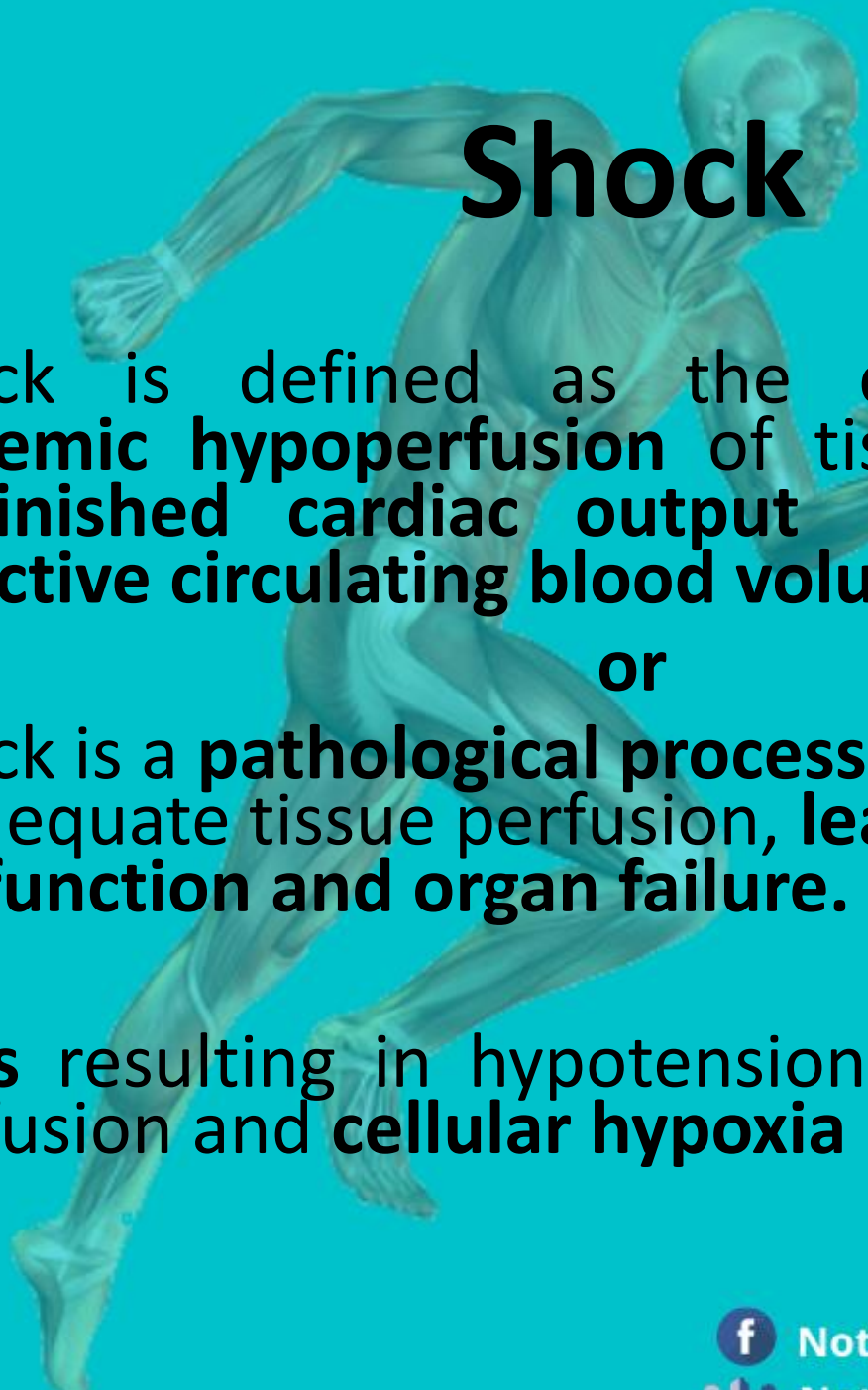
Shock



- Shock is defined as the characterized by **systemic hypoperfusion** of tissues, caused by **diminished cardiac output** or by **reduced effective circulating blood volume.**

or

- Shock is a **pathological process that results** from inadequate tissue perfusion, **leading to cellular dysfunction and organ failure.**

- **It is** resulting in hypotension, impaired tissue perfusion and **cellular hypoxia**

Characteristic features:

Extreme and widespread failure of the circulatory system

↓

Systemic hypotension

↓

Life-threatening inadequate/impaired tissue perfusion (hypoperfusion)

↓

Tissue hypoxia

↓

Reversible cellular injury

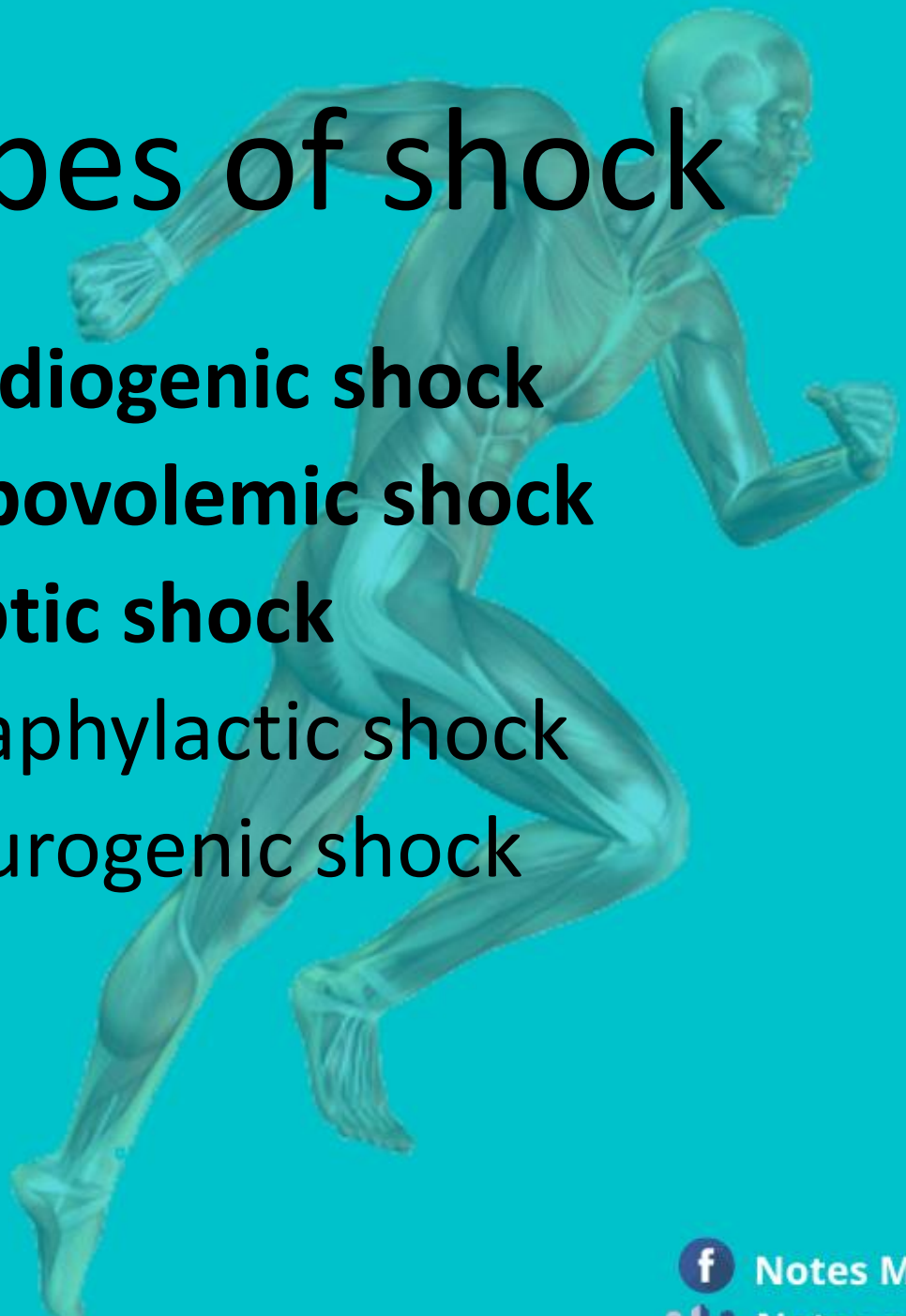
↓

Reversible tissue injury and organ failure

↓

Death

Types of shock



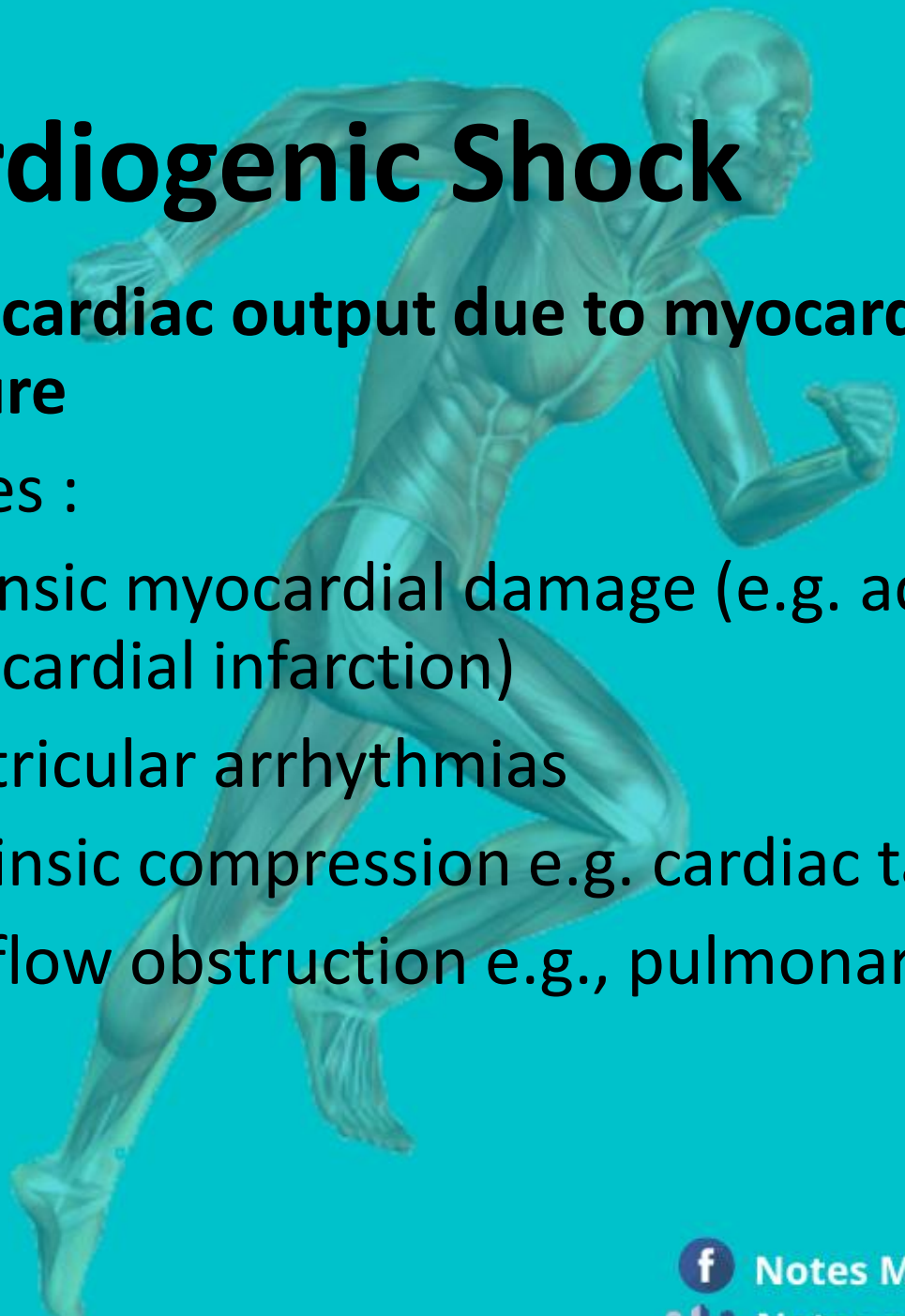
- **Cardiogenic shock**
- **Hypovolemic shock**
- **Septic shock**
- Anaphylactic shock
- Neurogenic shock

Cardiogenic Shock

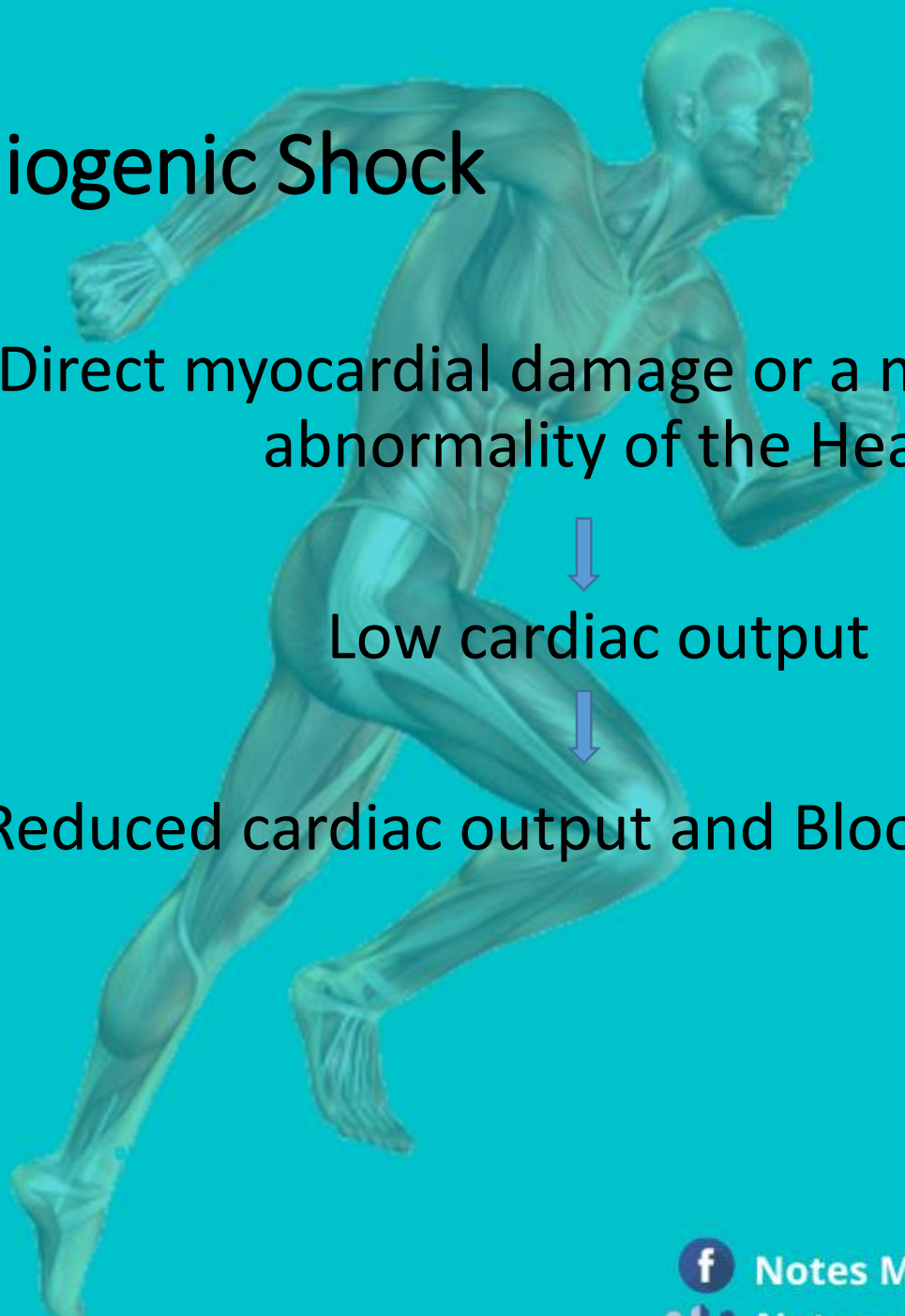
- **low cardiac output due to myocardial pump failure**

Causes :

- intrinsic myocardial damage (e.g. acute myocardial infarction)
- Ventricular arrhythmias
- Extrinsic compression e.g. cardiac tamponade
- Outflow obstruction e.g., pulmonary embolism



Cardiogenic Shock



Direct myocardial damage or a mechanical abnormality of the Heart

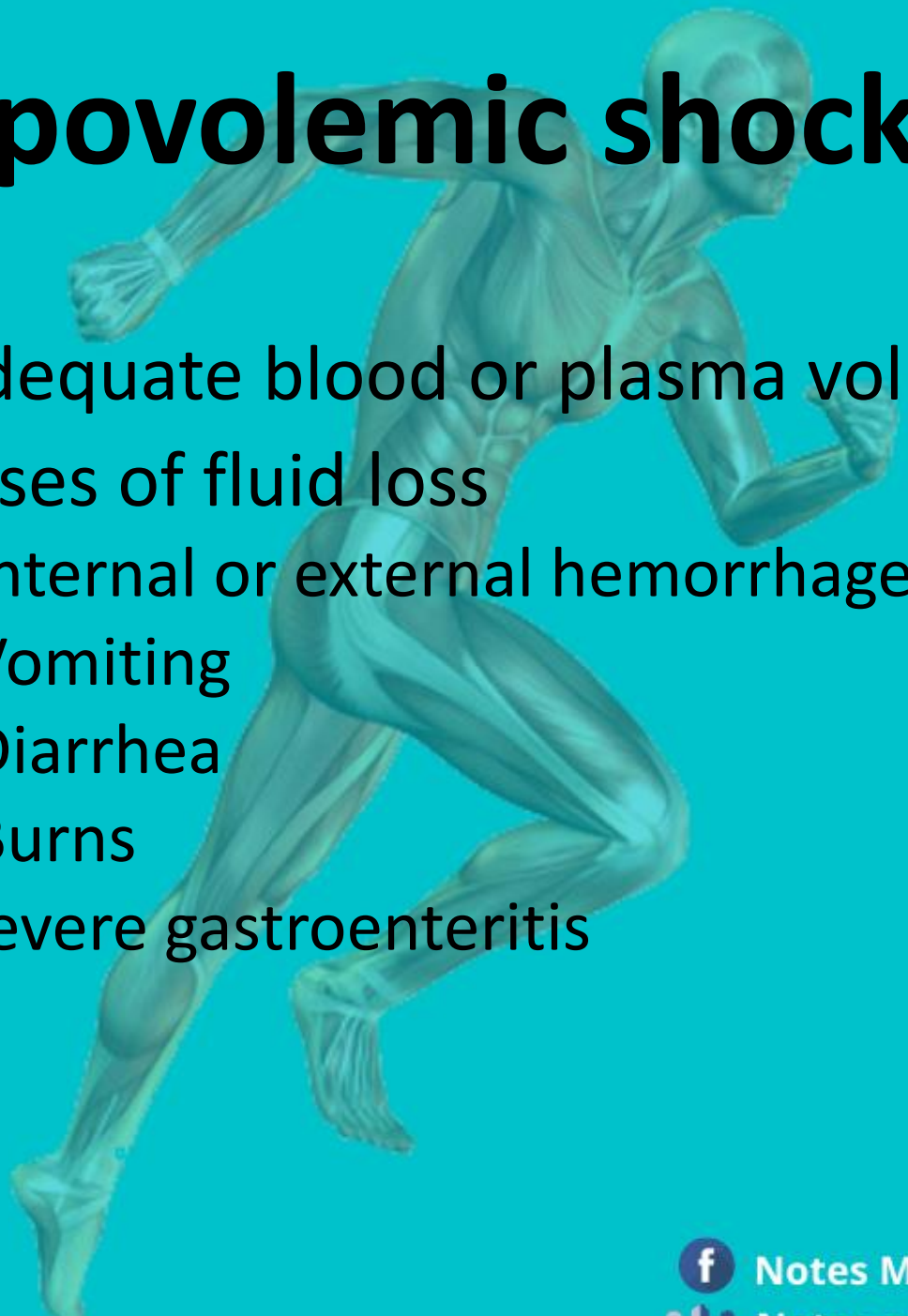
↓

Low cardiac output

↓

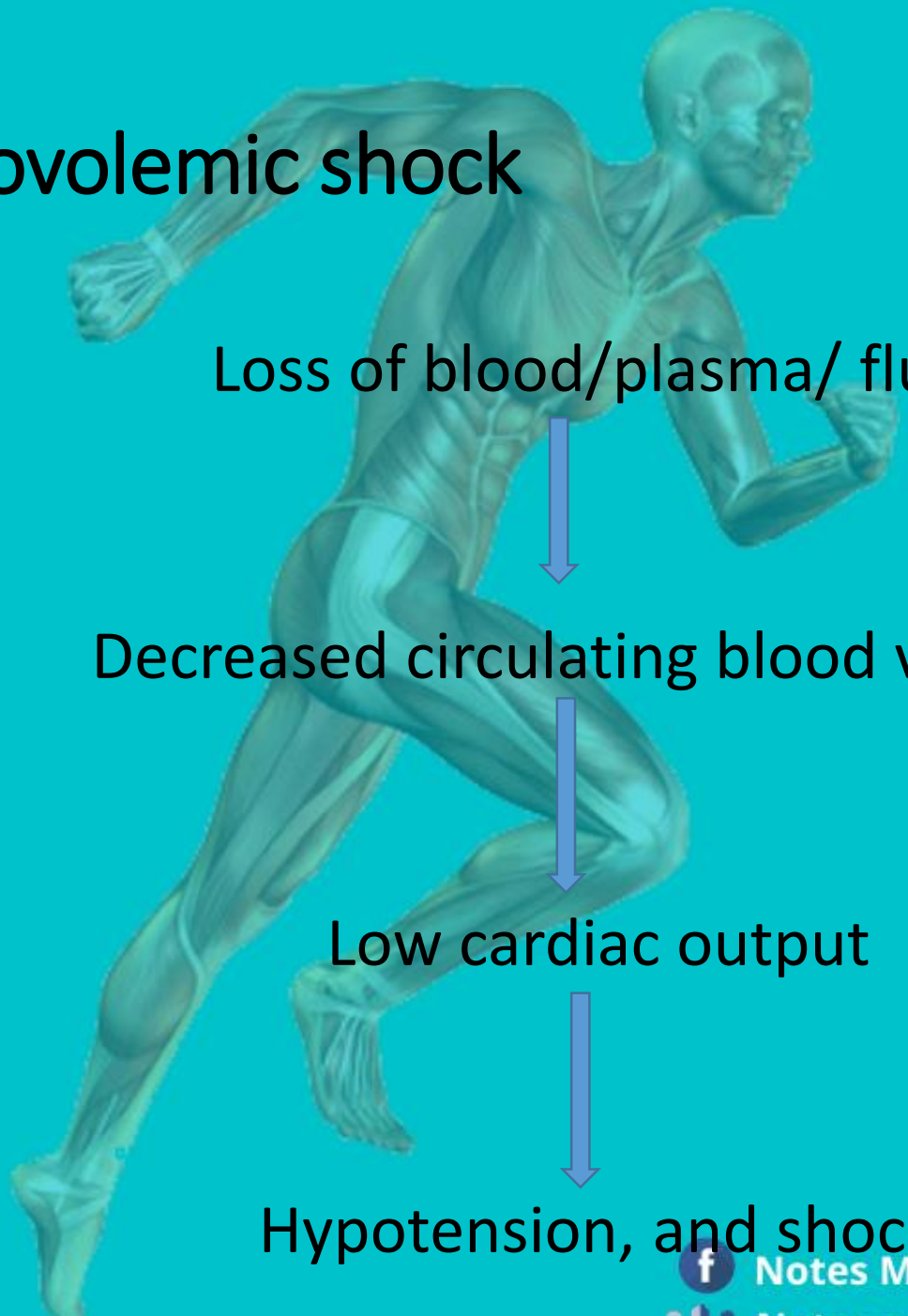
Reduced cardiac output and Blood pressure

Hypovolemic shock



- Inadequate blood or plasma volume
- Causes of fluid loss
  - Internal or external hemorrhage
  - Vomiting
  - Diarrhea
  - Burns
  - Severe gastroenteritis

Hypovolemic shock



Loss of blood/plasma/ fluid

↓

Decreased circulating blood volume

↓

Low cardiac output

↓

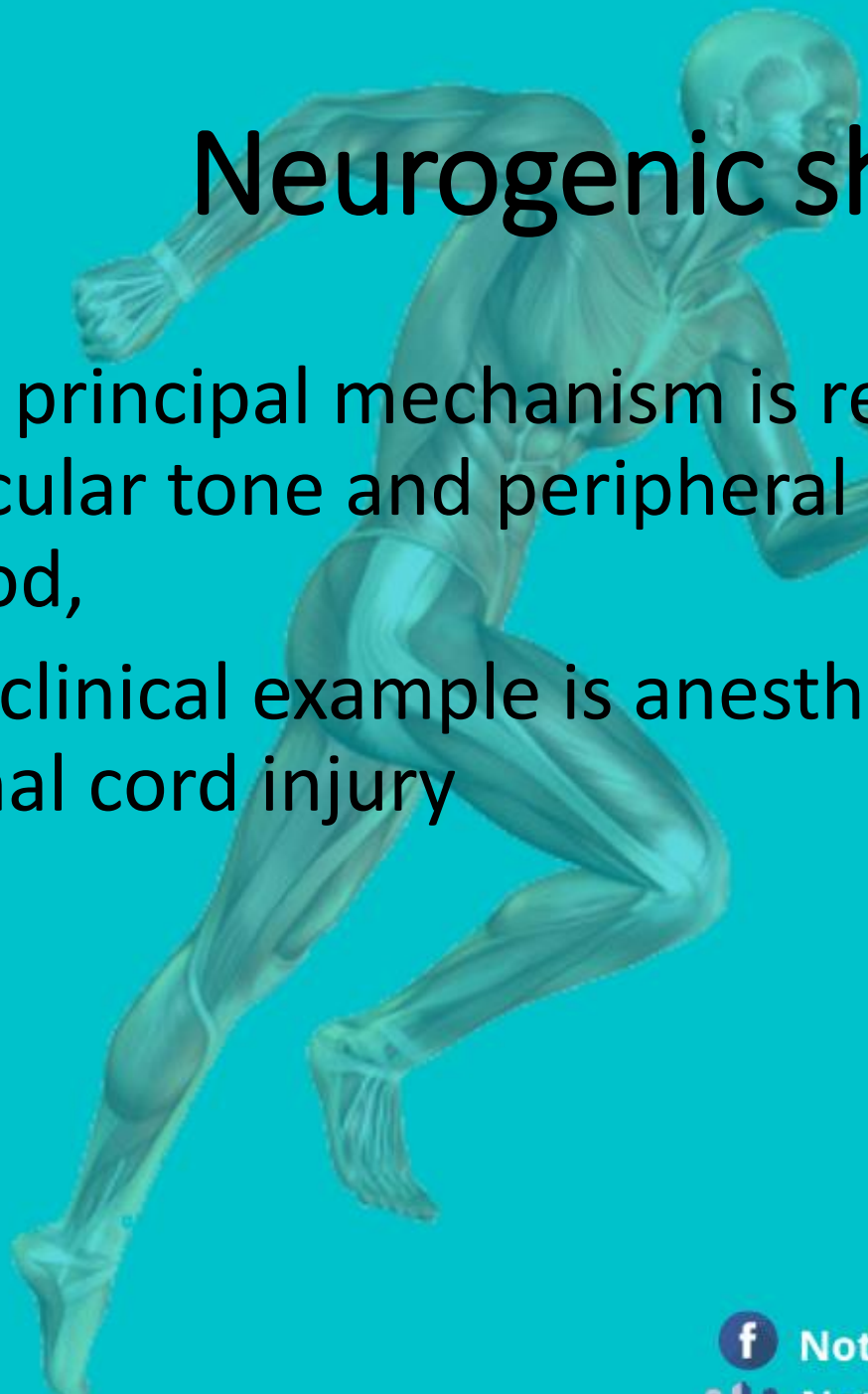
Hypotension, and shock

Anaphylactic shock

- Systemic form of IgE – mediated hypersensitivity reaction
- Systemic vasodilation + increased vascular permeability
- Peripheral pooling of blood and hypotension

Neurogenic shock

- The principal mechanism is result of loss of vascular tone and peripheral pooling of blood,
- For clinical example is anesthetic accident or spinal cord injury

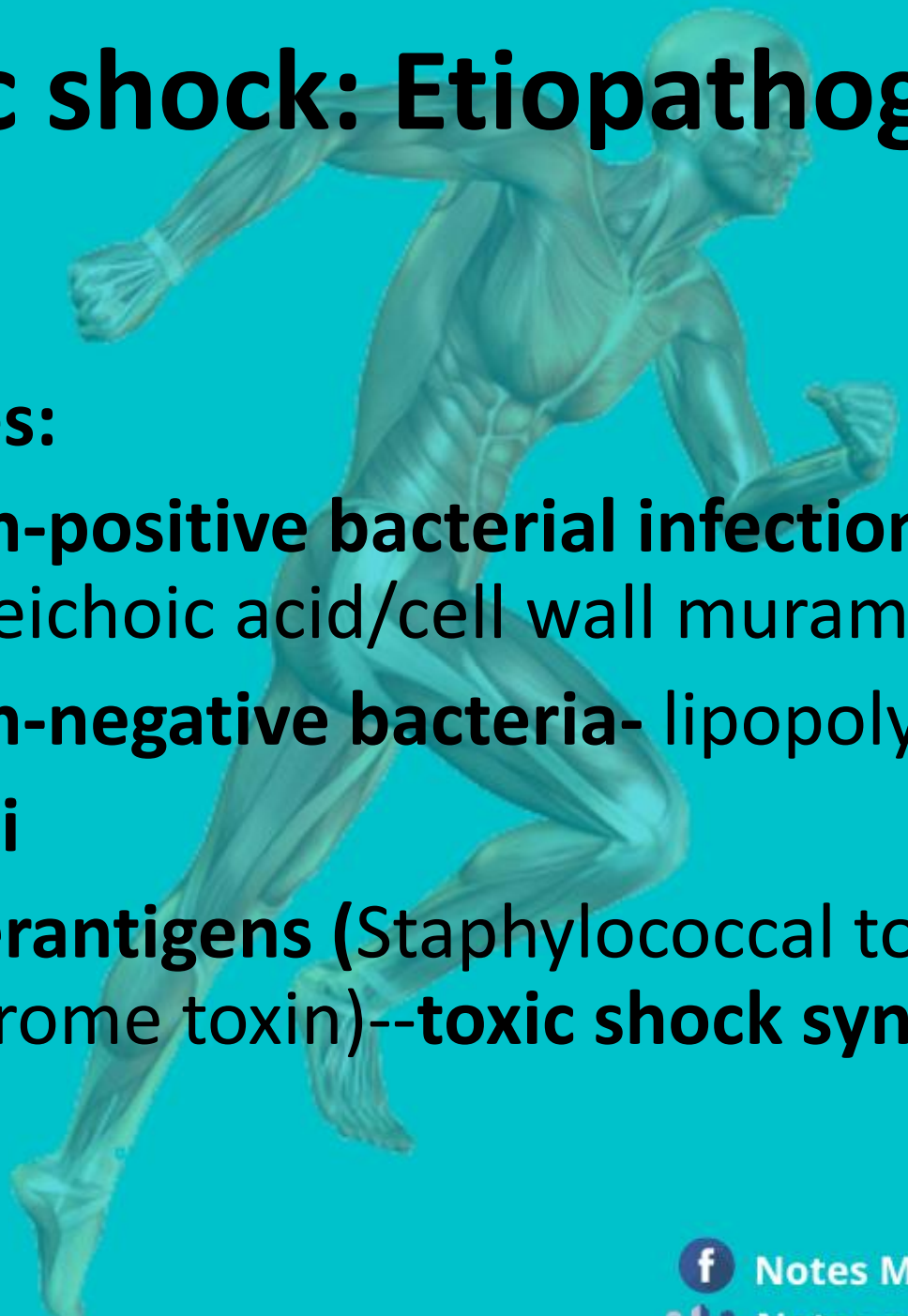


Septic shock

- It is defined as shock due to **severe sepsis with hypotension,** which cannot be corrected by infusing fluids.

- It results from vasodilation and peripheral pooling of blood and is associated with dysfunction of multiple organs distant from the site of infection.

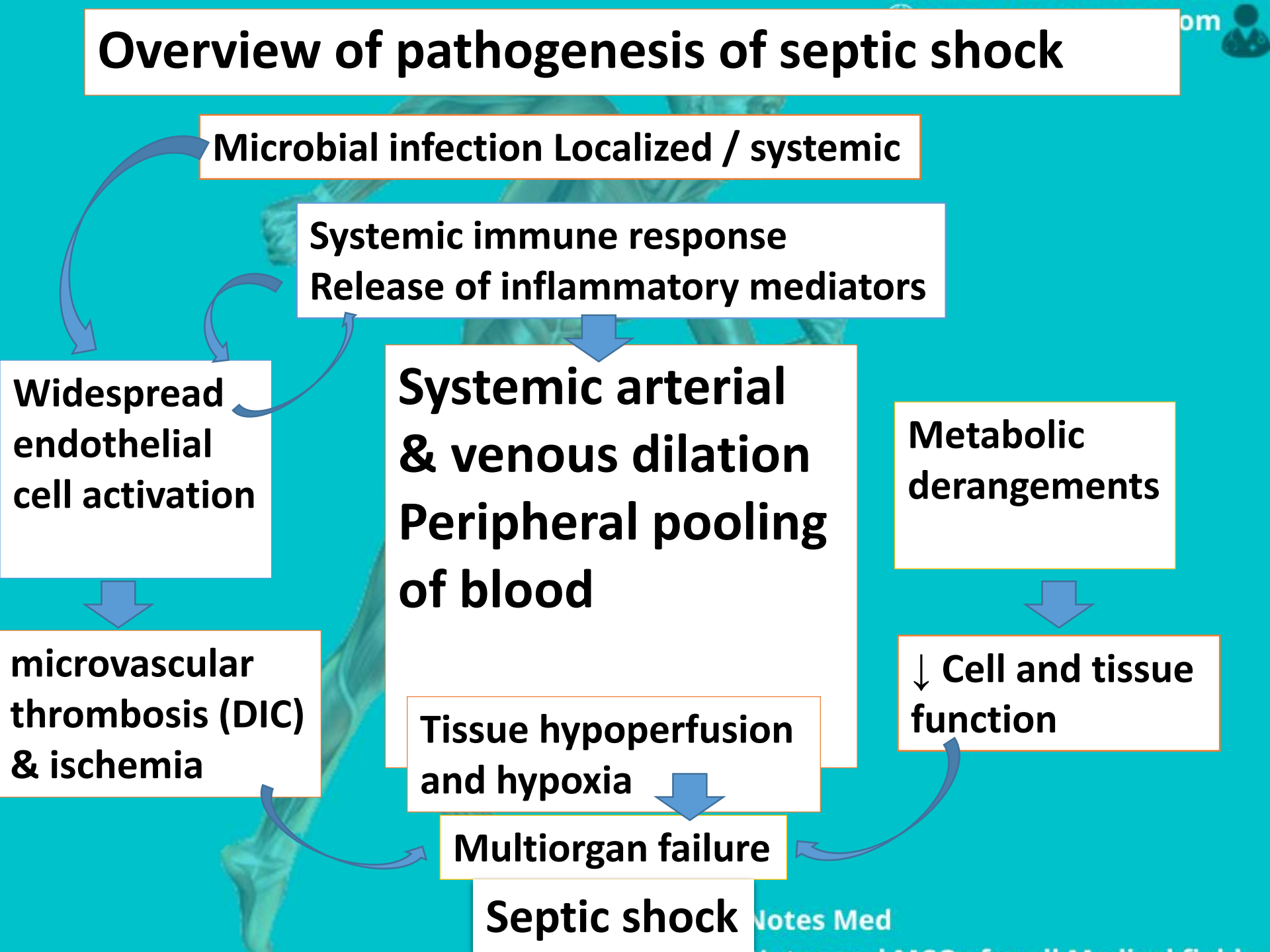
Septic shock: Etiopathogenesis

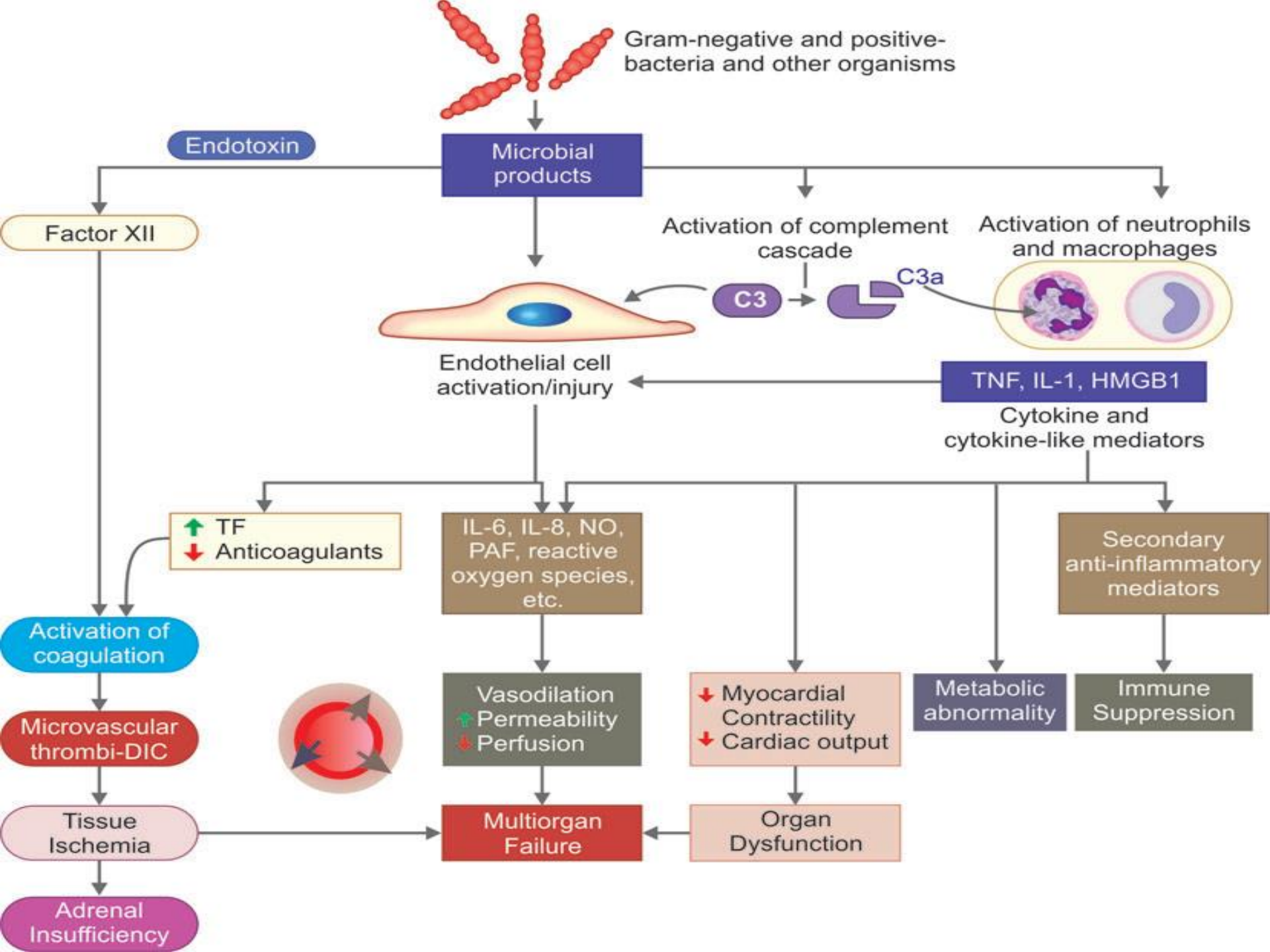


Causes:

- **Gram-positive bacterial infections –** lipoteichoic acid/cell wall muramyl peptides
- **Gram-negative bacteria-** lipopolysaccharide
- **Fungi**
- **Superantigens (**Staphylococcal toxic shock syndrome toxin)--**toxic shock syndrome**

Overview of pathogenesis of septic shock




Gram-negative and positive-bacteria and other organisms
Endotoxin
Microbial products
Factor XII
Activation of complement cascade
Activation of neutrophils and macrophages
C3
C3a
Endothelial cell activation/injury
TNF, IL-1, HMGB1
Cytokine and cytokine-like mediators
TF
Anticoagulants
IL-6, IL-8, NO, PAF, reactive oxygen species, etc.
Secondary anti-inflammatory mediators
Activation of coagulation
Vasodilation
Permeability
Perfusion
Myocardial Contractility
Cardiac output
Metabolic abnormality
Immune Suppression
Microvascular thrombi-DIC
Tissue Ischemia
Multiorgan Failure
Organ Dysfunction
Adrenal Insufficiency

Factors contributing septic shock

- **Inflammatory mediators**
  - Microbe derived substances- PAMP(pathogen associated molecular pattern)
  - Recognized by host innate immune system
    - Cells- neutrophils, macrophages, endothelial cells
    - Plasma component- complement system, factor XII
  - Activated cells-> proinflammatory cytokines and cytokine like mediators- TNF, IL-1, IL_12, IL-18HMGB-1; ROS, PAF→ activate endothelial cells → release of secondary waves of cytokines

Factors contributing septic shock

- Activation of complement cascade: direct activation by microbes or indirectly by factor XII activation and generation of plasmin
  → generation of anaphylatoxins C3a, C5a, chemoattractants C5a, opsonins C3b
- Factor XII activation → activation of coagulation cascade

Factors contributing septic shock

- Endothelial cell activation and injury
  - Activated directly by microbes or inflammatory mediators
  1. **Thrombotic effect**
  - ↑Procoagulant effect- ↑ TF
  - ↓Anticoagulant effect- ↓ TFPI, thrombomodulin expression, protein C
  - ↑ Antifibrinolytic effect- ↑ PAI

  - microvascular thrombosis – **tissue ischemia** – full blown DIC– extensive haemorrhage

Endothelial cell activation and injury

2. **Peripheral vasodilation**
   by release of cytokines and platelet activating factor (PAF), NO
→ peripheral pooling of blood and hypotension
3. ↑**vascular permeability** (loosening of endothelial tight junction)- tissue edema

→impaired tissue perfusion

Factors contributing septic shock

- Metabolic abnormalities
  1. Hyperglycemia→↓ Neutrophil function→ ↓ bactericidal activity
  - Due to gluconeogenesis stimulated by
    - Cytokines- TNF, IL-1
    - Stress induced hormones- catecholamines, glucagon, GH, glucocorticoids
  - ↓Insulin secretion and insulin resistance
    - Induced by proinflammatory cytokines

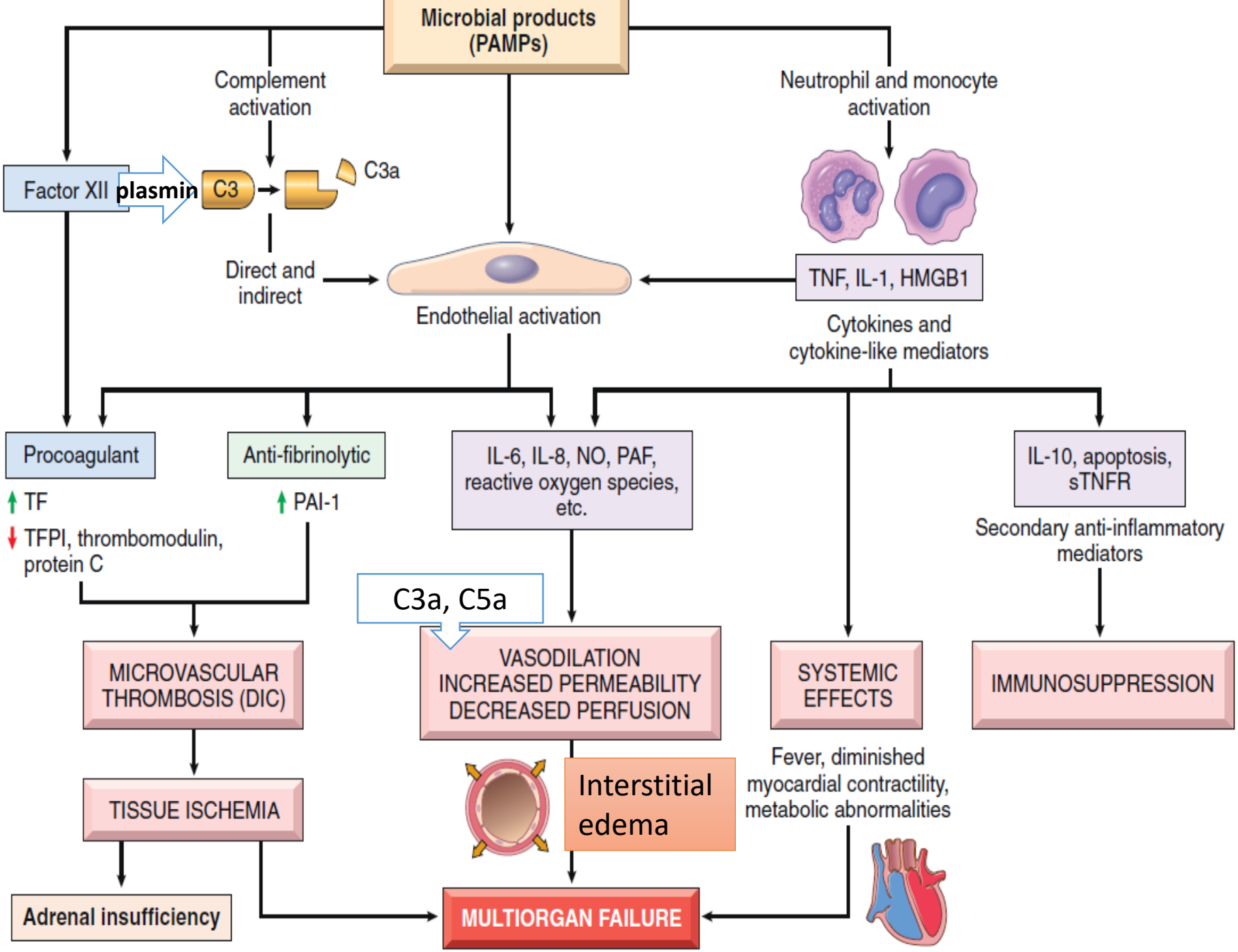
Metabolic abnormalities

- Later- adrenal insufficiency→ ↓glucocorticoids
  - Due to DIC → adrenal necrosis or
  - Due to functional exhaustion of intact adrenal gland

- Cellular hypoxia and anaerobic glycolysis→lactic acidosis→ vasodilation

Factors contributing septic shock

- Multi organ dysfunction and it is due to;
  - Systemic vasodilation and hypotension
  - Interstitial edema
  - Thrombosis
  - Heart- ↓myocardial contractility and cardiac output
  - Lungs- increased vascular permeability and endothelial injury→ ARDS
  - Kidneys- Acute tubular necrosis and renal failure
  - Liver failure
  - Death


Microbial products (PAMPs)
Complement activation
Neutrophil and monocyte activation
Factor XII
plasmin
C3
C3a
Direct and indirect
Endothelial activation
TNF, IL-1, HMGB1
Cytokines and cytokine-like mediators
Procoagulant
Anti-fibrinolytic
IL-6, IL-8, NO, PAF, reactive oxygen species, etc.
IL-10, apoptosis, sTNFR
TF
TFPI, thrombomodulin, protein C
PAI-1
Secondary anti-inflammatory mediators
C3a, C5a
MICROVASCULAR THROMBOSIS (DIC)
VASODILATION INCREASED PERMEABILITY DECREASED PERFUSION
SYSTEMIC EFFECTS
IMMUNOSUPPRESSION
Interstitial edema
Fever, diminished myocardial contractility, metabolic abnormalities
TISSUE ISCHEMIA
Adrenal insufficiency
MULTIORGAN FAILURE

STAGES OF SHOCK

- Nonprogressive phase
- Progressive stage
- Irreversible stage

- Seen mainly in hypovolemic and cardiogenic shock

Shock: Non progressive stage

- Reflex compensatory mechanisms activated→ maintains perfusion of vital organs by maintaining cardiac output
- Neurohumoral mechanism:
  - Baroreceptor reflexes
  - Release of Catecholamines
  - Activation of the renin- angiotensin- aldosterone axis
  - Release of ADH
  - Sympathetic stimulation
- Tachycardia, peripheral vasoconstriction and renal conservation of fluid

Progressive phase

- If the underlying causes are not corrected, shock passes to the progressive phase
- Tissue hypoperfusion
- Metabolic acidosis due to anaerobic glycolysis
- vasodilation and peripheral pooling of blood
- further endothelial cell injury
- DIC
- Tissue hypoxia of vital organs

Irreversible stage

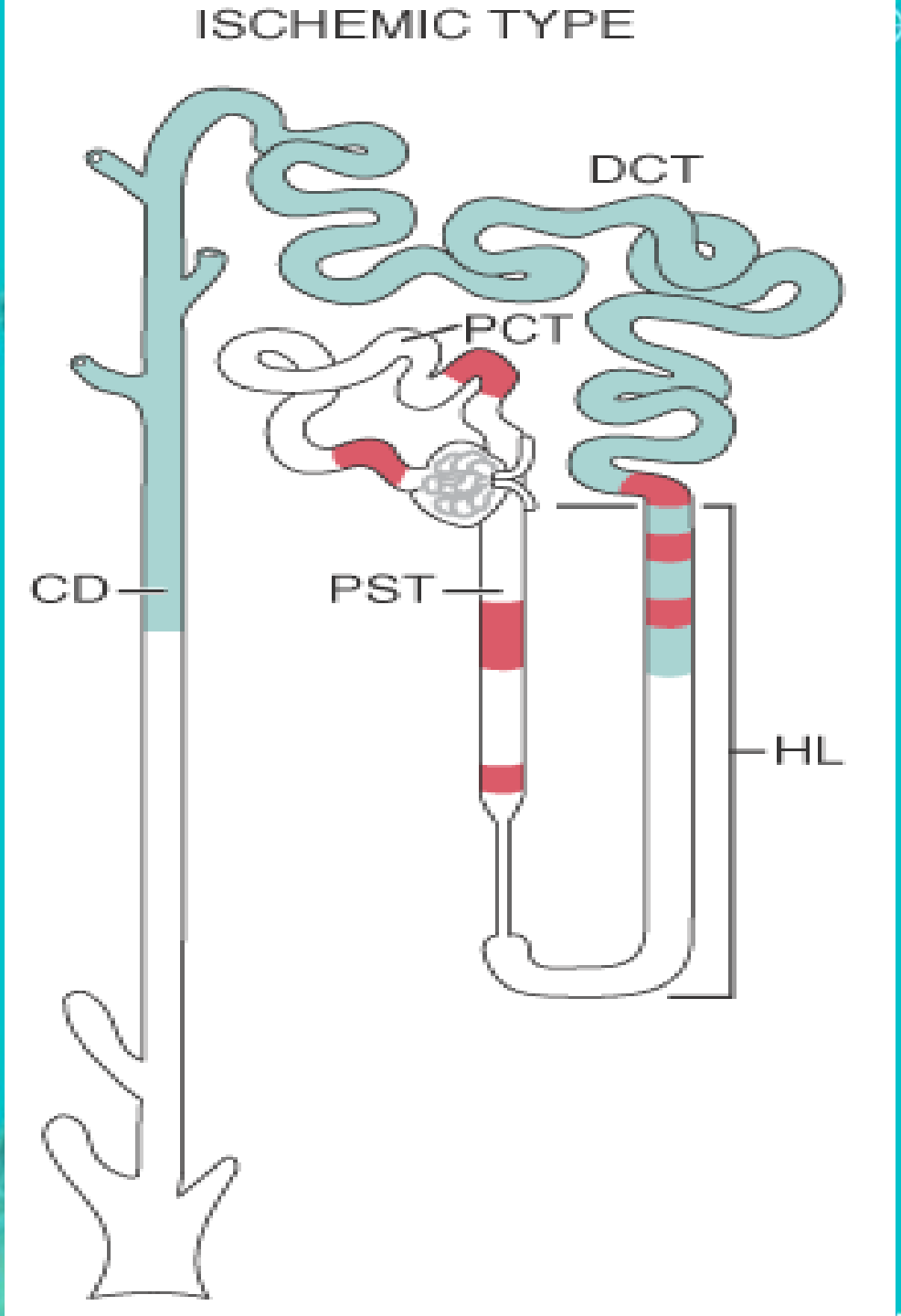
- **Without intervention, the shock eventually enters** an **irreversible stage.**
- Severe tissue injury
- No survival even with vigorous correction of circulatory imbalances
- Heart- myocardial contractility fails
- Kidney- acute tubular necrosis– acute renal failure
- Bowel- intestinal flora may enter circulation and superimposed septic shock
- Inevitable death

Morphology

Coagulation necrosis in vital organs:

- Heart- **petechial hemorrhages** in the epicardium and endocardium.
- Kidneys – patchy tubular necrosis
- Lungs- diffuse alveolar damage
- Adrenal glands- cortical cell lipid depletion
- GI tract- mucosal haemorrhage and ischemic necrosis
- Liver- fatty change
- Septic shock- widespread microthrombi formation and petechial haemorrhages on serosal surface and the skin

Organ	Changes
Adrenal	Lipid depletion in the cortical cells
Kidney	Acute tubular necrosis
Lungs	Relatively resistant to hypoxic injury. However, in septic shock shows diffuse alveolar damage (shock lung) with hyaline membrane
Heart	Coagulative necrosis and contraction band necrosis
Liver	Congestion and necrosis of centrilobular region of the liver
Brain	Encephalopathy (ischemic or septic) and cortical necrosis
Gastrointestinal tract	Diffuse gastrointestinal hemorrhage. Erosions of the gastric mucosa and superficial ischemic necrosis in the intestine



Acute tubular necrosis in shock

Clinical features

- Depends upon the initiating cause
- Hypovolemic and cardiogenic shock
  - Weak rapid pulse, tachypnea; **cool clammy cyanotic skin**
- Septic shock
  - **Warm and flushed skin**
- Initial threat to life depends upon the precipitating cause of shock- MI, sepsis
- soon- multiorgan failure– heart, brain, lungs aggravate the condition
- Worsening renal function – progressive oliguria, acidosis, electrolyte imbalance
- Death