CHS 2413
(Pathology and Physiopathology)

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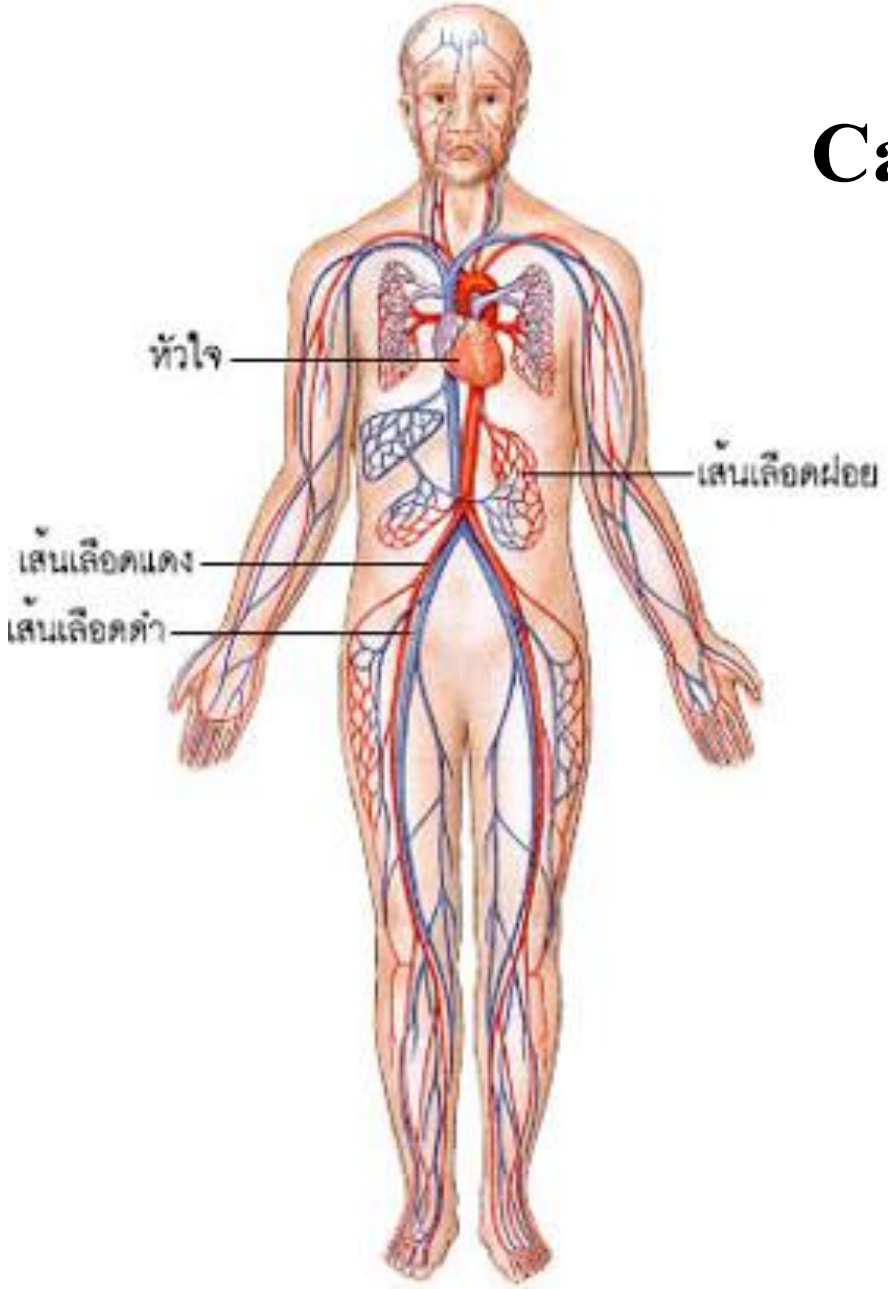
Hemodynamic Disorders

Cardiovascular system



Normal fluid homeostasis

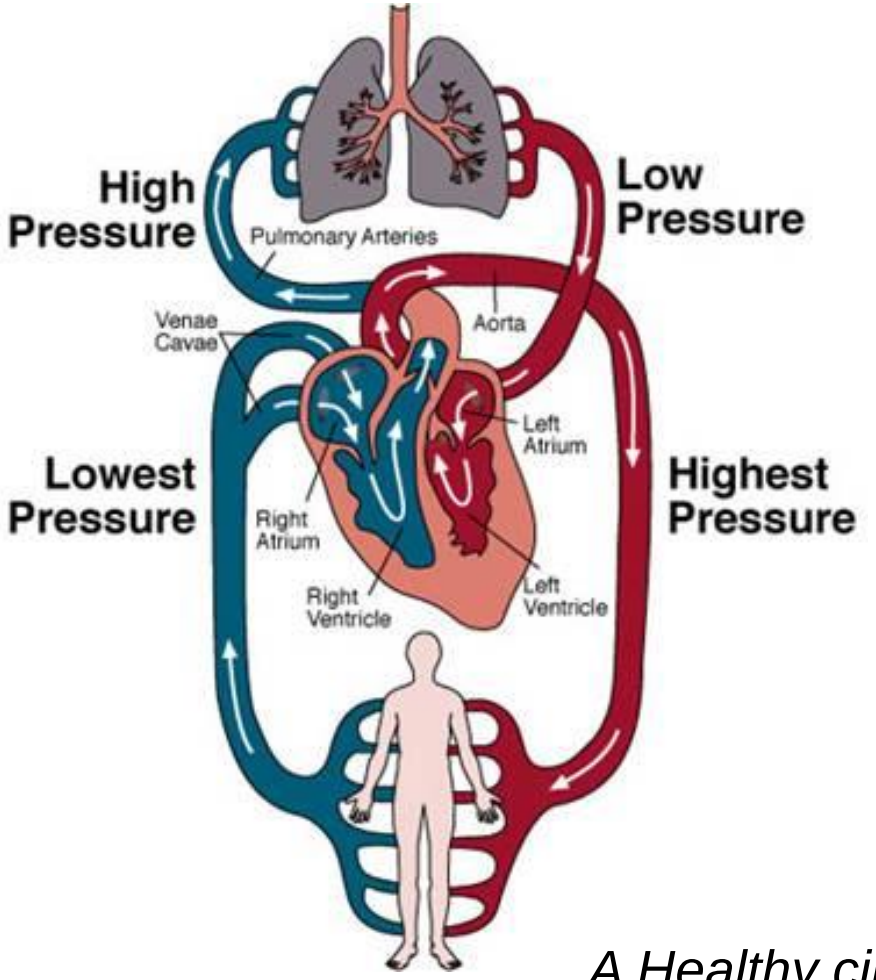
- vessel wall integrity
  - hemorrhage
- Intravascular pressure or vascular volume
  - ischemia
  - hyperemia
  - edema
- Maintenance of blood as a liquid
  - thrombosis
  - embolism
  - infarction

WATER

- 60% of body
- 2/3 of body water is INTRA-cellular
- The rest is INTERSTITIAL
- Only 5% is INTRA-vascular

EDEMA is SHIFT to the INTERSTITIAL SPACE

- HYDRO-
  - -THORAX,
  - -PERICARDIUM (EFFUSIONS)
  - -PERITONUM (ASCITES)
- ANASARCA (total body edema)



Containing

- Heart, artery, Vein
- General circulation
  Pulmonary circulation

Functions

- Deliver oxygen and nutrients
- Carry away metabolic wastes

A Healthy circulatory system

♠ *Normal blood volume*

♠ *Homeostasis*

Normal homeostasis

- *vessel wall integrity*
- *intravascular pressure*
- *osmolarity*
- *normal hemostasis*

- Edema
- Hemorrhage
- Shock
- Hyperemia & congestion
- Thrombosis & Embolism
- Infarction

Three Major Causes of morbidity and mortality

- ♦ Myocardial infarction
- ♦ Pulmonary embolism
- ♦ Cerebral vascular accident

Pathology of Hemodynamics

1. **Edema (increased fluid in the ECF)**
2. Hyperemia (INCREASED flow)
3. Congestion (INCREASED backup)
4. Hemorrhage (extravasation)
5. Shock (circulatory failure/collapse)
6. Hemostasis (keeping blood as a fluid)
7. Thrombosis (clotting blood)
8. Embolism (downstream travel of a clot)
9. Infarction (death of tissues w/o blood)

Fluid Homeostasis
Starling's Law

Homeostasis is maintained by the opposing effects of:

- **Vascular Hydrostatic Pressure**

and

- **Plasma Colloid Osmotic Pressure**

ปรากฏการณ์ที่แรงบีบตัวของหัวใจ (stroke volume)ขึ้นกับปริมาตรเลือดในหัวใจขณะคลายตัวเต็มที่ (End-diastolic volume; EDV) เรียกว่ากฎสตาร์ลิง (Starling's law) ของหัวใจ

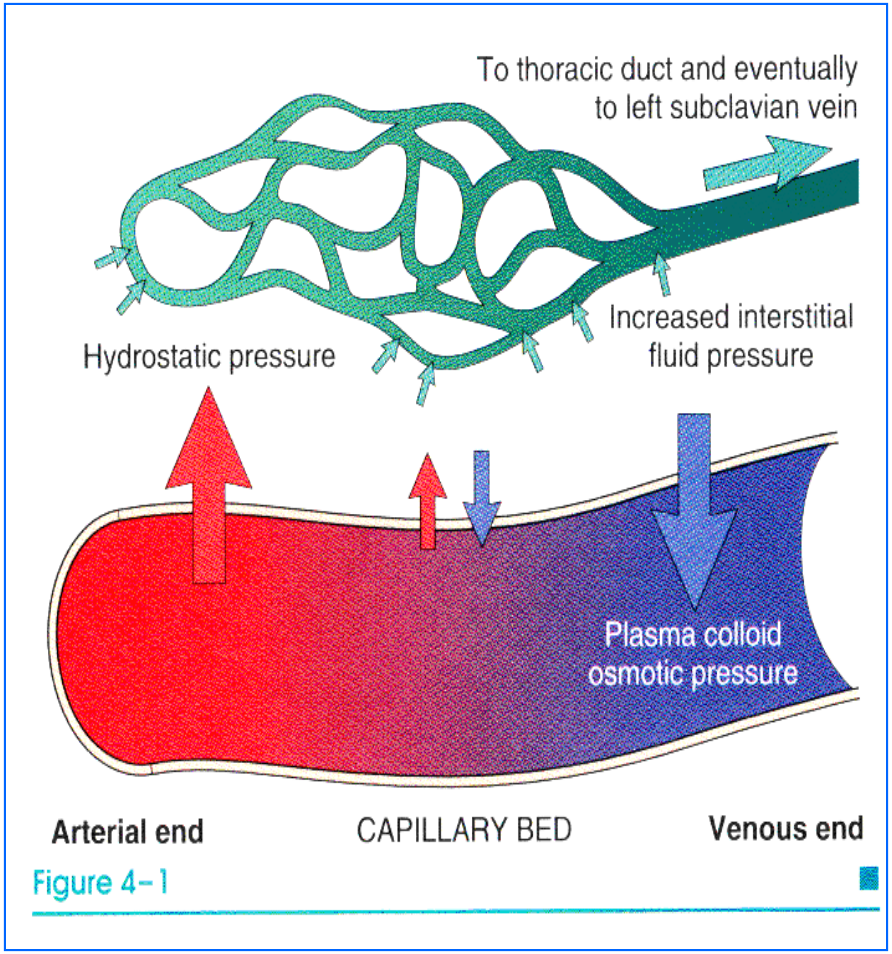
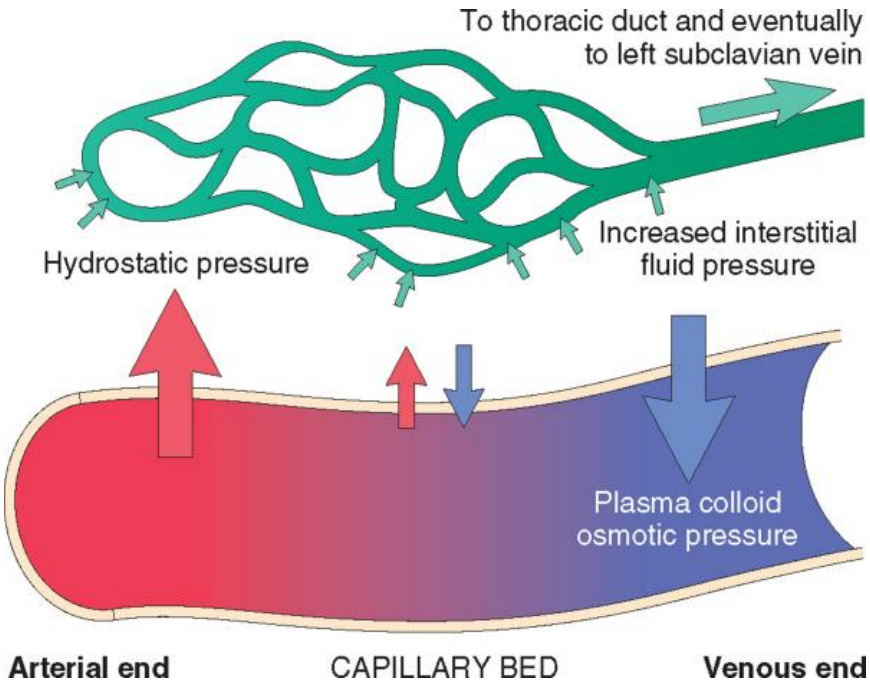


Figure 4–1

EDEMA

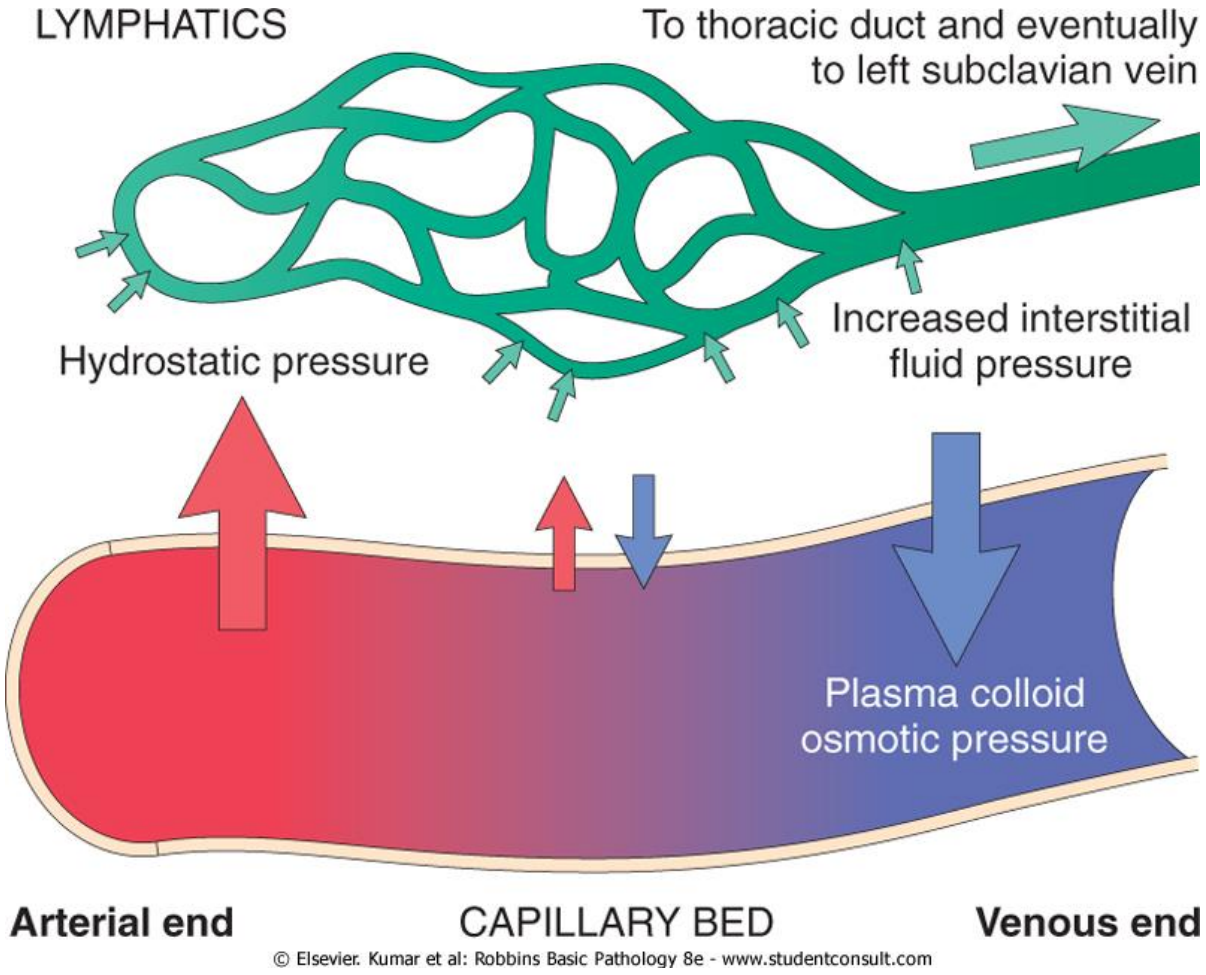


- Increased fluid in the interstitial tissue spaces
- General & local
- Pathogenesis
  - Vascular hydrostatic pressure
  - Plasma colloid osmotic pressure
  - Lymphatic drainage

Fluid Homeostasis

Total extracellular tissue fluid volume

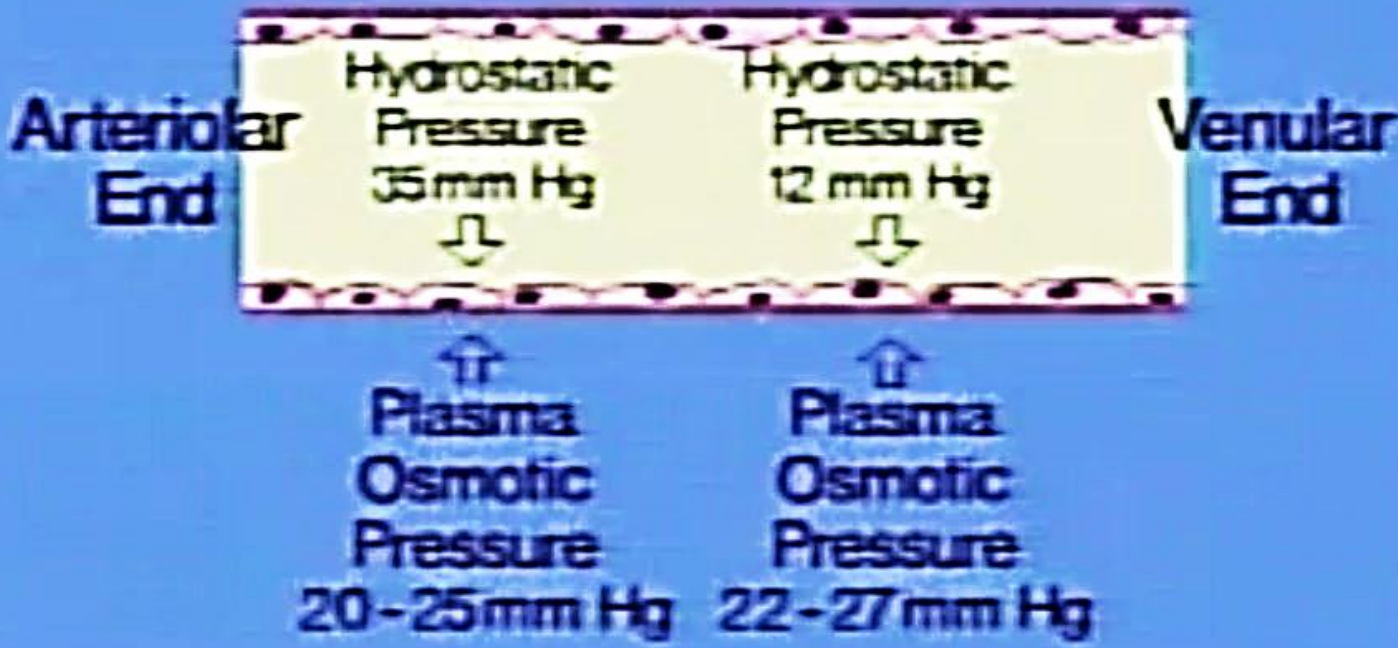
= hydrostatic pressure – [colloid osmotic pressure + lymphatic drainage]



Disruption in fluid homeostasis = edema

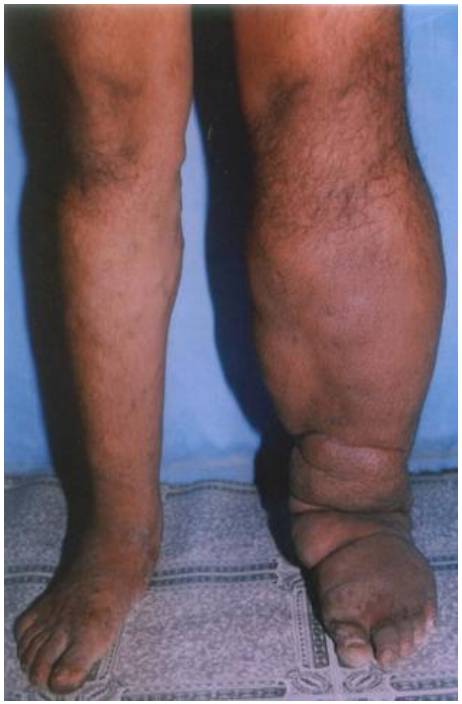
Relationship (Normal)

Hydrostatic & Plasma Osmotic Pressure

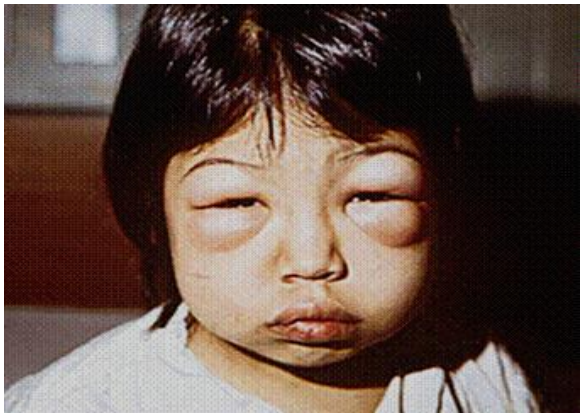


EDEMA

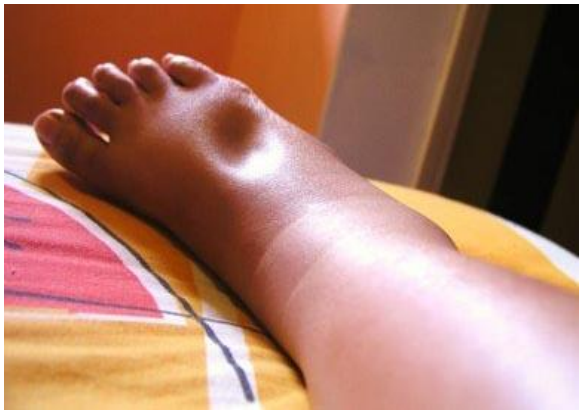
- Increased hydrostatic pressure *(cardiac edema, etc.)*
- Reduced plasma osmotic pressure *(nephrotic, hepatic, malnutrient edema, etc.)*
- Lymphatic obstruction *(filariasis infection — elephantiasis， breast surgery, etc)*
- Sodium and water retention *(ARF, etc)*



elephantiasis



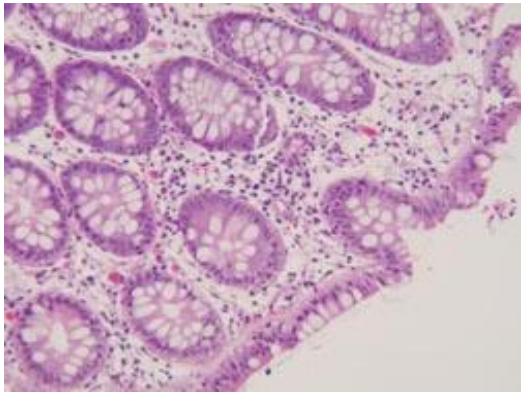
Minimal Change Disease

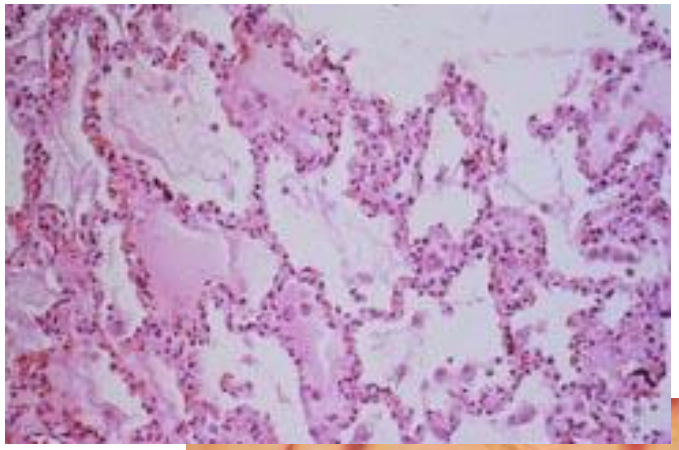


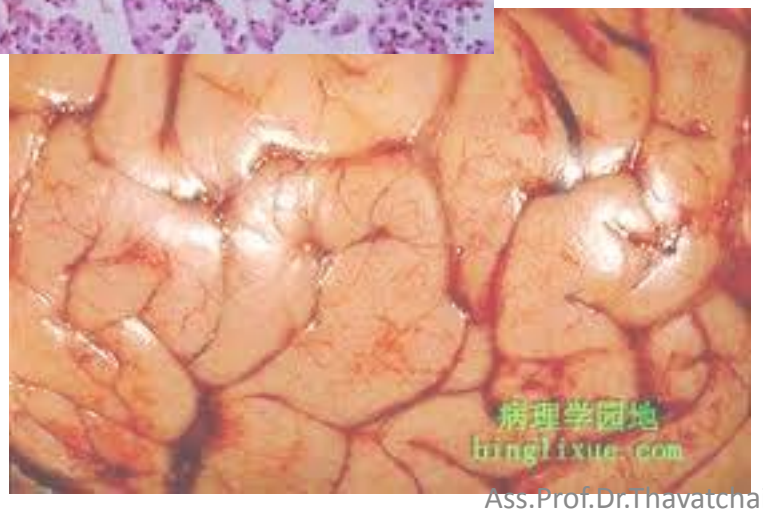
Pitting edema

EDEMA

- Morphology







LM:

Clearing and separation of the extracellular matrix elements

Cell swelling

Subcutaneous edema

Pulmonary edema

Edema of the brain

EDEMA

- Hydrothorax
- hydropericardium
- hydroperitoneum (ascites)
- anasarca

- ***Clinical correlation***

  - from annoying to fatal

  - indicate subtle disease

EDEMA

Increased fluid in the *interstitial tissue spaces or body cavities.*

- Increased hydrostatic pressure:
  - Impaired venous return
    - *Congestive heart failure* (poor right ventricular function)
    - *Constrictive pericarditis*
    - *Ascites* (*peritoneal dropsy*; e.g. from liver *cirrhosis*)
    - Venous obstruction or compression (thrombosis, external pressure, dependency of lower limbs)

- Arteriolar dilation (heat; neurohumoral dysregulation)

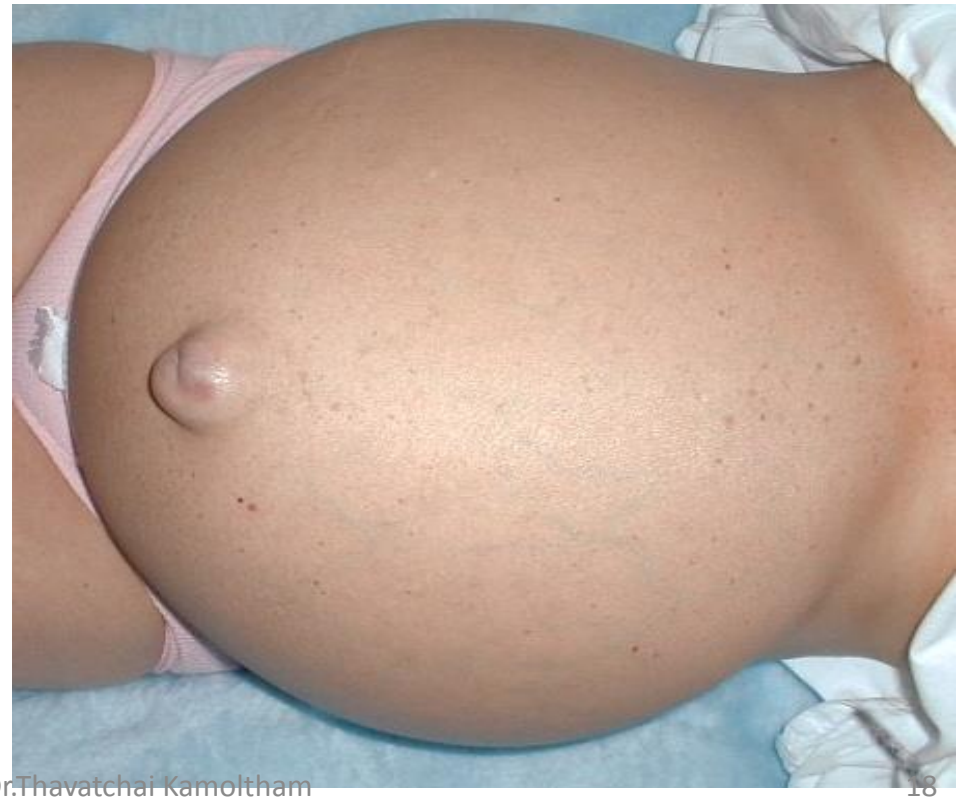
- Reduced plasma osmotic pressure (*hypoproteinemia*)
  - *Nephrotic syndrome* (protein-losing glomerulopathies)
  - Liver cirrhosis (ascites)
  - Malnutrition
  - Protein-losing gastroenteropathy

- Lymphatic obstruction
  – Interstitial fluids are removed via lymphatic drainage, to thoracic duct and left subclavian vein
  – Inflammation, neoplasm, surgery, irradiation

- Sodium retention (water follows sodium)
  – Excess salt intake with renal insufficiency
  – Increased tubular reabsorption of sodium (renal hypertension;renal hypoperfusion-- increased renin-angiotensin-aldosterone secretion)
- Inflammation (acute, chronic, angiogenesis)

HEPATIC ASCITES

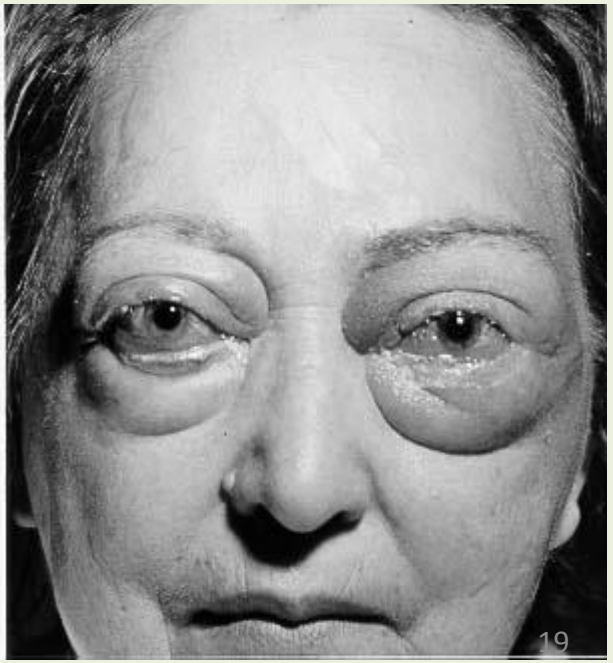
- PORTAL HYPERTENSION
- HYPOALBUMINEMIA



RENAL EDEMA

- SODIUM RETENTION

- PROTEIN LOSING GLOMERULOPATHIES (NEPHROTIC SYNDROME)



GENERALIZED EDEMA (Anasarca)

- HEART
- LIVER
- KIDNEY

Dependent Edema is a prominent feature of Congestive Heart Failure; in legs if standing or sacrum in sleeping patient

Periorbital edema is often the initial manifestation of Nephrotic Syndrome, while late cases will lead to generalized edema.

Pulmonary Edema

- is most frequently seen in Congestive Heart Failure
  - May also be present in renal failure, adult respiratory distress syndrome (ARDS), pulmonary infections and hypersensitivity reactions

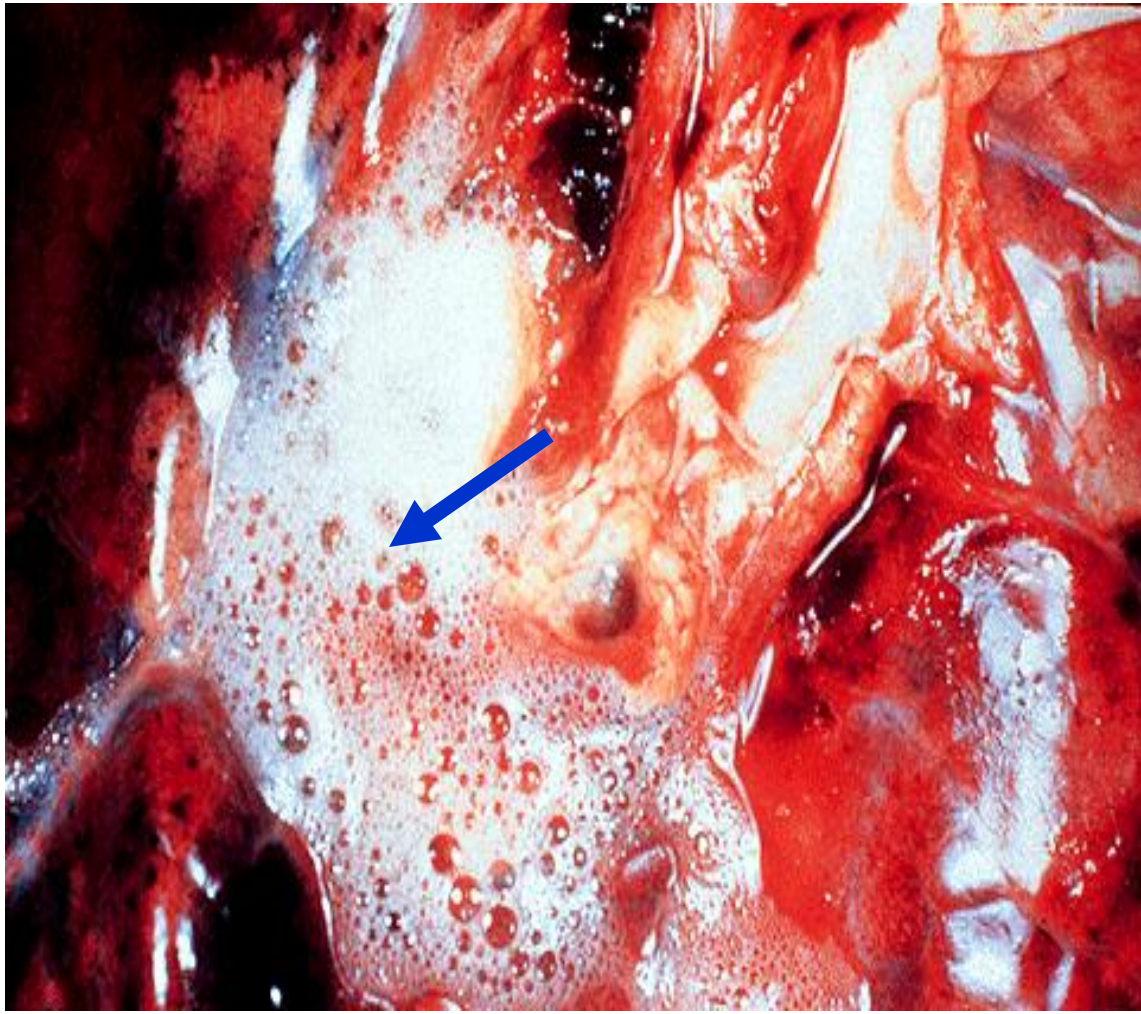
(634) Congestive Heart Failure: Left-sided vs Right-sided, Systolic vs Diastolic, Animation. - YouTube

Pulmonary Edema

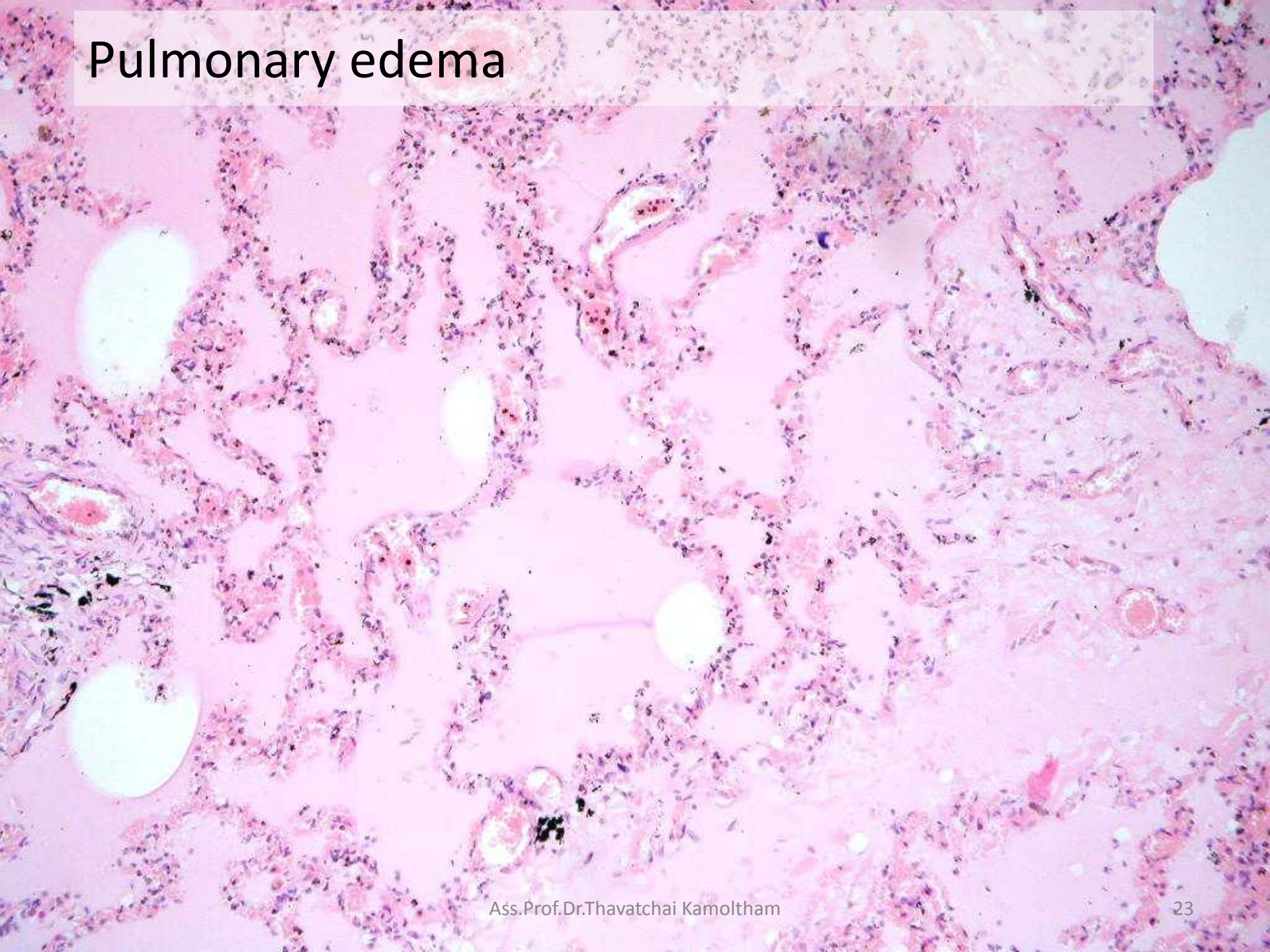
- The Lungs are typically 2-3 times normal weight
- Cross sectioning causes an outpouring of frothy,

  sometimes blood-tinged fluid
- It may interfere

  with pulmonary function



Pulmonary edema



Edema in Congestive Heart Failure

Right-sided Heart Failure:

Right atrial pressure **Increases**

Systemic venous pressure **Increases**

Congestion where?

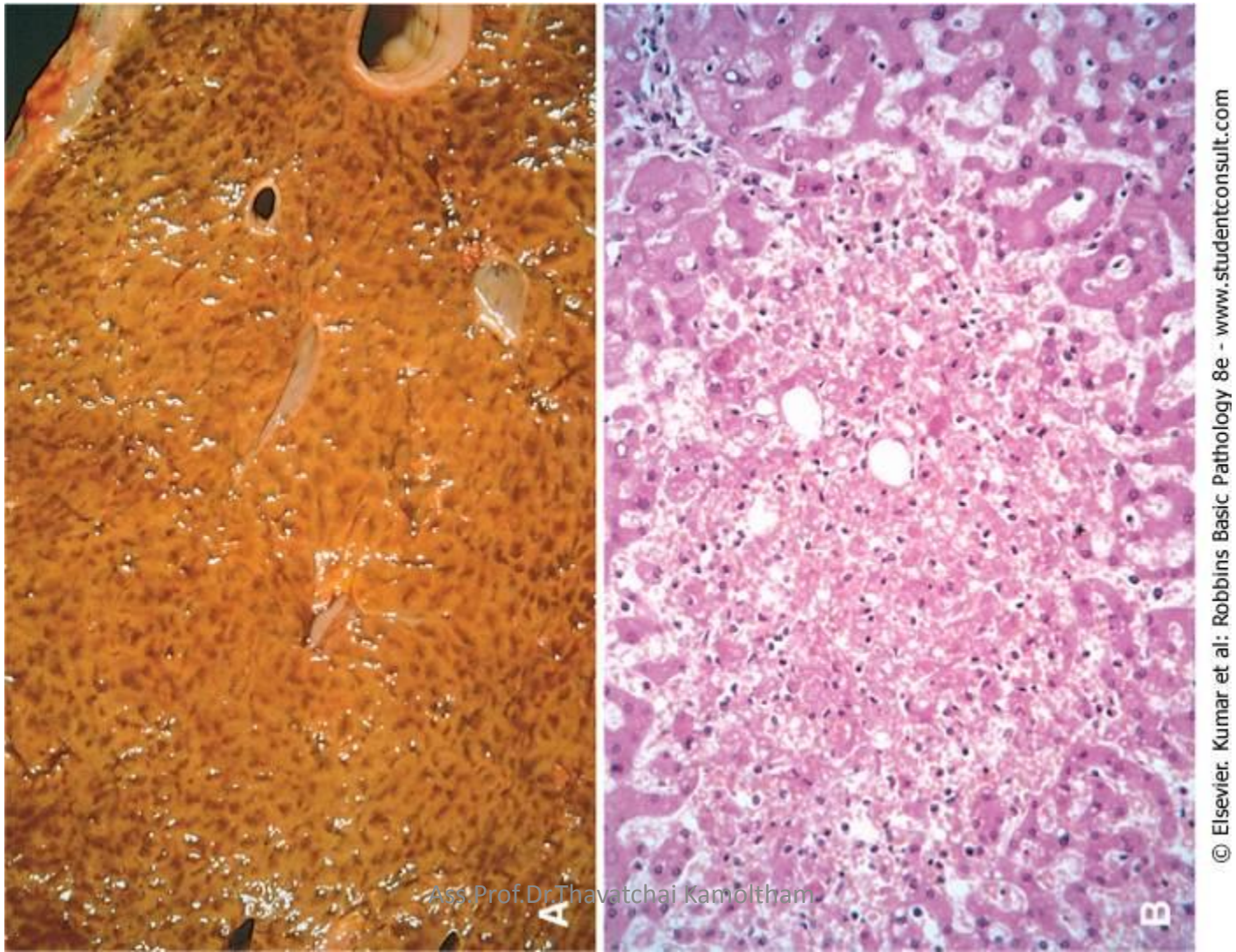
Systemic

- Centrilobular Liver Congestion (venous)

- Lower Extremity Edema

Centrilobular Hepatic Congestion

Blood backs up in liver and impedes flow of oxygenated blood into deepest zones (around central veins), thus causing “central” necrosis and giving the liver a mottled, “nutmeg” appearance.



Edema in Congestive Heart Failure

Left-sided Heart Failure:

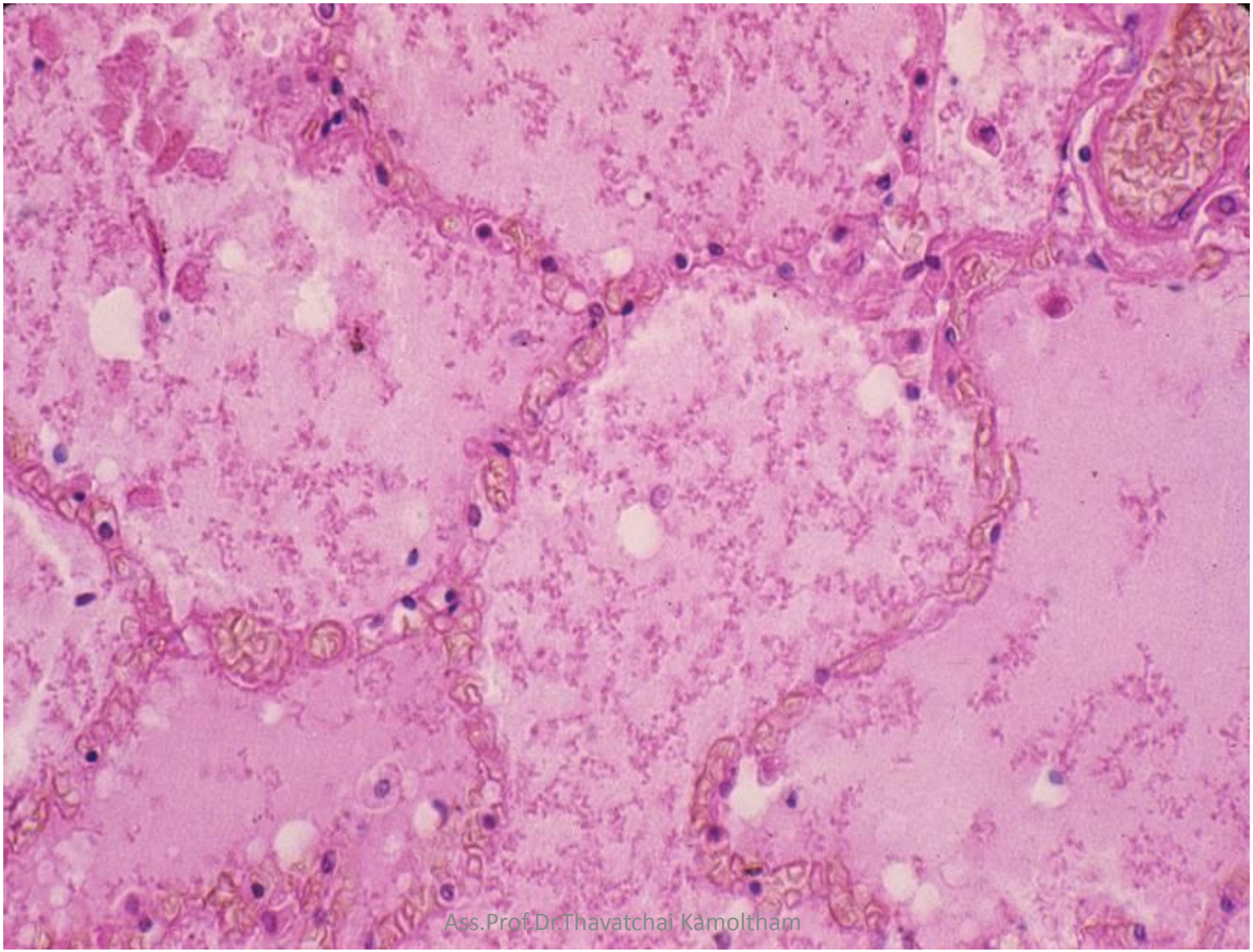
Left atrial pressure: Increases

Pulmonary venous pressure: Increases

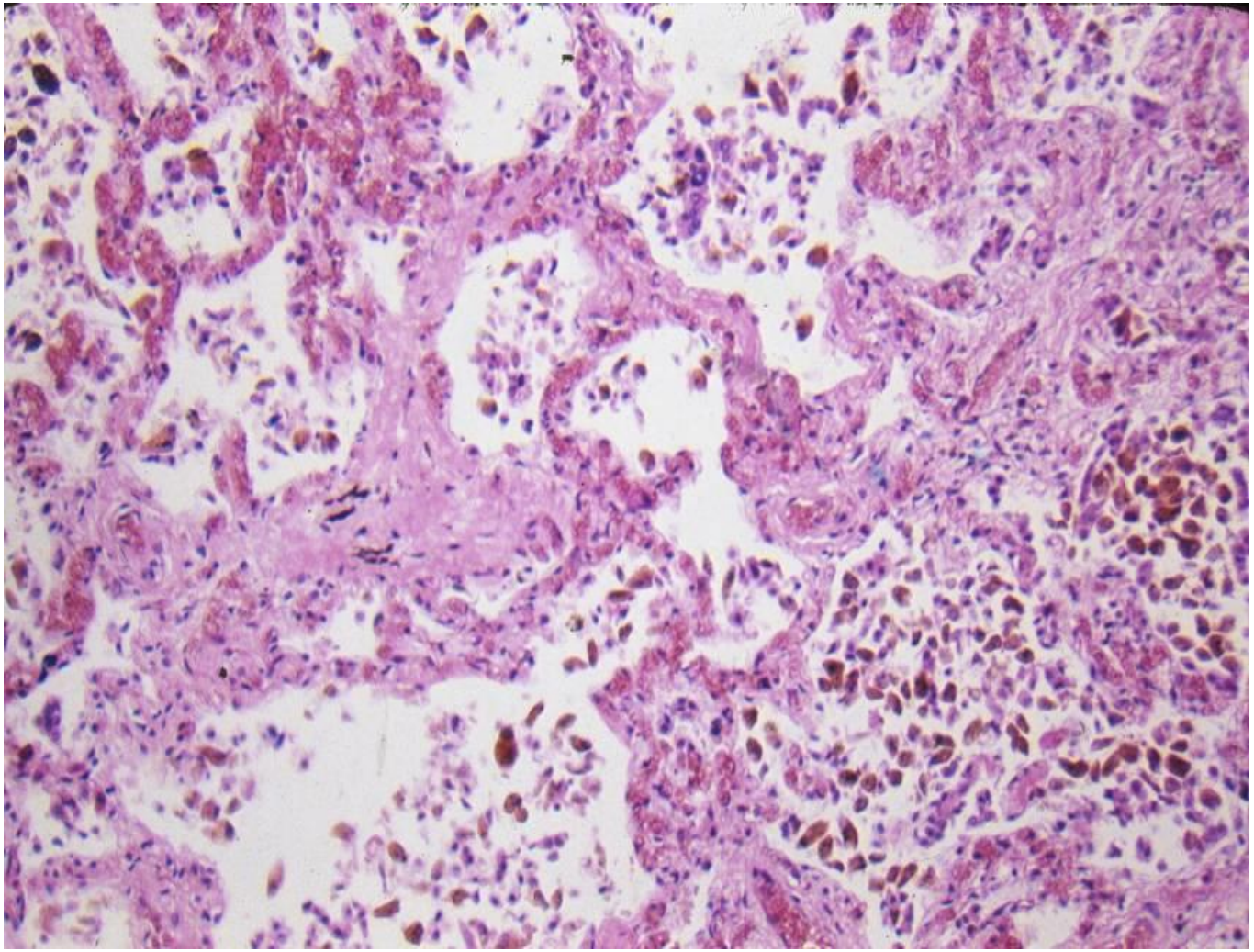
Pulmonary edema/congestion: Key feature of left heart failure, can lead to pulmonary edema

Right atrial pressure: No initial change

Pulmonary edema

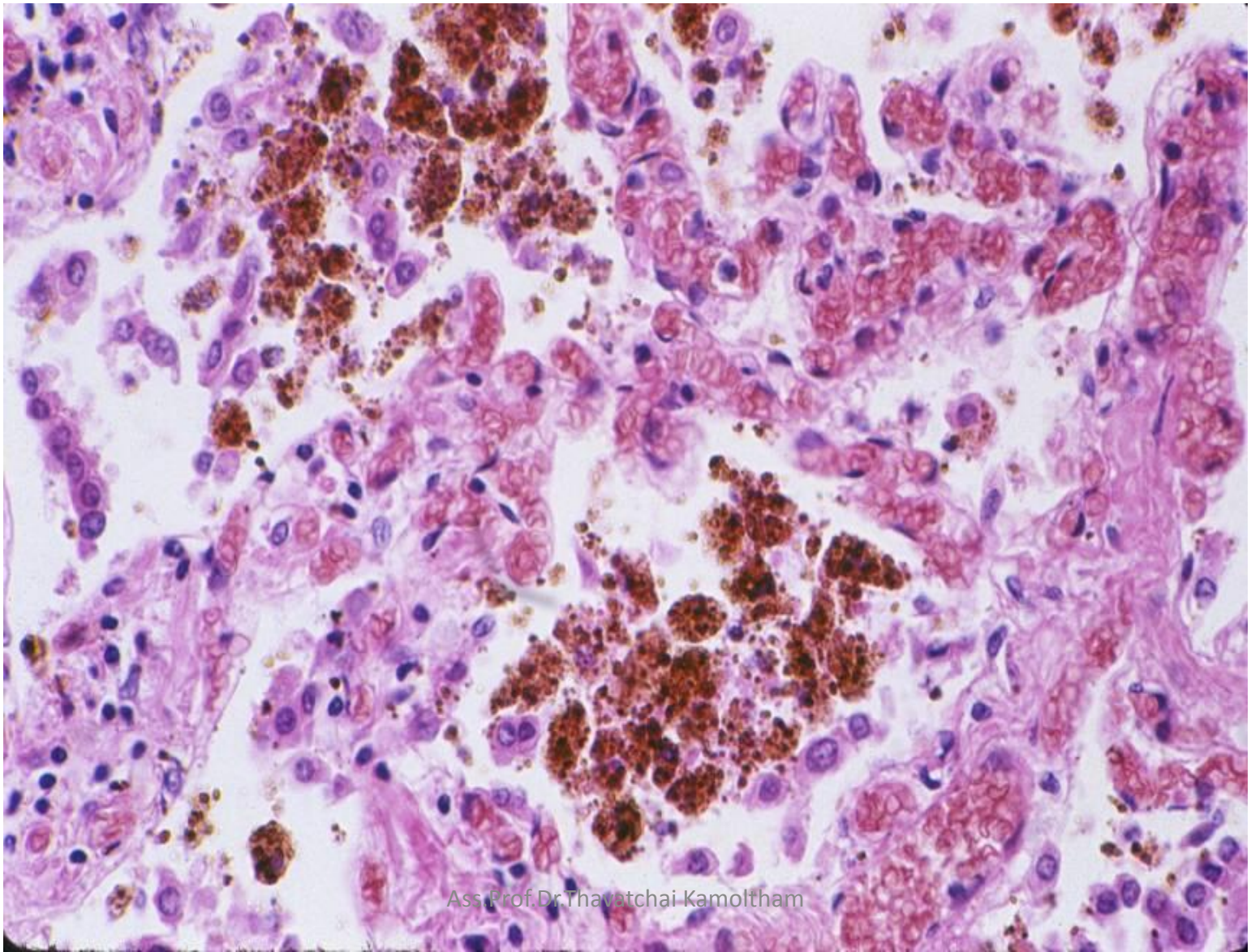


Chronic Pulmonary Congestion



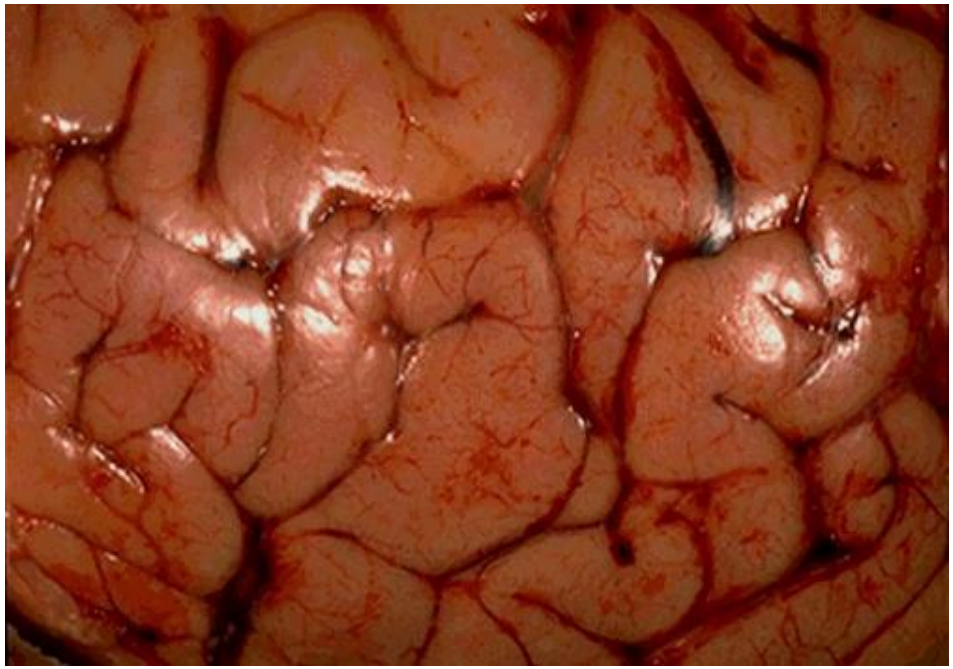
Chronic Pulmonary Congestion

Blood extravasates from capillaries and is taken up by resident macrophages that become engorged with hemosiderin at which point they are commonly referred to as “heart failure cells.”



Brain Edema

- Trauma, Abscess, Neoplasm, Infection (Encephalitis due to say… West Nile Virus), etc



The surface of the brain with cerebral edema demonstrates widened gyri with a flattened surface. The sulci are narrowed

Brain Edema

Clinical Correlation

The big problem is: There is no place for the fluid to go!

- Herniation into the foramen magnum **will kill**

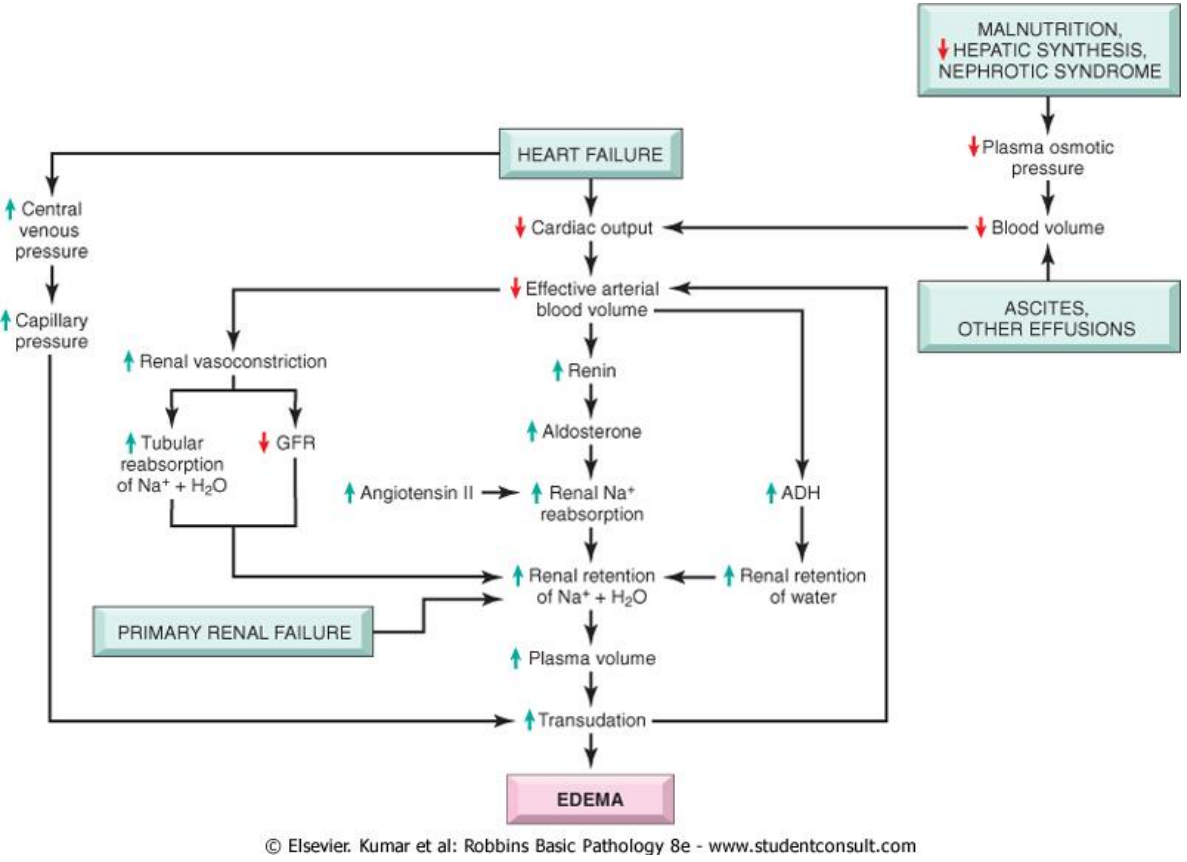
Localized Edema

- Inflammatory
  - Combination of increased blood flow due to arteriolar vasodilation AND increased leakiness of capillary endothelium
- Mechanical
  - Blockage of lymph vessels
    - Filariasis (nematode infection)
    - Neoplasia
    - Chemoterapy/radiotherapy damage to lymphatics

Systemic Edema

- Increased hydrostatic pressure
  - Gravity
  - Congestive Heart Failure
  - Venous Obstruction
    - DVT, Vena cava obstruction
    - Cirrhosis –backs up blood in hepatic portal system
    - Constrictive Pericarditis –similar to CHF, heart can't pump
- Reduced Osmotic Pressure
  - Liver failure (not making enough albumin)
  - Nephrotic syndrome (losing too much albumin)
- Sodium (and water) retention
  - Acute renal failure

Pathways to systemic edema



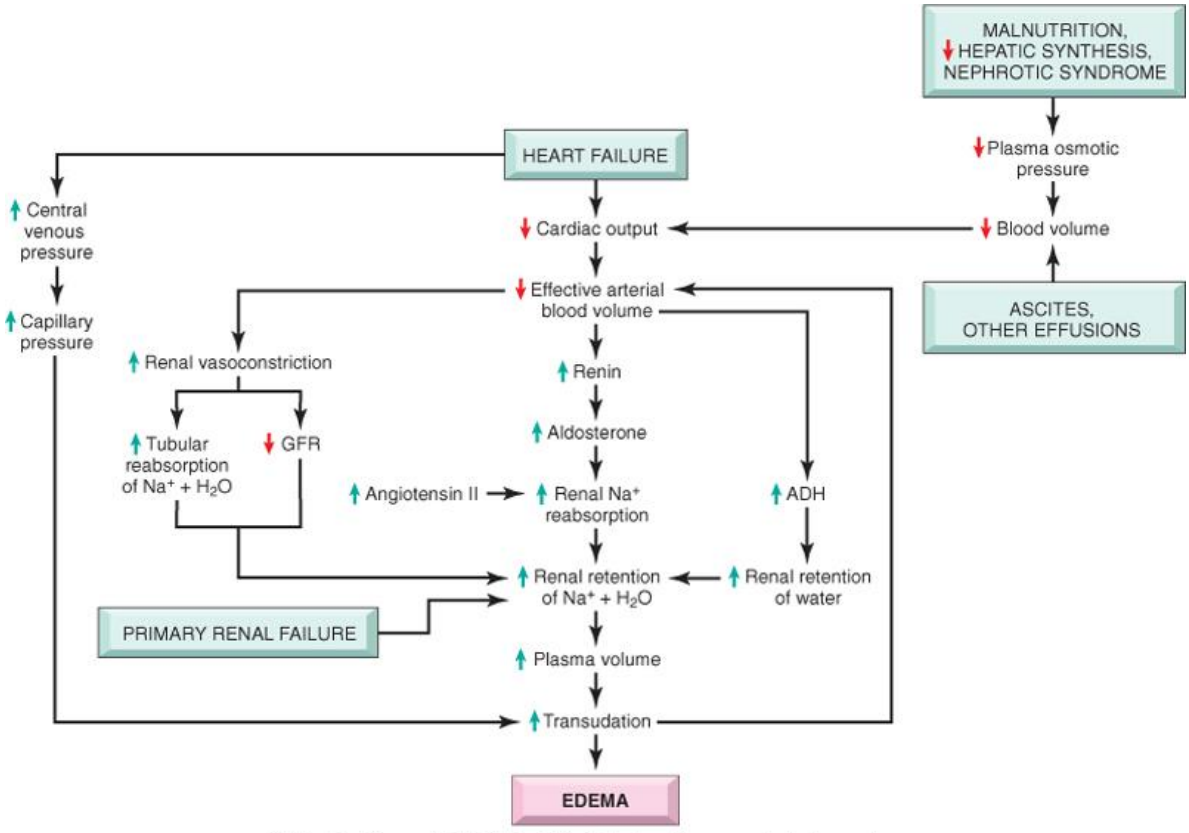
Reduced Oncotic Pressure

- Malnutrition
- Liver failure/dysfunction
  - Can't make enough albumin
  - Also causes hepatic portal congestion
- Nephrotic syndrome
  - Glomerular capillaries too leaky and albumin is lost in urine

Pathways to systemic edema

Congestive Heart Failure

- RV failure: blood backs up in vena cava
- LV failure: blood backs up first in lungs, then vena cava
- Low cardiac output stimulates Renin-Angiotensin-Aldosterone pathway and sets up vicious cycle in kidneys
  - AngII raises systemic BP
  - Aldosterone increases Na+ retention
  - ADH increases water retention



Pathology of Hemodynamics

1. Edema (increased fluid in the ECF)
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9. Infarction (death of tissues w/o blood)

HYPEREMIA & CONGESTION

A local increased volume of blood in a particular tissue

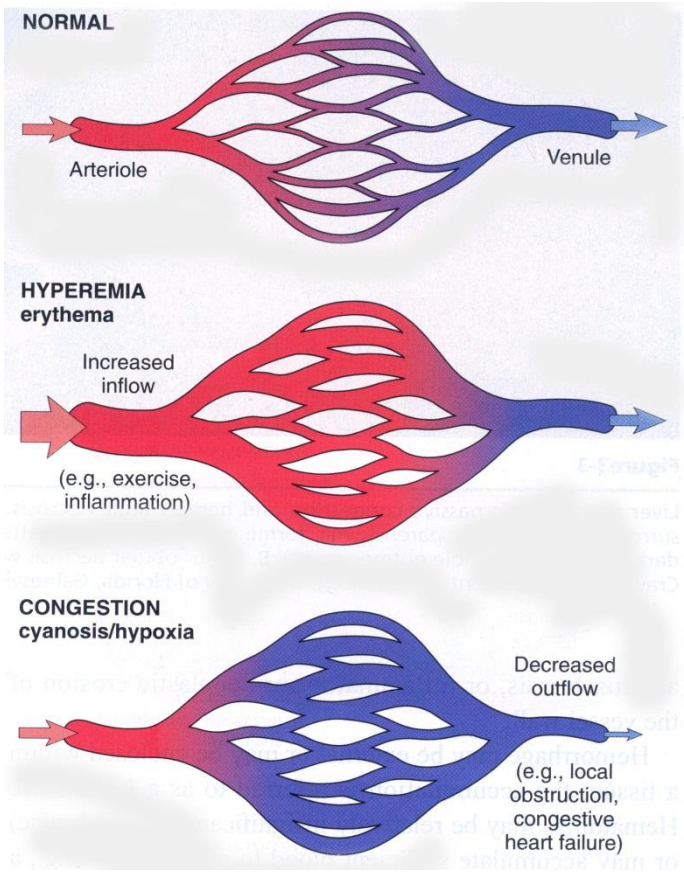
Arterial hyperemia (hyperemia)

An augmented blood flow inducing arteriolar and capillary dilation

Venous hyperemia (congestion)

Accumulation of Blood in Small Veins and capillaries result from drainage difficulty of veins

HYPEREMIA & CONGESTION



Hyperemia:

Active process;

Red, raised tempreture, increased volume ;

Enhanced function;

Congestion:

passive process;

general of local;

Reddish blue color (cyanosis), low temperature, increased volume, edema;

Decreased function

HYPEREMIA

- **Types**

  Physiological: Shy, exercise, taking Meal

  Pathological: Inflammatory, post-decompressed

- **Significance**

  – Benefits

  Plenty supply of O2, functional enhancement, nutrition substance

  – Hazards

  Headache , hemorrhage, stroke

CONGESTION

Causes:

Systemic: general or pulmonary

Cardiac dysfunction (right or left)

Local: local venous compression or obstruction

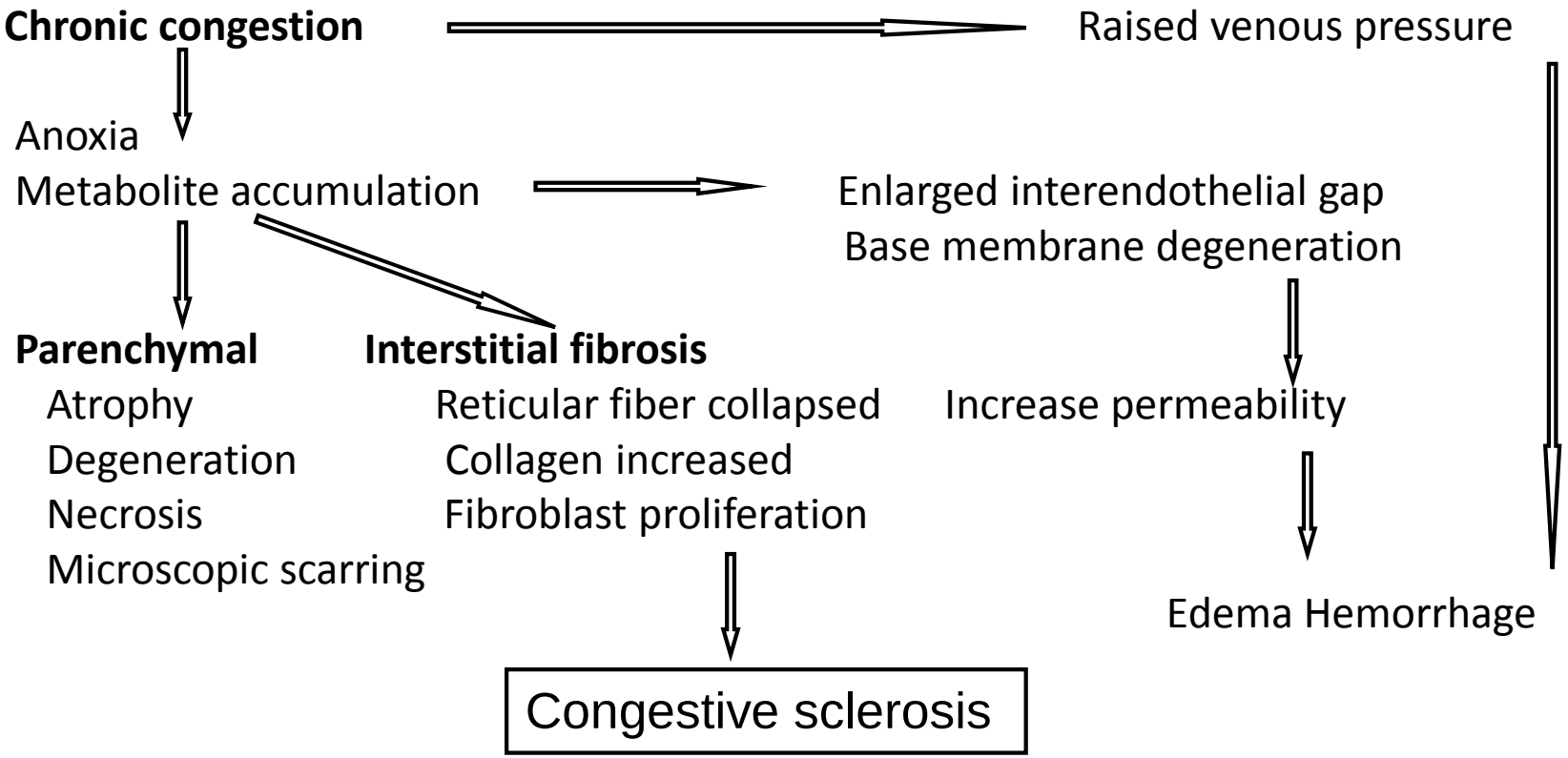
External Compression --- Tumor, Bandage

Occlusion of lumen --- Thrombosis, Embolism

Thickening of venous wall

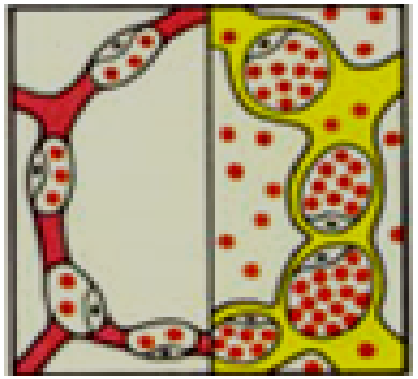
Paralysis of neurogenic modulation --- Burn, frostbite

CONGESTION


Chronic congestion
Raised venous pressure
Anoxia
Metabolite accumulation
Enlarged interendothelial gap
Base membrane degeneration
Parenchymal
Atrophy
Degeneration
Necrosis
Microscopic scarring
Interstitial fibrosis
Reticular fiber collapsed
Collagen increased
Fibroblast proliferation
Increase permeability
Edema Hemorrhage
Congestive sclerosis

CONGESTION

Morphology

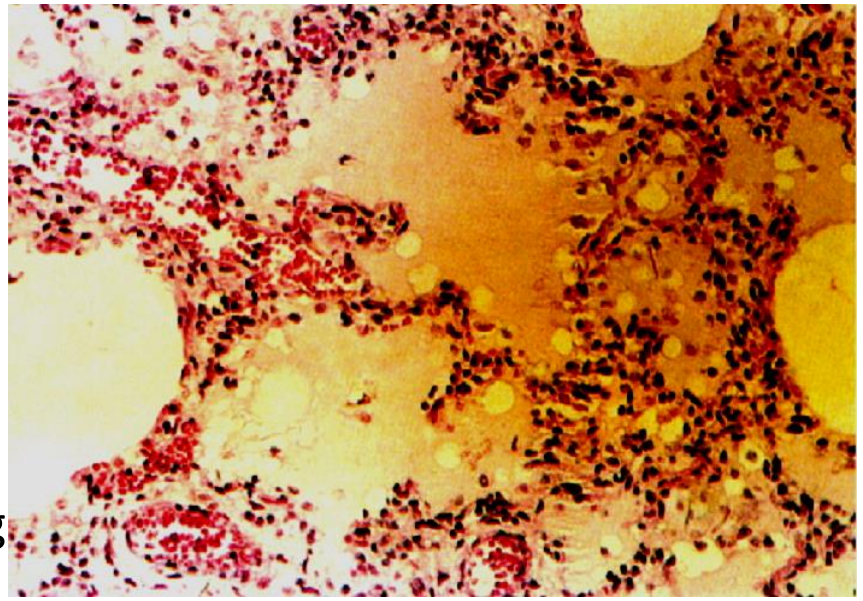


- Grossly hemorrhagic and wet
- Microscopically rich of red blood cells in small vessels

CONGESTION

Lung:

Acute pulmonary congestion

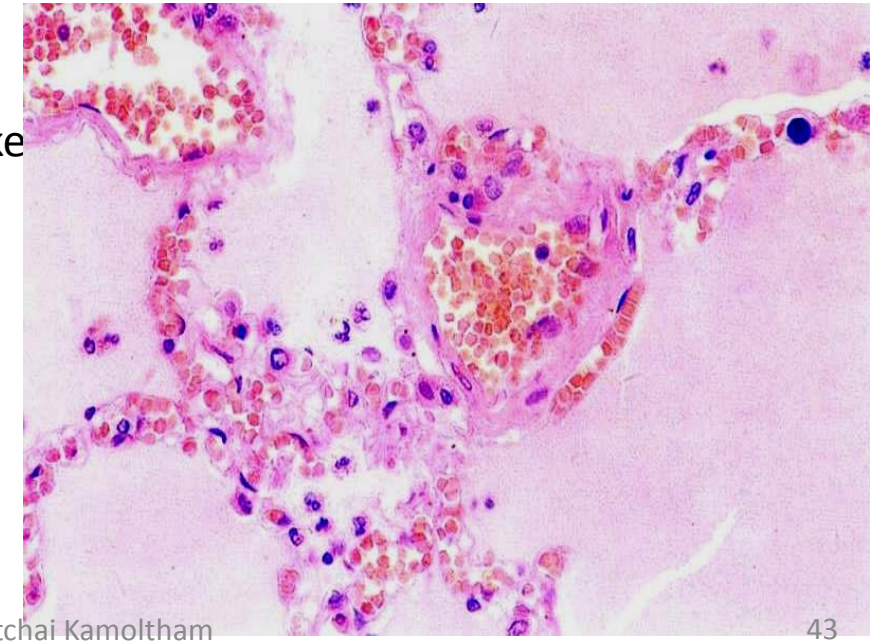


Gross: Plump swollen lung with shining pleura, edematous fluid flowing out while cutting the lung

LM:

Alveolar capillaries highly dilated (rosary- like appearance) and engorged with blood

Alveolar cavity filled with eosinophilic edema fluid



Manifestation

Pink colored foamy sputum

CONGESTION

Lung:

Chronic pulmonary congestion

Gross: Hard, with brown spots scattered

—— Brown induration

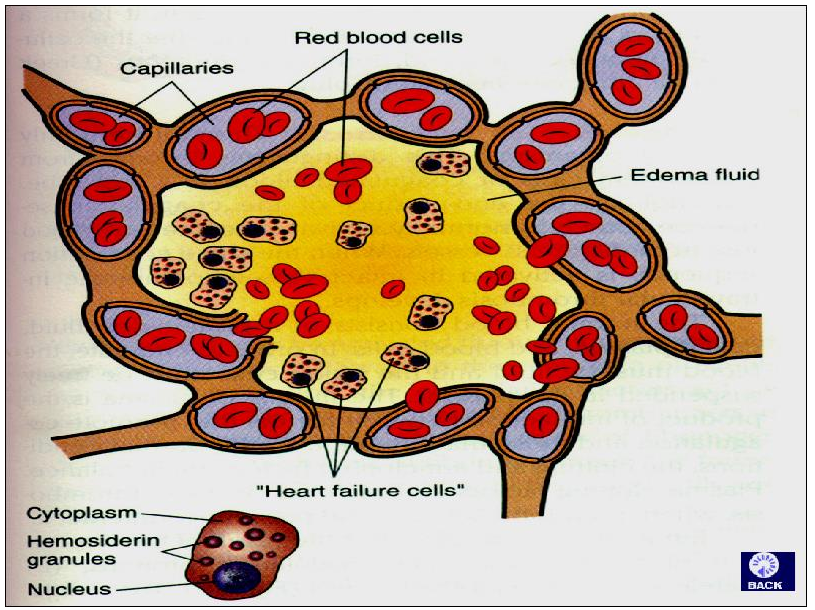
LM:

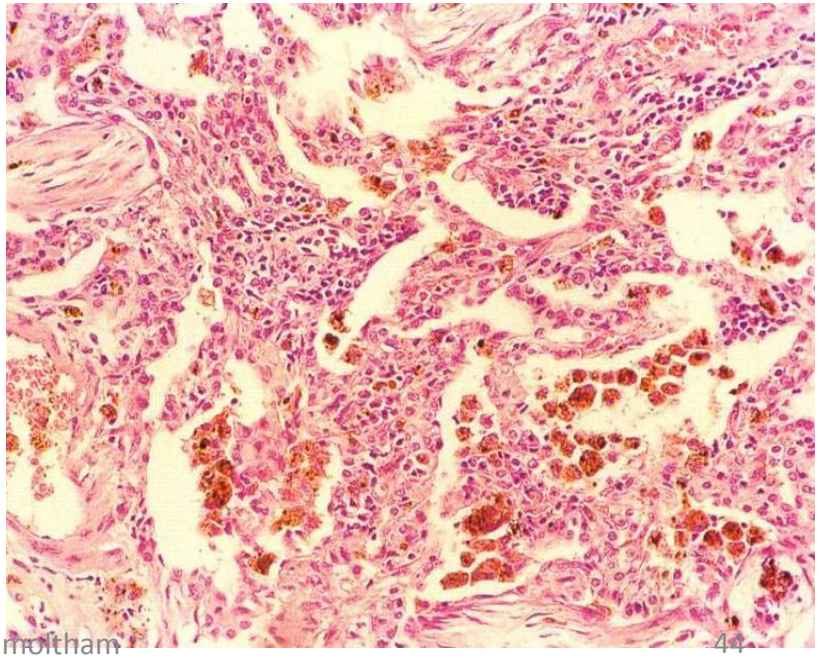
Septa thickened and fibrosis

Alveolar spaces containing 'heart failure cells'— hemosiderin-laden macrophages

Manifestation

Rusty sputum, dyspnea, etc.





CONGESTION

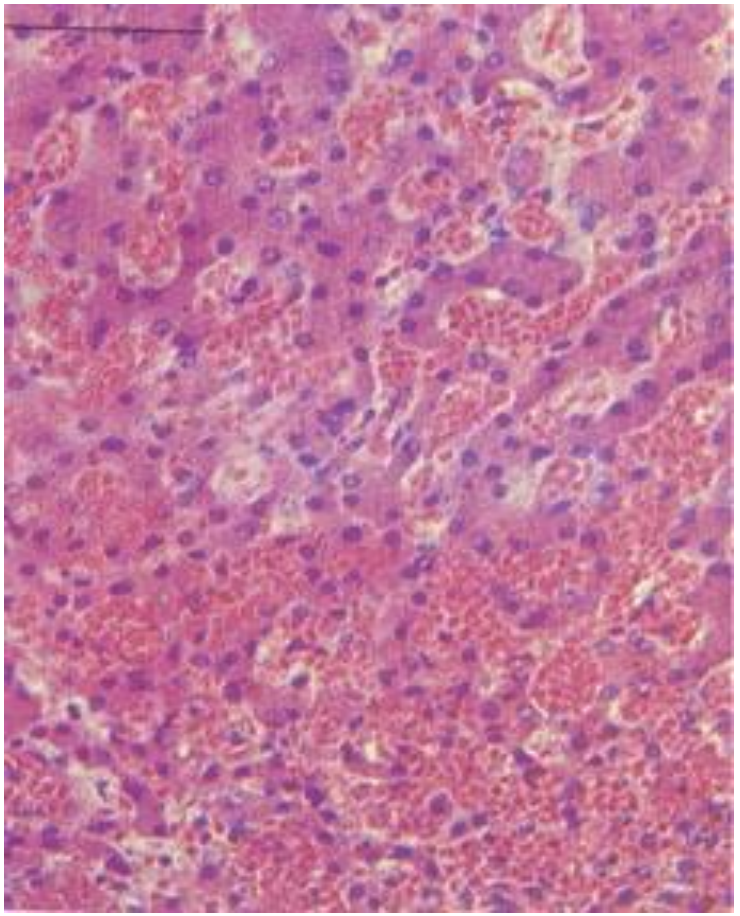
Liver:

Acute hepatic congestion

LM:

— Dilation of central vein and sinusoids with blood

— Atrophy, degeneration and necrosis of central hepatocytes



CONGESTION

Liver:

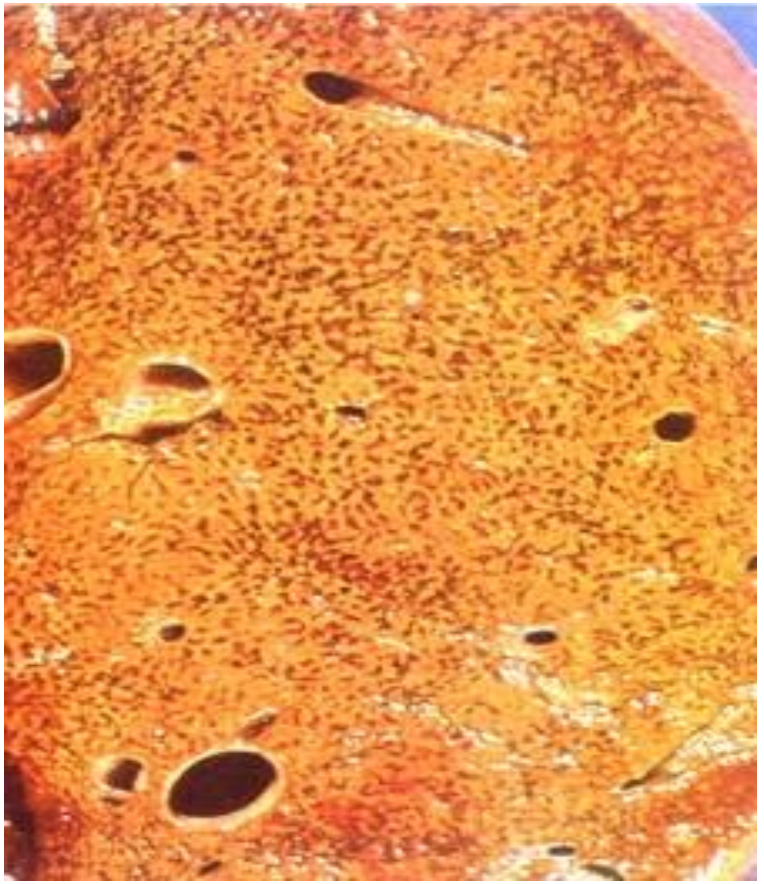
Chronic hepatic congestion

Nutmeg liver

Gross: red-brown zones accentuated against the yellow surrounding zones

LM: centrilobular necrosis and congestion, and perilobular fatty change; fibrosis

Long-standing, severe hepatic congestion: hepatic fibrosis (cardiac cirrhosis)



Transudate vs Exudate

- **Transudate**
  - results from disturbance of Starling forces
  - specific gravity < 1.012
  - protein content < 3 g/dl,
- **Exudate**
  - results from damage to the capillary wall
  - specific gravity > 1.012
  - protein content > 3 g/dl,

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Hemorrhage

In skin, mucous membranes, or serosal surfaces:

Petechiae - tiny (1-2 mm)

Purpura - medium-sized ($\geq$ 3 mm & $\leq$ 1 cm)

Ecchymoses - bruises (> 1 cm)

Hematoma = collection of blood in an organ or tissue:

Hemothorax: in the thorax

Hemoperitoneum: in the peritoneum

Hemopericardium: in the pericardium

Hemarthrosis: in joint

HEMORRHAGE

Causes

- **Rupture of blood vessels**

  Trauma

  Peptic ulcer, aneurism, atherosclerosis

- **Diapedesis**

  Enlarged interendothelial gap (basement membrane injury).

  The intergrity of the vessels remains intact

  Injury to vascular wall: sever infection, anoxia, toxins

  Change in number and quality of platelets

  uremia, leukemia, idiopathic

  Disturbance of coagulation mechanism

  congenital disease, DIC , deficiency of Vit. K

HEMORRHAGE

- *Petechiae*
- *Purpuras*
- *Ecchymoses*
- *Hematoma*
- *Hemothorax*
- *Hemopericardium*
- *Hemoperitoneum*
- *hemoarthrosis*

The clinical significance

depends on the volume, the rate of loss and the site.

- Hemorrhagic shock
- Stroke

Shock

Systemic hypoperfusion caused by **reduced cardiac output** or **reduced blood volume**, resulting in **1) hypotension**, **2) impaired tissue perfusion**, and **3) cellular hypoxia**.

General categories are:

Cardiogenic: reduced cardiac output

Hypovolemic: reduced blood volume

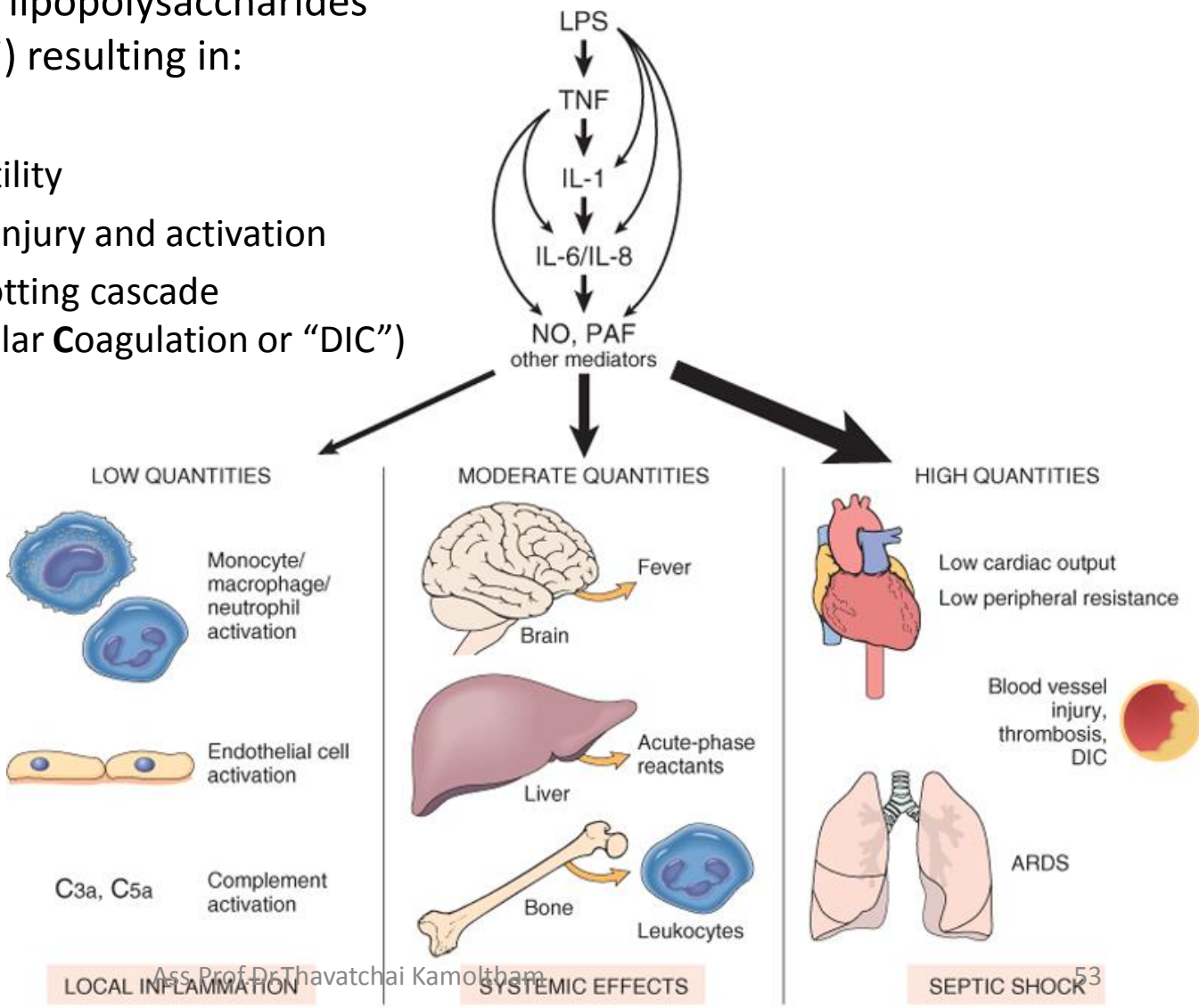
- **Hemorrhagic:** blood loss
- **Neurogenic:** vasodilation following nerve cord injury, spinal block
- **Anaphylactic:** systemic vasodilation and respiratory insufficiency

Septic: over-reactive inflammatory response to infection

Septic shock

Cytokine storm of TNF, IL-1, and IL-6 in response to bacterial antigens (usu. lipopolysaccharides from gram-negative bacilli) resulting in:

1) Systemic vasodilation
2) Reduced cardiac contractility
3) Widespread endothelial injury and activation
4) Systemic activation of clotting cascade (**D**isseminated **I**ntravascular **C**oagulation or "DIC")



General stages of shock

- **Nonprogressive stage:** reflex compensatory mechanisms (tachycardia, peripheral vasoconstriction, renal fluid retention) compensate for hypoperfusion.
  - Causes common symptoms associated with shock: weak, rapid pulse; shallow, rapid breathing; and cool, clammy skin (the **exception** is **septic shock** that may present with **flushing** due to widespread inflammatory response).
- **Progressive stage:** metabolic lactic acidosis blunts vasomotor response and blood starts to pool in peripheral tissues (increasing hypercoagulative risk), vital organs perfused less and begin to fail.
  - Clinical symptoms associated with this phase are reduced urine output, acidosis, and electrolyte imbalances
- **Irreversible stage:** widespread tissue necrosis induces systemic inflammatory response (vasodilation, etc.), reduced cardiac function, and acute renal failure.

SHOCK

- **Definition: CARDIOVASCULAR COLLAPSE**
- **Common pathophysiologic features:**
  - **INADEQUATE CARDIAC OUTPUT and/or**
  - **INADEQUATE BLOOD VOLUME**
- **Pathogenesis**
  - **Cardiac** (634) Shock, Pathology of Different Types, Animation - YouTube
  - **Septic**
  - **Hypovolemic**

GENERAL RESULTS

- INADEQUATE TISSUE PERFUSION
- CELLULAR HYPOXIA
- UN-corrected, a FATAL outcome

TYPES of SHOCK

- **CARDIOGENIC**: (Acute, Chronic Heart Failure)
- **HYPOVOLEMIC**: (Hemorrhage or Leakage)
- **SEPTIC**: ("ENDOTOXIC" shock, #1 killer in ICU)
- NEUROGENIC: (loss of vascular tone)
- ANAPHYLACTIC: (IgE mediated systemic vasodilation and increased vascular permeability)

CARDIOGENIC shock

- MI
- VENTRICULAR RUPTURE
- ARRHYTHMIA
- CARDIAC TAMPONADE
- PULMONARY EMBOLISM (acute RIGHT heart failure or “cor pulmonale”)

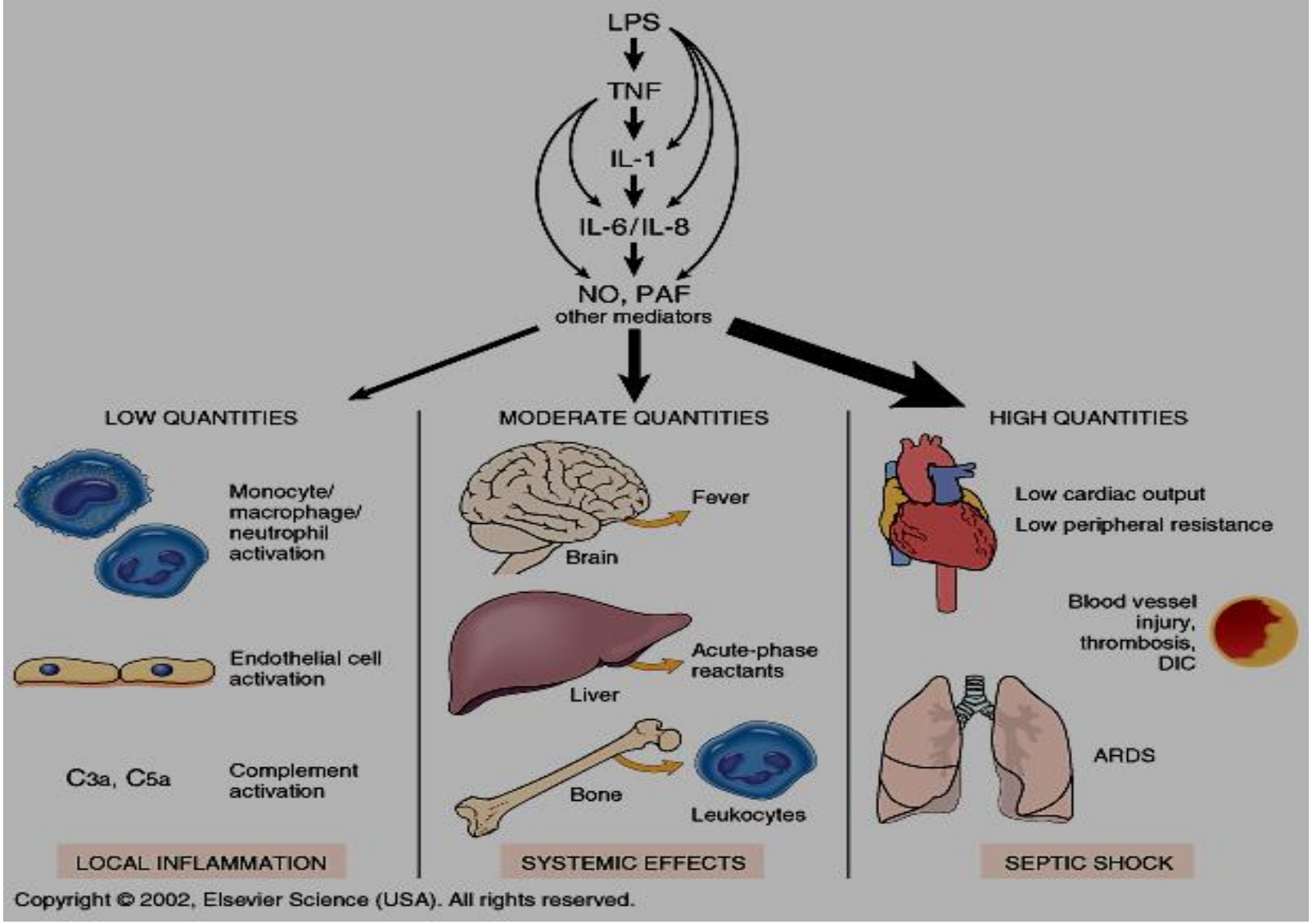
HYPOVOLEMIC shock

- HEMORRHAGE, Vasc. compartment→H2O
- VOMITING, Vasc. compartment→H2O
- DIARRHEA, Vasc. compartment→H2O
- BURNS, Vasc. compartment→H2O

SEPTIC shock

- OVERWHELMING INFECTION
- "ENDOTOXINS", i.e., LPS (Usually Gm-)
- Degraded bacterial cell wall products
- Also called "LPS", because they are **L**ipo-**P**oly-**S**accharides
- Attach to a cell surface antigen known as CD-14

- Gm+
- FUNGAL
- "SUPERANTIGENS", (Superantigens are polyclonal T-lymphocyte activators that induce systemic inflammatory cytokine cascades similar to those occurring downstream in septic shock, "toxic shock" antigents by staph are the prime example.)



LPS = lipopolysaccharide

TNF = tumor necrosis factor

IL = interleukin

NO = nitric oxide

PAF = platelet-activating factor

Effects of Lipopolysaccharide

SEPTIC shock events

(linear sequence)

- SYSTEMIC VASODILATION (hypotension)→
- ↓ MYOCARDIAL CONTRACTILITY→
- DIFFUSE ENDOTHELIAL ACTIVATION→
- LEUKOCYTE ADHESION→
- ALVEOLAR DAMAGE→ (ARDS)
- DIC
- VITAL ORGAN FAILURE→ CNS

CLINICAL STAGES of shock

NON-PROGRESSIVE

- COMPENSATORY MECHANISMS
- CATECHOLAMINES
- VITAL ORGANS PERFUSED

PROGRESSIVE

- HYPOPERFUSION
- EARLY "VITAL" ORGAN FAILURE
- OLIGURIA
- ACIDOSIS

IRREVERSIBLE

- HEMODYNAMIC CORRECTIONS of no use

Morphologic Features of Shock

- Brain: ischemic encephalopathy
- lung :DAD (Diffuse Alveolar Damage,)
- Heart: subendocardial hemorrhages and necrosis
- Kidneys: acute tubular necrosis or diffuse cortical necrosis
- Gastrointestinal tract: patchy hemorrhages and necrosis
- Liver: fatty change or central hemorrhagic necrosis
- DIC
- MULTIPLE ORGAN FAILURE

CLINICAL PROGRESSION of SYMPTOMS(linear sequence)

- Hypotension →
- Tachycardia →
- Tachypnea →
- Warm skin→ Cool skin→ Cyanosis
- Renal insufficiency→
- Obtundance
- Death