# ***Pathophysiology***

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**Lecture 10**

# IV. Disorders of cardiovascular system

## X. Pulmonary edema

*An abnormal accumulation of fluid in the air sacs of the lungs and parenchyma, which leads to shortness of breath and can cause problems with the exchange of gas (oxygen and carbon dioxide), resulting in poor oxygenation of blood.*

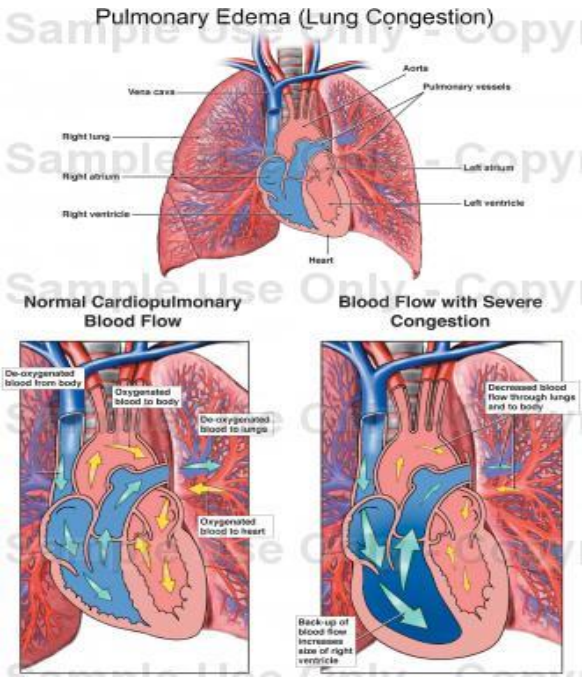
The person with severe pulmonary edema is usually seen

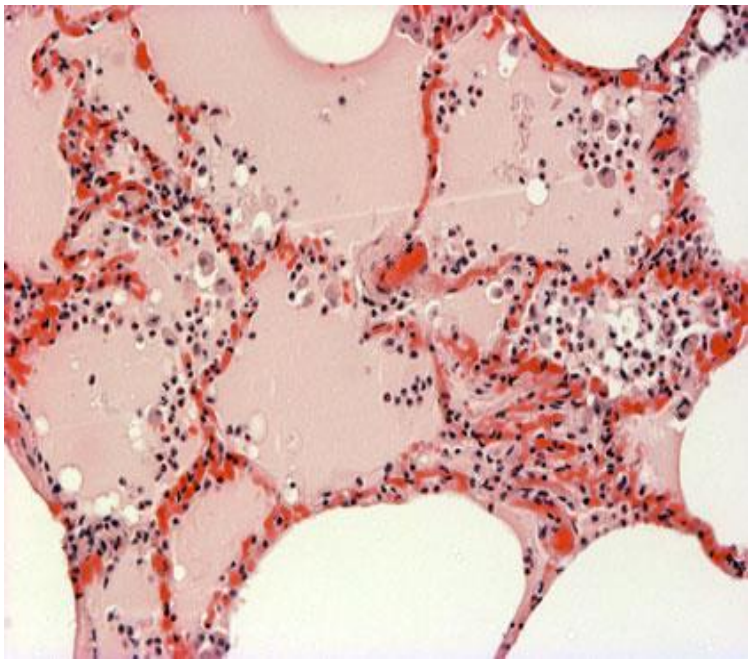
1. Sitting and gasping for air.
2. The pulse is rapid,
3. The skin is moist and cool,
4. The lips and nail beds are cyanotic.
5. As the pulmonary edema worsens and oxygen supply to the brain drops, confusion and stupor appear.
6. Dyspnea and air hunger are accompanied by a productive **cough with frothy** (resembling beaten egg whites) and often blood-tinged sputum—the effect of air mixing with the serum albumin and red blood cells that have moved into the alveoli.
7. The movement of air through the alveolar fluid produces fine crepitate sounds called **crackles**, which can be heard with chest auscultation. As fluid moves into the larger airways, the crackles become louder and coarser.

Pulmonary edema could be divided in to two types according to the causes:

***I. Cardiogenic***

**Pathophysiology**: Caused by rapid transudation of fluid into lungs secondary to increased **pulmonary wedge pressure(** *is the pressure measured by wedging a pulmonary catheter with an inflated balloon into a small pulmonary arterial branch***).** without time for compensation of pulmonary bed. Increased wedge pressure translates to increased pulmonary venous pressure and elevated microvascular pressure, leading to transudation of fluid (Starling's forces at work!). Can occur at wedge pressures as low as 18mmHg or not until >25mmHg if chronic condition has resulted in increased lymphatic drainage capacity.



**Myocardial infarction**

↓

**A Decrease in the left ventricular function**

↓

**Increase in the left ventricular end diastolic function**

↓

**Transmission back to the left atrium & pulmonary Artery**

↓

**Increase venous pressure**

↓

**Increase capillary hydrostatic pressure**

↓

**Increase transcapillary gradients**

↓

**Movement of fluid into the interstitium**

↓

**edema**

***Etiology:***

**A. Heart muscle:**

1. **Systolic dysfunction:** Coronary arterial disease, systemic hypertension, valvular disease.
2. **Diastolic dysfunction:** Increase in ventricular stiffness impairs filling leading to proximal pressure rise. Causes include hypertrophic and restrictive cardiomyopathies, ischemia, HTN crises.

**B. Valvular problems:**

1. **Mitral stenosis.**
2. **Aortic stenosis.**
3. **Aortic regurgitation.**

**C. Other:**

1. **Renal artery stenosis.**
2. **Atrial myxoma.**

***II. Non cardiogenic***

***A.*** *Radiographic evidence of alveolar fluid accumulation without elevated pulmonary capillary wedge pressure.*

**Pathophysiology:**

Alveolar-capillary membrane becomes damaged and leaky, resulting in movement of proteins and water into interstitial space. **Note: hypoalbuminemia does NOT cause pulmonary edema.**

**Etiologies:**

**A. Acute respiratory distress syndrome (ARDS).** Multiple etiologies, including sepsis, DIC, inhaled toxins, radiation pneumonia, inhalation of high oxygen concentrations, severe trauma (thoracic or otherwise).

**B. Re-expansion** pulmonary edema: can occur after re-expansion of pneumothorax or following removal of large amounts of pleural fluid (>1.0-1.5 L).

**C. High altitude pulmonary edema**.

**D. Narcotic overdose**: From overdose of heroin or methadone. Usually occurs within 2 hours of injection. Pathophysiology unknown but believed due to direct toxicity, hypoxia, hyperventilation, or cerebral edema.

**E. Pulmonary embolism.**

## *The arterial blood pressure*

***Reflects the rhythmic ejection of blood from the left ventricle into the aorta. It rises as the left ventricle contracts and falls as it relaxes pressure***.

**Systolic pressure** ideally is less than 120 mm Hg, and the lowest pressure, called the **diastolic pressure**, is less than 80 mm Hg. The difference between the systolic and diastolic pressure (approximately 40 mm Hg) is the **pulse pressure**. The mean arterial pressure (approximately 90 to 100 mm Hg).

| Category | Systolic BP(mmHg) | Diastolic BP(mmHg) |
|---|---|---|
| Optimal blood pressure | <120 | <80 |
| Normal blood pressure | <130 | <85 |
| High-normal blood pressure | 130–139 | 85–89 |
| Grade 1 hypertension (mild) | 140–159 | 90–99 |
| Grade 2 hypertension (moderate) | 160–179 | 100–109 |
| Grade 3 hypertension (severe) | !180 | !110 |
| Isolated systolic hypertension(Grade 1) | 140–159 | <90 |
| Isolated systolic hypertension (Grade 2) | !160 | <90 |

## XI. Essential hypertension

In **90% of all cases the reason for hypertension remains unclear**. This is called **essential hypertension**. Hypertension is generally a product of genetic predisposition with environmental and lifestyle factors.

**Genetic predisposition: a family history**

1. Hypertension.
2. Heart disease.
3. Type 2 diabetes.

**Environmental factors:**

1. Age.
2. Hormone state.

There is no significant difference in the development of hypertension between men and women although the ***prevalence of hypertension increases sharply with*** **age, especially for women**.

**Lifestyle – influential risk factors**:

1. Smoking.
2. Heavy drinking.
3. Being overweight
4. Sodium and calorie-rich diet.
5. Lack of physical activity.
6. Stress.

**Essential hypertension** *is characterized by a sustained systolic pressure of greater than 140 mm Hg and a diastolic BP at greater than 90 mm Hg*.

**Pathophysiologic characteristics of essential hypertension.**

- No known cause.
- Diastolic pressure repeatedly > 90 mm Hg.
- Total peripheral resistance usually increased.
- Pulse pressure possibly increased or decreased.
- Cardiac output normal, or elevated in some, possibly early in the disease.
- Cardiac work increased.
- Altered renal physiology, with accelerated natriuresis and reduced renal blood flow.
- **Normal** blood flow to most regions; **diminished** renal and skin blood flow and **increased** muscle flow may develop.
- Plasma volume **reduced** (may be inversely related to diastolic pressure).
- **Hyper-reactivity** of pressure to stress, abnormal vascular reactivity and impaired circulatory homeostasis.

## XII. Secondary hypertension

Is defined as *any hypertension with an identifiable underlying cause*. It is much less common than the other type, essential hypertension, affecting only **5% of hypertensive patients**. Unlike primary hypertension many of the conditions causing secondary hypertension can be corrected or cured by surgery or specific medical treatment. It has many different causes including

endocrine diseases, kidney diseases, and tumors. It also can be a side effect of many medications.

**Common causes**

Intrinsic Renal Disease
Renovascular Disease
Mineralocorticoid excess/ aldosteronism

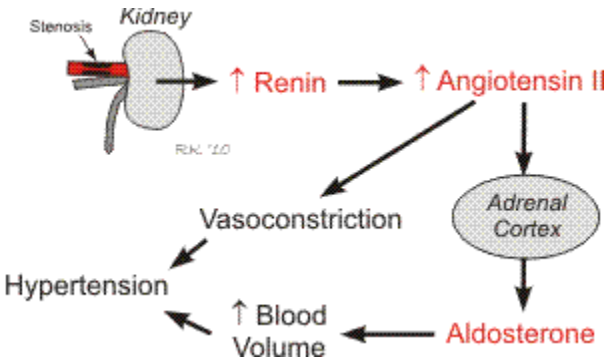
**Uncommon causes**

Pheochromocytoma
Glucocorticoid excess/ Cushing's disease
Coarctation of Aorta
Hyper/hypothyroidism

**<u>Causes of Secondary hypertension</u>**

1. **Renal diseases**: ( ***Most common causes of Secondary HPT***)

a) **Renal artery stenosis:** The normal physiological response to low blood pressure in the renal arteries is to **increase cardiac output** (CO) to maintain the pressure needed for glomerular filtration. Here, however, increased CO cannot solve the structural problems causing renal artery hypotension, with the result that CO remains chronically elevated.




b) **Renal parenchymal disease.**
c) **Renal vascular disease.**
d) **Renin-producing tumors.**
e) **Primary sodium retention (Liddle's syndrome).**
f) **Increased intravascular volume.**

**2- Endocrine:**

a) **Acromegaly.**
b) **Hypothyroidism.**
c) **Hyperthyroidism.**
d) **Hyperparathyroidism.**
e) **Adrenal cortical.**
f) **Cushing syndrome.**
g) **Primary aldosteronism.**
h) **Apparent mineralocorticoid excess.**
i) **Adrenal medulla.**
j) **Pheochromocytoma.**
k) **Carcinoid syndrome.**

**3- Drugs and exogenous hormones**

**4- Neurological causes**

a) **Increase intracranial pressure**
b) **Quadriplegia**
c) **Guillain–Barre syndrome**

**5- Obstructive sleep apnea (OSA)**

**6- Acute stress related secondary HTN**

**7- Diseases of the aorta**

a) **Rigidity of the aorta**
b) **Coarctation of the aorta**

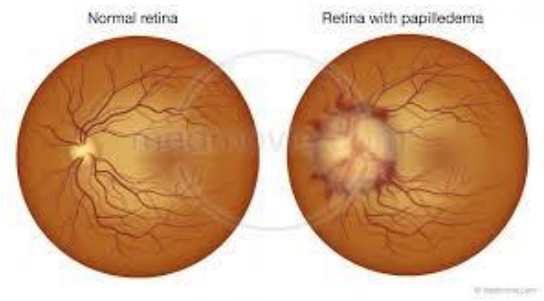
**8- Pregnancy induced HTN**

9- **Isolated systolic HTN due to an increased cardiac output.**

## XIII. Malignant hypertension

A hypertensive emergency *is a condition in which elevated blood pressure results in target organ damage.* The systems primarily involved include the **central nervous system**, the **cardiovascular system, and the renal system**. **Malignant hypertension and accelerated hypertension are both hypertensive emergencies**, with similar outcomes and therapies. In order to diagnose malignant hypertension, **papilledema must be present**.

***Blood Pressure.*** In patients with malignant hypertension, the range of presenting BP is wide, with diastolic BP ranging from 100 to 180 mmHg and systolic BP from 150 to 290 mmHg. Pre-existing stable hypertension is often, but not always, present for several years before the onset of the malignant phase.




**Pathophysiology of Malignant hypertension**

The **renin-angiotensin system plays a central role in the homeostasis of BP.** A rise in plasma renin activity stimulates the production of angiotensin II, a vasoconstrictor that results in increased vascular resistance and BP. In severe HTN there is amplification of the renin-angiotensin system; a rise in levels of renin and angiotensin II leading to **high aldosterone secretion, resulting in damage to the endothelium of blood vessels**, as evidenced by fibrin thrombi in the vessels. It is proposed that high BP leads to high vascular reactivity and critical levels of vasoactive agents such as norepinephrine, angiotensin II, and vasopressin leading to natriuresis, which brings about hypovolemia, triggering even more elevation of the vasoconstrictive agents. This leads to **arteriolar fibroid necrosis** which precipitates endothelial damage followed by platelet deposition and release of thromboxane which can result in a **microangiopathic hemolytic anemia**. It further results in myointimal proliferation/damage with an endpoint of ischemia.

Ischemia releases further vasoconstrictive agents, which propagates the cycle.

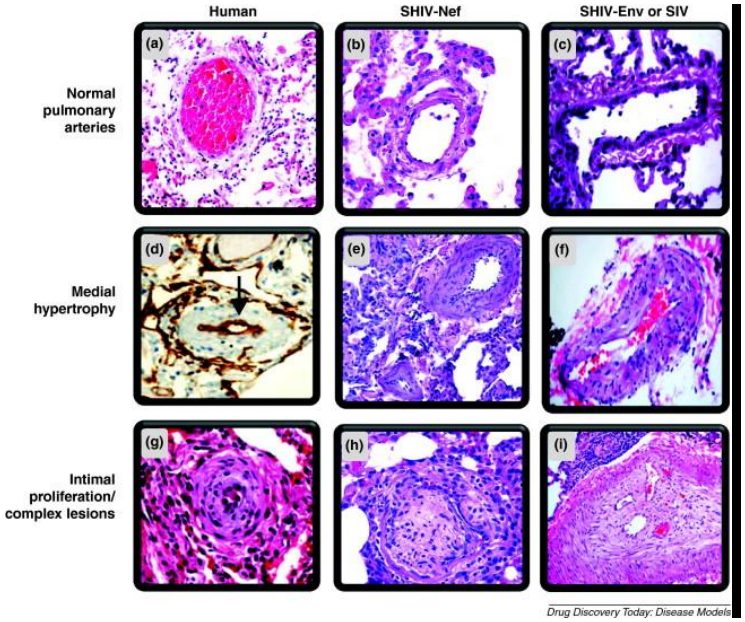
BP =PVR. X CO. (SV. X HR.)

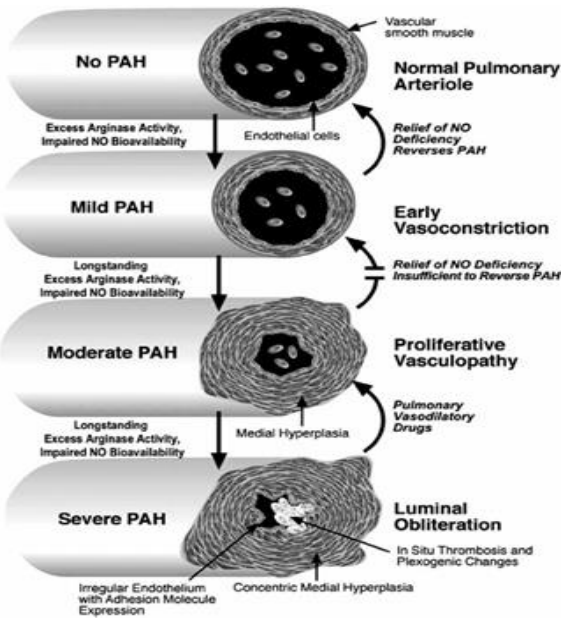
Rate at which MAP rises more important than absolute rise

**Acute rise in BP** → **Failure of vasoconstriction by auto regulation** → **Endothelial damage** → **Deposition. of proteins/ fibrinogen in vessel wall** → **Activates coagulation and inflammation** → **FIBRINOID NECROSIS** → **Acute rise in BP**

***- Renin-angiotensin-aldosterone system plays an important role in initiating and perpetuating BP rise by causing vasoconstriction and fluid retention.***

***- THIS CYCLE MUST BE STOPPED IN ORDER TO PREVENT FURTHER VASCULAR INJURY AND TISSUE ISCHEMIA!***


Human
SHIV-Nef
SHIV-Env or SIV
Normal pulmonary arteries
Medial hypertrophy
Intimal proliferation/ complex lesions
(a)
(b)
(c)
(d)
(e)
(f)
(g)
(h)
(i)
Drug Discovery Today: Disease Models


Vascular smooth muscle
No PAH
Normal Pulmonary Arteriole
Excess Arginase Activity, Impaired NO Bioavailability
Endothelial cells
Relief of NO Deficiency Reverses PAH
Mild PAH
Early Vasoconstriction
Longstanding Excess Arginase Activity, Impaired NO Bioavailability
Relief of NO Deficiency Insufficient to Reverse PAH
Moderate PAH
Proliferative Vasculopathy
Pulmonary Vasodilatory Drugs
Longstanding Excess Arginase Activity, Impaired NO Bioavailability
Medial Hyperplasia
Severe PAH
Luminal Obliteration
In Situ Thrombosis and Plexogenic Changes
Irregular Endothelium with Adhesion Molecule Expression
Concentric Medial Hyperplasia

Life has 2 rules:
#1: Never Quit
#2: Always remember rule #1
-Unknown
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