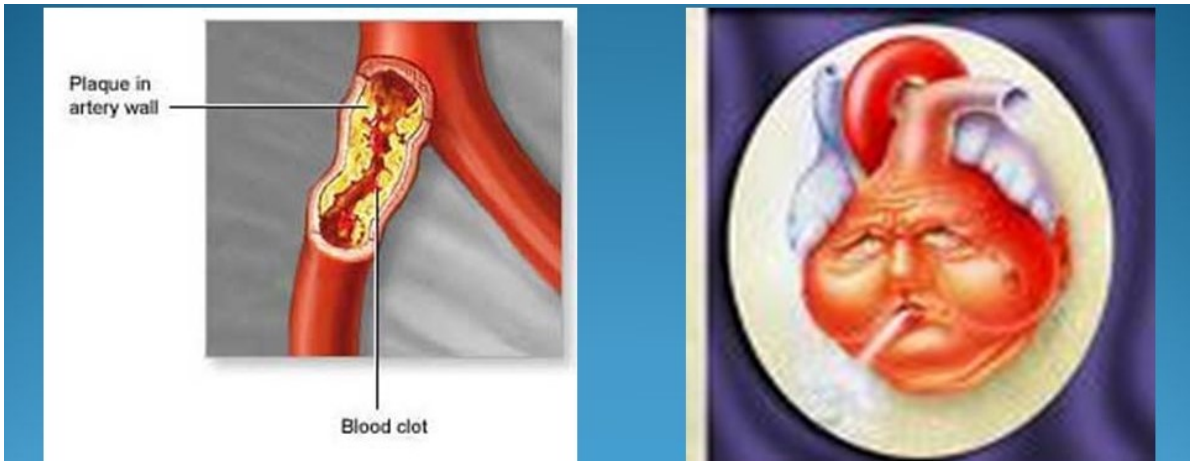
PATHOPHYSIOLOGY OF CARDIOVASCULAR DISORDERS



Course Name: Pathophysiology

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HYPERTENSION and HYPOTENSION

Key Facts (WHO , 2023)

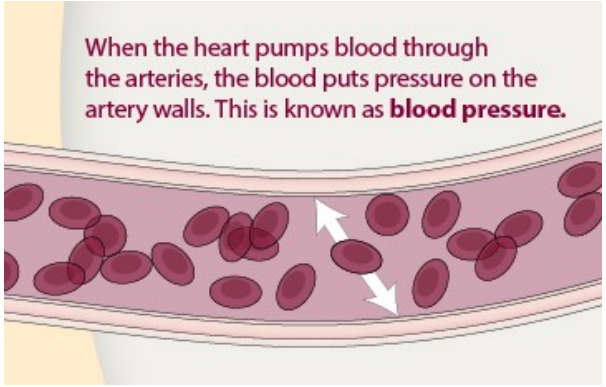
- An estimated 1.28 billion adults aged 30–79 years worldwide have hypertension, most (two-thirds) living in low- and middle-income countries
- An estimated 46% of adults with hypertension are unaware that they have the condition.
- Less than half of adults (42%) with hypertension are diagnosed and treated.
- Approximately 1 in 5 adults (21%) with hypertension have it under control.
- Hypertension is a major cause of premature death worldwide.
- One of the global targets for noncommunicable diseases is to reduce the prevalence of hypertension by 33% between 2010 and 2030.

What is blood pressure?

- Blood pressure is the pressure of blood pushing against the walls of your arteries. Arteries carry blood from your heart to other parts of your body. → (*PERFUSION*)

- Arterial BP is hemodynamically generated by the interplay between blood flow and the resistance to blood flow. It is mathematically defined as the product of cardiac output (CO) and total peripheral resistance (TPR) according to the following equation:

- $BP = CO \times TPR$



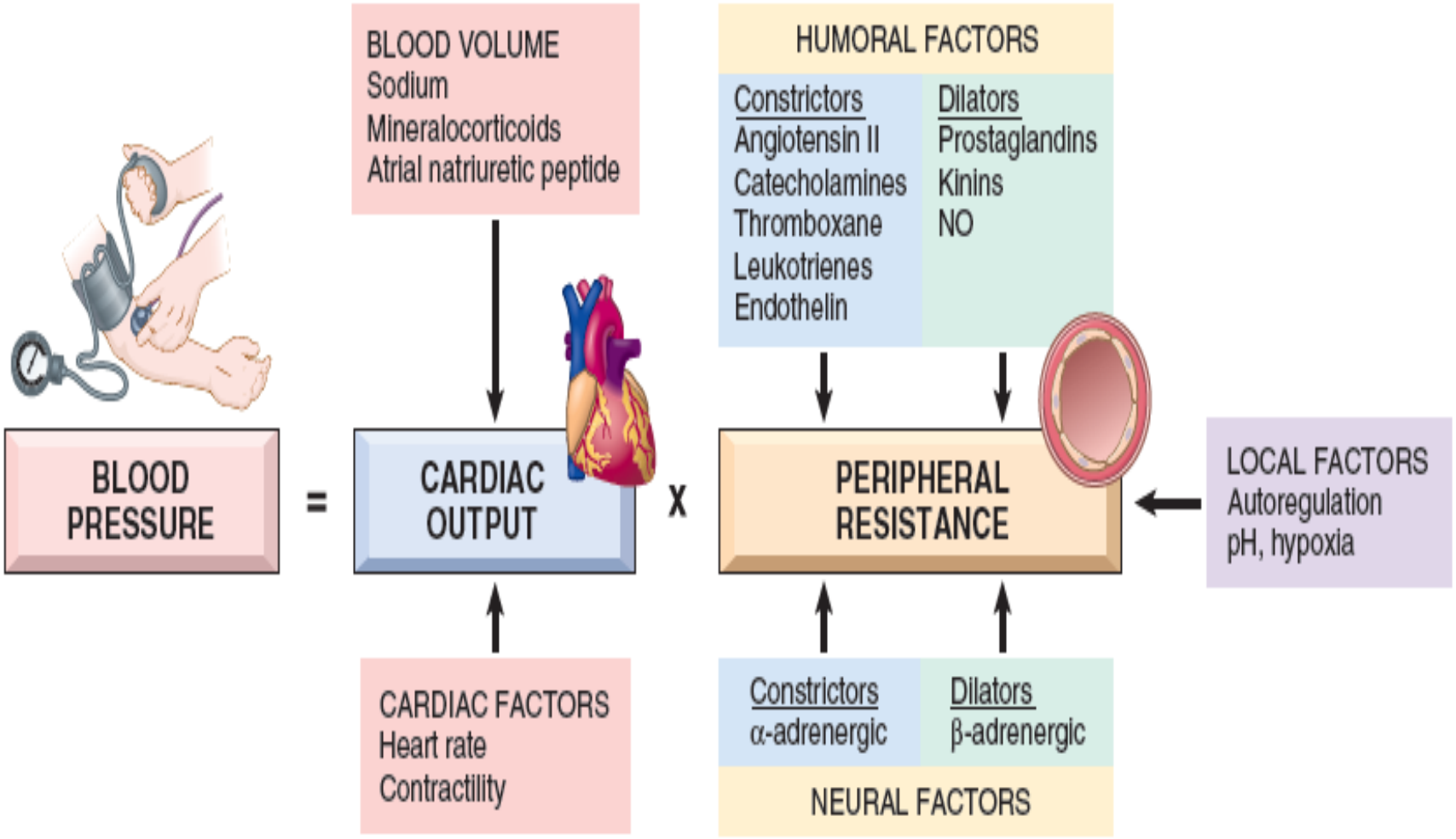


Fig. 10.3 Blood pressure regulation.

ARTERIAL BLOOD PRESSURE

- Arterial BP is the pressure in the arterial wall measured in millimeters of mercury (mm Hg).
- The two typical arterial BP values are *systolic BP* (SBP) and *diastolic BP* (DBP).
- SBP is achieved during cardiac contraction and represents the peak value.
- DBP is achieved after contraction when the cardiac chambers are filling, and represents the nadir (lower) value.
- The difference between SBP and DBP is called the pulse pressure and is a measure of arterial wall tension.
- Mean arterial pressure is the average pressure throughout the cardiac cycle of contraction. It is sometimes *used clinically* to represent overall arterial BP, especially in hypertensive emergency.
- During a cardiac cycle, two-thirds of the time is spent in diastole and one-third in systole.

ARTERIAL BLOOD PRESSURE (continued)

- Under normal physiologic conditions, arterial BP fluctuates throughout the day. It typically follows a circadian rhythm, where it decreases to its lowest daily values during sleep. This is followed by a sharp rise starting a few hours prior to awakening with the highest values occurring midmorning. BP is also increased acutely during physical activity or emotional stress.
- If the measurement reads 120 systolic and 80 diastolic, you would say, “120 over 80,” or write, “120/80 mmHg.”
- A normal blood pressure level is **less** than 120/80 mmHg. (*guidelines of 2017)*

Measuring Blood Pressure

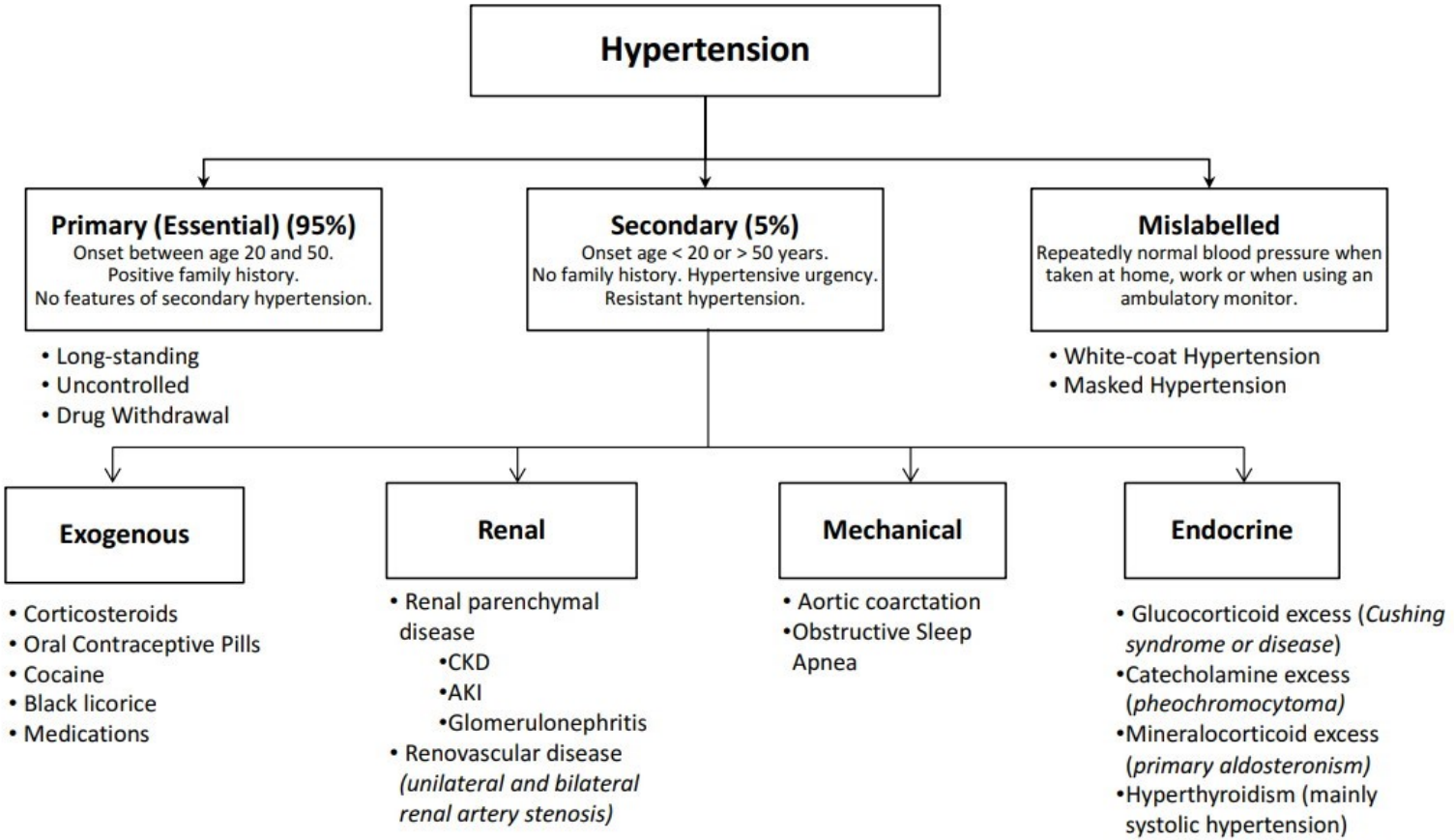
1- Direct Measurement of Blood Pressure

Requires an intraarterial catheter and specialized equipment

2- Indirect Measurement of Blood Pressure

- ✓ Blood pressure is most commonly measured by indirect means at the brachial artery, using a **sphygmomanometer** and a **stethoscope**
- ✓ Systolic pressure is recorded as the onset of the **Korotkoff sounds**, and their disappearance is recorded as the diastolic pressure.

Hypertension



Definition of hypertension:
Systolic BP ≥ 140mmHg or Diastolic BP ≥ 90mmHg
Isolated systolic hypertension in the elderly: ≥ 160mmHg
Diabetes mellitus ≥ 130/80mmHg
Note: In children, the definition of hypertension is different (either systolic or diastolic BP >95%ile), **but the approach is the same**.

Hypertensive Urgency: BP usually >180/110mmHg or asymptomatic Diastolic BP >130mmHg with target organ damage usually present but not acutely changing
Hypertensive Emergency: BP usually >220/140mmHg with evolving target organ damage

Cardiovascular

TABLE 15-2 Potential Mechanisms of Pathogenesis

Blood pressure is the mathematical product of cardiac output and peripheral resistance. Elevated blood pressure can result from increased cardiac output and/or increased total peripheral resistance.

Increased cardiac output	Increased cardiac preload: • Increased fluid volume from excess sodium intake or renal sodium retention (from reduced number of nephrons or decreased glomerular filtration) Venous constriction: • Excess stimulation of the RAAS • Sympathetic nervous system overactivity
Increased peripheral resistance	Functional vascular constriction: • Excess stimulation of the RAAS • Sympathetic nervous system overactivity • Genetic alterations of cell membranes • Endothelial-derived factors Structural vascular hypertrophy: • Excess stimulation of the RAAS • Sympathetic nervous system overactivity • Genetic alterations of cell membranes • Endothelial-derived factors • Hyperinsulinemia resulting from obesity or the metabolic syndrome

RAAS= Renin- Angiotensin- Aldosterone system

PRIMARY OR ESSENTIAL HYPERTENSION

- The **primary** cause of primary hypertension is still **unknown**.

- The development of primary hypertension involves interplay between genetic and environmental factors interacting with multiple physiological systems including neural, renal, hormonal, and vascular.

Pathophysiology include:

- The pathophysiology of primary hypertension is heterogeneous but ultimately exerts its effects through two primary determinants of BP: cardiac output (CO) and peripheral vascular resistance (PVR).

TABLE 16.5 Risk Factors for the Development of Primary Hypertension

Nonmodifiable Risk Factors	Modifiable Risk Factors
Increasing age	Obesity
Family history	Sedentary lifestyle
	Metabolic syndrome
	Dietary factors
	• Increased fat intake
	• Increased sodium intake
	• Inadequate potassium intake
	• Inadequate calcium intake
	Tobacco use
	Laboratory data
	• Elevated blood glucose
	• Elevated total cholesterol
	• Elevated triglycerides
	• Decreased high-density lipids (HDL)
	• Elevated low-density lipids (LDL)

PATHOGENESIS

1- HUMORAL MECHANISMS

A- The Renin–Angiotensin–Aldosterone System

B- Natriuretic Hormone

C- Insulin Resistance and Hyperinsulinemia

2- NEURONAL REGULATION

Pathologic disturbances in any of the four major components (autonomic nerve fibers, adrenergic receptors, baroreceptors, and central nervous system)

3- PERIPHERAL AUTOREGULATORY COMPONENTS

Abnormalities in renal or tissue autoregulatory systems

→ Renal defect in sodium excretion

PATHOGENESIS (continued)

4- VASCULAR ENDOTHELIAL MECHANISMS

- ✓ A deficiency in the local synthesis of vasodilating substances (prostacyclin , bradykinin and nitric oxide)
- ✓Or excess vasoconstricting substances (angiotensin II and endothelin I)

5- ELECTROLYTES AND OTHER CHEMICALS

- ✓Excess sodium intake → The exact mechanisms are unknown
- ✓Altered calcium homeostasis
- ✓Potassium depletion

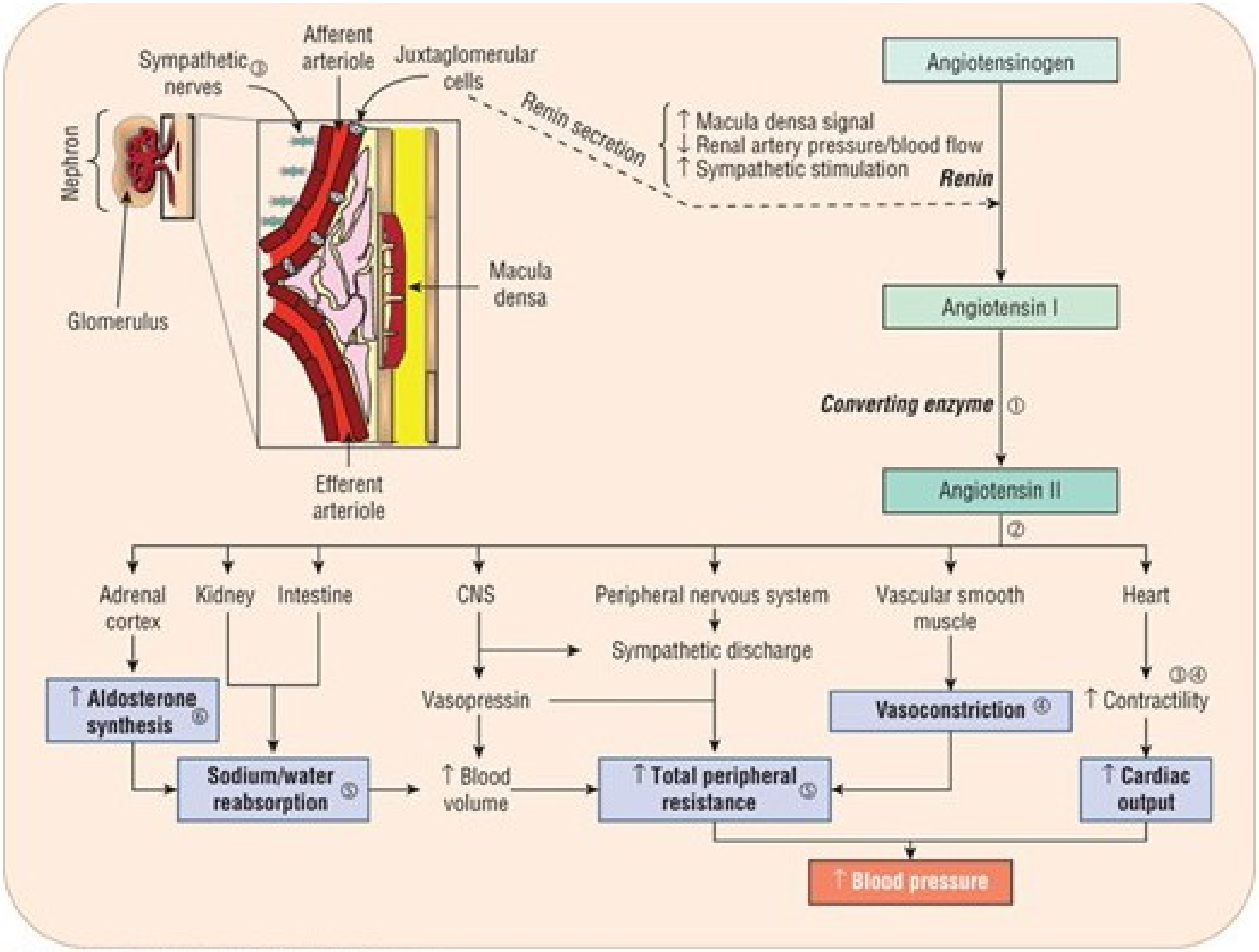
1- HUMORAL MECHANISMS
A- The Renin–Angiotensin–Aldosterone System

- Renin is produced and stored in the juxtaglomerular cells of the kidney, and its release is stimulated by impaired renal perfusion, salt depletion, and 1-adrenergic stimulation.

- The release of renin is the rate-limiting step in the eventual formation of angiotensin II, which is a potent vasoconstrictor.

- The renin-angiotensin-aldosterone system (RAAS) in primary hypertension is supported by the presence of high levels of renin, suggesting the system is inappropriately activated

Primary hypertension pathophysiology



1- HUMORAL MECHANISMS
B- Natriuretic Hormone

- This hormone is thought to block the active transport of sodium out of arteriolar smooth muscle cells.
- The increased intracellular sodium concentration ultimately would increase vascular tone and BP.

C- Insulin Resistance and Hyperinsulinemia

- Hypothetically, increased insulin concentrations may lead to hypertension because of increased renal sodium retention and enhanced sympathetic nervous system activity.
- Insulin has growth hormonelike actions that can induce hypertrophy of vascular smooth muscle cells.
- Insulin also may elevate BP by increasing intracellular calcium, which leads to increased vascular resistance.
- The exact mechanism by which insulin resistance and hyperinsulinemia occur in hypertension is unknown.

Classifications Of Primary Hypertension

JNC7= The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

- The JNC7 classification of BP in adults (age ≥18 years) is based on the average of two or more properly measured BP readings from two or more clinical encounters. It includes four categories***: normal, Elevated, stage 1 hypertension, and stage 2 hypertension.***
- Elevated is not considered a disease category, but identifies patients whose BP is likely to increase into the classification of hypertension in the future.
- *Hypertensive crises* are clinical situations where BP values are very elevated, typically greater than 180/120 mm Hg.7 They are categorized as either a *hypertensive emergency* or *hypertensive urgency*.
- Hypertensive emergencies are extreme elevations in BP that are accompanied by acute or progressing target-organ damage.
- Hypertensive urgencies are high elevations in BP without acute or progressing target-organ injury.

2017 Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure

https://www.ahajournals.org/doi/full/10.1161/HYP.0000000000000065#d1e2541

Classification of Blood Pressure in Adults (Age ≥18 Years) *without other risk factors*			
BP Category	**Systolic Blood Pressure (mm Hg) SBP**		**Diastolic Blood Pressure (mm Hg) DBP**
Normal	<120 mm Hg	AND	<80 mm Hg
Elevated	120–129 mm Hg	AND	<80 mm Hg
HYPERTENSION			
Stage 1 hypertension	130-139 mm Hg	OR	80-89 mm Hg
Stage 2 hypertension	≥140 mm Hg	OR	≥90 mm Hg

If systolic and diastolic blood pressure values yield different classifications, the highest category is used for the purpose of determining a classification.

→ *For patients with diabetes mellitus, significant chronic kidney disease, known coronary artery disease (myocardial infarction, stable angina, unstable angina), noncoronary atherosclerotic vascular disease (ischemic stroke, transient ischemic attack, peripheral arterial disease, abdominal aortic aneurism), or a Framingham risk score of 10% or greater, values ≥ 130/80 mm Hg are considered above goal; patients with left ventricular dysfunction have a blood pressure goal of less than 120/80 mm Hg.*

Clinical Presentation of Hypertension

- **General**

The patient may appear very healthy, or may have the presence of additional CV risk factors:

✓Age (≥ 55 years for men and 65 years for women)

✓Diabetes mellitus

✓Dyslipidaemia (elevated low-density lipoprotein-cholesterol, total cholesterol, and/or triglycerides; low high-density lipoprotein-cholesterol)

✓Microalbuminuria

✓Family history of premature CV disease

✓Obesity (body mass index ≥30 kg/m2)

✓Physical inactivity

✓Tobacco use

Clinical Presentation of Hypertension (continued-1)

- **Symptoms**

Most patients are asymptomatic.

- **Signs**

Previous BP values in the prehypertension or hypertension category.

- **Laboratory Tests**

→ Blood urea nitrogen/serum creatinine, fasting lipid panel, fasting blood glucose, serum electrolytes, spot urine albumin-to-creatinine ratio. The patient may have normal values and still have hypertension. However, some may have abnormal values consistent with either additional CV risk factors or hypertension-related damage.

Clinical Presentation of Hypertension (continued-2)

Other Diagnostic Tests

- ✓12-lead electrocardiogram (to detect left ventricular hypertrophy), estimated glomerular filtration rate (using Modification of Diet in Renal Disease equation).

- ✓10-year risk of fatal coronary heart disease or non-fatal myocardial infarction, based on Framingham scoring.

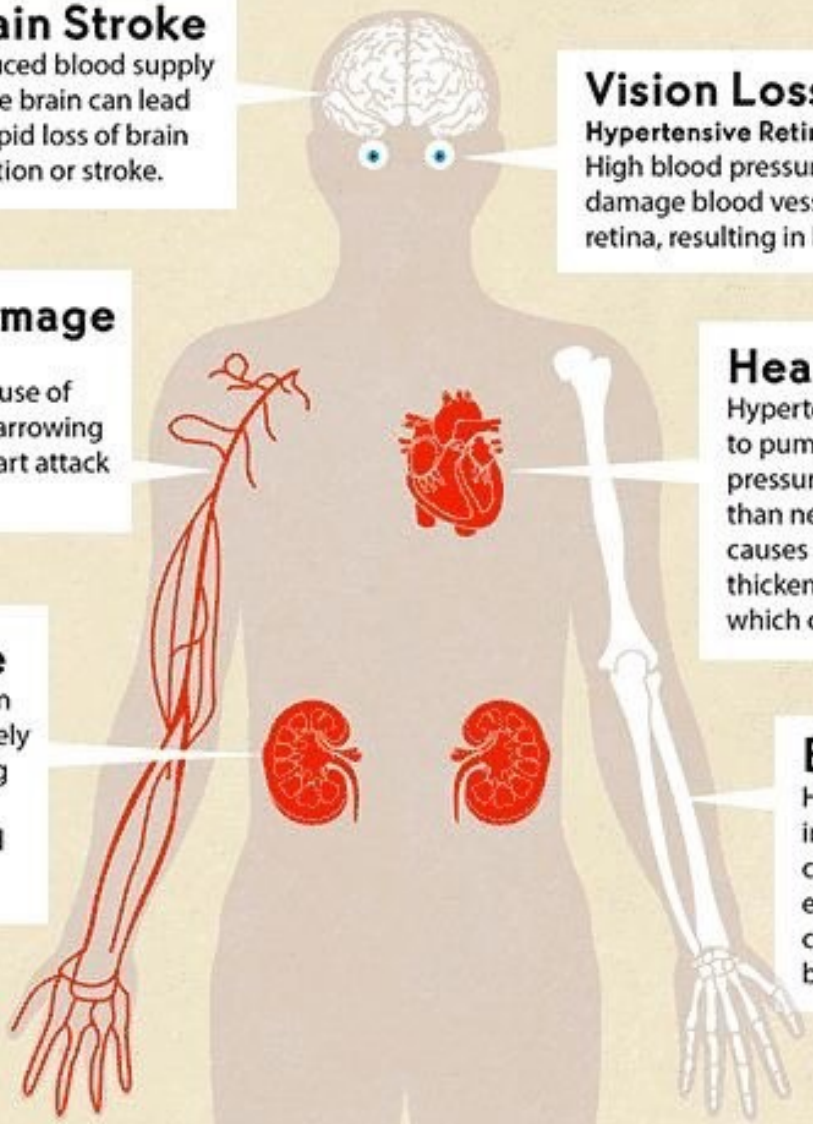
Clinical Presentation of Hypertension (continued-3)

Target-Organ Damage

The patient may have a previous medical history or diagnostic findings that indicate the presence of hypertension-related target-organ damage:

1. Brain (stroke, transient ischemic attack)
2. Eyes (retinopathy)
3. Heart (left ventricular hypertrophy, angina or prior MI, prior coronary revascularization, heart failure)
4. Kidney (chronic kidney disease)
5. Peripheral vasculature (peripheral arterial disease)

Complications of Hypertension



Brain Stroke
Reduced blood supply to the brain can lead to rapid loss of brain function or stroke.

Vision Loss
Hypertensive Retinopathy
High blood pressure can damage blood vessels in the retina, resulting in loss of vision.

Blood Vessel Damage
Atherosclerosis
Hypertension is a leading cause of atherosclerosis, the artery-narrowing process that can result in heart attack and stroke.

Heart Attack
Hypertension causes the heart to pump against high blood pressure, making it work harder than necessary. Over time, this causes the heart muscle to thicken, restricting blood flow which can lead to heart failure.

Kidney Failure
Damaged blood vessels in the kidneys can't effectively filter your blood, resulting in a dangerous accumulation of fluid and waste.

Bone Loss
High blood pressure may increase the amount of calcium in your urine. That excessive elimination of calcium may lead to loss of bone density (osteoporosis).

Secondary Hypertension

TABLE 15-1 Secondary Causes of Hypertension

Diseases	Drugs Associated with Hypertension in Humans[a]
Chronic kidney disease Cushing's syndrome Coarctation of the aorta Obstructive sleep apnea Parathyroid disease Pheochromocytoma Primary aldosteronism Renovascular disease Thyroid disease	**Prescription drugs** • Adrenal steroids (e.g., prednisone, fludrocortisone, triamcinolone) • Amphetamines/anorexiants (e.g., phendimetrazine, phentermine, sibutramine) • Antivascular endothelin growth factor agents (bevacizumab, sorafenib, sunitinib), estrogens (usually oral contraceptives) • Calcineurin inhibitors (cyclosporine and tracolimus) • Decongestants (phenylpropanolamine and analogs) • Erythropoiesis stimulating agents (erythropoietin and darbepoietin) • Nonsteroidal antiinflammatory drugs, cyclooxygenase-2 inhibitors • Others: venlafaxine, bromocriptine, bupropion, buspirone, carbamazepine, clozapine, desulfrane, ketamine, metoclopramide Situations: β-blocker or centrally acting α-agonists (when abruptly discontinued); β-blocker without α-blocker first when treating pheochromocytoma **Street drugs and other natural products** Cocaine and cocaine withdrawal Ephedra alkaloids (e.g., Ma-huang), "herbal ecstasy," other phenylpropanolamine analogs[a] Nicotine withdrawal, anabolic steroids, narcotic withdrawal, methylphenidate, phencyclidine, ketamine, ergotamine and other ergot-containing herbal products, St. John's wort **Food substances** Sodium Ethanol Licorice Tyramine-containing foods if taking a monoamine oxidase inhibitor

Malignant hypertension

- In a small percentage of patients with chronic essential hypertension, dramatic increases in blood pressure (greater than 120 to 130 mmHg **diastolic pressure**) may occur suddenly.

- These sudden increases in blood pressure are termed **malignant hypertension** and are especially dangerous because dramatic increases in pressure may damage the **retina or kidneys** and lead to **cerebral edema and stroke**.

- Malignant hypertension requires immediate medical treatment with powerful intravenous vasodilators such as diazoxide or sodium nitroprusside

Hypotension

- Hypotension is an **abnormally low blood pressure**.

- One common form of hypotension is orthostatic hypotension (also called postural hypotension) that occurs upon standing.

- The act of standing initiates a series of reflex responses in the body that are designed to prevent pooling of blood in the lower extremities and a decrease in blood pressure. These reflexes include **vasoconstriction in the lower limbs and a reflex increase in heart rate.**

Table 8.3 Causes of Orthostatic Hypotension

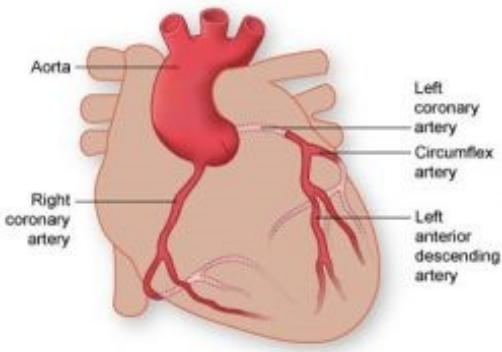
Aging — Associated with reduced baroreceptor responses, decreased cardiac output and reduced vascular responsiveness
Decreased blood or fluid volume — Caused by dehydration, diarrhea, diuretic use
Autonomic nervous defects — An inability to initiate vasoconstriction and increased heart rate reflexes
Prolonged bed rest — Associated with reduced plasma volume, decreased vascular tone
Drug-induced — Examples: antihypertensive drugs, calcium channel blockers, vasodilators
Idiopathic — Cause is not known

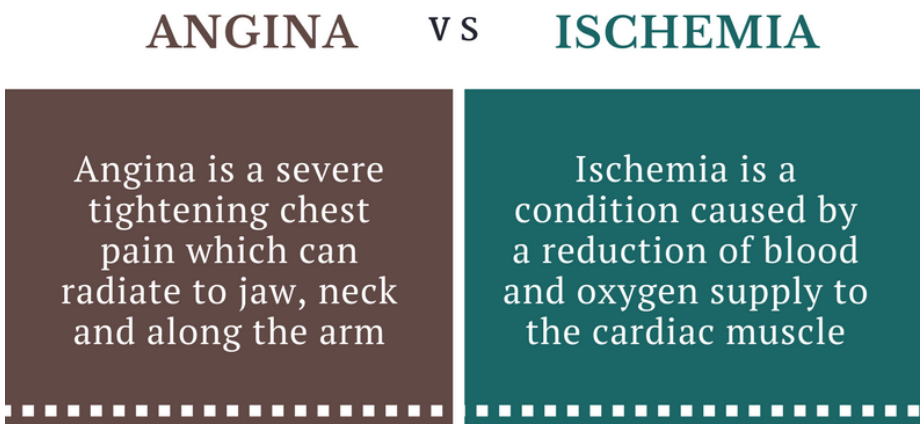
Manifestations

- Dizziness (*syncopy*)
- Decreased cardiac output
- Reduced brain blood flow
- Pooling of blood in the extremities
- Falls and injuries, particularly in elderly individuals

❑ Diseases of coronary arteries (CAD)

- The two main coronary arteries supplying the myocardium are the **left coronary artery** and the **right coronary artery**.
- Ischemic heart disease (IHD) is also called coronary heart disease (CHD) or coronary artery disease (CAD).
- The term ***ischemic*** refers to a **decreased supply of oxygenated blood to the heart muscle**. IHD is caused by stenosis, or narrowing, in one or more of the major coronary arteries that supply blood to the heart, most commonly by atherosclerotic plaques.
- Most **heart attacks** are the direct result of **occlusion of a coronary blood vessel by a lipid deposit (MI)**, but **spasm of coronary arteries causes ischemia and it is called angina**





Plaque and thrombus formation

- Reductions in coronary blood flow (secondary to atherosclerotic plaques, vasospasm, or thrombus formation) and arterial oxygen content (secondary to hypoxia) decrease myocardial oxygen supply.

- **Coronary Atherosclerosis**
- Endothelial damage and dysfunction, commonly caused by hypertension, diabetes, and smoking, allow low-density lipoprotein (LDL) cholesterol and inflammatory cells (eg, monocytes and T lymphocytes).

- The process of plaque and thrombus formation :

1. monocyte- derived macrophages ingesting lipoproteins to form **foam cells**. Macrophages also secrete growth factors that promote smooth muscle cell migration from the media to the intima. The result is the development of early atherosclerosis in the form of a **fatty streak** consisting of lipid-laden macrophages and smooth muscle cells.
2. The fatty streak enlarges as foam cells, smooth muscle cells, and necrotic debris accumulate in the sub-endothelial space.
3. A collagen matrix forms a fibrous cap that covers the lipid core of the lesion to establish an **atherosclerotic plaque.**

- The atherosclerotic plaque may progress until it protrudes into the artery lumen and impedes blood flow. When the plaque occludes 70% or more of a major coronary artery or 50% or more of the left main coronary artery, the patient may experience angina during activities that increase myocardial oxygen demand.

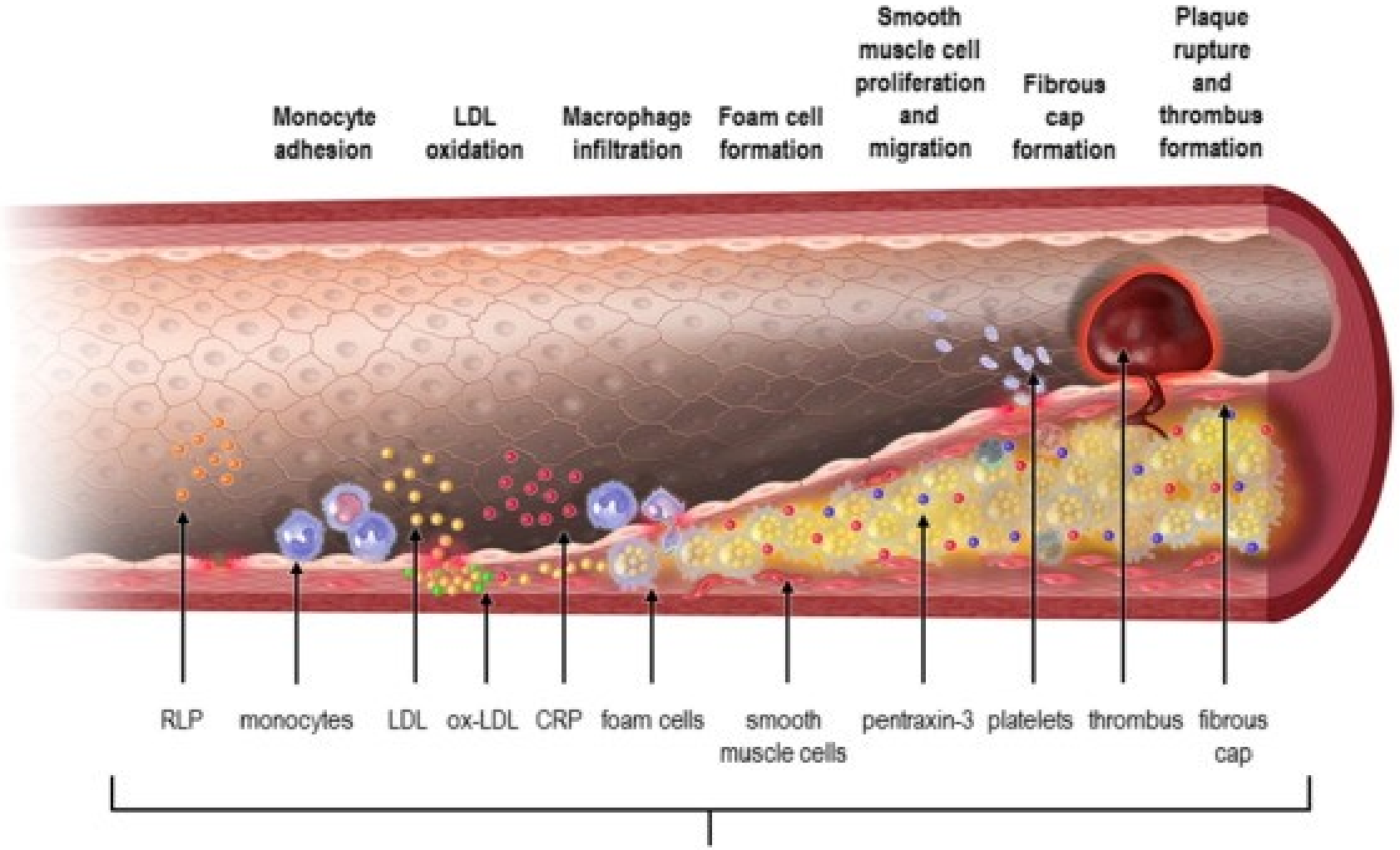
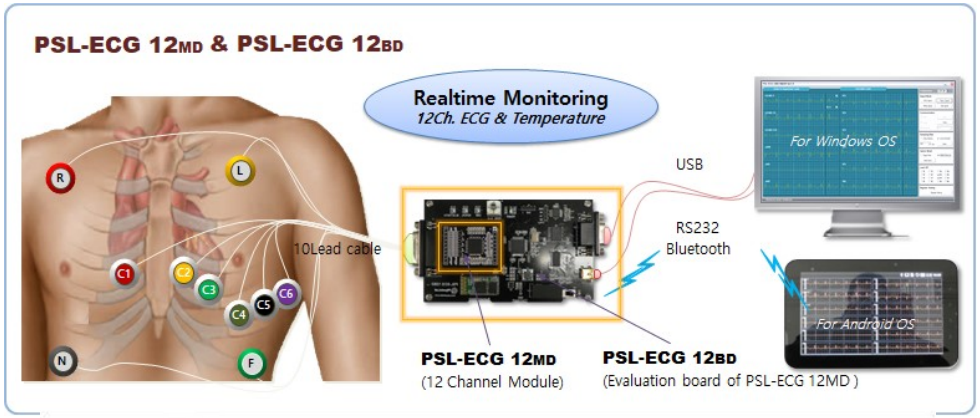
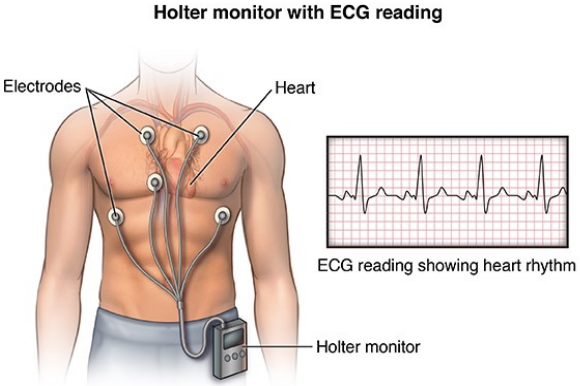

Monocyte adhesion
LDL oxidation
Macrophage infiltration
Foam cell formation
Smooth muscle cell proliferation and migration
Fibrous cap formation
Plaque rupture and thrombus formation
RLP
monocytes
LDL
ox-LDL
CRP
foam cells
smooth muscle cells
pentraxin-3
platelets
thrombus
fibrous cap
EPA reported to exert beneficial effects at multiple steps in the atherogenic pathway

Table 10.1 Diagnosis of Myocardial Ischemia

Electrocardiograph
Holter monitoring — 24 ambulatory electrocardiograph
Stress testing with electrocardiograph
Nuclear imaging
Cardiac catheterization





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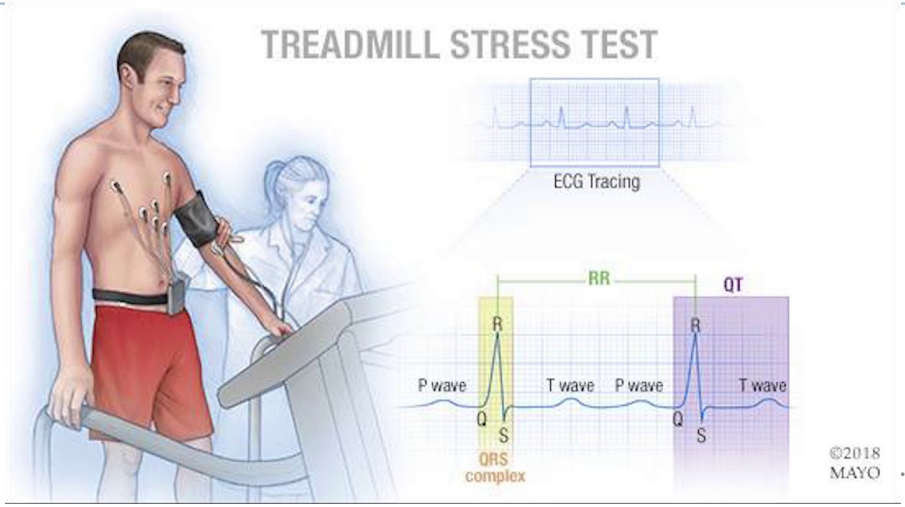
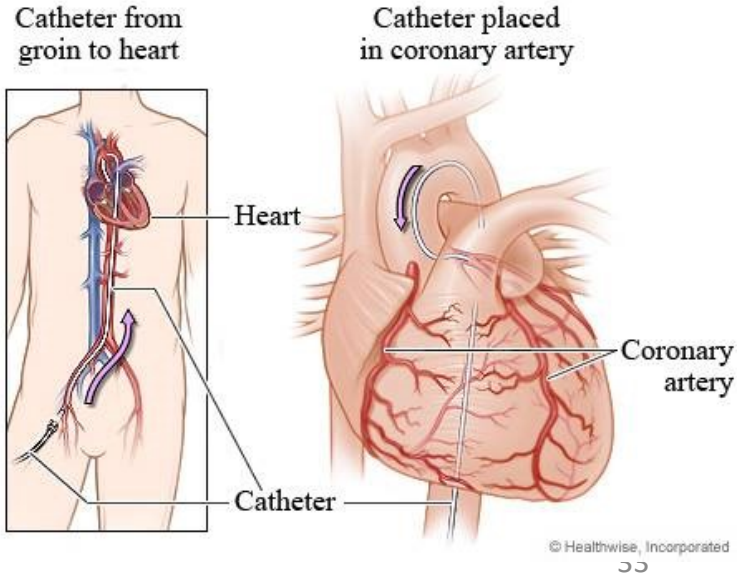
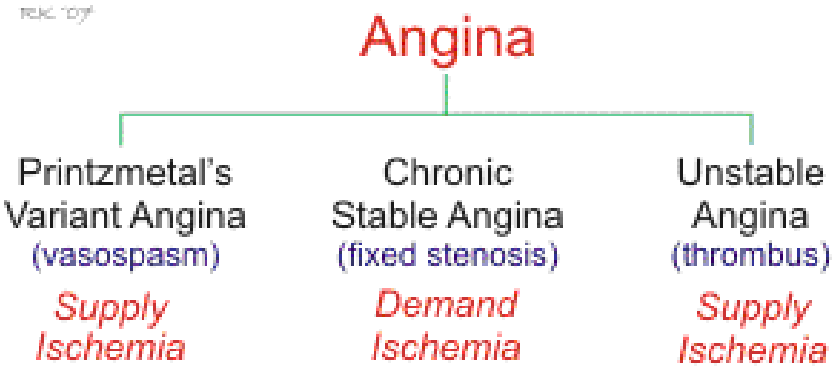


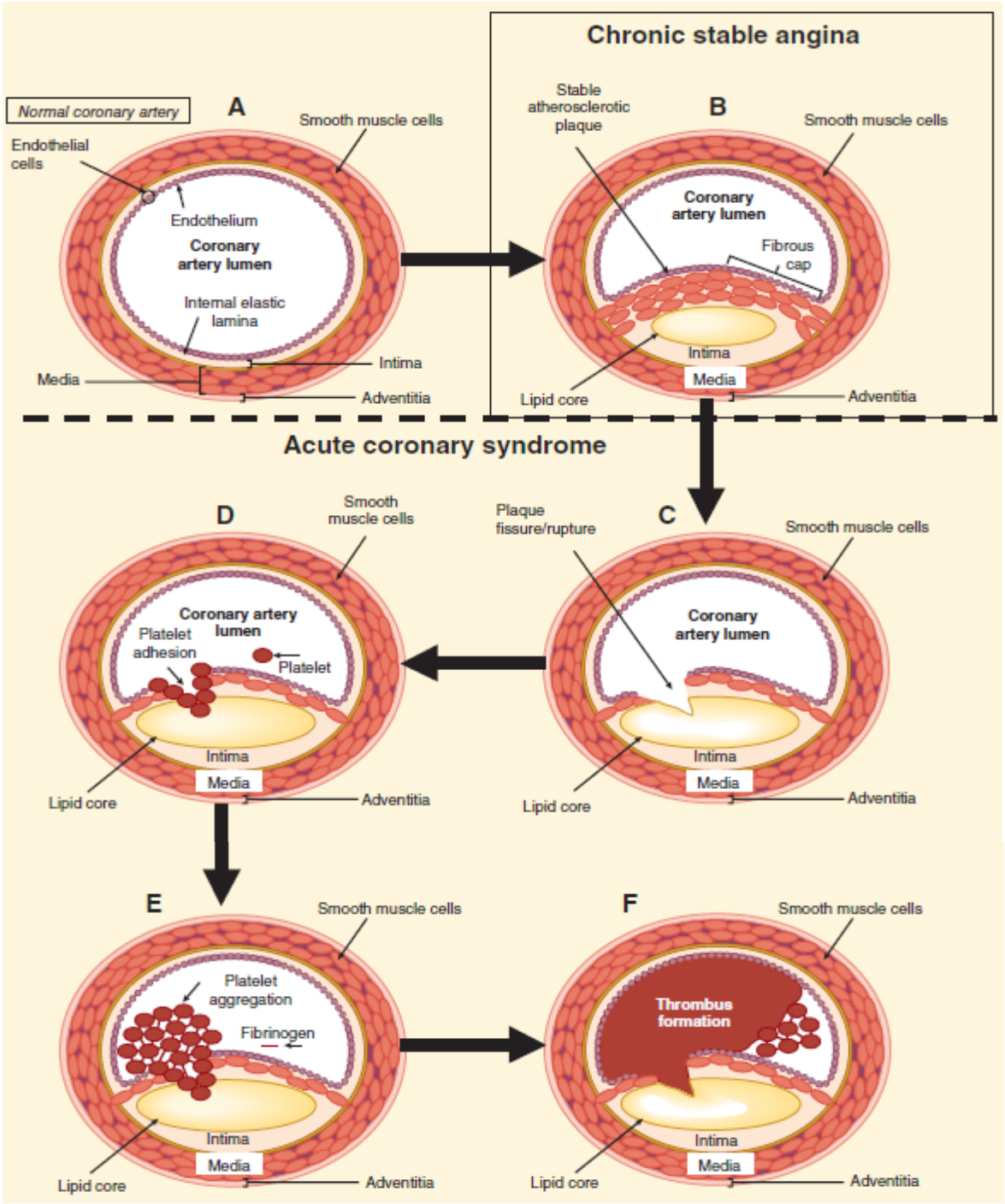


1. Angina

- is the major symptom of **myocardial ischemia**.
- **Angina pectoris** most commonly presents as **pain, pressure or a burning sensation in the area of the sternum**.

- There are three types of angina pectoris:
- Classic or exertional angina (Stable)
- Unstable
- Variant angina (vasospastic angina, Prinzmetal's angina)




Chronic stable angina
Normal coronary artery
A
Smooth muscle cells
Endothelial cells
Endothelium
Coronary artery lumen
Internal elastic lamina
Intima
Media
Adventitia
Stable atherosclerotic plaque
B
Smooth muscle cells
Coronary artery lumen
Fibrous cap
Intima
Media
Lipid core
Adventitia
Acute coronary syndrome
D
Smooth muscle cells
Coronary artery lumen
Platelet adhesion
Platelet
Intima
Media
Lipid core
Adventitia
Plaque fissure/rupture
C
Smooth muscle cells
Coronary artery lumen
Intima
Media
Lipid core
Adventitia
E
Smooth muscle cells
Platelet aggregation
Fibrinogen
Intima
Media
Lipid core
Adventitia
F
Smooth muscle cells
Thrombus formation
Intima
Media
Lipid core
Adventitia

1. Classic or exertional angina
   - Pain is precipitated by increased workload on the heart. May be caused by exercise, emotions, stress and cold exposure.

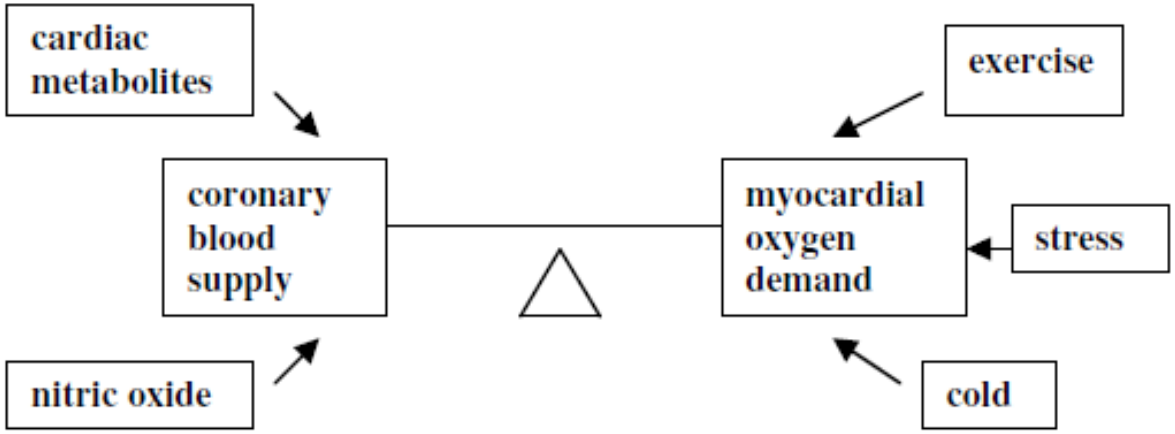


Figure 10.1 Myocardial oxygen balance.

Symptoms may remain "stable" for a number of years or progress in severity.

2. Unstable angina

- Angina that occurs at **rest.**
- Also referred to as “pre-infarct” angina since it is usually associated with extensive blockage of coronary arteries. Coronary blood flow does not meet the needs of the heart even at rest.
- Requires intensive treatment and evaluation.

3. Variant angina (vasospastic angina, Prinzmetal’s angina)

- Caused by **vasospasm of the coronary arteries.**
- Usually associated with coronary artery disease but may result from excess sympathetic activity.
- Frequently occurs at **night, at rest or during minimal exercise.**
- May be precipitated by stress, cold exposure or smoking.

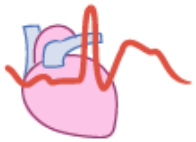
Types of Angina

✓ Stable Angina

- "Effort" angina: Triggered by physical or mental exertion.
- Resolves with rest or nitrates.

✓ Unstable Angina

- New onset or worsening angina that is unpredictable.
- Rest/meds do not resovle.
- Acute coronary syndrome; May lead to MI



✓ Vasospastic Angina

- Aka, Variant/Prinzmetal
- Occurs spontaneously, often at rest. Common at night & early morning (esp. w/ exercise).

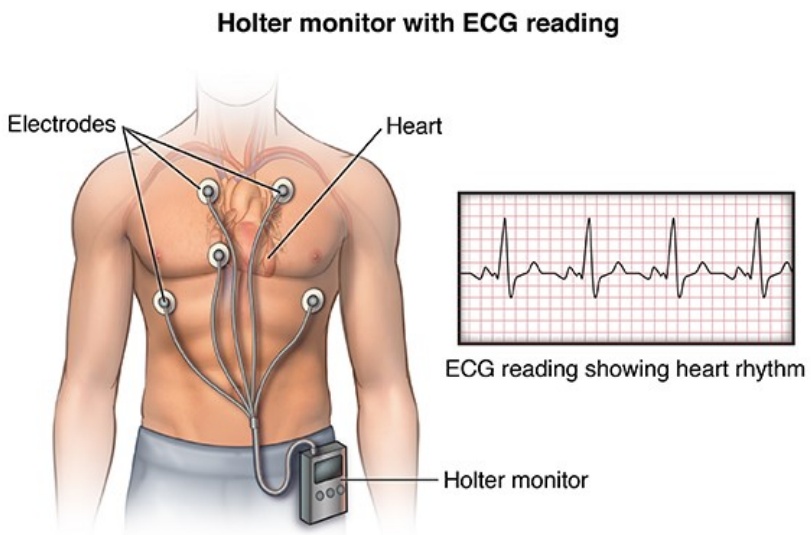
- More common in women & smokers.
- Responds to nitrates; Calcium-channel blockers suppress (Beta-blockers do not)

✓ Microvascular Angina

- Angina due to coronary microvascular dysfunction or vasospasm.
- Accounts for chest pain in up to 50% of patients w/out obstructive epicardial CAD.
- Can occur with exertion or at rest.
- May respond less well to nitrates.
- Can be difficult to distinguish from epicardial angina, Diagnose with PET or CMR.

2. Silent ischemia

- is a particularly dangerous form of myocardial ischemia as there is a lack of clinical symptoms, i.e., ischemia without angina.
- Usually diagnosed by exercise stress testing or Holter monitoring



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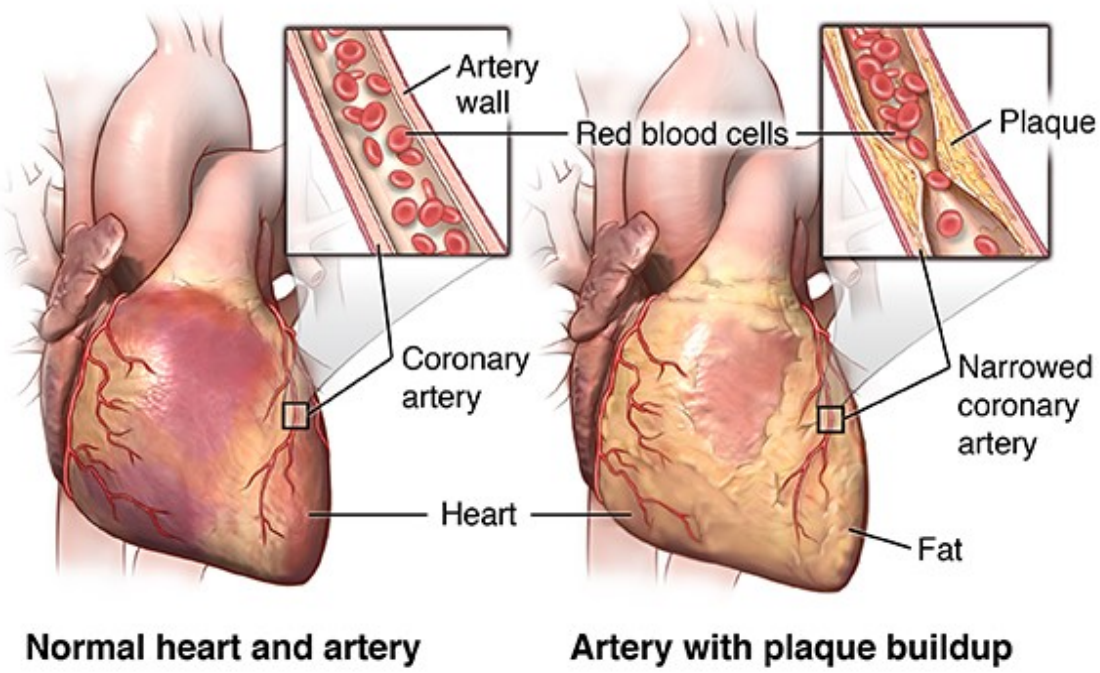
3. Myocardial infarction

lipid deposits may accumulate to the point where they completely block a coronary vessel or, more commonly, accumulated lipid plaques may break off from the vascular endothelium and act as a **thrombus that blocks a coronary artery** at a narrower point downstream.



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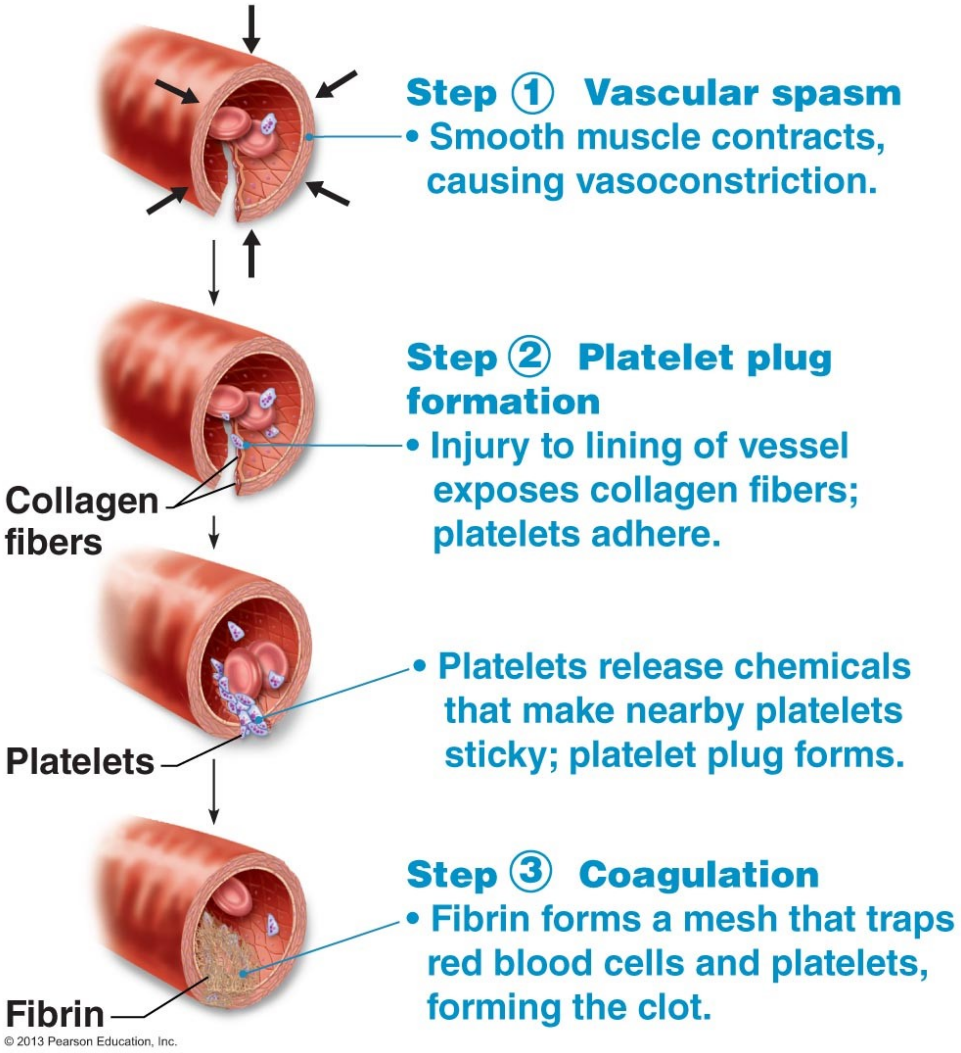
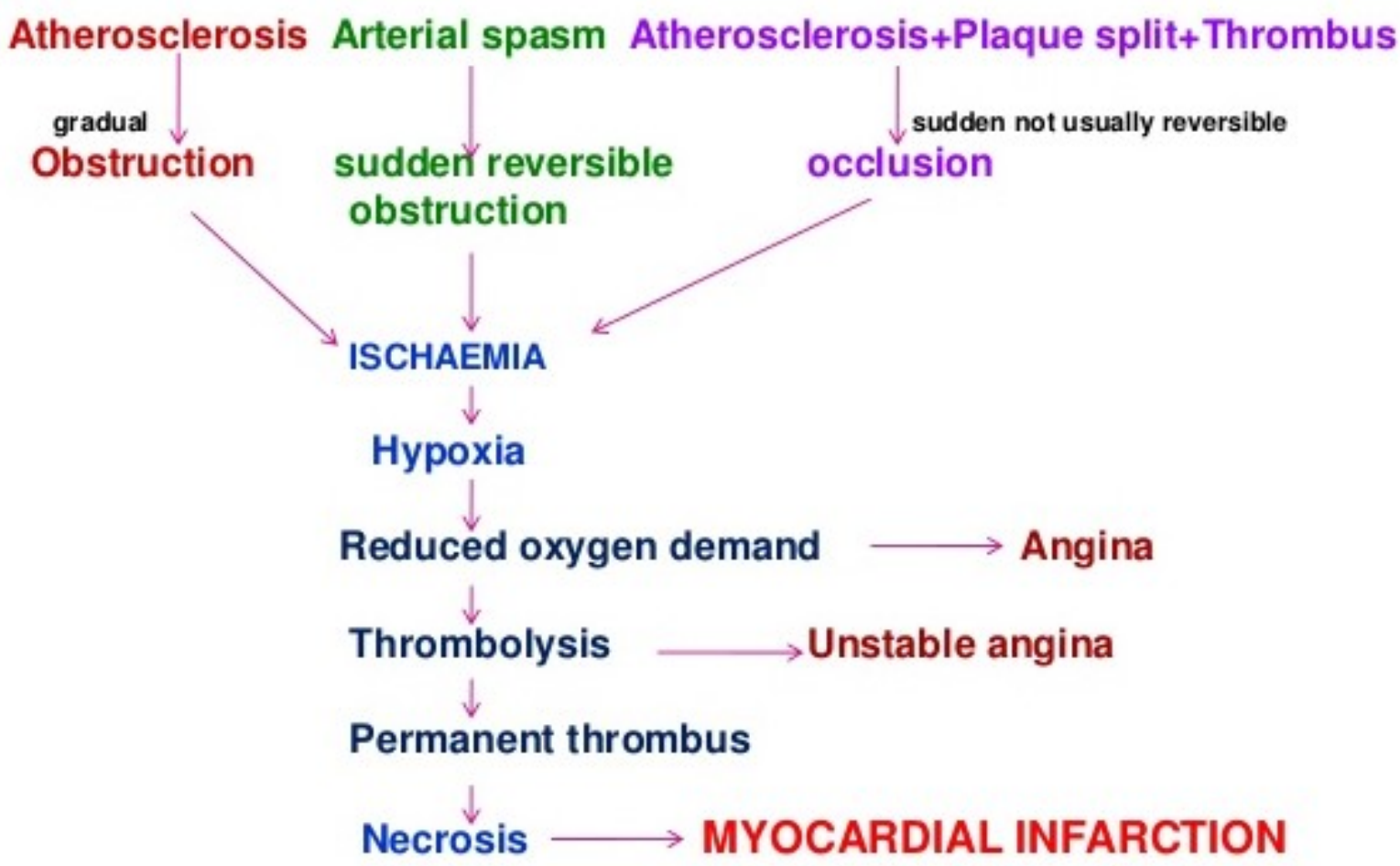
- **Myocardial infarction** or “heart attack” is an **irreversible injury** to and eventual death of myocardial tissue that results from ischemia and **hypoxia**.



Plug formation

PATHOPHYSIOLOGY

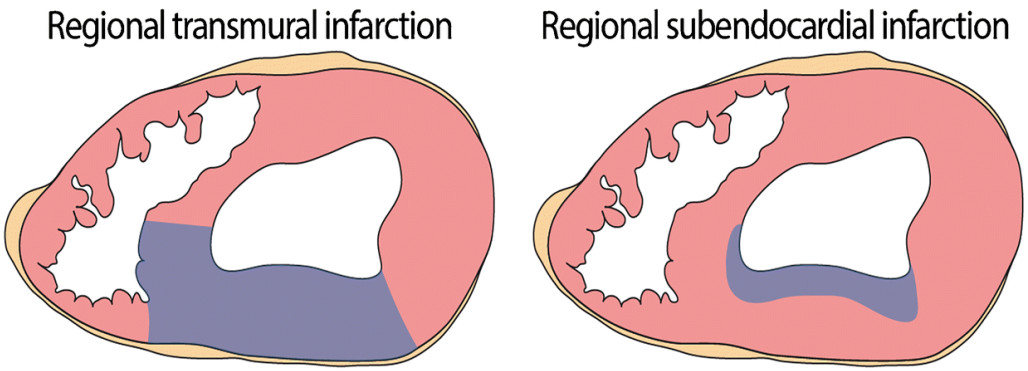


https://www.slideshare.net

- A myocardial infarction may be:

1. **Trans-mural** meaning it involves the full thickness of the ventricular wall
2. **Sub-endocardial** in which the inner one third to one half of the ventricular wall is involved.

- **Transmural infarcts** tend to have a greater effect on cardiac function and pumping ability since a greater mass of ventricular muscle is involved.



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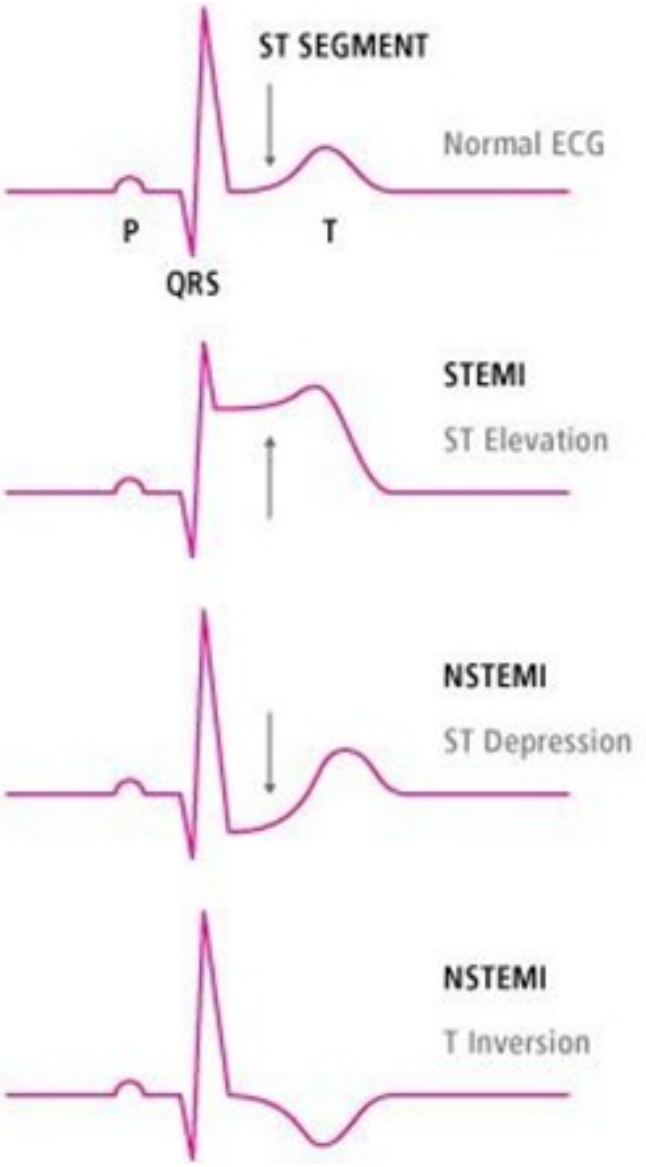
Manifestations of myocardial infarction

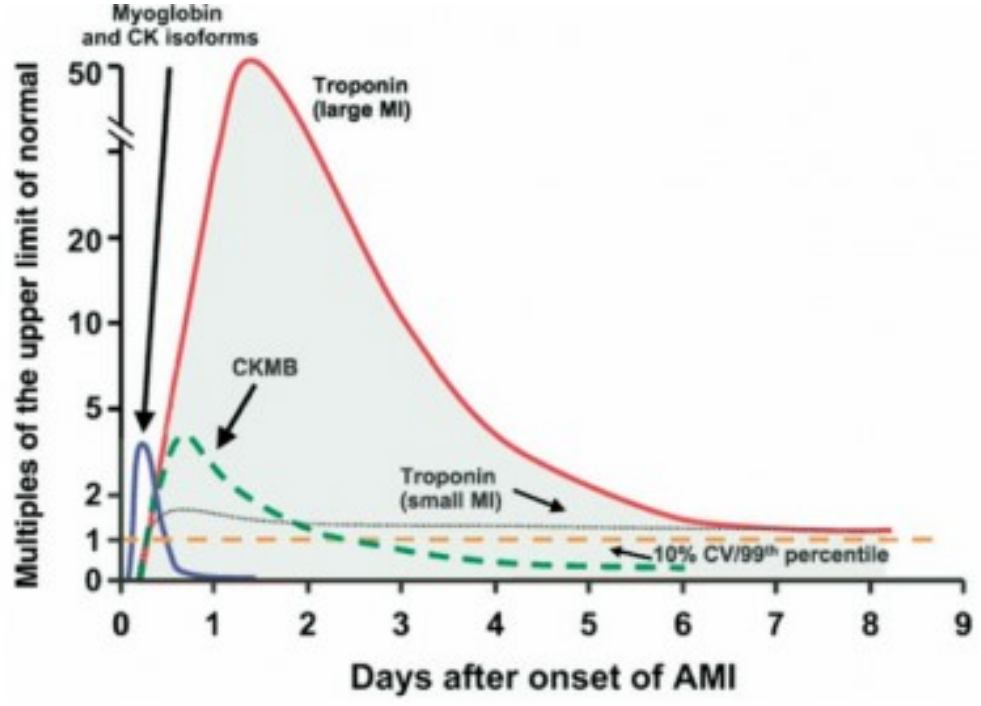
1. **Severe chest pain and discomfort** — Pressing or crushing sensation often accompanied by nausea, vomiting, sweating and weakness due to hypotension. Some myocardial infarctions are "silent" and have no symptoms.
2. **Irreversible cellular injury** — Generally occurs 20 to 30 minutes after the onset of complete ischemia.
3. **Release of myocardial enzymes** such as creatine phosphokinase (CPK-MB) and lactate dehydrogenase (LDH), and troponin into circulation from myocardial damaged cells.
4. **Electrocardiogram changes** — Inversion of T wave, ST elevation, pronounced Q waves.

5. **Inflammatory response** from the injured myocardium — Leukocyte infiltration, increased white blood cell counts, fever.

6. **Coagulative necrosis** of the area of the myocardium affected by the infarction.

7. **Repair of damaged areas** occurs by replacement with scar tissue and not functional muscle tissue; therefore, some alteration in function is inevitable.





Complications of myocardial infarction

1. **Rupture of weakened myocardial wall**. Bleeding into pericardium may cause cardiac **tamponade** and further impair cardiac pumping function. This is most likely to occur with a **transmural infarction**. Rupture of the septum between the ventricles might also occur if the septal wall is involved in the infarction.
2. **Formation of a thromboembolism** from pooling of blood in the **ventricles**.
3. **Pericarditis** — Inflammation due to pericardial friction rub. Often **occurs 1 to 2 days** after the infarction.
4. **Arrhythmia** — Common as a result of **hypoxia, acidosis** and **altered electrical conduction** through damaged and necrotic areas of the myocardium. May be life-threatening and lead to fibrillation.

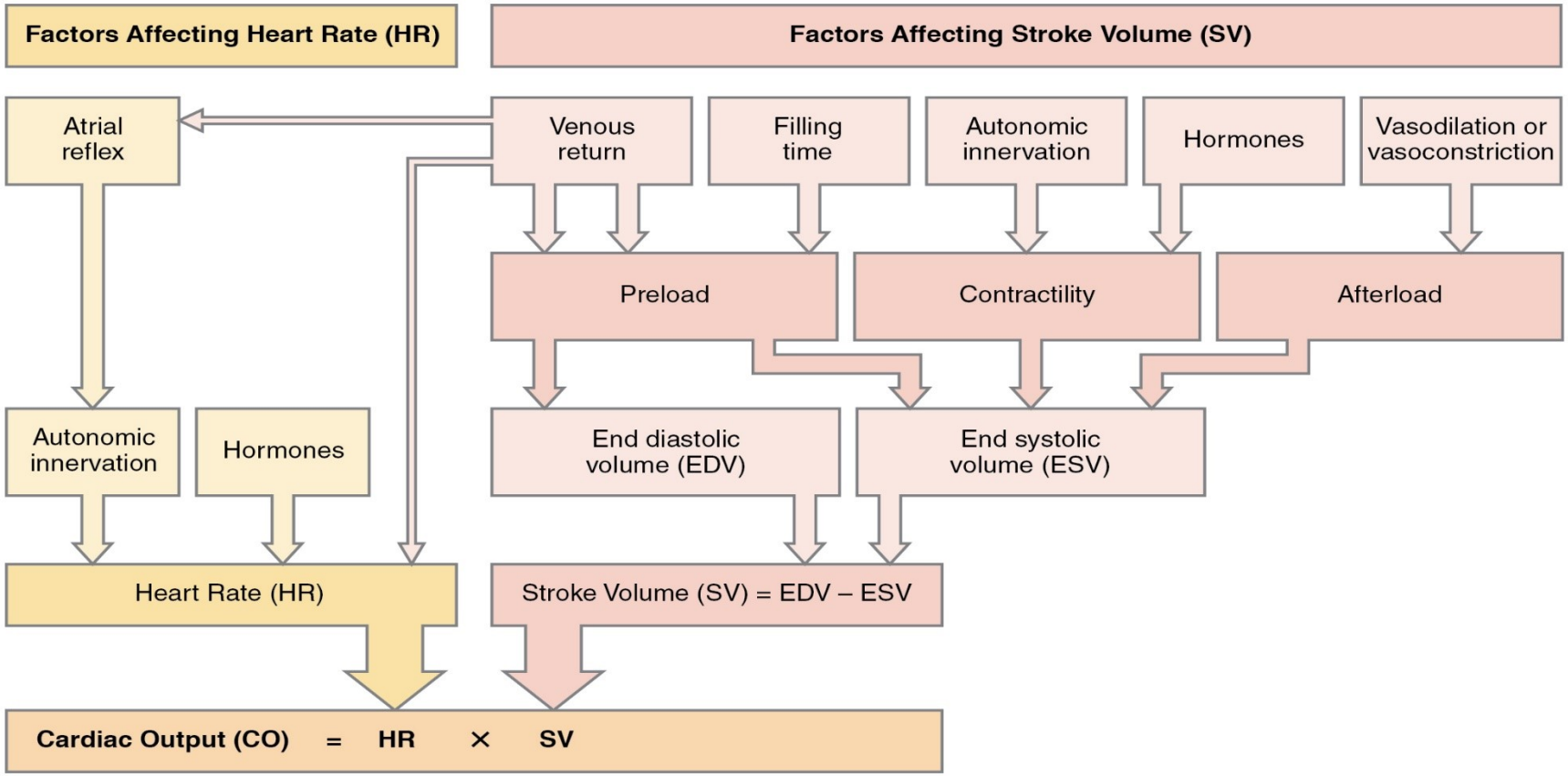
• Cardiac tamponade : Excessive pressure that develops from the accumulation of fluid in the pericardium

5. Reduced cardiac function — Typically presents with reduced **myocardial contractility**, reduced **wall compliance**, decreased **stroke volume** and increased **left ventricular end diastolic volume.**

6. Congestive heart failure may result if a large enough area of the myocardium has been damaged such that the heart no longer pumps effectively.

7. Cardiogenic shock — Marked hypotension that can result from extensive damage to the left ventricle. The resulting hypotension will trigger cardiovascular compensatory mechanisms that will further tax the damaged myocardium and exacerbate impaired function. Cardiogenic shock is associated with a mortality rate of 80% or greater.

Revision of physiology of cardiovascular



- Stroke volume — Volume of blood ejected from each ventricle per beat.
- End-diastolic volume — Volume of blood remaining in the ventricle at the end of systole (contraction).
- Preload — The degree to which the myocardium is stretched by venous return. Determined by LVEDV.
- LVEDV (left-ventricular end-diastolic volume) — The amount of blood that fills the left ventricle during relaxation.
- Ejection fraction — The fraction of the blood contained in the ventricle at the end of diastole that is expelled during its contraction (the stroke volume divided by end-diastolic volume).
- Afterload — The pressure the heart must overcome to pump blood out into the aorta.

Compensatory mechanisms for myocardial infarction

- **As a result of the hypotension and hemodynamic changes that accompany a myocardial infarction, the cardiovascular system initiates a number of reflex compensatory mechanisms designed to maintain cardiac output and adequate tissue perfusion:**

1. **Catecholamine release**: Increases heart rate, force of contraction and peripheral resistance. Catecholamines can, however, be arrhythmogenic.
2. **Sodium and water retention**.
3. **Activation of renin–angiotensin system** leading to peripheral vasoconstriction.
4. **Ventricular hypertrophy**

Unfortunately, these compensatory changes may increase oxygen demand and workload on the infarcted heart and worsen overall cardiac function.

Both myocardial infarction and less serious angina can present symptoms of severe chest pain. Treat all cases of chest pain as cardiac emergencies.

DISTINGUISHING ANGINA PECTORIS FROM MYOCARDIAL INFARCTION

	Angina Pectoris	Myocardial Infarction
Location of Discomfort	Substernal or across chest	Same
Radiation of Discomfort	Neck, jaw, arms, back, shoulders	Same
Nature of Discomfort	Dull or heavy discomfort with a pressure or squeezing sensation	Same, but maybe more intense
Duration	Usually 2 to 15 minutes, subsides after activity stops	Lasts longer than 10 minutes
Other symptoms	Usually none	Perspiration, pale gray color, nausea, weakness, dizziness, lightheadedness
Precipitating Factors	Extremes in weather, exertion, stress, meals	Often none
Factors Giving Relief	Stopping physical activity, reducing stress, nitroglycerin	Nitroglycerin may give incomplete or no relief

N&V

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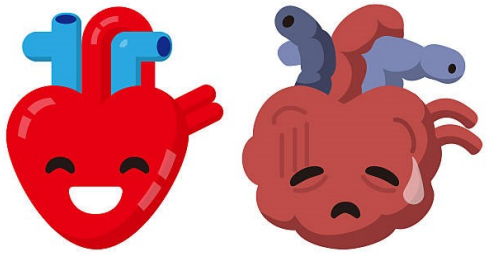
	Stable Angina	Unstable Angina	STEMI	NSTEMI
Character of pain	Exertional pain	Rest pain	Rest pain	Rest pain
Relievers	Responds to GTN	No GTN effect	No GTN effect	No GTN effect
Enzymes	Normal	Normal	Elevated	Elevated
ECG	Often normal	Often ST depression	ST segment elevation	No ST segment elevation

❑Disease of cardiac muscle

(heart failure & shock)



- Heart failure is a condition in which the heart is no longer **pumping blood effectively**.

- Depending upon the **cause**, heart failure may be classified as:

- **Low- output failure**
- **High-output failure**.

- **Low-output failure:**
- is a reduced pumping efficiency of the heart that is caused by factors that impair cardiac function such as **myocardial ischemia, myocardial infarction or cardiomyopathy**.

- **High output failure:**
- the **cardiac output is normal or elevated** but still **cannot meet the metabolic and oxygen need of the tissues**.
- Common causes of high-output failure include **hyperthyroidism (hypermetabolism), pregnancy, and anemia (reduced oxygen- carrying capacity)**

Manifestations of heart failure

- Classically, the manifestations of heart failure can be divided into those occurring as a result of:
- **Left heart failure** (left atrium and ventricle)
- **Right heart failure** (right atrium and ventricle).

Left heart failure

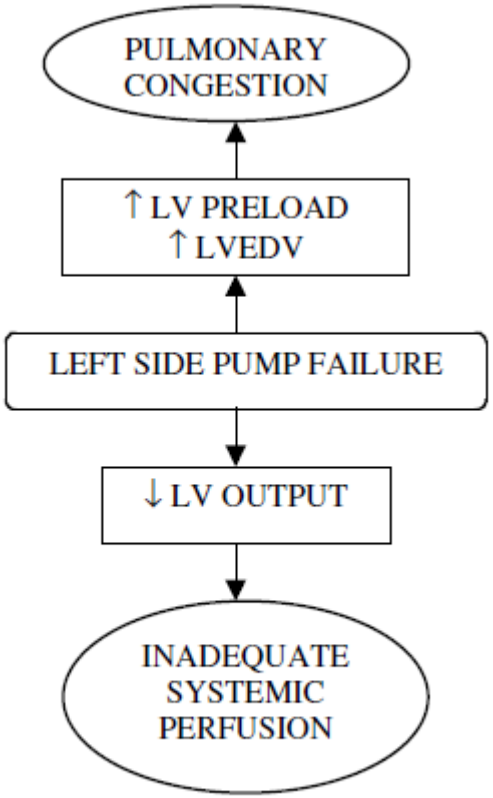
- The left side of the heart is responsible for pumping oxygenated blood from the lungs out to the peripheral tissues of the body.
- The most common causes of left heart failure include **myocardial infarction, cardiomyopathy and chronic hypertension.**
- Left heart failure is also referred to as **congestive heart failure** due to the pulmonary congestion of blood that accompanies the condition

Right heart failure

- arises as a consequence of left heart failure.
- increased pulmonary pressure that accompanies left heart failure, the resistance to blood flow now faced by the right ventricle is significantly increased as it pumps blood to the lungs **(cor-pulmonale)**
- Right heart failure may also result from chronic obstructive pulmonary disease, cystic fibrosis or adult respiratory distress syndrome

Manifestations of left heart failure include the following:

1. **Decreased stroke volume , increased left-ventricular end-diastolic volume (LVEDV), increased preload**
2. **Congestion of blood in the pulmonary circulation** leading to increased pulmonary pressure and **pulmonary edema**
3. **Dyspnea, cough, "rales" or crackling sounds** that may be heard through a stethoscope as a result of fluid accumulation in the lungs
4. **Orthopnea,** the accumulation of **fluids and dyspnea** that are often worse at night or when the patient lies in the supine position because blood and fluids from the lower limbs may redistribute into the pulmonary circulation
5. **Poor perfusion of systemic circulation** that may lead to cyanosis
6. **Generalized fatigue and muscle weakness**

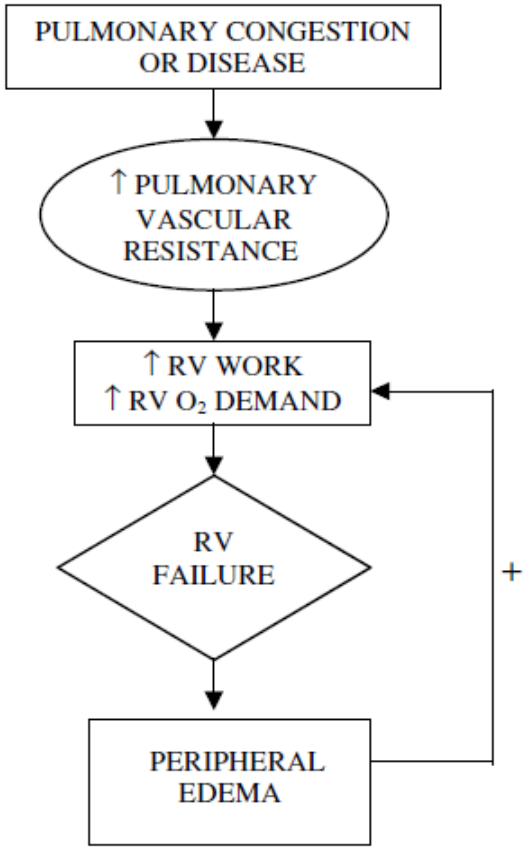


Consequences of left heart failure.

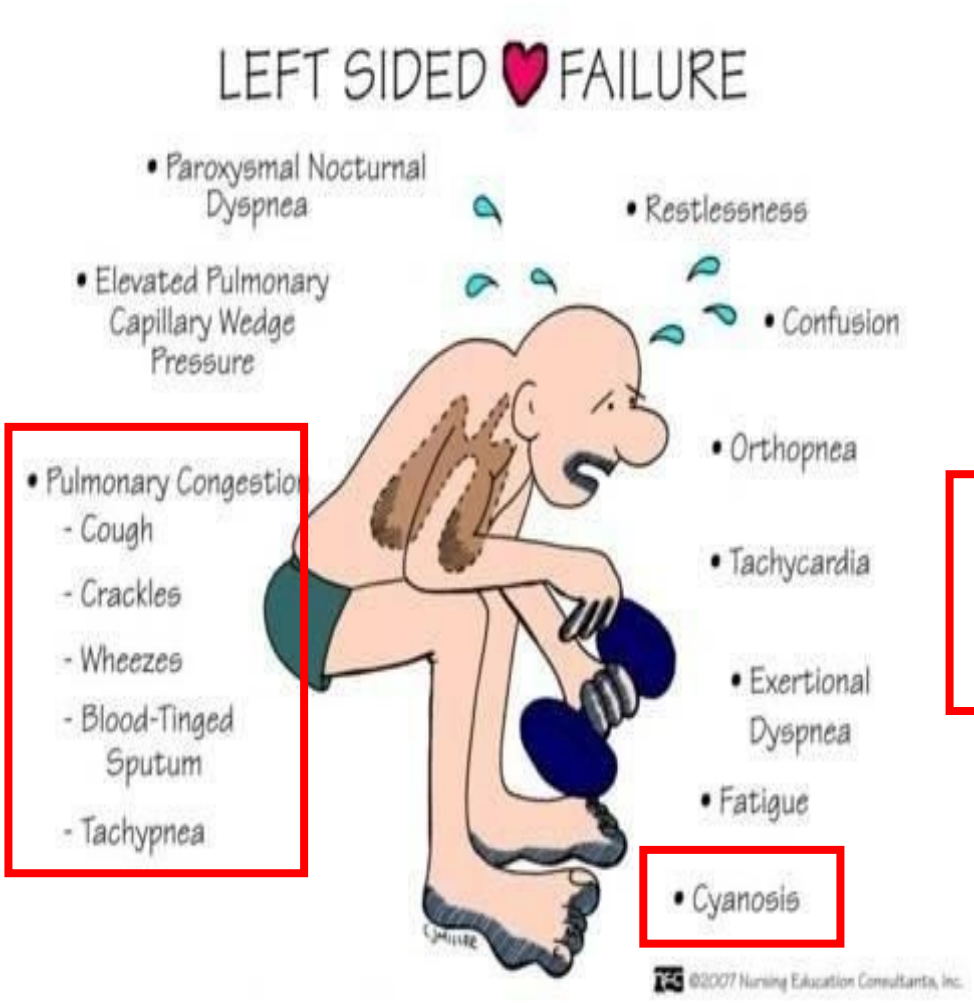
Manifestations of right heart failure

- include the following:

1. Increased right ventricular workload
2. Venous congestion and distention
3. Peripheral edema, ascites
4. Swelling of the liver with possible injury and eventual failure
5. Gastrointestinal symptoms



Consequences of right heart failure.


LEFT SIDED FAILURE
• Paroxysmal Nocturnal Dyspnea
• Restlessness
• Elevated Pulmonary Capillary Wedge Pressure
• Confusion
• Pulmonary Congestion
- Cough
- Crackles
- Wheezes
- Blood-Tinged Sputum
- Tachypnea
• Orthopnea
• Tachycardia
• Exertional Dyspnea
• Fatigue
• Cyanosis
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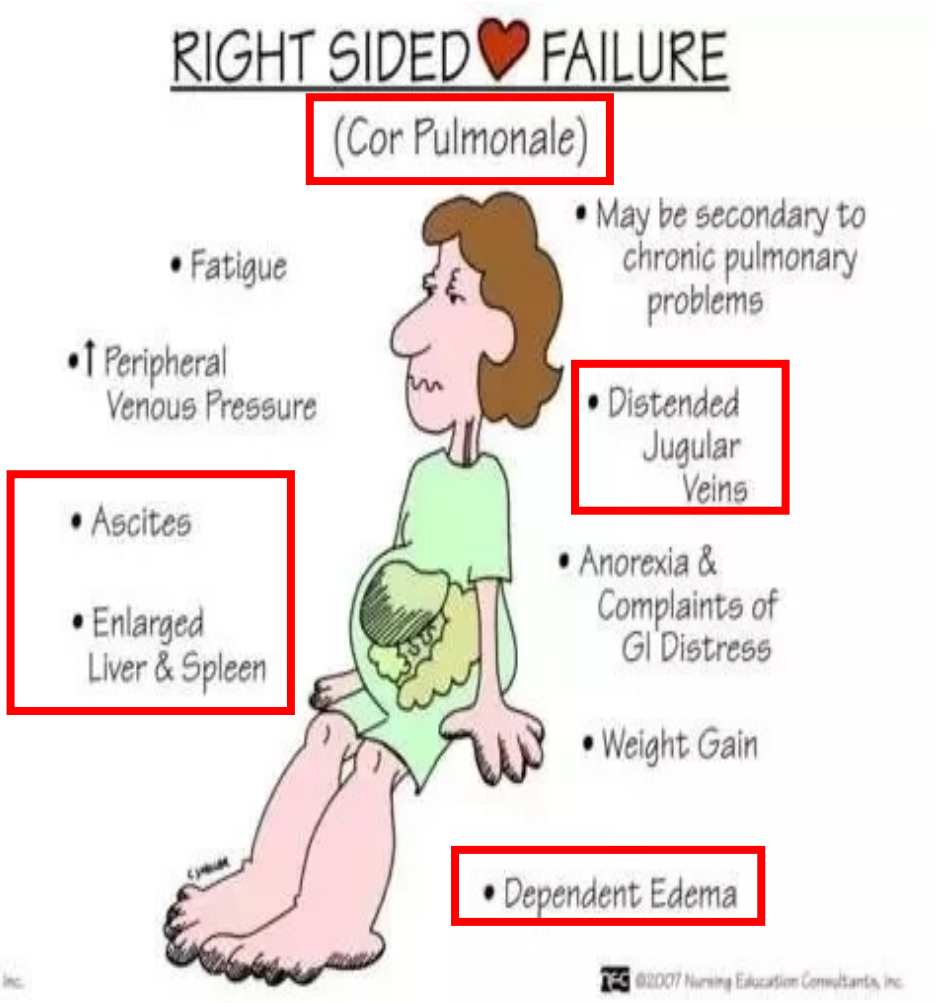
RIGHT SIDED FAILURE
(Cor Pulmonale)
• May be secondary to chronic pulmonary problems
• Fatigue
• ↑ Peripheral Venous Pressure
• Distended Jugular Veins
• Ascites
• Enlarged Liver & Spleen
• Anorexia & Complaints of GI Distress
• Weight Gain
• Dependent Edema
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Systolic failure vs. diastolic failure

- Recently, the American Heart Association issued guidelines for treating heart failure based upon whether patients experience:

- **Systolic failure:** a decreased ejection of blood from the heart during diastole

- **Diastolic failure:** filling of the ventricles during diastole is impaired

Systolic failure

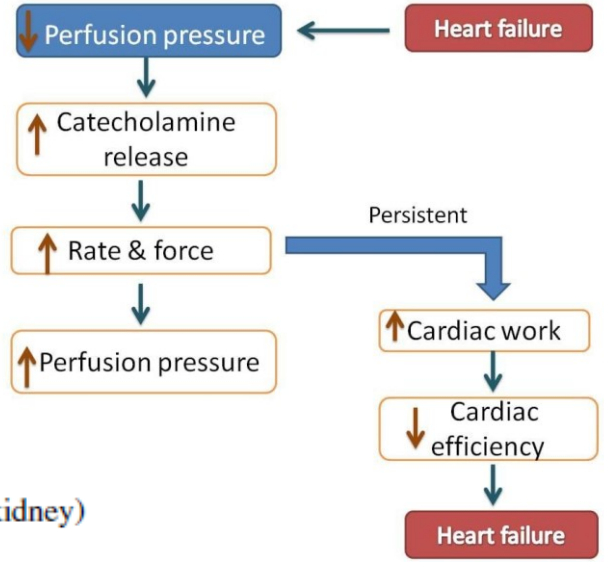
- Decreased myocardial contractility
- Decreased ejection fraction
- Most commonly caused by conditions that impair contractility such as ischemic heart disease, myocardial infarction and cardiomyopathy
- Symptoms mainly those of reduced cardiac output

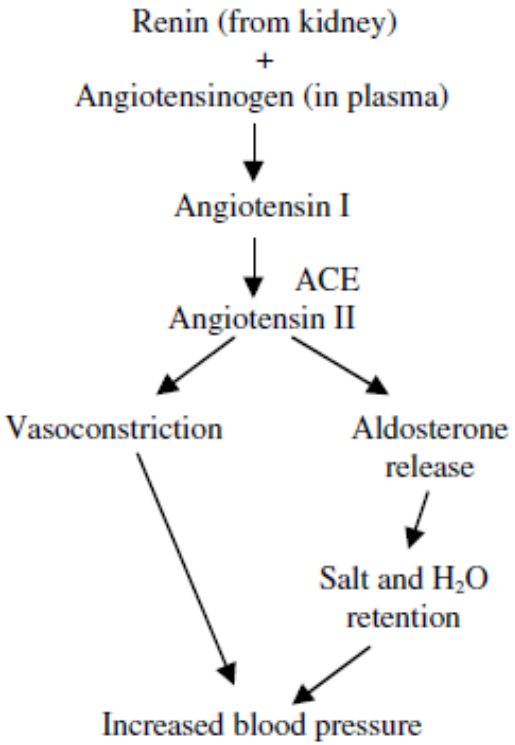
Diastolic failure

- Approximately 20 to 40% of patients with heart failure
- Preserved left ventricular systolic function but reduced ventricular filling that may be associated with impaired ventricular relaxation
- Associated with conditions such as restrictive and hypertrophic cardiomyopathy
- Symptoms primarily those of blood congestion and may include marked dyspnea and fatigue

Compensation for heart failure

- Increased cardiac output
- Increased sympathetic activity (catecholamines)
- Activation of renin–angiotensin system
- Ventricular hypertrophy and **remodeling of heart**





Shock

- Shock is a clinical condition of **reduced blood flow to organs and tissues.**
- Shock may be classified into three main categories based upon the cause of the shock. These categories of shock are : **distributive shock, cardiogenic shock, and, hypovolemic shock**.

Table 12.3 Distributive Shock

Neurogenic shock
Caused by a defect in sympathetic input to the blood vessels
May be caused by brain injury, central nervous system depressant drugs or spinal cord injury
Septic shock
Occurs most frequently with systemic infection by bacteria
May be triggered by an immune response to bacterial endotoxins
Widespread vasodilation occurs in response to the release of inflammatory mediators (examples: histamine, cytokines) and bacterial toxins
Anaphylactic shock
Triggered by an allergic reaction to antigens such as drugs, food, insect venom, etc.
Develops suddenly and manifests with marked vasodilation, bronchospasm and hypotension
May be rapidly fatal

2. **Cardiogenic shock**
   - Shock that occurs when the heart is unable to maintain normal cardiac output
   - Possible causes of cardiogenic shock:
     Heart failure
     Myocardial infarction
     Cardiomyopathy
     Cardiac tamponade
     Pneumothorax

3. **Hypovolemic shock**
   - Shock that occurs from decreased blood volume
   - Possible causes of hypovolemic shock:
     Hemorrhage
     Excess fluid loss from diarrhea, vomiting
     Shifting of fluids from the vasculature to the interstitial spaces (*ascites*)

Complications of shock

- **Adult respiratory distress syndrome** (shock lung) — A potentially fatal respiratory failure that accompanies severe shock. The exact cause is uncertain but the condition may involve ischemic injury to lung tissues.
- **Acute renal failure** due to reduced renal perfusion.
- **Disseminated intravascular coagulation** — Formation of multiple small blood clots that may be related to sluggish blood flow or abnormal clotting activity.
- **Multiple organ failure, cerebral hypoxia, death.**

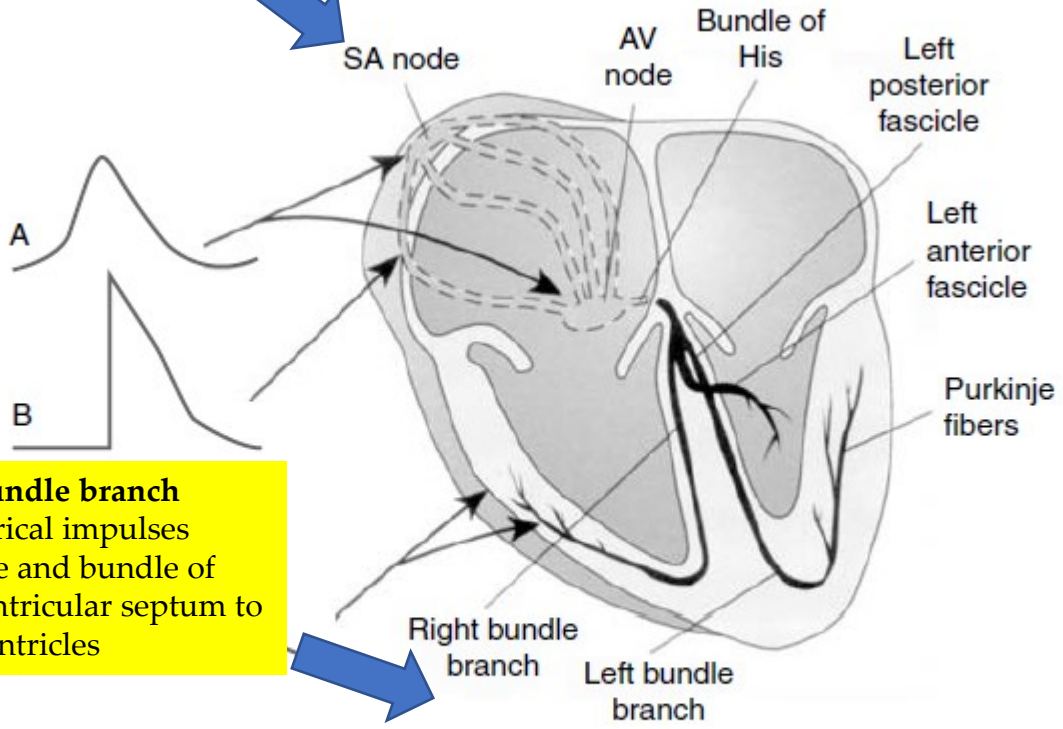
❑ Abnormalities of cardiac conduction

- A cardiac **arrhythmia or dysrhythmia** is any **disturbance that occurs to normal heart rhythm**.

- Cardiac arrhythmias can vary in severity from an occasional missed beat to serious abnormalities of rate and rhythm that severely impair the pumping ability of the heart and can be rapidly life-threatening

Sinoatrial (SA) node
- Located in the wall of the right atrium
- Primary pacemaker of the heart that sets normal rate and rhythm
- Depolarizes spontaneously 60 to 100 times per minute to set the resting heart rate
- Transmits depolarization impulses to AV node via conduction bundles

Atrioventricular (AV) node
- Located in the posterior wall of the septum
- Receives impulses from the SA node and transmits them via the bundle of His through the ventricular septum
- May take over as primary pacemaker if the SA node is defective,
but at a slower rate of depolarization



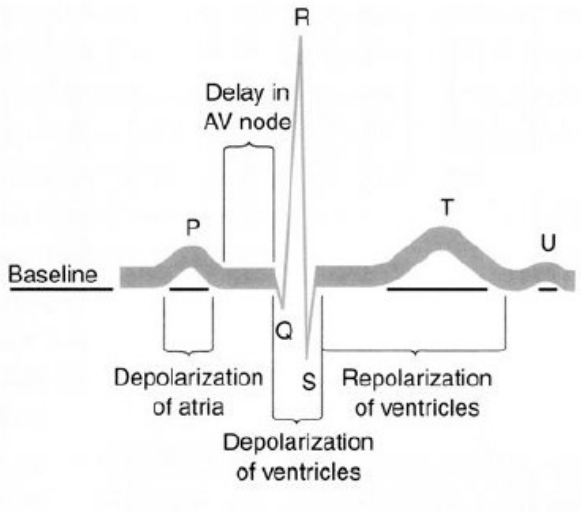
Left and right bundle branch
- Conducts electrical impulses from the AV node and bundle of His down the ventricular septum to the *apex* of the ventricles

Purkinje fibers
- Highly branched fibers that carry electrical impulses up through the muscle mass of the ventricles
- May act as a tertiary pacemaker in the event of SA and AV node failure but have a very low rate of depolarization that yields a very low cardiac output if pacing the heart

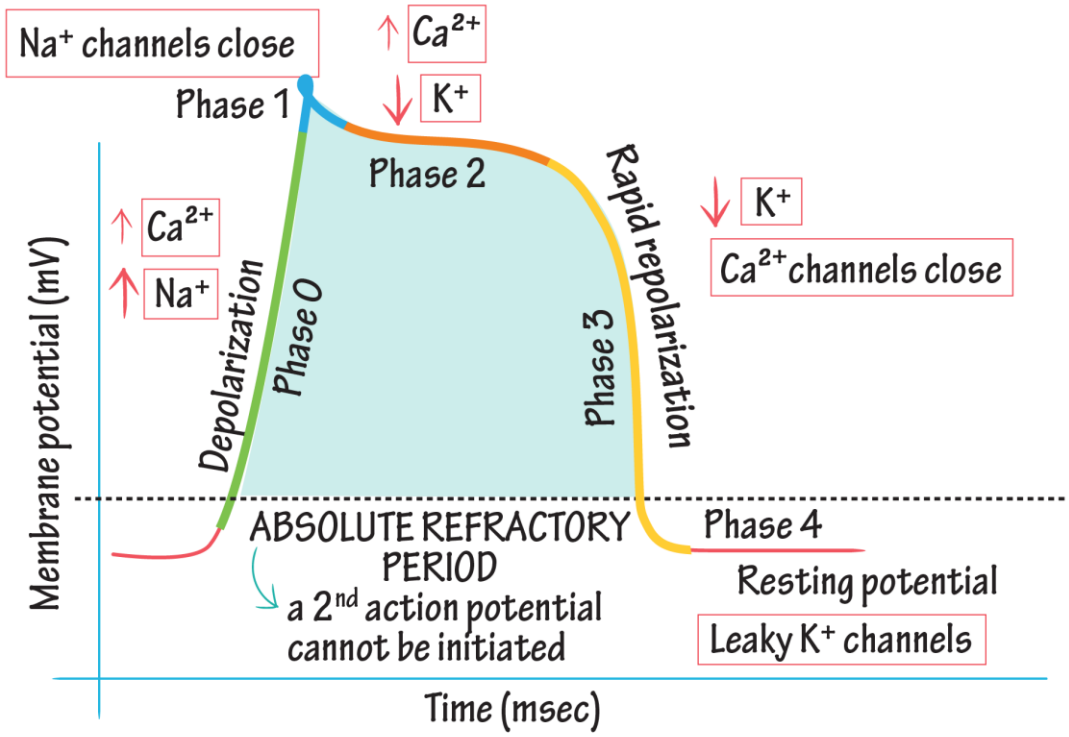
Figure 13.1 Cardiac conduction system. (From Porth, C.M., *Pathophysiology: Concepts of Altered Health States*, 5th ed., Lippincott, Philadelphia, 1998. With permission.)

Phases of cardiac muscle cell action potential

- **Phase 0 :** Opening of Na channels, rapid depolarization of cell membrane
- **Phase 1:** Inactivation of Na channels, some small influx of Ca2+ occurs
- **Phase 2:** Plateau phase , some K efflux, Ca2+ enters for actual muscle contraction
- **Phase 3:** Rapid outward movement of K+ that reestablishes resting membrane potential, but Na + and K + ions on the wrong side of the membrane
- **Phase 4:** Active Na + /K + pump, which switches location of ions and restores normal resting membrane potential



CARDIAC ACTION POTENTIAL



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Key terms

- Threshold potential — The minimum depolarization required to initiate an action potential.
- Conduction velocity — Rate at which electrical impulses are carried through the myocardium; directly affected by the speed of the action potential in various cells.
- Absolute refractory period — A period of time immediately following an action potential during which a second action potential cannot be triggered by a stimulus of any size.
- Relative refractory period — A period immediately following an action potential during which a greater-than-normal stimuli can start another action potential.

Factors that may contribute to the development of a cardiac arrhythmia

- Ischemia
- Myocardial infarction
- Electrolyte imbalance
- Altered cellular pH
- Administration of certain drugs
- Congenital defects in the heart

Pathophysiology

- Cardiac arrhythmias are caused by (a) abnormal impulse initiation, (b) abnormal impulse conduction, or (c) both.

1. Abnormal Impulse Initiation:

- Abnormal initiation of electrical impulses occurs due to abnormal automaticity. A decrease in sinus node automaticity results in a reduced rate of impulse generation and a slow heart rate (sinus bradycardia). Conversely, an increase in sinus node automaticity results in an increased rate of impulse generation and a rapid heart rate (sinus tachycardia)

- Abnormal atrial automaticity: atrial tachycardia or atrial fibrillation (AF)
- Abnormal AV nodal automaticity : “junctional tachycardia”
- Abnormal automaticity originating from the pulmonary veins is a precipitant of AF.
- Abnormal automaticity in the ventricles: premature ventricular complexes (PVCs) or may precipitate ventricular tachycardia (VT) or ventricular fibrillation (VF).

2. Abnormal Impulse Conduction:

abnormal premature electrical impulse (abnormal automaticity).

Reentry: There are two pathways for impulse conduction, slowed impulse conduction down pathway and a longer refractory period in pathway

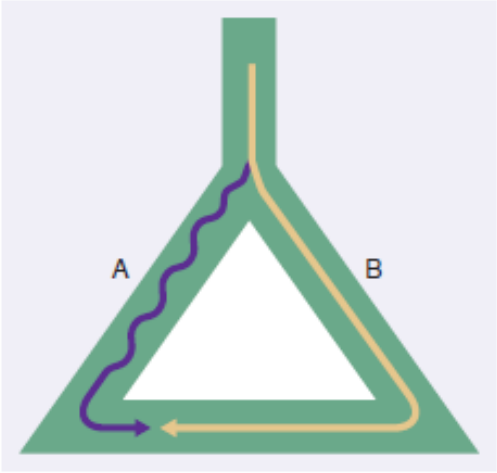


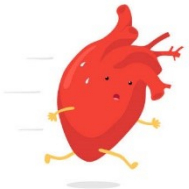
FIGURE 9–3. The process of initiation of reentry. There are two pathways for impulse conduction, slowed impulse conduction down pathway A and a longer refractory period in pathway B.

Types of arrhythmia

- Arrhythmias are classified into two broad categories: supraventricular (those occurring above the ventricles) and ventricular (those occurring in the ventricles).
- **SUPRAVENTRICULAR ARRHYTHMIAS**

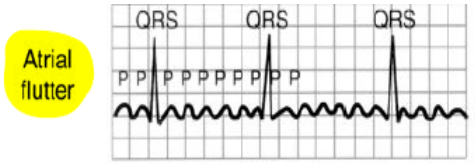
1. **Sinus Bradycardia (Abnormal Impulse Initiation) :**Sinus bradycardia is defined by a sinus rate less than 60 beats/min. result of fibrotic tissue in the sinus node, which replaces normal sinus node tissue
2. **AV Block (Abnormal Impulse Conduction) :** occurs when conduction of electrical impulses through the AV node is impaired to varying degrees. AV block is classified into three categories. First-degree (1°) AV block is defined simply as prolongation of the PR interval to greater than 0.2 seconds, up to third-degree (3°) AV block, also referred to as "complete heart block,"
3. **Atrial Fibrillation and flutter (Abnormal Impulse Initiation): AF** un-coordinated contractions, flutter atrial beating of 300 beat/min

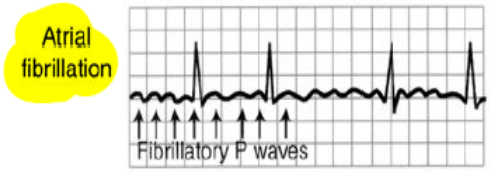
4. Paroxysmal Supraventricular Tachycardia – atrial paroxysmal tachycardia: sudden trial beating to 150 beat/ min



Sinus node arrhythmia

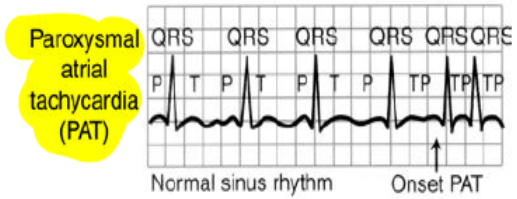
- *Sinus bradycardia* — Excessively slow heart rate (<60 beats per minute, bpm)
- *Sinus tachycardia* — Excessively fast heart rate (>100 bpm)
- *Sinus arrest* — Failure of SA node to discharge, secondary pacemakers may take over (i.e., AV node)

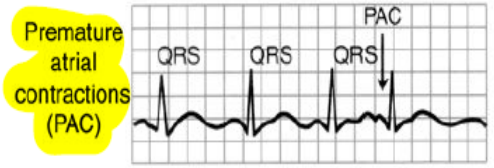




Atrial arrhythmia

- Premature atrial contractions
  Contraction of the heart before the normal contraction
  Most occur from ectopic impulses
  Also called *premature beats* or *extrasystole*
- Atrial paroxysmal tachycardia
  Sudden increase in atrial contraction rate to approximately 150 bpm
- Atrial flutter
  Atrial beating rates of approximately 300 bpm
- Atrial fibrillation
  Uncoordinated contraction of atria





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- **VENTRICULAR ARRHYTHMIAS**

1. **Premature Ventricular Complexes:** PVCs are ectopic electrical impulses originating in ventricular tissue, resulting in wide, misshapen, abnormal QRS complexes. PVCs have also been known by other terms, ventricular premature beats (VPBs), ventricular premature contractions (VPCs), and ventricular premature depolarizations (VPDs).
2. **Ventricular Tachycardia:** VT is a series of three or more consecutive PVCs at a rate greater than 100 beats/min.

   Torsades de Pointes: TdP is a specific polymorphic VT associated with prolongation of the QTc interval (prolongation in the repolarization phase of the ventricular action potential) …… drugs

3. **Ventricular Fibrillation:** VF is irregular, disorganized, chaotic electrical activity in the ventricles resulting in the absence of ventricular depolarizations, and consequently, lack of pulse, cardiac output, and blood pressure.

Ventricular arrhythmia

- *Ventricular premature beats*
  One of the most common types of arrhythmia
  Can progress into ventricular tachycardia or fibrillation
- *Ventricular tachycardia*
  Excessive ventricular contraction rates
  Can have marked effects on cardiac output
- *Ventricular fibrillation*
  The most serious cardiac arrhythmia
  Characterized by a complete loss of ventricular coordination
  Cardiac output falls to zero
  Rapid death will ensue if not treated

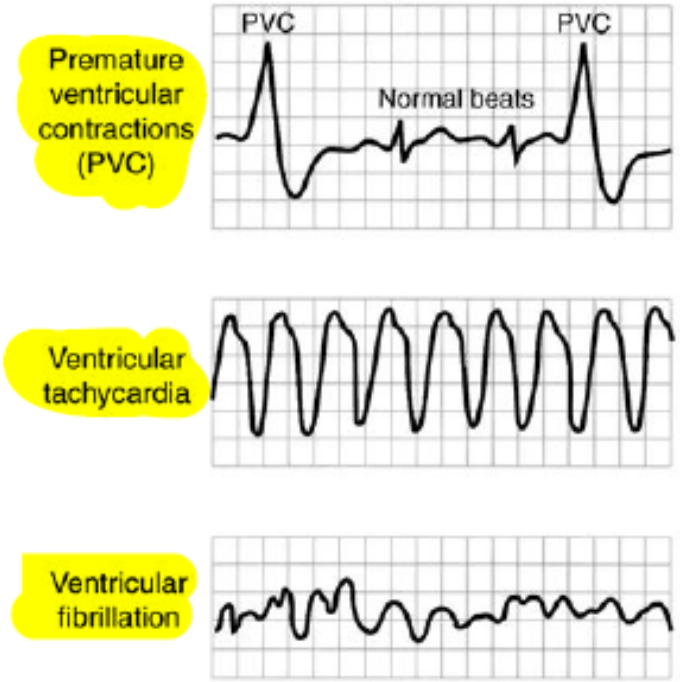

Figure 13.5 Ventricular arrhythmias. (From Porth, *Altered Health States*, 5th ed., Lippincott, Philadelp

Classification of Arrhythmias

- Normal sinus impulse formation
  - Normal sinus rhythm
  - Sinus arrhythmia
- Disturbances from sinus
  - Sinus bradycardia
  - Sinus tachycardia
- Disturbances of atrial impulse formation
  - Atrial premature complexes
  - Atrial tachycardia
  - Atrial flutter
  - Atrial fibrillation
- Disturbances of ventricular impulse formation
  - Ventricular premature complexes
  - Ventricular tachycardia
  - Ventricular asystole- no contraction
  - Ventricular fibrillation

Disturbances of impulse conduction

- Sinus arrest
- Atrial standstill
- First-degree AV block
- Second degree AV block
- Third degree AV block

Heart block

- Abnormal conduction of impulses by the bundle of His (AV bundle)
- Affects conduction of impulses between atria and ventricles
- May be a delay or complete block of impulse conduction

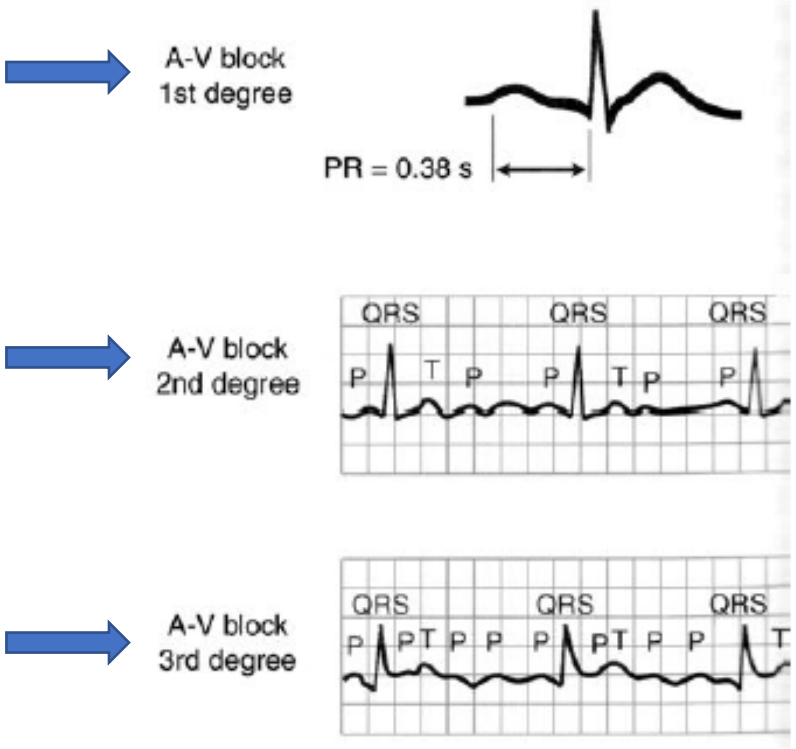

Figure 13.6 Degrees of heart block. (From Porth, C.M., *Pathophysiology: Concepts of Altered Health States*, 5th ed., Lippincott, Philadelphia, 1998. With permission.)