Pathophysiology

Dr. Yasser Mufid

Lecture 10

II. Disorders of cardiovascular system

VI. Shock

is a medical emergency in which the organs and tissues of the body are ***not receiving an adequate flow of blood.*** This deprives the organs and tissues of oxygen (carried in the blood) and allows the buildup of waste products. Shock can result in serious damage or even death.

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Shock is an acute state in which tissue perfusion is inadequate to maintain the supply of oxygen and nutrients necessary for normal cell function. **The main cause is circulatory failure**, which produces a fall in blood pressure and cardiac output which will results in widespread hypoxia. This leads to a lack of blood perfusion of the key organs (brain, lungs, heart, etc.), which is ultimately life threatening. There are ***three reasons why tissue perfusion might become inadequate*** & these are:

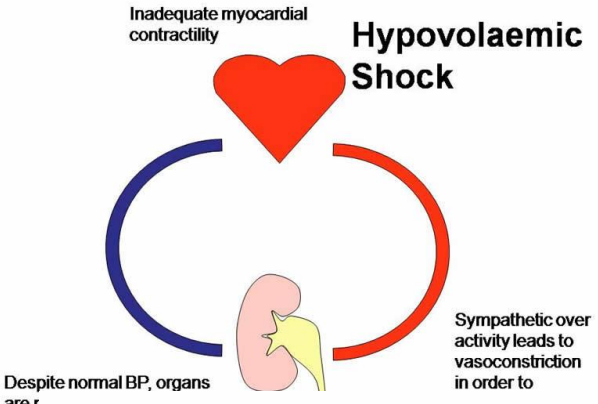
1. A decreased circulating blood volume.
2. A failure of the heart to pump effectively.
3. A massive increase in peripheral vasodilation.

Types of Shock

1. **Hypovolemic shock: Severe bleeding or loss of body fluid** *from trauma, burns, surgery, or dehydration from severe nausea and vomiting*. Blood pressure decreases, thus blood flow is reduced to cells, tissue, and organs.

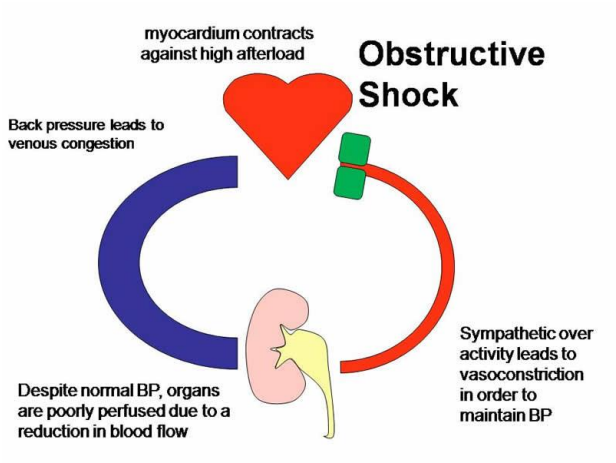
Degree of volume loss which leads to response

a. 10% **well tolerated** (tachycardia).
b. 20 - 25% failure of compensatory mechanisms (hypotension, orthostasis, decreased Cardiac Output (CO)).
c. > 40% loss **associated with overt shock** (*marked hypotension, decreased Cardiac Output (CO), lactic acidemia, anuria, air hunger, coma then death*).

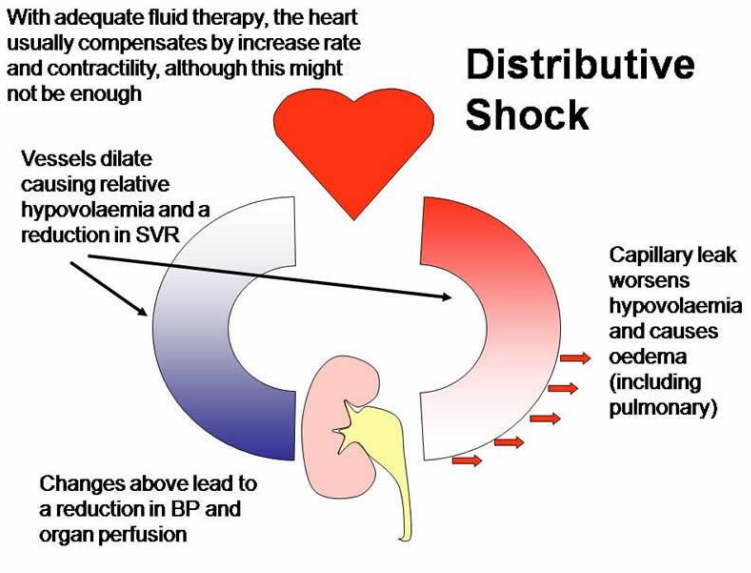


2. **Cardiogenic shock:** Myocardial Infarction with damage to heart muscle; the heart is unable to pump effectively which will lead to Inadequate cardiac output. Body cells do not receive enough oxygen. Requires at least 40% loss of functional myocardium (single Myocardial Infarction or cumulative damage) - stunned, nonfunctional, but viable myocardium may contribute to post-MI cardiogenic shock.

3. **Extra-cardiac obstructive shock:** Is due to obstruction to flow in the cardiovascular circuit and characterized by **either impairment of diastolic filling or excessive afterload.**



4. **Distributive**: which includes:
   a) **Septic shock:** (**bacterial, fungal, viral, rickettsia**): Occurs when the sepsis has progressed to the point **where it is affecting many organ systems.**
   b) **Toxic shock syndrome**: An acute infection caused by *Staphylococcus aureus* or *Streptococcus pyogenes* toxic shock syndrome toxin (***a Superantigen toxin that allows the nonspecific binding of MHC II with T cell receptors, resulting in polyclonal T cell activation);*** usually systemic, that overwhelms the body (toxic shock syndrome). The blood pressure decreases, impairing blood flow to cells, tissues, and organs.



   c) **Anaphylactic shock:** Results from reaction to substance to which patient is hypersensitive or allergic (**allergen extracts, bee sting, medication, food**). Outpouring of histamine results in dilation of blood vessels throughout the body is ***a type I hypersensitivity reaction***.
   d) **Neurogenic (spinal shock):** Injury or trauma to the nervous system (spinal cord, brain). The Nerve impulse to blood vessels is impaired, **blood vessels remain dilated and blood pressure decreases**. **Psychogenic Shock:** Shock caused by **overwhelming emotional factors**. Sudden dilation of blood vessels results in fainting because of lack of blood supply to the brain.

VII. Coronary Heart Disease & Myocardial Infarction (Coronary artery disease)

Coronary artery disease is a narrowing or blockage of the arteries and vessels that provide oxygen and nutrients to the heart.

It is caused by atherosclerosis, an accumulation of fatty materials on the inner linings of arteries. The resulting blockage restricts blood flow to the heart. When the blood flow is completely cut off, the result is a heart attack.

Pathophysiology

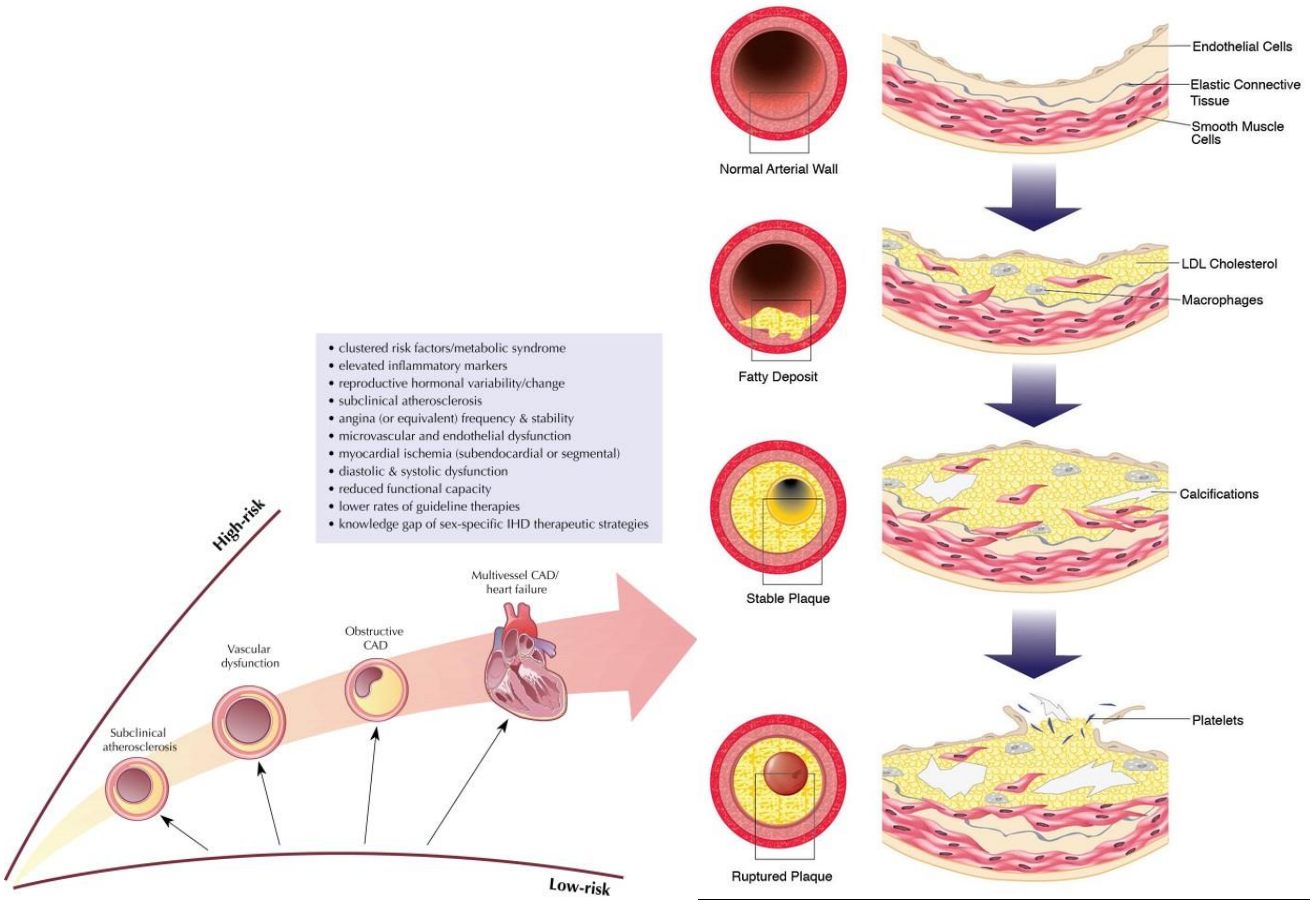
Coronary artery disease is almost always due to atheromatous *narrowing and subsequent occlusion of the vessel.* Early atheroma is present from young adulthood onwards. A mature plaque is composed of two constituents, each associated with a particular cell population.

A. The **lipid core** is mainly released from necrotic "**foam cells**"—monocyte derived macrophages, which migrate into the intima and ingest lipids.
B. The **connective tissue matrix** is derived from **smooth muscle cells**, which migrate from the media into the intima, where they proliferate and change their **phenotype to form a fibrous capsule around the lipid core**.

Limitation of blood flow to the heart causes ischemia (cell starvation secondary to a lack of oxygen) of the myocardial cells. Myocardial cells may die from lack of oxygen and this is called a myocardial infarction. It leads to heart muscle damage, heart muscle death and later myocardial scarring without heart muscle regrowth.

Chronic high-grade stenosis of the coronary arteries can induce transient ischemia which leads to the induction of a ventricular arrhythmia, which may terminate into ventricular fibrillation leading to death.

When a plaque produces a >50% diameter stenosis (or >75% reduction in cross sectional area), reduced blood flow through the coronary artery during exertion may lead to angina.



Risk factor for Coronary Heart disease

1) Tobacco Smoke.
2) High Blood Cholesterol .
3) High Blood Pressure .
4) Physical Inactivity.
5) Obesity and Overweight.
6) Diabetes Mellitus.
7) Stress.
8) Alcohol.
9) Diet and Nutrition.
10) Age.

Clinical manifestations are those of Ischemic Heart disease

Myocardial Infarction (STAMI)

ST-segment elevation acute myocardial infarction

The term acute myocardial infarction (MI) should be used when there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia. Under these conditions any one of the following criteria meets the diagnosis for MI:

• **Detection of a rise and/or fall of cardiac biomarker values** [preferably cardiac troponin (cTn)] and with at least one of the following:

1. Symptoms of ischemia.
2. New or presumed **new significant ST-segment–T wave (ST–T) changes or new left bundle branch block (LBBB).**
3. Development of **pathological Q waves** in the ECG.
4. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality by **Echo cardiogram**.
5. Identification of an intracoronary thrombus by **angiography or autopsy**.

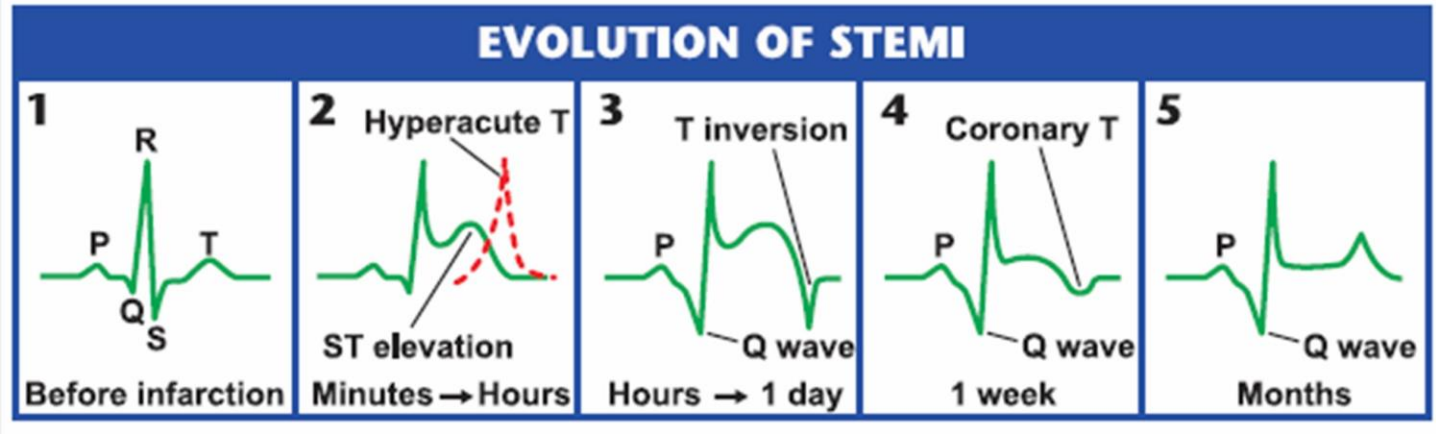
Initial Diagnosis of STEMI

• **History of chest pain** / discomfort lasting for 10-20 minutes or more (not responding to nitroglycerine).

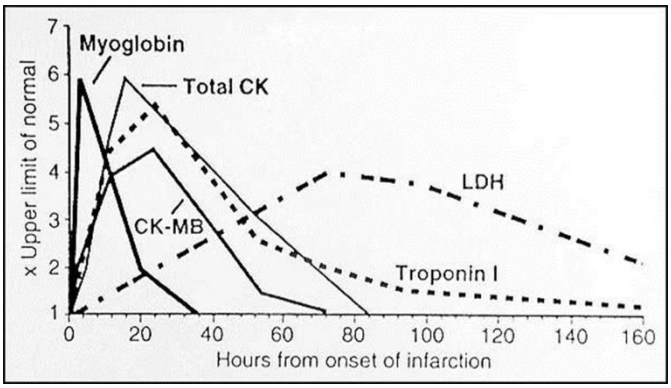
• **ECG:** Persistent ST-segment elevation or (presumed) new left bundle-branch block. Repeated ECG recordings often needed since ECG can be equivocal in early hours.

• **Elevated markers** of myocardial necrosis (**CK-MB, troponins**) can be sometimes helpful in deciding to perform coronary angiography (eg. in LBBB) but one should not wait for the results to initiate reperfusion therapy.

• **2D-echocardiography** rules out major myocardial ischemia by demonstrating **absence of wall motion abnormalities**. Valuable in cases when diagnosis of STEMI is in doubt.
• **Older age**, **elevated heart rate**, **lower systolic blood pressure** and **anterior location of the infarct** are important factors in risk-stratification of STEMI patients.
• Other important predictors are **previous infarction**, height, time to treatment, diabetes and smoking status.



Cardiac biomarker



In the past, measurement of nonspecific markers such as:

1. **Aspartate transaminase**,
2. **Lactate dehydrogenase** (LDH),
3. **Total creatine kinase** (CK) were performed.

Creatine Kinase, an enzyme presents in many tissues, including the myocardium and skeletal muscle, has 3 isoenzymes: **MM, MB, and BB**. CK-MB is present in a relatively high concentration in the myocardium, whereas the concentration of CK-MM is highest in skeletal muscle while the CK-BB is present in the brain.
1- **CK-MB** can **be found in patients with renal failure and chronic myopathic skeletal muscle injury** (as occurs in polymyositis and dermatomyositis) or in the **muscle tissue of trained athletes** **making it lesser sensitive** than the other biomarkers.
Following myocardial injury, the initial CK-MB rise occurs **4 to 9 hours after the onset of chest pain**, peaks at 24 hours, and returns to baseline at 48 to 72 hours.

2- Myoglobin is an **oxygen-binding protein**, found in a high concentration in both cardiac and skeletal muscle.
Myoglobin is a relatively small protein molecule that is released into serum as early as **1 hour after STEMI**, reaches a peak in the range of 4 to 12 hours, then is rapidly cleared.
The major advantage of myoglobin as a cardiac marker is that it is released earlier from damaged cells than other cardiac markers, permitting earlier detection of STEMI.
3- Troponin I (cTnI) **control the calcium-mediated interaction of actin and myosin**.
cTnI **completely specific for the heart**. Troponin increases in serum within **4 to 9 hours after STEMI**, peak at 12 to 24 hours, and remain **elevated for up to 14 days**.
Elevated levels can persist in blood for weeks; the cardiac specificity of troponins thus make them the ideal marker for retrospective diagnosis of infarction.