Pathology of Cardiovascular System

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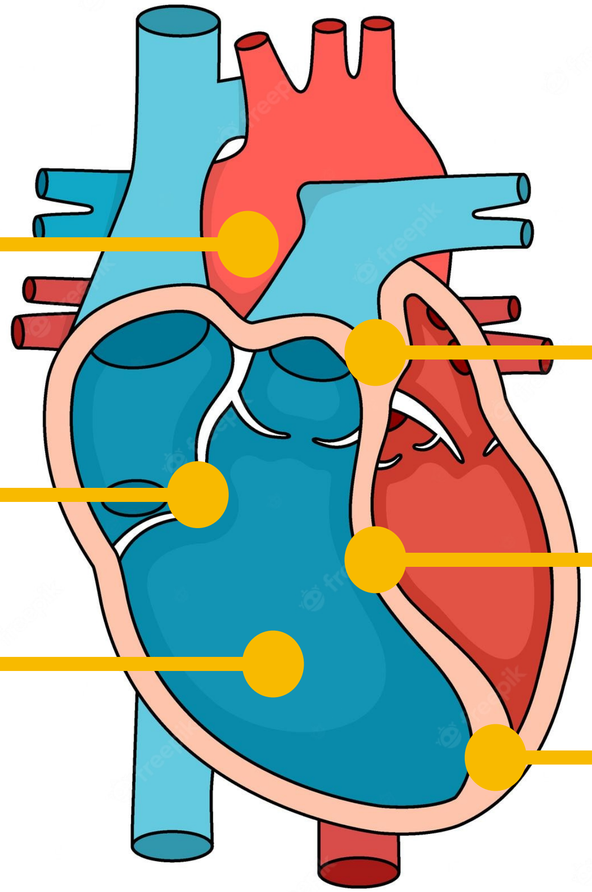
Overview of Heart Disease



Obstruction

Regurgitation

Failure to pump

Disorder of conduction

Shunted flow

Rupture of heart or major vessel

Failure of the pump

- The cardiac muscle contracts weakly and the chambers cannot empty properly - called *Systolic dysfunction*

- The cardiac muscle cannot relax sufficiently to permit ventricular filling - called *Diastolic dysfunction*

Obstruction to Flow

- Lesion that prevent valve opening or cause increased ventricular chamber pressures can overwork the myocardium, which has to pump against the obstruction

Regurgitant Flow

- Valve pathology that allows backward flow of blood results in increased volume overload and may overwhelm the pumping capacity of the affected chambers.

Shunted Flow

- Defects that divert blood inappropriately from one chamber to another, or from one vessel to another, lead to pressure and volume overloads.

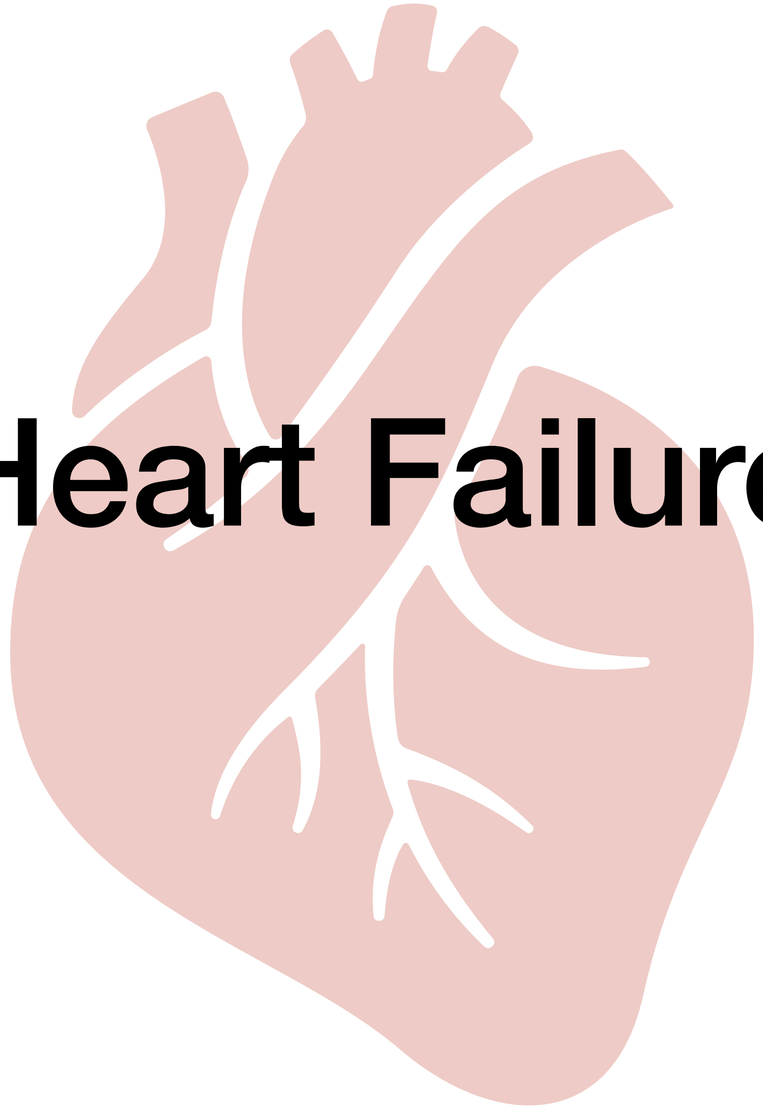
Disorders of Cardiac Conduction

- Uncoordinated cardiac impulses or blocked conduction pathway can cause arrhythmias that slow contractions or prevent effective pumping altogether.

Rupture of the Heart or Major Vessel

- Loss of circulatory continuity may lead to massive blood loss, hypotensive shock, and death.

Heart Failure



Heart Failure

- Heart failure (Congestive Heart Failure, CHF) occurs when the heart cannot generate sufficient output to meet the metabolic demands of the tissues.
- In most cases, CHF develops gradually owing to the cumulative effects of chronic work overload or progressive loss of myocardium
- Systolic dysfunction: inadequate myocardial contractile function
- Diastolic dysfunction: inability of the heart to adequately relax and fill

Compensation

- The Frank-Starling mechanism:
  - Increase end-diastolic volumes -> dilate the heart -> increased cardiac myofiber stretching -> increase cardiac output
- Activation of neurohormonal system:
  - Release NE
  - Activate RAAS system
  - Release ANP
- Myocardial structural changes

Left-sided Heart Failure

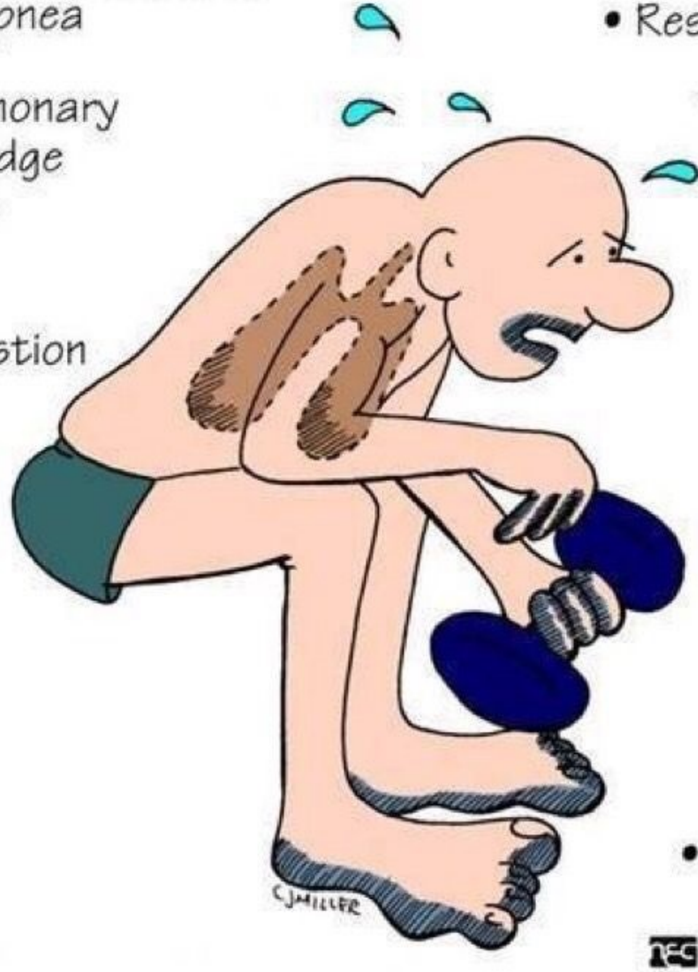
- The most common causes are
  - Ischemic Heart Disease
  - Systemic Hypertension
  - Mitral or Aortic Valve Disease
  - Primary Disease of Myocardium
- Effects of Left-sided HF:
  - diminished systemic perfusion and elevated back-pressures within the pulmonary circulation

Left-sided Heart Failure

- Clinical Features:
  - Dyspnea on exertion
  - Orthopnea (dyspnea when recumbent)
  - Paroxysmal Nocturnal Dyspnea

LEFT SIDED ♥ FAILURE

- Paroxysmal Nocturnal Dyspnea
- Elevated Pulmonary Capillary Wedge Pressure
- Pulmonary Congestion
  - Cough
  - Crackles
  - Wheezes
  - Blood-Tinged Sputum
  - Tachypnea



- Restlessness
- Confusion
- Orthopnea
- Tachycardia
- Exertional Dyspnea
- Fatigue
- Cyanosis

Right-sided Heart Failure

- Right-sided HF usually the consequences of Left-sided HF:
    - Pressure increase in the pulmonary circulation produces and increased burden of the right side of the heart
- Clinical Features:
    - Systemic and portal venous congestion -> Pleural effusion, peripheral edema, ascites, splenomegaly

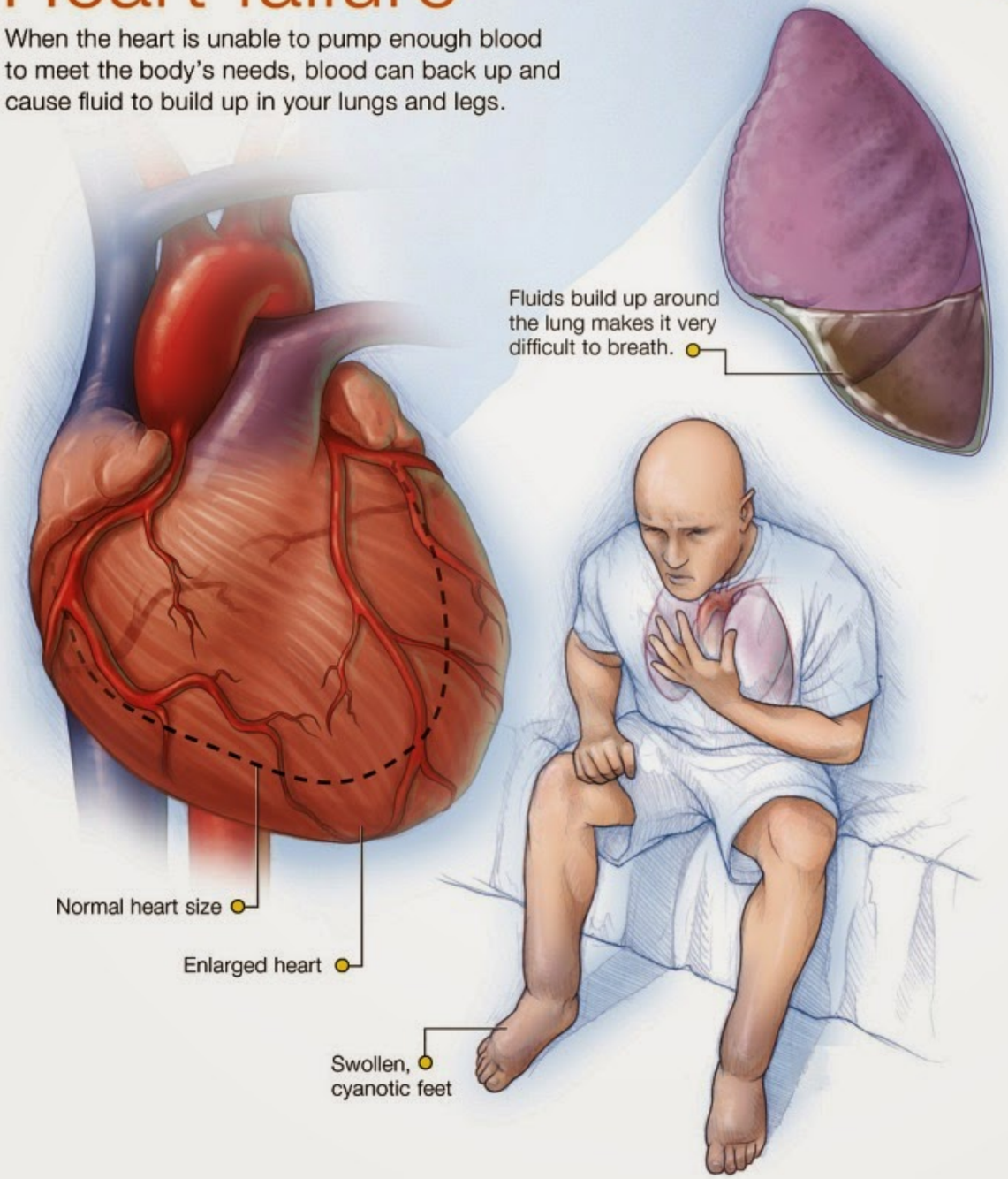
RIGHT SIDED ♥ FAILURE

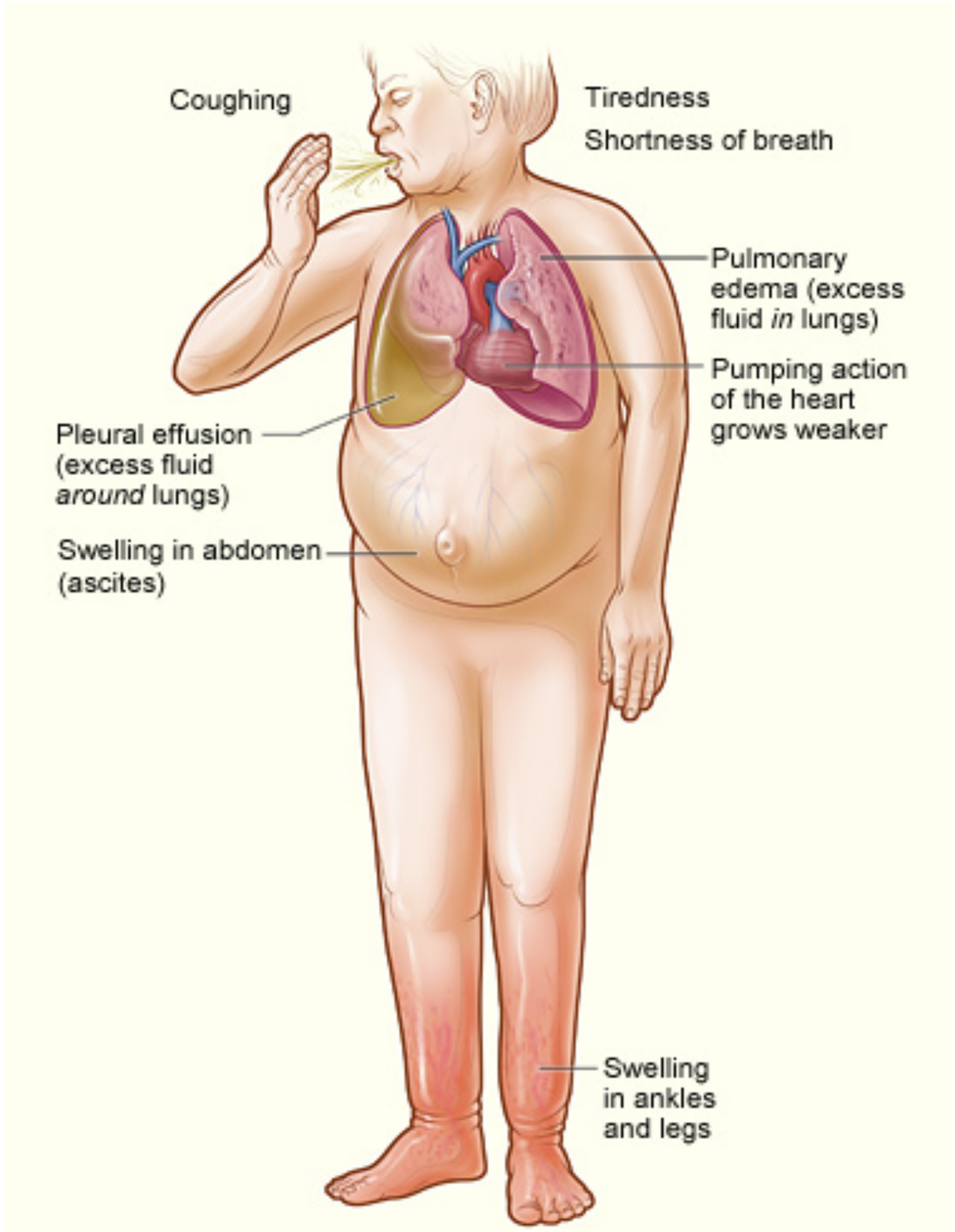
(Cor Pulmonale)

- Fatigue
- ↑ Peripheral Venous Pressure
- Ascites
- Enlarged Liver & Spleen
- May be secondary to chronic pulmonary problems
- Distended Jugular Veins
- Anorexia & Complaints of GI Distress
- Weight Gain
- Dependent Edema

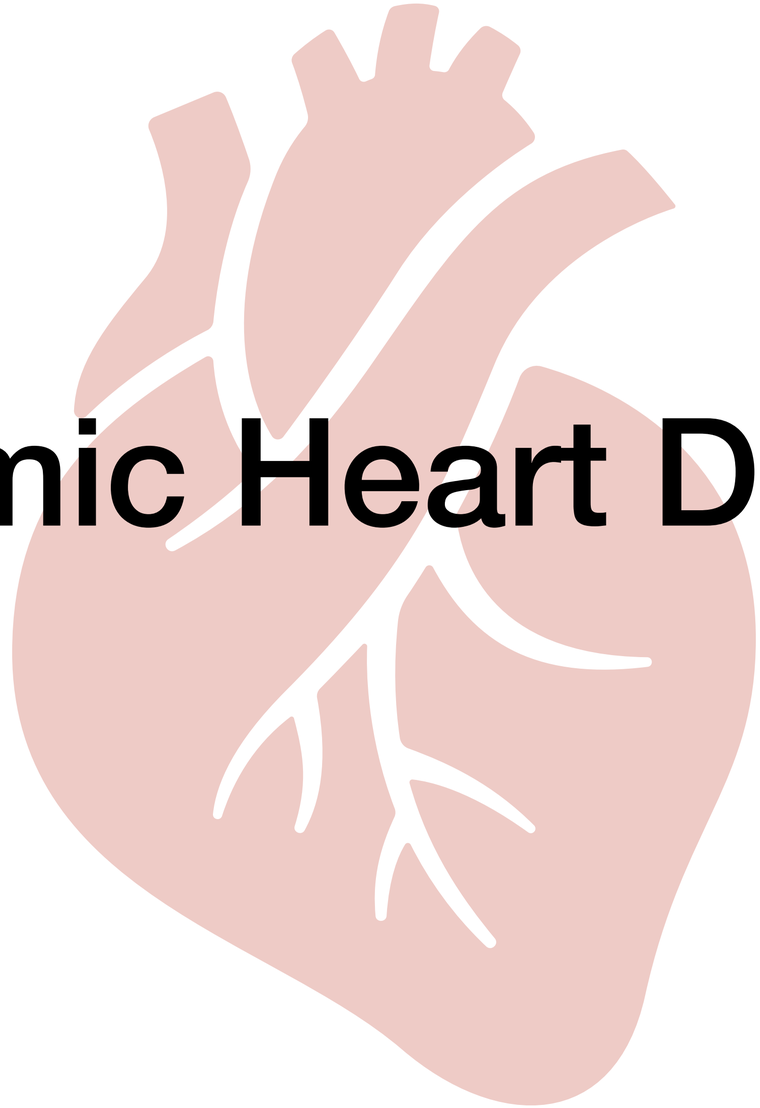
Heart failure

When the heart is unable to pump enough blood to meet the body's needs, blood can back up and cause fluid to build up in your lungs and legs.





Ischemic Heart Disease

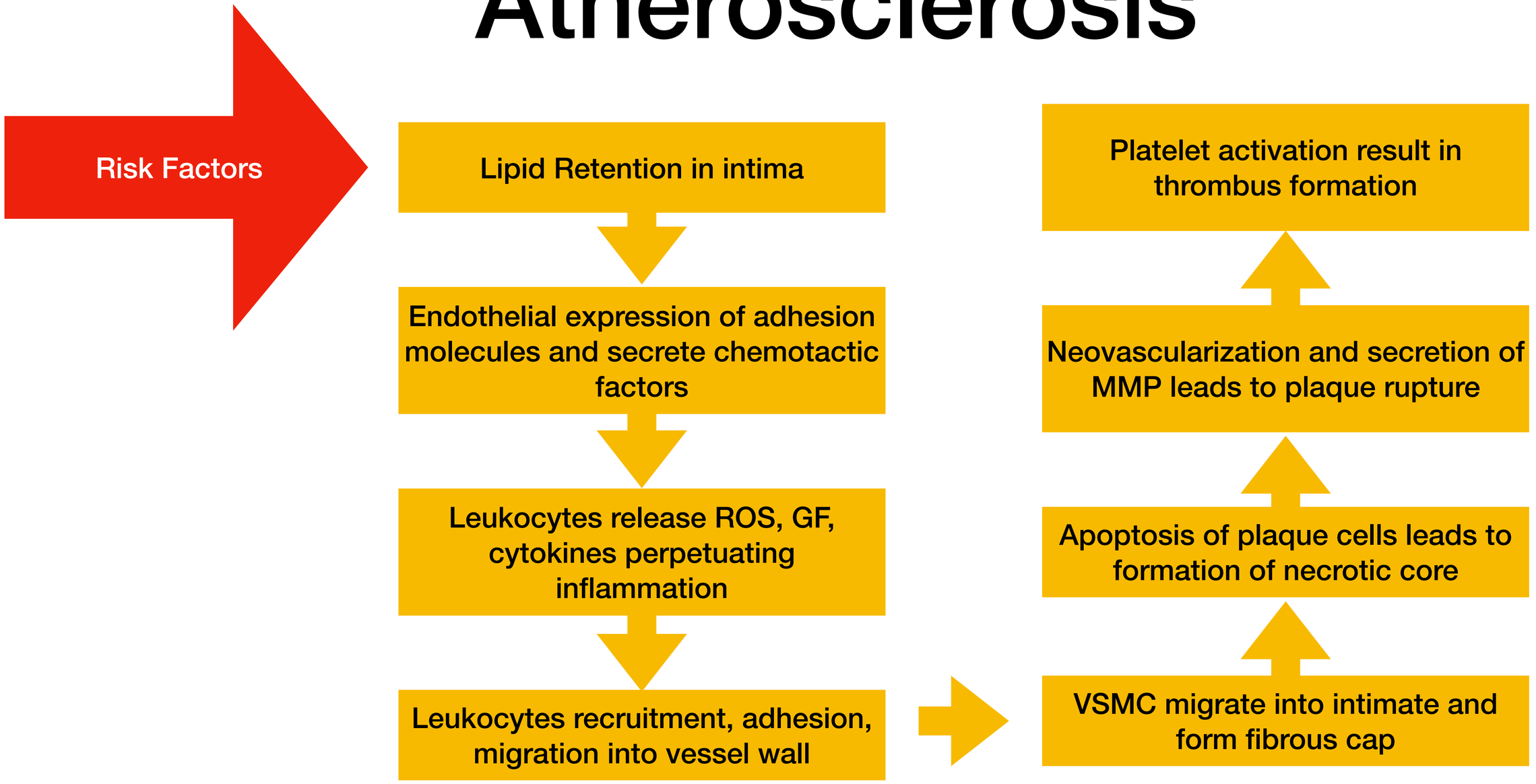


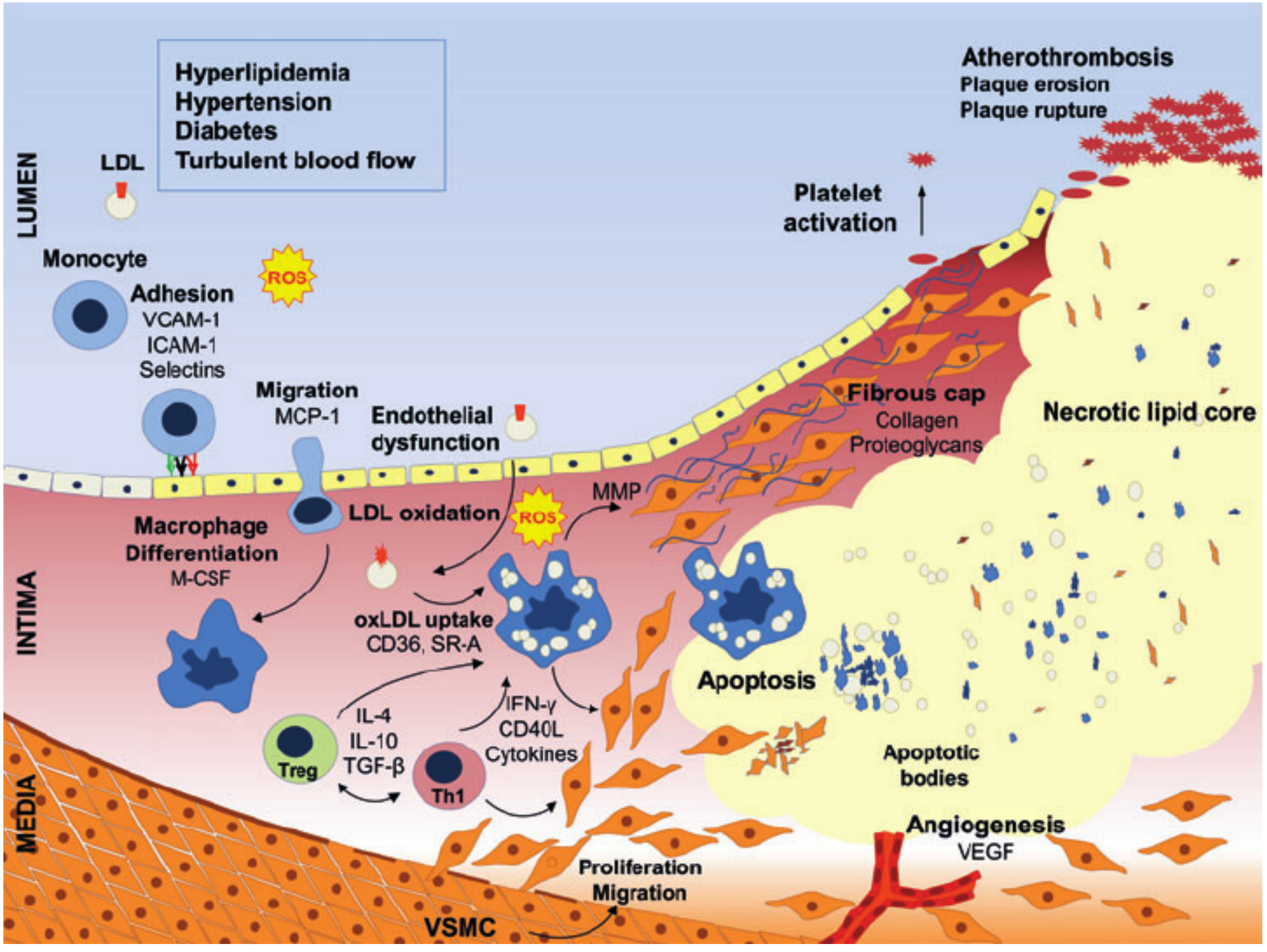
Ischemic Heart Disease

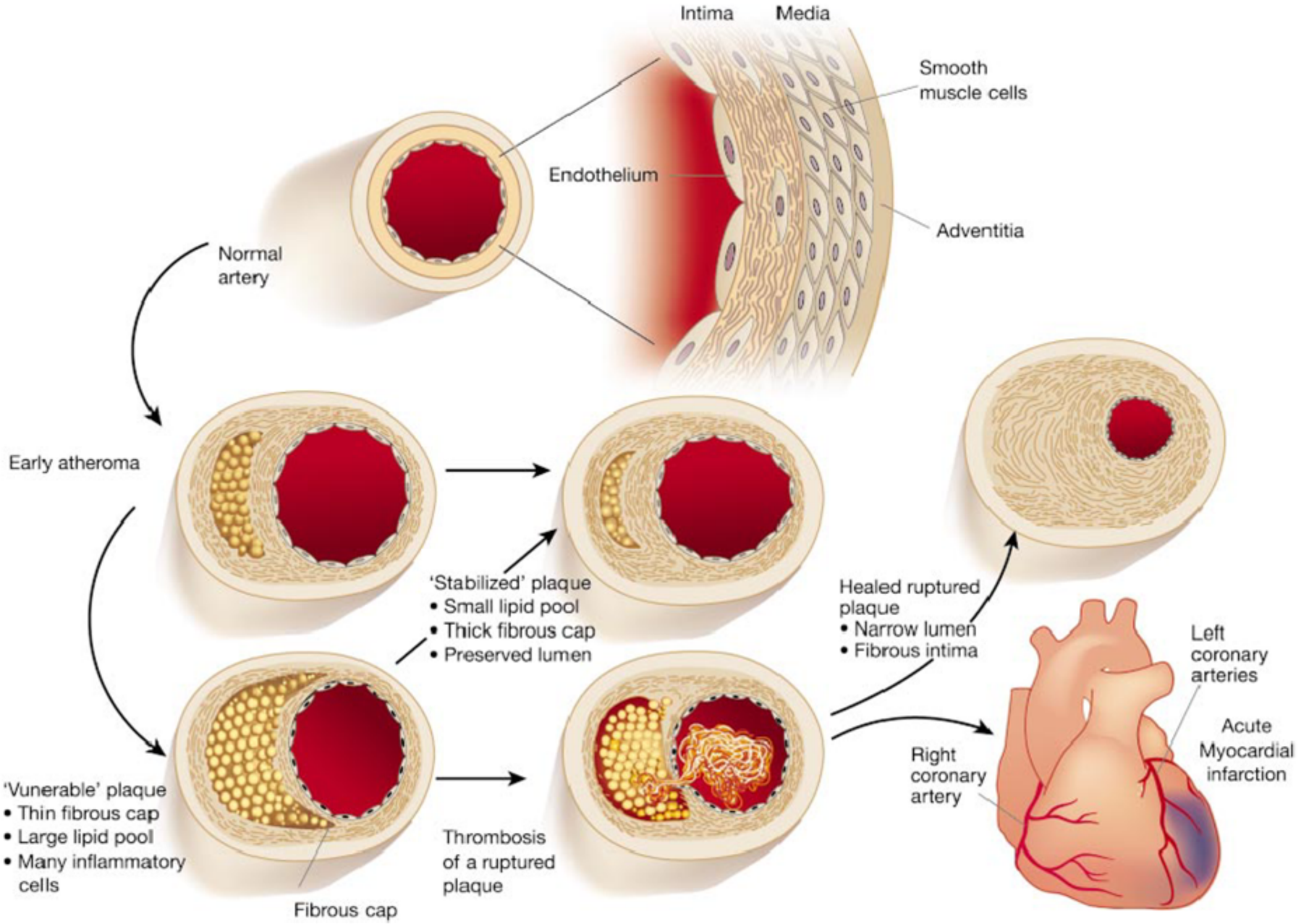
- An imbalance between cardiac blood supply and myocardial oxygen requirement -> Myocardial ischemia

- In more than 90%, IHD is a consequence of reduced coronary blood flow secondary to obstructive atherosclerotic vascular disease.

Atherosclerosis




Hyperlipidemia
Hypertension
Diabetes
Turbulent blood flow
Atherothrombosis
Plaque erosion
Plaque rupture
LUMEN
LDL
Platelet activation
Monocyte
ROS
Adhesion
VCAM-1
ICAM-1
Selectins
Migration
MCP-1
Endothelial dysfunction
Fibrous cap
Collagen
Proteoglycans
Necrotic lipid core
MMP
LDL oxidation
ROS
Macrophage Differentiation
M-CSF
INTIMA
oxLDL uptake
CD36, SR-A
Apoptosis
IL-4
IL-10
TGF-β
IFN-γ
CD40L
Cytokines
Treg
Th1
Apoptotic bodies
Angiogenesis
VEGF
MEDIA
Proliferation
Migration
VSMC



Libby P: Inflammation in Atherosclerosis. Nature 202;420:868

Angina Pectoris

- Angina Pectoris is an intermittent chest pain caused by transient, reversible myocardial ischemia

- Types of Angina Pectoris

    1. Typical or Stable angina: predictable episodic chest pain associated with exertion. The pain is described as a crushing substernal chest pain radiate to left jaw or left arm. The pain is usually relieved by rest or NTG.

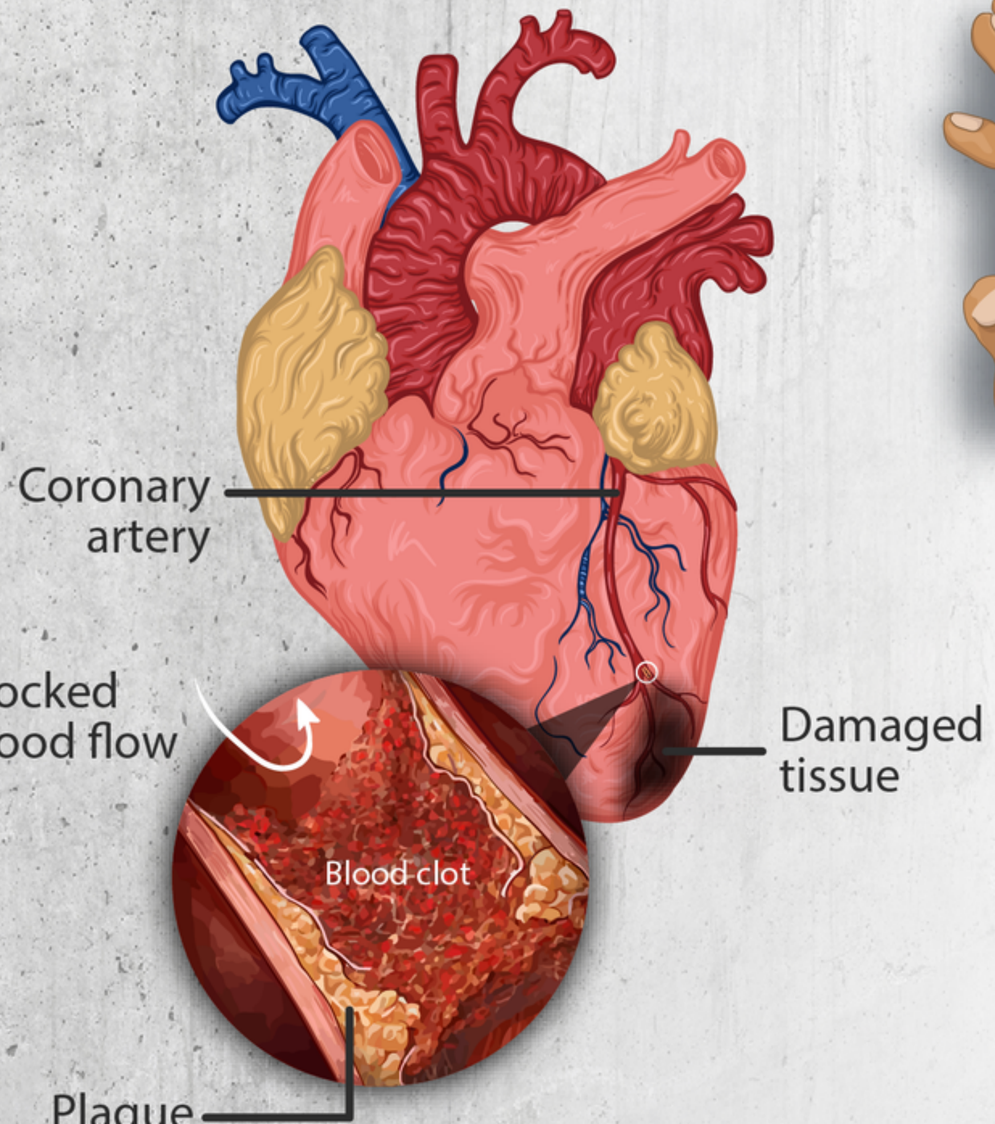
    2. Prinzmetal or variant angina: occur at rest and usually relieved by NTG.

    3. Unstable angina: frequent pain, precipitated by less exertion or at rest.

Myocardial Infarction

- Myocardial Infarction (MI) is necrosis of the heart muscle resulting from ischemia.
- Pathogenesis:
  - Majority of MI is caused by acute thrombosis within coronary arteries.
  - In 10% of MI is caused by vasospasm or embolization from AF or valve vegetations.

Myocardial Infarction
(Heart Attack)



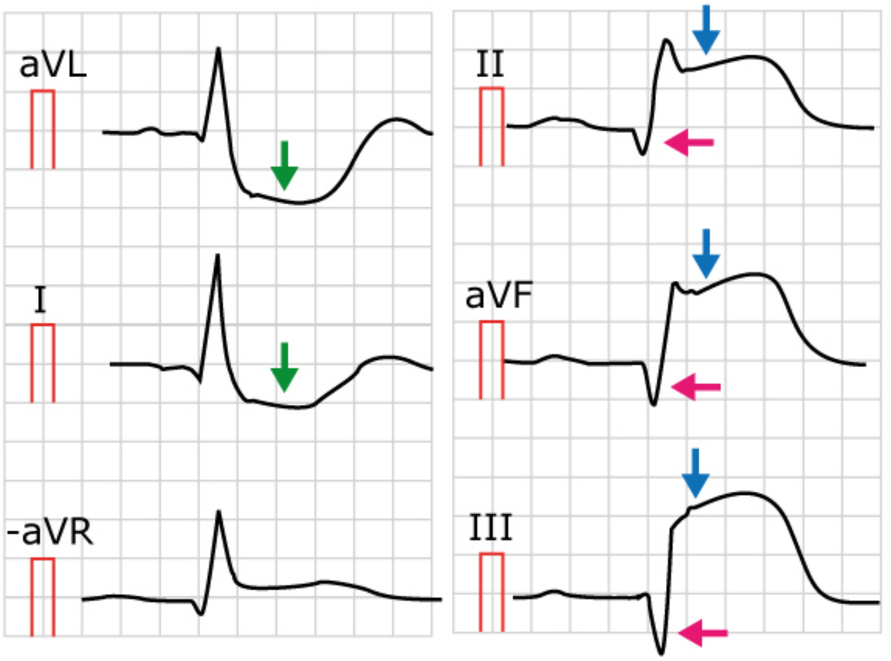
Patterns of Infarction

- Transmural Infarction:
  - Involve full thickness of the ventricle
  - ECG = ST segment elevation/ negative Q wave/ loss of R wave amplitude
- Subendocardial Infarction
  - Limited to the inner third of the myocardium
  - ECG = ST segment depression/ T wave abnormalities
- Microscopic Infarction
  - Small vessel occlusion
  - May not show any diagnostic ECG

Clinical Features

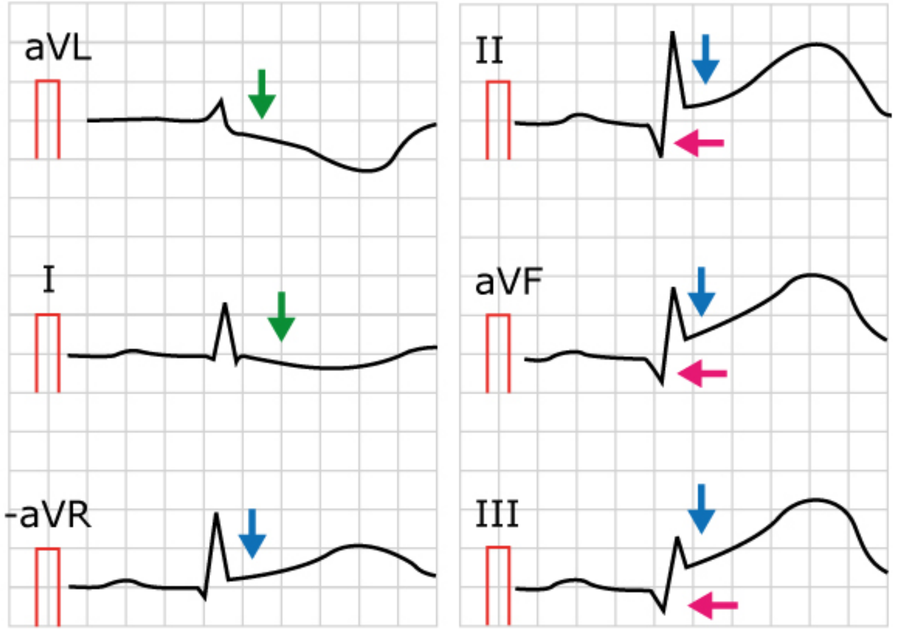
Clinical	ECG	Laboratory
Substernal chest pain radiate to the neck, jaw, epigastrium, or left arm Duration: several minutes to hours NTG: not relieve pain	STEMI: ST elevation NSTEMI: ST depression	TroponinI and TroponinT positive: detectable within 2 to 4 hrs, peaking at 48 hrs, and remaining 7 to 10 days

A Acute STE-ACS (STEMI) example 1



60 year old male with retrosternal chest pain. ECG shows ST segment elevations in inferior leads (II, aVF and III). There are reciprocal ST segment depressions in aVL and I. There are also pathological Q-waves in the inferior leads.

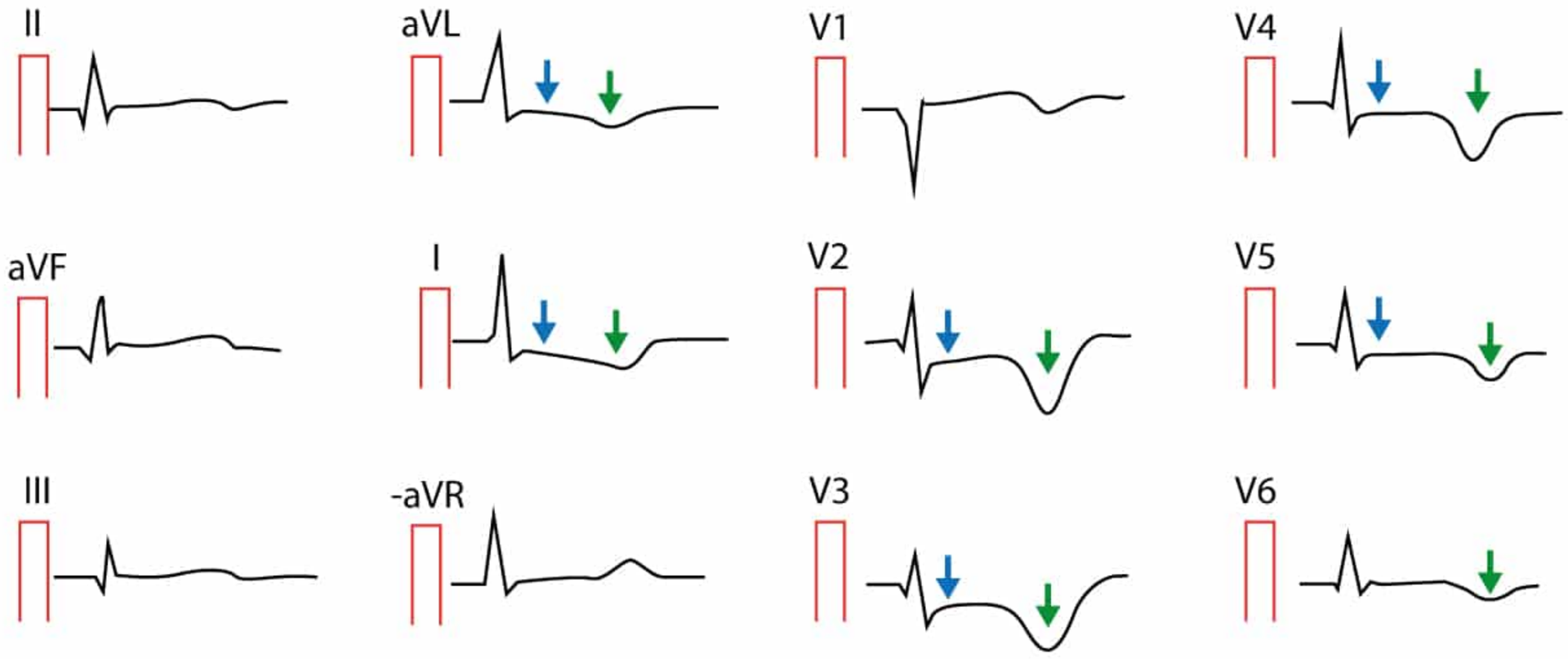
B Acute STE-ACS (STEMI) example 2

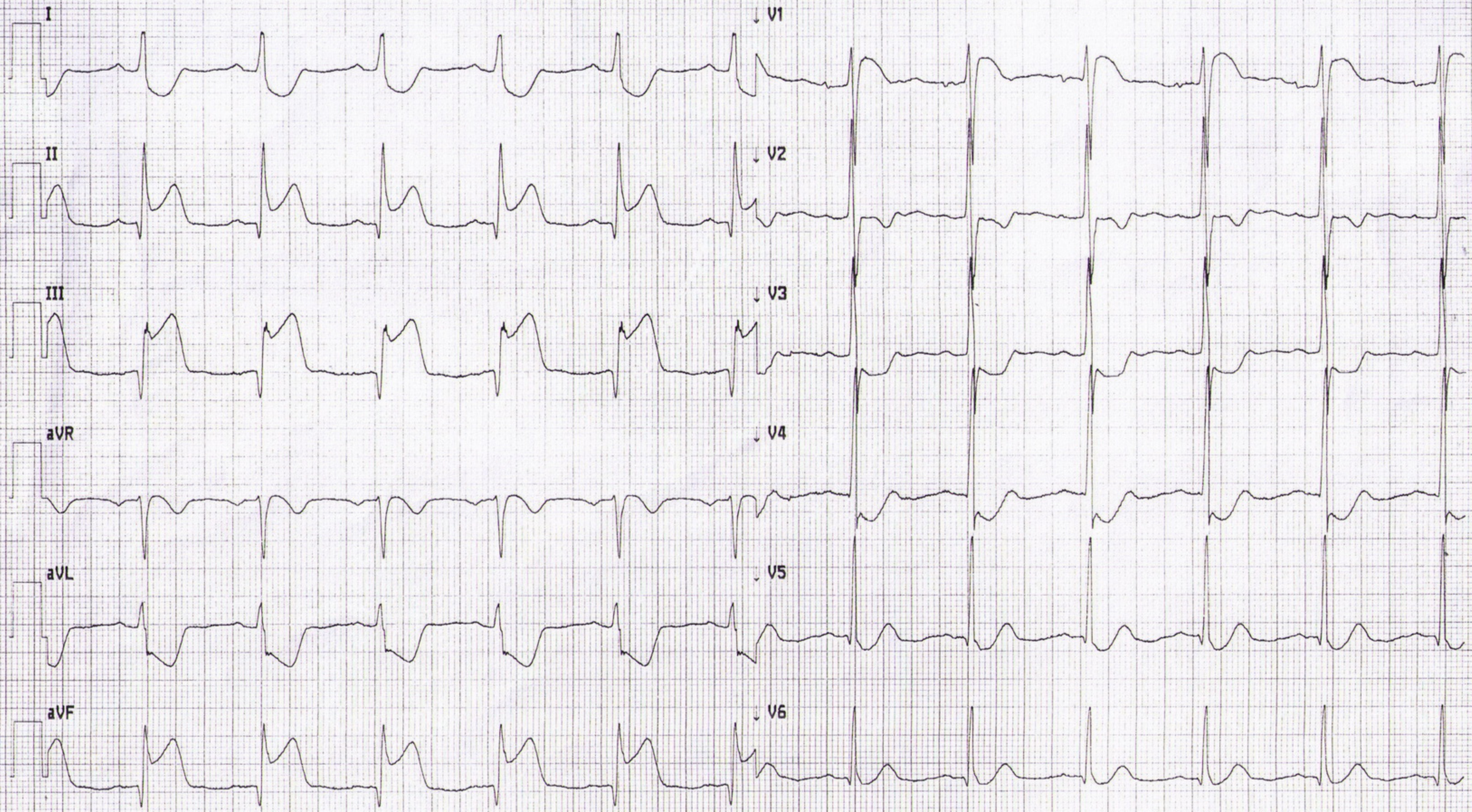


65 year old diabetic with 3 hours duration of chest pain. ECG shows ST-segment elevations, reciprocal depressions and pathological Q-waves.

- ST segment elevation
- Pathological Q-waves
- Reciprocal ST-segment depression

NSTEMI


II
aVL
V1
V4
aVF
I
V2
V5
III
-aVR
V3
V6
ST segment depression
T-wave inversions (negative T-waves)


I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6

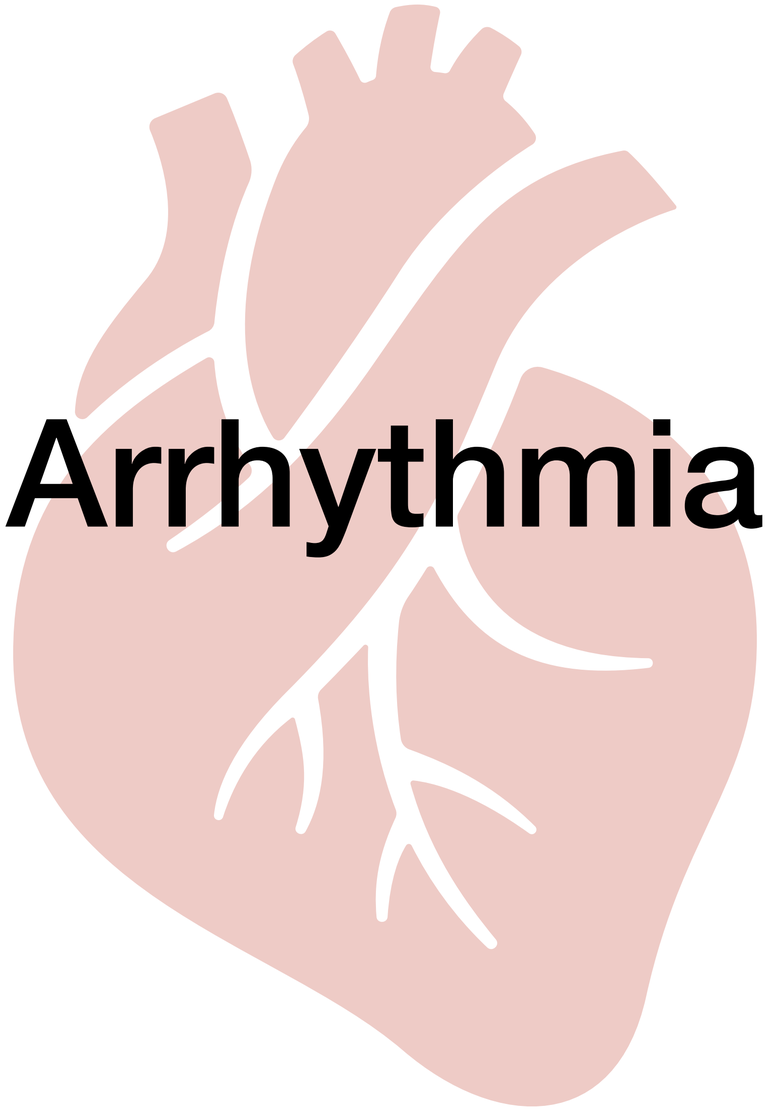
Complications

Contractile dysfunction	Pericarditis
Papillary muscle dysfunction	Chamber dilation
Right ventricular infarction	Mural thrombus
Myocardial rupture	Ventricular aneurysm
Arrhythmia	Heart failure

Chronic Ischemic Heart Disease

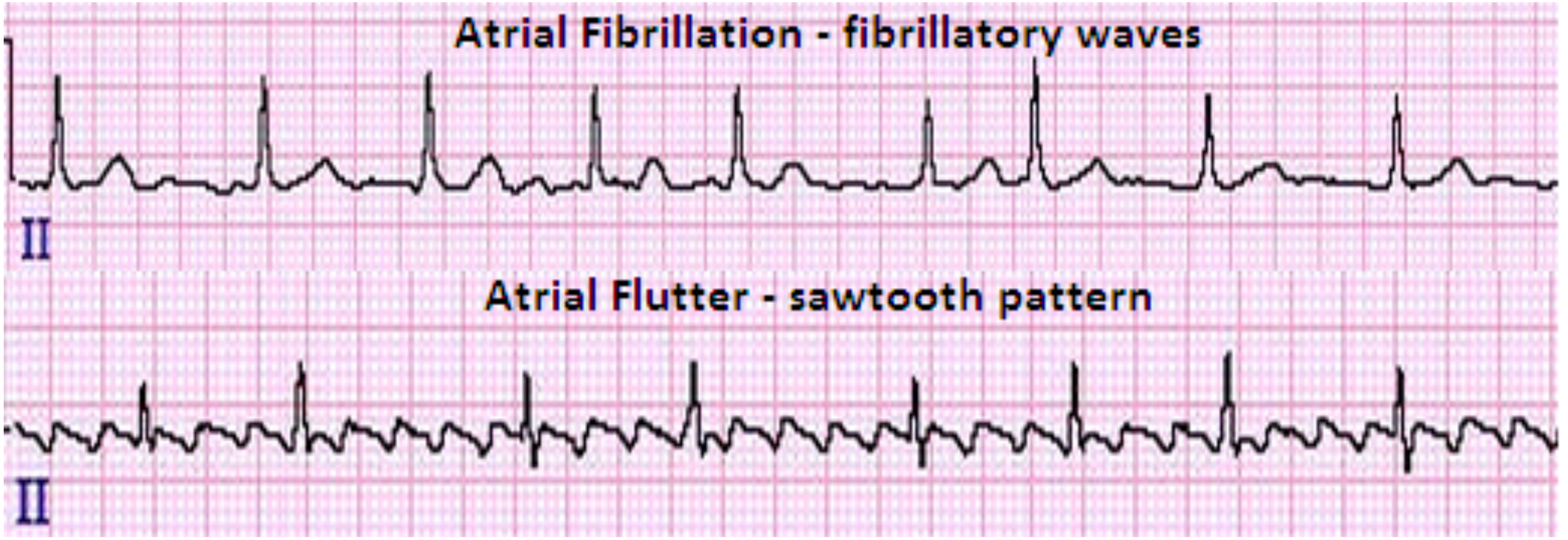
- Chronic IHD or Ischemic cardiomyopathy
- Progressive heart failure secondary to ischemic myocardial damage

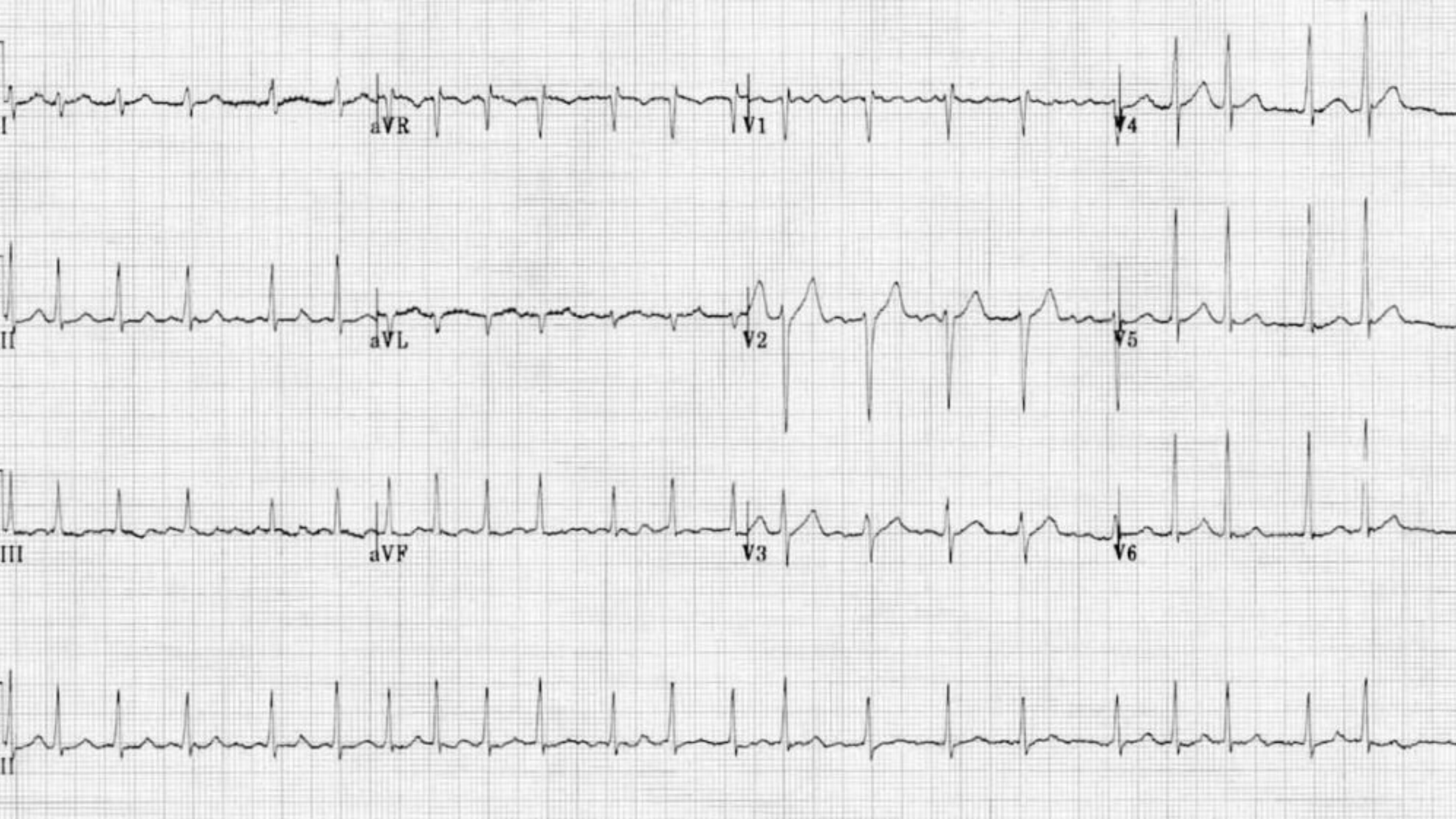
Arrhythmia



Arrhythmia

- Aberrant rhythm can be initiated anywhere in the conduction system; typically originating from the atrium (supra ventricular) or within ventricle
- Abnormalities in myocardial conduction can be sustained or sporadic (paroxysmal)
- They can manifest as
  - tachycardia,
  - bradycardia,
  - an irregular rhythm,
  - No electrical activity (asystole)


Atrial Fibrillation - fibrillatory waves
II
Atrial Flutter - sawtooth pattern
II


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

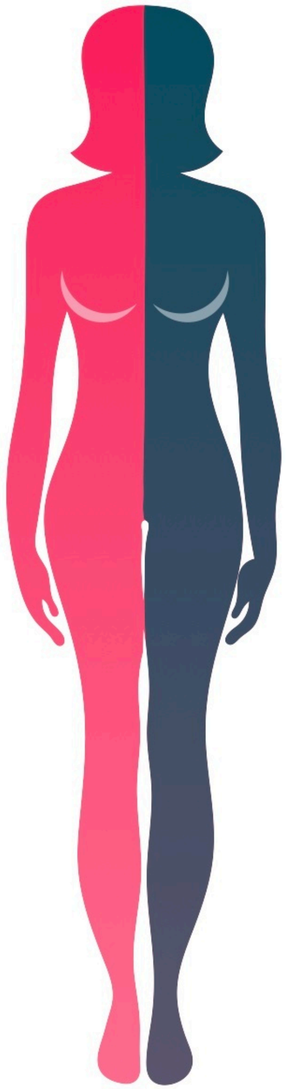
Clinical Features

- Palpitation
- Syncope
- Sudden cardiac death

SYNCOPE

PALPITATIONS
CHEST PAIN
DYSPNOEA

FREQUENTLY
ASYMPTOMATIC



ABSENT ‘A’ WAVES

TACHYCARDIA

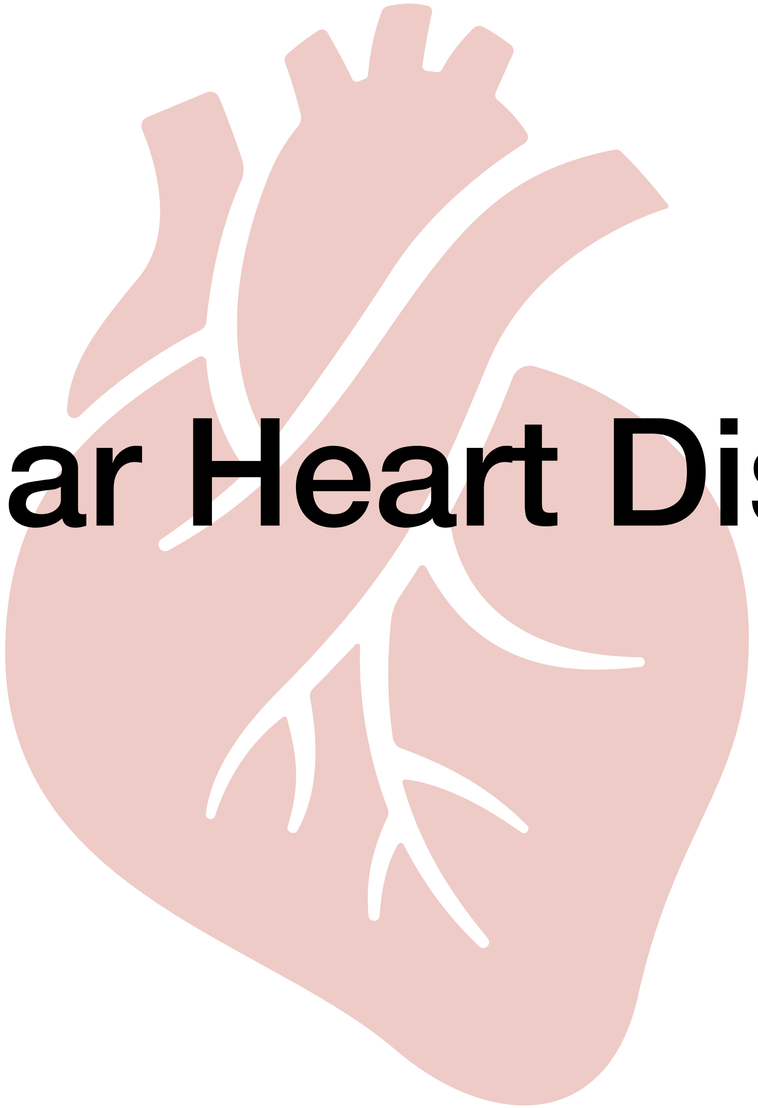
90 60 mmHg

IRREGULAR PULSE
HYPOTENSION

SYMPTOMS

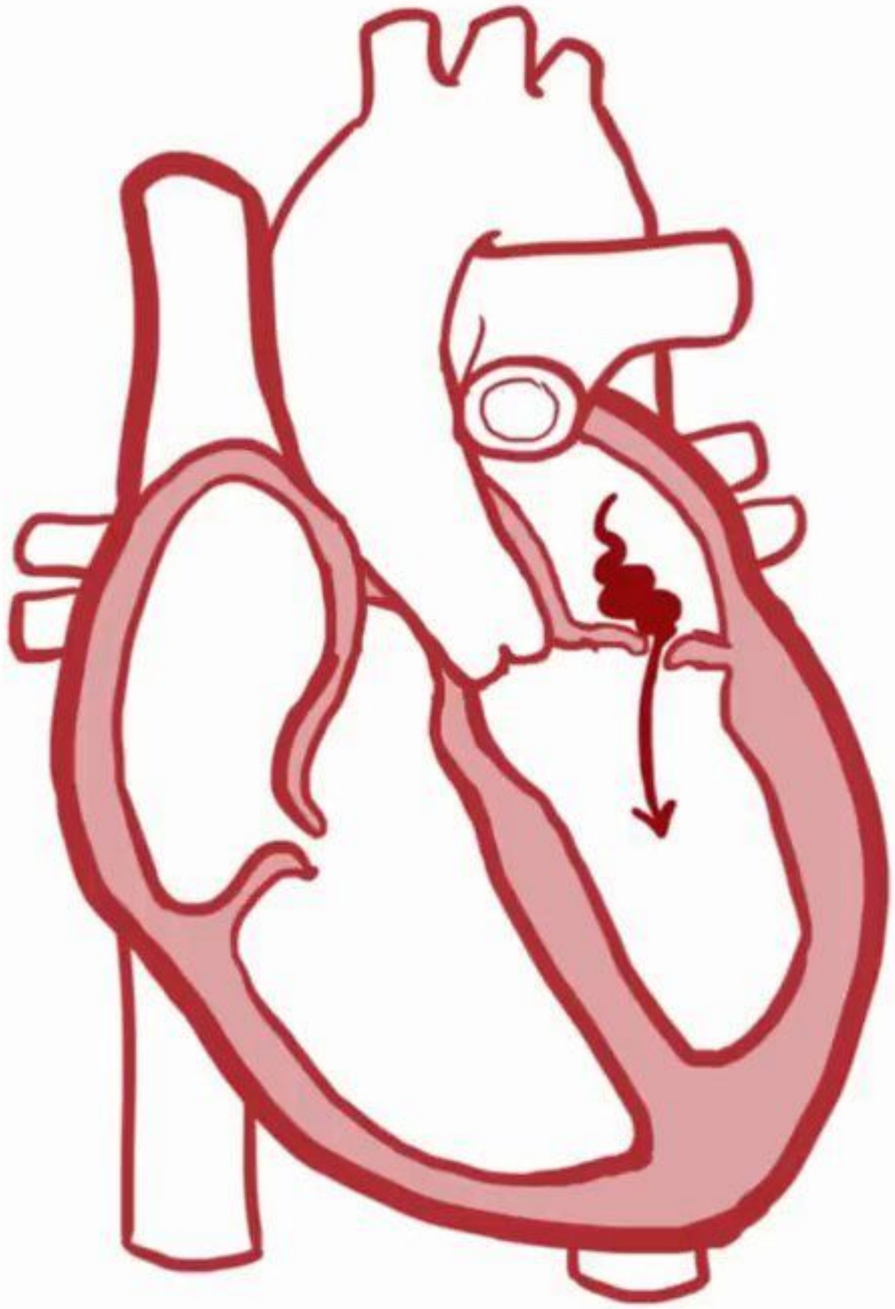
SIGNS

Valvular Heart Disease

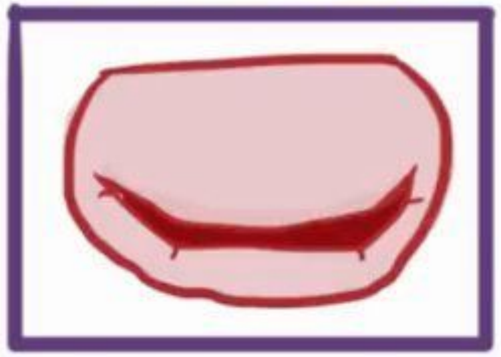


Valvular Heart Disease

Stenosis	Insufficiency
Failure of the valve to open completely -> obstructing forward flow	Failure of the valve to close completely -> regurgitation (back flow) of blood



MITRAL VALVE



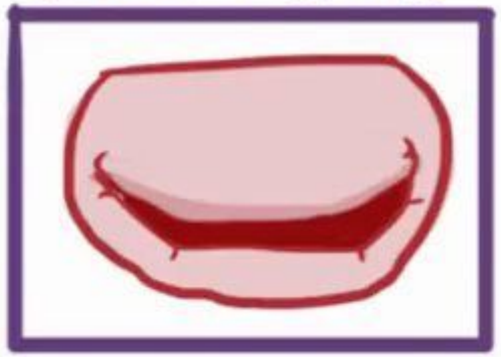
Systole ~ CLOSED

doesn't close all the way

↓

REGURGITATION

MITRAL VALVE



Diastole ~ OPEN

doesn't open all the way

↓

STENOSIS

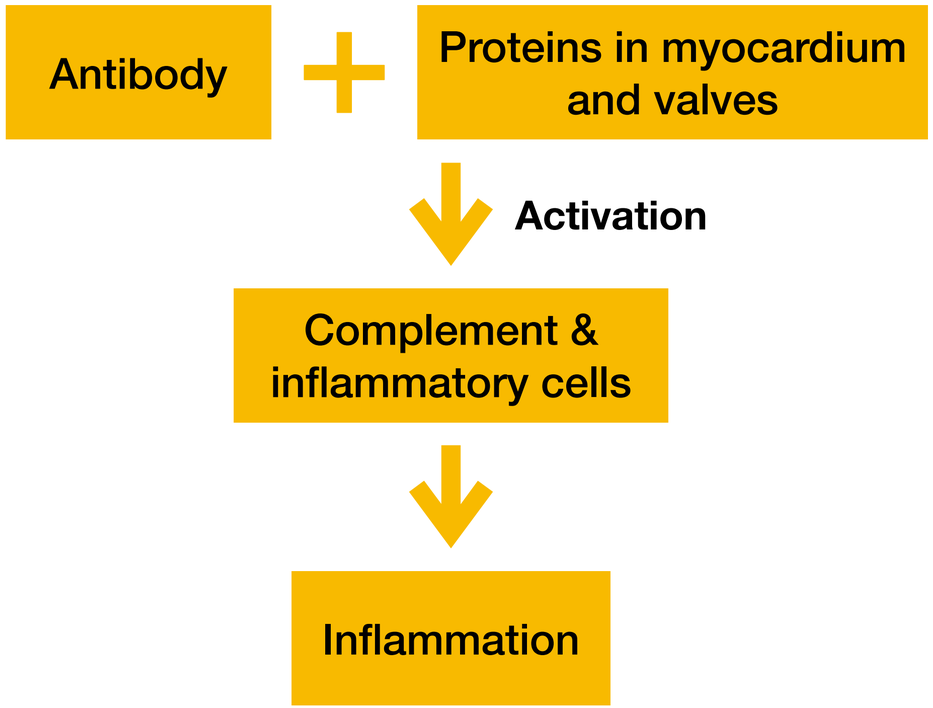
Rheumatic Valvular Disease

- Rheumatic heart disease is the cardiac manifestation of rheumatic fever.
- It is associated with inflammation of all parts of the heart, but valvular inflammation produce the most important clinical features.

Rheumatic fever is an acute, immunologically mediated, multi system inflammatory disease that occurs after group A beta-hemolytic streptococcal infections.

Pathogenesis

Acute rheumatic fever is a hypersensitivity reaction contributed to antibodies directed against group A streptococcal molecules that cross-react with host myocardial antigens



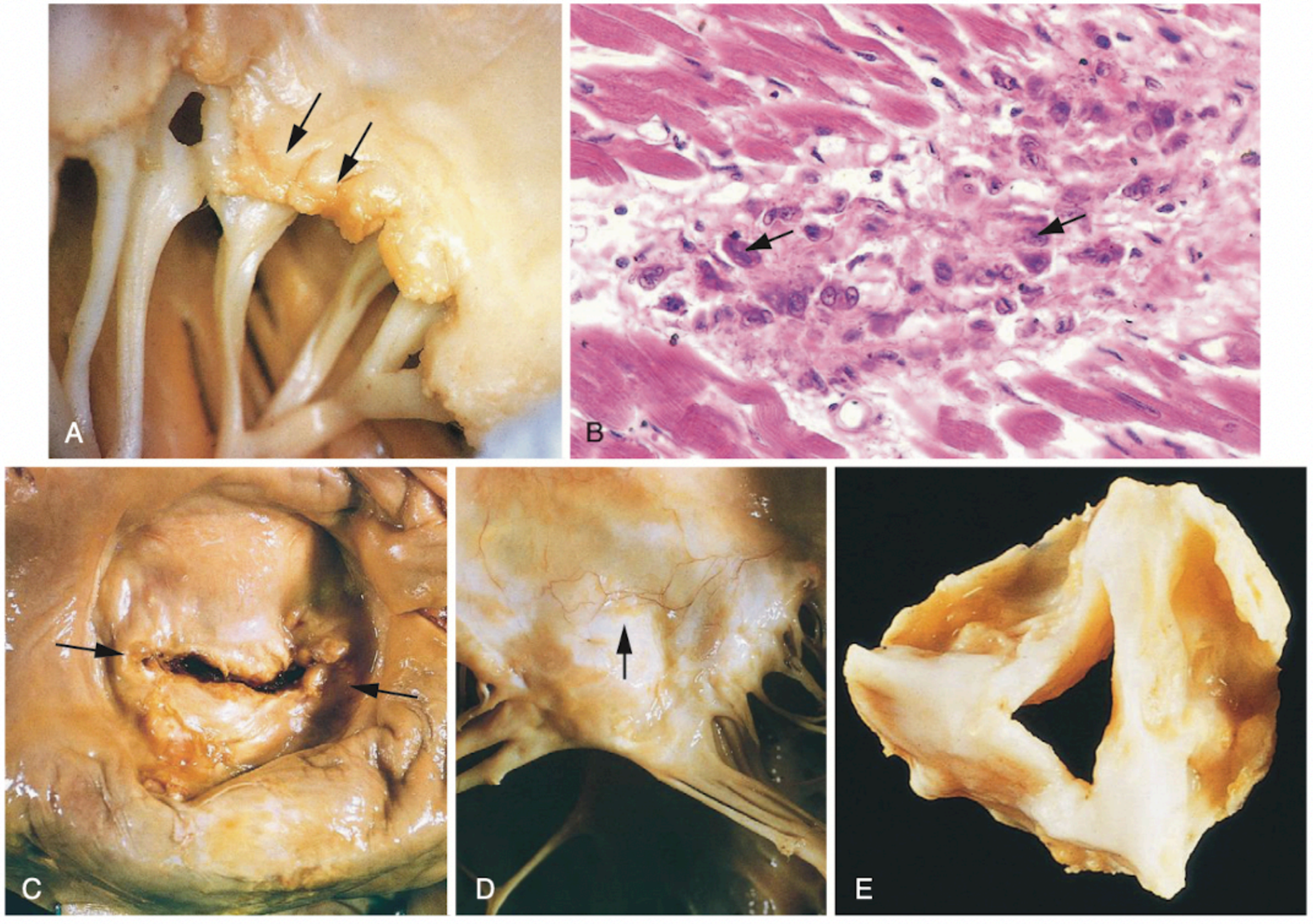


Figure 12-23 Acute and chronic rheumatic heart disease. **A,** Acute rheumatic mitral valvulitis superimposed on chronic rheumatic heart disease. Small vegetations (verrucae) are visible along the line of closure of the mitral valve leaflet *(arrows).* Previous episodes of rheumatic valvulitis have caused fibrous thickening and fusion of the chordae tendineae. **B,** Microscopic appearance of an *Aschoff body* in a patient with acute rheumatic carditis. The myocardium exhibits a circumscribed nodule of mixed mononuclear inflammatory cells with associated necrosis; within the inflammation, large activated macrophages show prominent nucleoli, as well as chromatin condensed into long, wavy ribbons (caterpillar cells; *arrows*). **C** and **D,** Mitral stenosis with diffuse fibrous thickening and distortion of the valve leaflets and commissural fusion (*arrows*, **C**), and thickening of the chordae tendineae (**D**). Note neovascularization of anterior mitral leaflet (*arrow*, **D**). **E,** Surgically resected specimen of rheumatic aortic stenosis, demonstrating thickening and distortion of the cusps with commissural fusion. (**E,** Reproduced from Schoen FJ, St. John-Sutton M: Contemporary issues in the pathology of valvular heart disease. Hum Pathol 18:568, 1967.)

Clinical Features

- Fever
- Palpitation
- Chest pain
- Dyspnea

Infective Endocarditis

- Infective Endocarditis (IE) is a microbial infection of the heart valves that leads to the formation of vegetations composed of thrombotic debris and organisms.

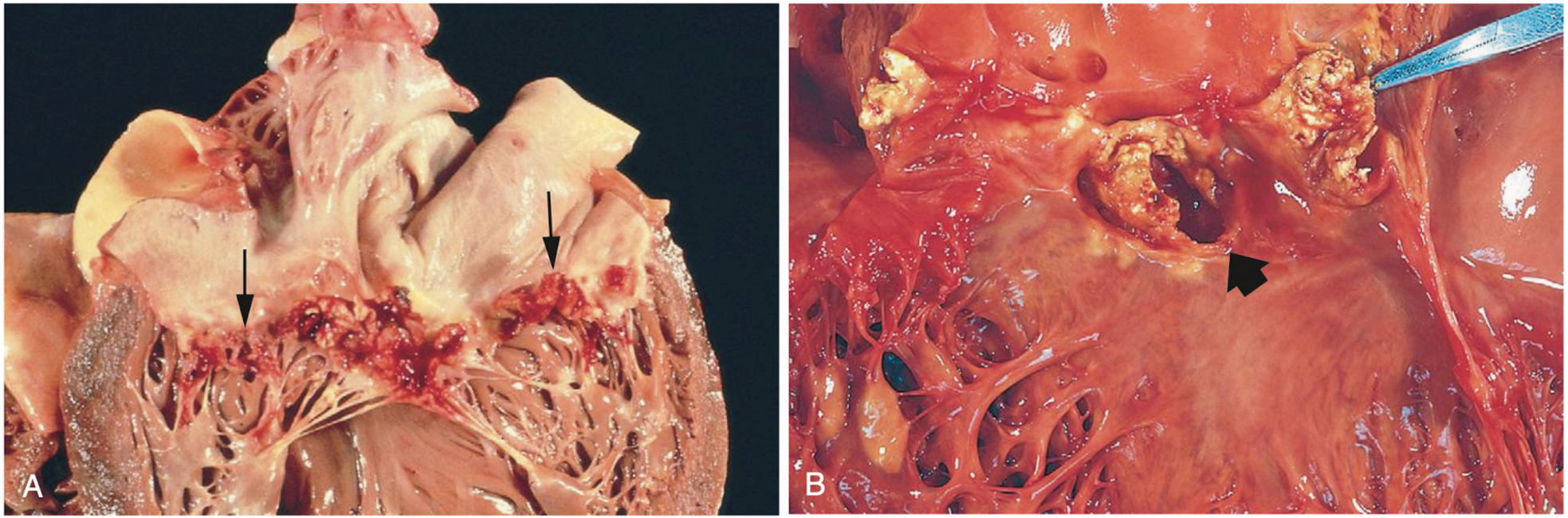


Figure 12-25 Infective (bacterial) endocarditis. **A,** Endocarditis of mitral valve (subacute, caused by *Streptococcus viridans*). The large, friable vegetations are denoted by *arrows.* **B,** Acute endocarditis of congenitally bicuspid aortic valve (caused by *Staphylococcus aureus)* with extensive cuspal destruction and ring abscess *(arrow).*

Pathogenesis

Predisposing Factors

Infections
Mitral valve prolapse
Bicuspid aortic valve
Calcific valvular stenosis
Prosthetic heart valve

Endocardial damage by turbulence flow

Bacterial seeding

Causative organisms
S.viridans
S.aureus
HACEK gr

Clinical Features

- History
  - Fever with chills
  - Weakness
- Physical examination
  - Murmur
  - Nail bed (Splinter) hemorrhage
  - Retinal hemorrhage (Roth spots)
  - Painless palm and sole erythematous lesions (Janeway lesion)
  - Painful fingertip nodules (Osler nodes)

Diagnosis
positive blood cultures and echocardiographic findings

Table 14-2a Modified Duke Criteria for the Diagnosis of Infective Endocarditis

Major Criteria

I. Positive blood cultures for IE

1. Two separate blood cultures with viridans streptococci, *Streptococcus bovis*, *Staphylococcus aureus*, HACEK group, or community-acquired enterococci (no primary focus)
2. Persistently positive blood cultures drawn more than 12 hours apart **OR** all of three or a majority of four separate blood cultures, drawn 1 hour apart
3. Single positive blood culture for *Coxiella burnetii*

II. Evidence of endocardial involvement

1. Positive echocardiogram for IE
2. Oscillating intracardiac mass on a valve or supporting structure, in the path of regurgitant jets, or on implanted materials in the absence of another anatomic explanation
3. Abscess
4. New partial dehiscence of a prosthetic valve
5. New valvular regurgitation (change in preexisting murmur not sufficient)

Minor Criteria

1. Predisposing heart condition or intravenous drug use
2. Fever ≥38°C (100.4°F)
3. Vascular phenomena: Arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, Janeway lesions
4. Immunologic phenomena: Glomerulonephritis, Osler's nodes, Roth spots, rheumatoid factor
5. Microbiologic evidence: Positive blood culture but not meeting major criteria or serologic evidence of infection with an organism consistent with IE

HACEK, *Haemophilus, Actinobacillus*, *Cardiobacterium*, *Eikenella*, *Kingella*; IE, infective endocarditis.

Table 14-2b Classification of Infective Endocarditis by Modified Duke Criteria

Definite IE

Pathologic Criteria:

Vegetation or intracardiac abscess confirmed by histology showing active endocarditis **AND** an associated microorganism demonstrated by culture or histology

Clinical Criteria:

2 major criteria **OR**
1 major and 3 minor criteria **OR**
5 minor criteria

Possible IE

1 major and 1 minor criteria **OR**
3 minor criteria

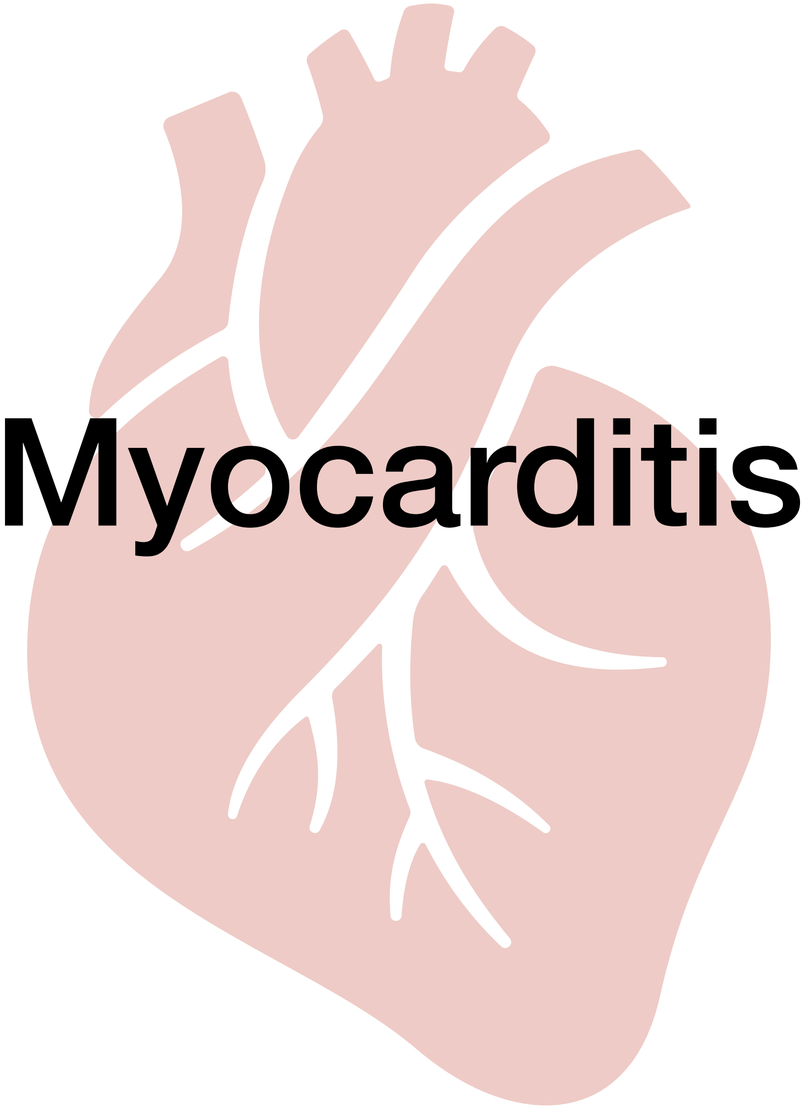
Rejected IE

Firm alternative diagnosis **OR**
Resolution of manifestations with therapy for ≤4 days **OR**
No pathologic evidence at surgery or autopsy after antibiotic therapy ≤4 days

IE, infective endocarditis.

Adapted from Li JS, Sexton DJ, Mick N, et al. Proposed Modifications to the Duke Criteria for the Diagnosis of Infective Endocarditis. *Clin Infect Dis* 2000;30:633–638.

Myocarditis



Myocarditis

- Myocarditis encompasses a group of clinical entries in which infectious agents and/or inflammatory process target the myocardium.

Causes of myocarditis

Infection	Viral	- Coxsackievirus A and B - Cytomegalovirus (CMV) - Human immunodeficiency virus (HIV) - Influenza virus
	Nonverbal	- Trypanosome cruzi - Toxoplasma gondii - Borrelia burgdorferi
Noninfection	- Systemic lupus erythematosus - Polymyositis - Hypersensitivity myocarditis	

Clinical Features

- Asymptomatic
- Heart failure
- Arrhythmia
- Sudden death

Thank You