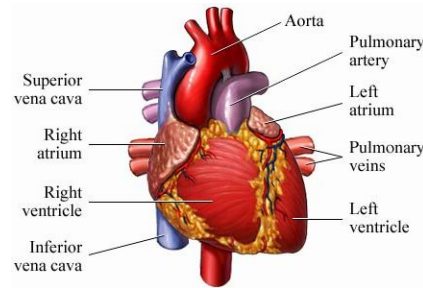


Cardiovascular System



Valvular Heart Diseases

له امراض ال Valvular heart يمكن يكون :-

- Congenital
- Obstruction (stenosis)
له تضيق الشرايين مثل Fibrosis
- Regurgitation (incompetence)
له الصمام من تآكل بـ backflow

- Prolapse

له تآكل الصمام من collagen خصله مضطرب وعرضه واحد، وبالتالي الدم يتحرك من خلاله بكل سهولة

- Calcification

له تصلب الشرايين (old age)

- Infection

له بكتيريا أو Fungal

Lecture I: Valvular heart diseases & Endocarditis

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2

MAJOR CAUSES OF ACQUIRED HEART VALVE DISEASE

Mitral Valve Disease

Stenosis ① acquired
Regurgitation ②

Mitral Stenosis: obstruction, closure of the cardiac valve (واحد من الأجزاء) →

★★ Postinflammatory scarring (rheumatic heart disease)

التهاب شرايين (مرض الالتهابي)
Regurgitation أو Stenosis

Mitral Regurgitation:

تساقط

Abnormalities of leaflets and commissures:

- ★ Postinflammatory scarring
- ★ Infective endocarditis
- ★ Mitral valve prolapse
→ cardiac dilatation severe anemia

Abnormalities of tensor apparatus:

- Rupture of papillary muscle
- Papillary muscle dysfunction (fibrosis)
- Rupture of chordae tendineae

Abnormalities of left ventricular cavity and/or annulus:

- ★ Left ventricular enlargement

3

MAJOR CAUSES OF ACQUIRED HEART VALVE DISEASE

Aortic Valve Disease

Aortic Stenosis:

- ★ Postinflammatory scarring (rheumatic heart disease)
- ★ Senile calcific aortic stenosis
- Calcification of congenitally deformed valve

Aortic Regurgitation:

تساقط

Intrinsic valvular disease

- ★ Postinflammatory scarring (rheumatic heart disease)
- ★ Infective endocarditis (Sub acute)

Aortic disease

- Degenerative aortic dilation
- Syphilitic aortitis
- Ankylosing spondylitis
- Rheumatoid arthritis
- ★ Marfan syndrome

4

Rheumatic Fever and Heart Disease

- Definition:** acute, immunologically mediated, multi-system inflammatory disease that follows an episode of group **A streptococcal pharyngitis** after an interval of a few weeks.

- Rarely follows infection by streptococci at other sites
- Incidence has declined in recent years
- Rheumatic fever cause two types of disease:**

1. **Acute RF:** manifest as acute rheumatic carditis

↳ days or weeks
↳ neutrophils

2. **Chronic RF:** manifest as valvular deformities

↳ more than 1 week
↳ types from macrophages & lymphocyte.

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Rheumatic Fever: Diagnosis

- Modified Jones' Major criteria:**

1. **Pancarditis:** pericardial friction rub, weak heart sounds

because of pericardial effusion, tachycardia, & arrhythmias

2. **Polyarthritis:** migratory, large joints, non deforming = Without ankylosis

3. **Sydenham's chorea** ⇒ involuntary jerky movement

4. **Erythema marginatum:** maculopapular rash

5. **Subcutaneous nodules**

Rheumatic Fever

- Pathogenesis:** a hypersensitivity that is induced by group A streptococci. The **antibodies** that are formed as a reaction to the M protein of streptococci cross react with the **normal** protein present in the cardiac valves, joints, and other tissue
- Peak incidence** between **5-15 years**

- Diagnosis of rheumatic fever based on Jones' criteria:**

- Two major Jones' criteria, or
- One major, and two minor Jones' criteria

2 major OR 1 major + 2 minor together

6

Rheumatic Fever: Diagnosis

- Minor clinical:**

• Previous history of RHD/RF

• Arthralgia

• Fever

- Minor Laboratory:**

• **Acute phase reactions**

– High ESR (erythrocyte rate)

– Increased C reactive protein

– Leukocytosis

• **Prolonged PR interval** on ECG

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Rheumatic Fever: Diagnosis

Streptococcal infection • There should also be supporting evidence of preceding

There should also be supporting evidence of preceding streptococcal infection:

1. Positive throat culture

2. Increased titer of antibodies to one or more streptococcal enzymes:
 DNAase B و Streptolysin o لے متحر

- Streptolysin O
- DNase B

- These are present in the sera of most patients.
- There are reliable assays such as streptozyme test for the detection of these antibodies

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Rheumatic Fever: Morphology

1. **Acute rheumatic fever:** inflammation, but not in valve.

- occurs anywhere from 10 days to 6 weeks after an episode of pharyngitis caused by group A streptococci.
- The peak incidence** is between the ages of 5 and 15
- Inflammatory infiltrate** occur in wide range of sites: skin, synovium, joints, and heart
- Initial tissue reaction is **fibrinoid necrosis** → dehydration in collagen

2. Chronic rheumatic heart disease

- characterized by **irreversible deformity** of one or more cardiac valves, resulting from previous episodes of acute valvulitis

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Rheumatic Fever: Morphology

Acute rheumatic carditis:

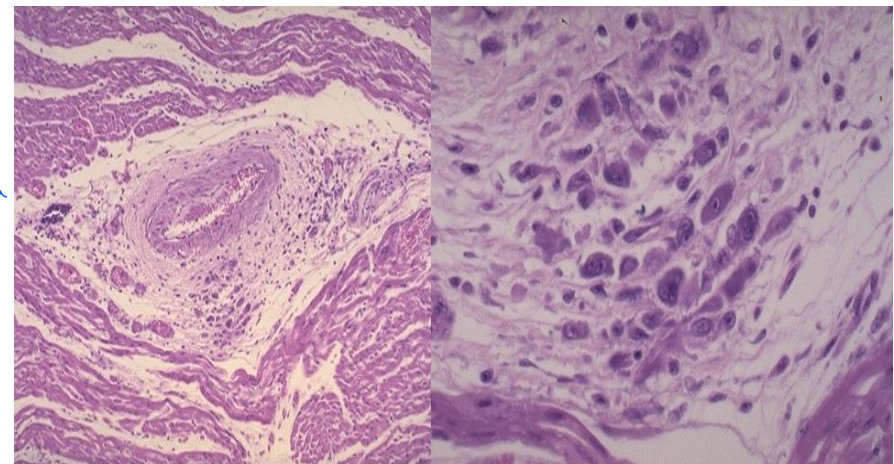
- characterized by the presence of **Aschoff bodies**: *specific type of granuloma in acute R.F*
 - multiple foci of inflammation within the connective tissues *around for ailed Blood vessels* of the heart
 - central fibrinoid necrosis surrounded by a chronic mononuclear inflammatory infiltrate & large macrophages with vesicular nuclei and abundant basophilic cytoplasm.

↓
نوع الـ macrophage الموجودة

called **Anitschkow cells**.

لما أنه يكون ذا خُرَادي أُرْكانًا مع بعضهم البعض مَجْمُوعَات
giant cells

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Acute rheumatic carditis is marked by granulomatous inflammation called **Aschoff nodules** centered in the interstitium around blood vessels

(macrophage) antischow ϕ , cells $\rightarrow$ cells
cells
die new inflammation $\rightarrow$ "عادة" around for B.V $\rightarrow$ ϕ
Fibroid necrosis $\rightarrow$ B.V wall $\rightarrow$ necrosis $\rightarrow$ necrosis

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RF: Chronic rheumatic heart disease

Mitral stenosis:

- more common in **females** than males
- narrowed to a slit like opening called **fish mouth** deformity (scarring) يشبه السمكة
- mural thrombi may occur in the dilated and hypertrophied left atrium giving rise to systemic emboli → حبيبات الدم في الأترية الأمامية يتصلب في دوائها Systemic emboli وهذه الدم نقل
- lungs are heavy & firm due to **chronic passive congestion** of the lung.
- in long standing cases the right ventricle and atrium are dilated and hypertrophied



The mitral valve as seen from above in the left atrium. The MV demonstrates the **fish-mouth** deformity seen as an end result to scarring in chronic rheumatic heart disease

Mitral regurgitation:

- the leaflets are retracted → impaired in closing.

causes LV dilation and hypertrophy

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RF: Chronic rheumatic heart disease

Clinical Features:

- usually does not cause clinical manifestations for years or even decades after the initial episode of rheumatic fever. (rheumatic fever) Group-A streptococcus
- depend on which cardiac valve or valves are involved:
 - cardiac murmurs** → abnormal heart sound other than S1, S2 (Signs)
 - S1: Sound closer mitral & tricuspid valve
 - S2: Sound closer aortic valve
 - S3: Physiological aortic valve close before pulmonary.
 - cardiac hypertrophy and dilation**
 - congestive heart failure** (regurgitation & stenosis mainly stenosis)
 - arrhythmias (e.g. atrial fibrillation in mitral stenosis)** → ball arrhythmia ⇒ Blood stay in Lt. atrium
 - thromboembolic complications** → المنعرج بغيره (التهاق Systematic)
 - infective endocarditis**

- Treatment:** surgical replacement of diseased valves

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→ chronic heart disease → irreversible in one or more heart valves

Aortic stenosis:

- more often in **males** than in females
- the valve cusps are thickened, firm, and adherent to each other
- the resultant aortic orifice is **reduced to a rigid triangular channel**
- causes dilation and concentric hypertrophy of LV

Aortic regurgitation:

- fibrosis, scarring and retraction of the valve leaflets (normal) لا يتحرك
- LV hypertrophy and dilation.

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متردية
في تانيه
دنيا مع على
الرسمه

causes LV dilation and hypertrophy
mitral stenosis
aortic stenosis
regurgitation
L.V. ventricle

Calcific Aortic Stenosis

acquired disease →
normal valve or in congenital abnormality aortic valve.

- Also called degenerative calcific aortic stenosis
- Degenerative changes of the aging process
- Sclerosis and calcification** are the most common causes of aortic stenosis
- May occur in a congenitally bicuspid (2%) or unicuspid aortic valve, or it may develop in normal valve
- Valve sclerosis occurs most frequently in the aortic and mitral valves
- Calcification of the mitral valve typically involves the valve annulus and is usually asymptomatic → not effect on value function
a sympt for many years

Calcific Aortic Stenosis: Clinical features:

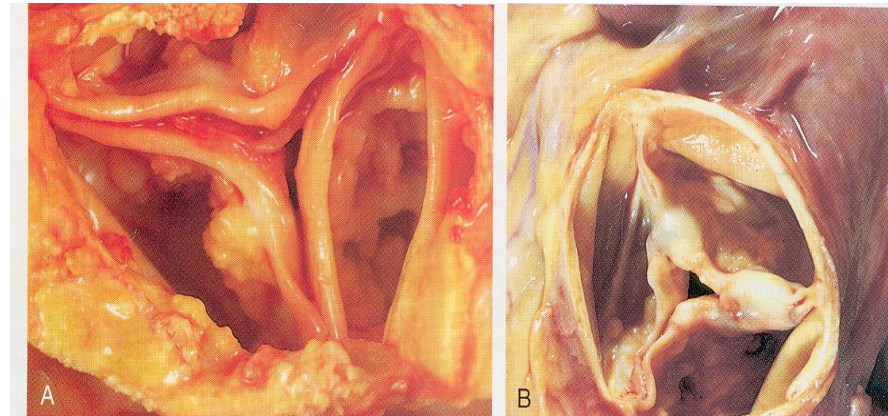
- Stenosis arising in a previously normal valve is usually asymptomatic until the eighth or ninth decade
- Stenosis arising in a congenitally bicuspid (2%) or unicuspid aortic valve clinically manifested 10 to 20 years earlier
- Cardinal clinical manifestation:**
 - Angina pectoris** → in ischemic heart disease.
 - Syncope** → not pumping normal amount Blood → ↓ Blood in Brain → (loss conscious).
 - CHF** (congestive heart failure) → close in aortic valve → not normal cardiac output → not normal perfusion in tissue
 - harsh crescendo-decrescendo systolic murmur**
 - LVH** left ventricular hypertrophy.
- Untreated stenosis will cause death in 3-4 years of onset of symptoms either due to arrhythmia or from CHF
- Treatment:** surgical valve replacement

⊗ abnormal sound → systole or diastole

⊗ loudness → mitral regurgitation & aortic stenosis

MORPHOLOGY

Calcium deposits lie behind the valve cusps



- A) Degenerative calcific aortic stenosis, leaflets are not fused
- B) Fused valves and commissures in rheumatic aortic valvulitis
↓
diseased value → effusion in reflex → symptomatic stenosis

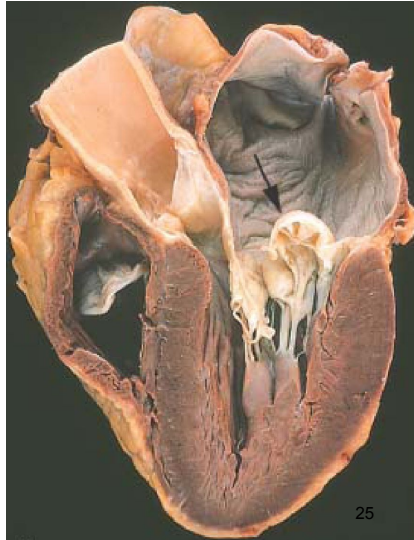
Mitral Valve Prolapse

- The most common cause of isolated mitral regurgitation
- Occurs in 3-5% of population
- Most cases are discovered between 20-40 yrs
- More common in women → من مرضات السيد
- The mitral valve is floppy and incompetent during systole
- complication of marfan syndrome

diastolic murmur ← regurgitation ← left atrium → mitral valve projection ← mitral stenosis or aortic regurgitation

Mitral Valve Prolapse: Morphology

- The cusps, particularly the posterior cusp is soft, large causing **ballooning** of the valve leaflet into the left atrium during systole
- The **chordae tendineae** which are **elongated** and fragile may rupture
- The mitral **annulus** may be **dilated**



ballooning weak & elongation ← chordae tendineae
 chordae contraction during Lt. atrium in the valve tendineae
 → rupture

Prosthetic cardiac valves

Complications for both types:

- Thrombosis**, occur in **bioprosthetic**, but less common compared to **mechanical valves**
- Infective Endocarditis**: occur in all types of the **bioprosthetic valves**, but in the mechanical valves it involves the **suture line** and adjacent **perivalvular tissue**, this may result in perforation of the leaflets and valvular regurgitation

collagen between RBCs
 metallic substance in the prosthetic valve
 → hemolysis
 because of the shearing effect of the
 mechanical valve on erythrocytes
 → RBCs lysis
 → hemolysis

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Prosthetic cardiac valves

There are two types:

1. Bioprosthetic valves:

- Glutaraldehyde fixed **porcine** or **bovine** tissue
- Cryopreserved **human** valves

2. Mechanical valves: are synthetic valves

Complication confined to the bioprosthetic valves:

- Undergo stiffening
- stenosis
- Calcification
- valvular insufficiency due to tearing or perforation

regurgitation

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Endocarditis

Types of Endocarditis:

- Infective Endocarditis (IE)
- Nonbacterial thrombotic endocarditis (NBTE)** → no infection
- Libman-Sacks Endocarditis (specific type).

usually

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Infective Endocarditis ⇒ cause microorganism

- **Definition:** infection of the cardiac valves or the mural surface of the endocardium with formation of vegetations.

• Classifications:

1. **Acute endocarditis:** infection of the valves by **highly virulent organisms** (e.g. staphylococcus aureus).
 ↳ normal valve, virulent organism → عند السطح القلبي
 ↳ Value له

- infects structurally **normal valve**
- causes **rapidly progressive** infection with little local host reaction

2. **Subacute endocarditis:** infection with **low virulent** organisms (e.g. alpha hemolytic streptococci)

- Infects previously **abnormal valves** ⇒ Rheumatic fever, prolapse, infective
 ↳ التهاب قلبية، حمى، تضيق، عدوى
- **Progresses slowly** and with the development of local inflammatory reaction and granulation tissue

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IE: Causative organisms

1. Native valve endocarditis: ↳ = original الأصلي

- **Alpha hemolytic streptococci:** streptococcus viridans
 ↳ abnormal valve ينتج له
 accounts for 50-60% of cases
- **Staphylococcus aureus:** in 20% of cases
 ↳ normal valve ينتج له
- **Enterococci and the HACEK group** (hemophilus, Actinobacillus, Cardiobacterium, Eikenella, and Kingella) **in the oral cavity** are responsible for the rest of cases

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Infective Endocarditis (IE)

Conditions that increase the risk of infective endocarditis:

1. Preexisting cardiac abnormalities: Congenital heart disease

- VSD Ventricular Septum defect.
- Calcific aortic stenosis → بترساق risk بآفة risk
 ↳ endocarditis
- Mitral valve prolapse

2. Prosthetic heart valves:

- Account for 10-20% of cases of IE

3. Intravenous drug abusers:

- IE occur on previously healthy valves
- Involves cardiac valves on the **right side** of the heart
 ↳ عادة
 ↳ tricuspid valve
 ↳ Value

30

IE: Causative organisms

2. Prosthetic valve endocarditis (PVE):

- **Early PVE** (occurs in the first two months of surgery):
 ↳ infective endocarditis in first two months
 - **Coagulase negative staphylococcus: S. epidermidis**
 - Coagulase positive staphylococcus
 ↳ common
 ↳ مظهر طبيعي في الفم
 - Gram negative bacteria
 - Fungi
- **Late PVE** (after two months of the postoperative period)
 - **Streptococcus viridans** is the most common.
 - Staphylococcus aureus
 - Coagulase negative staphylococcus is the cause in less than 20% of cases

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IE: Causative organisms

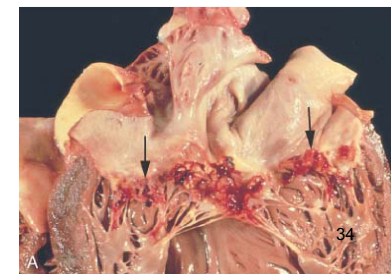
IE: diagnosis → duke university criteria

3. Endocarditis as a result of IV drug abuse: → Rt. side in the heart

- injection in skin → **S. aureus** is the organism most commonly involved
- Occurs on the right side
 - Tricuspid valve is the valve most commonly affected

• Based on Duke university criteria:

- Two major criteria
- One major and three minor criteria
- Five minor criteria



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Table 2
Duke Criteria for Clinical Diagnosis of IE

Major Criteria

- Positive blood cultures from at least two separate cultures drawn 12 hours apart
- Evidence of IE on echocardiogram (eg, a vegetation, abscesses or valve perforation)
- New regurgitant murmur

Minor Criteria

- Predisposing heart condition such as mitral valve prolapse, rheumatic or congenital heart disease, or intravenous drug abuse
- Temperature > 100.4°F (38°C)
- Presence of embolic disease or hemorrhage
- Presence of immunologic phenomena (eg, glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor)
- Positive blood cultures but major criteria are not met
- Echocardiogram is positive but major criteria are not met

Source: Adapted from reference 1

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Subacute infective endocarditis (Inflammatory reaction)

Osler's Nodes

Capillary in the tip of the finger
Painful, red, raised



Non-painful → Rheumatoid subcutaneous nodules

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Splinter hemorrhages in IE

(toxic manifestation)
 له خطوط صغيرة حمراء في nail
 rupture in small vessels

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Presenting Sign or Symptom	% of Cases
Fever	80 to 90
Heart murmur	85
Skin manifestations	18 to 50
Embolic phenomena	> 50
Splenomegaly	20 to 57
Clubbing of fingers	12 to 52
Chills	40
Weakness	40
Dyspnea	40
Sweats	25
Anorexia	25
Weight loss	25
Malaise	25
Cough	25
Nausea/vomiting	20
Headache	20
Myalgia/arthralgia	15
Chest pain	15
Abdominal pain	15
Retinal lesion	2 to 10

Adapted from reference 8

hyperplasia of C.T in nail bed
 clubbing of fingers
 Dr. Sameh Ghazy
 - hyperplasia of C.T in nail bed
 - ends of finger as drum sticks

valvular deformity
 result in inflammation
 systemic disease + complication

IE: Morphology of vegetations:

↳ fibrin + platelet + microorganism.

- The hallmark of IE is the presence of **valvular vegetations**

containing the **microorganisms** ⇒ the difference from R.h. fever.

mitral valve

abscesses formation

sterile vegetation ⇒ vegetations

- MV** is the most common valve involved

micro organism

- IE may affect **single** or **multiple** valves

- Fungal IE causes **larger** vegetations than bacterial IE

- Vegetations may obstruct the valve orifice

- Vegetations cause damage to the **valves**, leaflets, papillary muscles, and chordae tendineae may **rupture**

- Ring **microabscesses** may occur in the **perivalvular tissue**

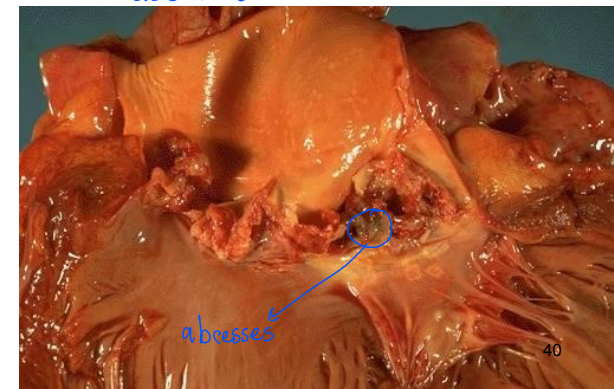
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IE: Complication

- Systemic **emboli** to brain, kidneys and myocardium

- Infarction → emboli نقل السواد

- Abscesses formation ⇒ emboli تجمع مكان آخر نقل abscesses



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non - infective endocarditis :-

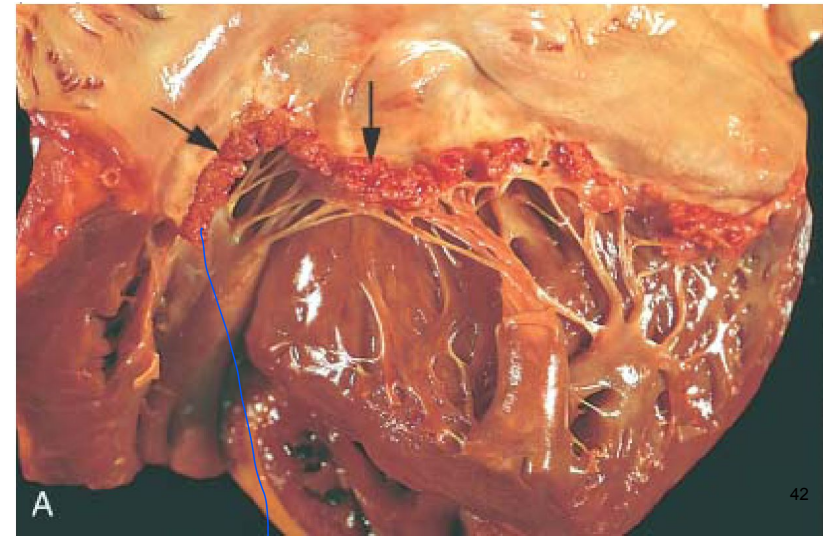
ثrombotic (من كبريتا الس) و يسمو

Nonbacterial Thrombotic Endocarditis (NBTE) ⇒ marantic endocarditis

- Deposition of small masses of fibrin, platelets, and other blood components on the leaflets of the cardiac valves
- **The vegetations of NBTE are sterile** and do not contain any microorganisms unlike infective endocarditis
- Condition is found in **previously normal valves**
- Most commonly affects the **aortic** and **mitral** valves
- Called **Marantic Endocarditis**: if occurred in diseases associated with general debility or wasting
- **Etiology**: this condition is associated with كثرة في الناس الي عندهم severe & chronic disease malnutriat
- Hypercoagulable conditions
- Malignancies

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Nonbacterial Thrombotic Endocarditis (NBTE)



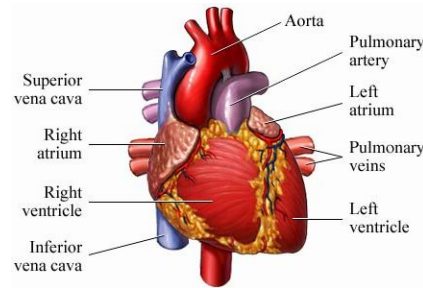
sterile vegetation ⇒ non-bacteria.

Libman-Sacks Endocarditis

- not contain microorganism Sterile vegetations that develop on the cardiac valves of patients with **systemic lupus erythematosus (SLE)**
- **Lesions occur on either or both sides of the valves**
- Occur mainly on ventricular surface of the mitral and tricuspid valves
- Less common these days because of the **use of steroids** in the treatment of **SLE**

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Cardiovascular System



Lecture II: Diseases of Myocardium, Pericardium and Tumors

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1

Primary diseases of the myocardium

- Myocarditis
- Cardiomyopathies
- immunologic diseases (e.g., rheumatic fever)

2

MAJOR CAUSES OF MYOCARDITIS

هناك الكثير من myocarditis (في كثير من الأحيان غير معروف سببها) ولكن يمكن أن تكون ناتجة عن أسباب معدية، مناعية، أو سببها دوائي.

Infections:

- ★★ **Viruses** (e.g., **coxsackievirus**, echovirus, influenza virus, HIV, CMV)
 - Chlamydia (e.g., *C. psittaci*)
 - Rickettsia (e.g., *R. typhi* [typhus fever])
 - Bacteria (e.g., *Corynebacterium* [diphtheria], *Neisseria* [meningococcus], *Borrelia* [Lyme disease])
 - Fungi (e.g., *Candida*)
 - Protozoa (e.g., *Trypanosoma* [Chagas disease], toxoplasmosis)
 - Helminths (e.g., trichinosis)

Immune-Mediated Reactions:

- Postviral
- ★ Poststreptococcal (**rheumatic fever**)
- Systemic lupus erythematosus
- **Drug hypersensitivity** (e.g., **methyldopa**^{Rx}, sulfonamides)
- Transplant rejection

Unknown:

- Sarcoidosis *Systemic Chronic granulomatous inflammatory disease.*
- Giant cell myocarditis

3

Cardiomyopathies ⇒ primary abnormality in myocardium
 له ضعف وظيفي في الـ myocardium بس سببها غير معروف. Cardiomyopathy لا يكون عندنا
 ← عتاه اقول عند هذا الشخص
 myocardiopathy
 ولكن ما معه HTN ولا IHD ولا valvular disease

Describe heart disease resulting from **primary** abnormality in the **myocardium**.

- Not associated with ^{hypertension} HTN, ^{ischemic heart disease} IHD, valvular disease, congenital heart disease, or inflammation
- **Divided into 3 major groups of diseases:**

1. Dilated cardiomyopathy

– the most common (90% of cases)

2. Hypertrophic cardiomyopathy

3. Restrictive cardiomyopathy

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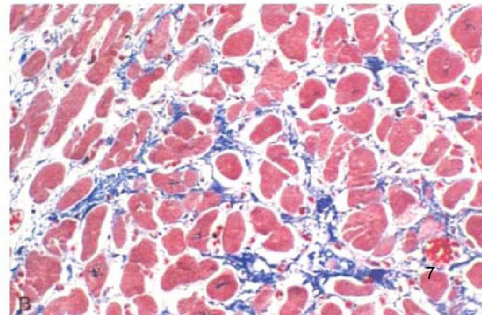
له سُمِّيَ بذلك : لأنه جدير Congestive نفس التي ينشأ عنه Congestive لا HF

- رہا تو کہ ہذا
الاسباب

Weakness 31
muscle
no nina 2
muscle 31
yo cardium.

-

5



↳ in chambers.

PROSIS

⑤ ثانياً ممكن يصير حتى الدم غير كافى
والثاني قلته يعني المرض فيه نقصه اعراضه
Congestive HF في وير Stasis in the heart
Blood
ويعتبر Thrombi Formation
development of embolism

6

8

Hypertrophic Cardiomyopathy

- most common change is hypertrophic not dilatation
- referred to as **asymmetric septal hypertrophy**
- referred to as **idiopathic hypertrophic subaortic stenosis**



stenosis

- Characterized by:**

1. myocardial hypertrophy of the 4 chambers mainly

septum (أكثر منطقة) interventricular septum maximum of hypertrophy
 (subaortic) hypertrophy (أكثر منطقة) interventricular septum

2. abnormal diastolic filling

3. ventricular outflow obstruction

- 50% of cases are autosomal dominant

below normal
 ↓
 below cardiac output.
 → HF

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Hypertrophic Cardiomyopathy: Morphology

Gross appearance: ليجر ديس ال hypertrophic كيث ؟

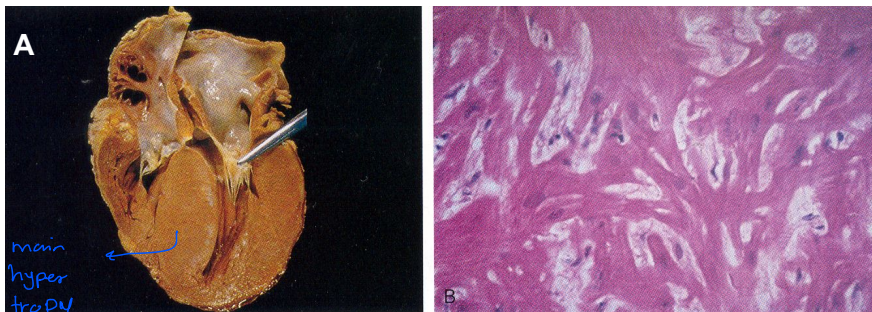
- The **hypertrophy** is prominent in the LV and in the septum
- The septum in most cases is thicker than the wall of the LV
- The septum thickness is maximum in the subaortic region
- Heart weight **usually > 800 gm**
- The hypertrophy of the septum is **asymmetric**, this causes the **outflow obstruction** during systole

Microscopic appearance:

- Hypertrophic, abnormally arranged myocytes, later there may be **cardiac fibrosis**

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Hypertrophic Cardiomyopathy: Morphology



A) Gross: The ventricular septum is **asymmetrically** thickened and bulges into the lumen of **LV**. Contact between the hypertrophic septum and the anterior leaflet of mitral valve may cause significant **LV** outflow obstruction.

B) Microscopic: hypertrophy and extreme disarray of fibers!¹

Hypertrophic Cardiomyopathy: Clinical features

- Exertional dyspnea:** secondary to **pulmonary HTN** (hypertension) → shorten in breath
- Systolic murmur:** due to abnormal movement of the anterior mitral valve leaflet, & LV outflow obstruction (aortic stenosis)
- Anginal pain** → Chest pain.
- Ventricular arrhythmia**
- Sudden death** in young athletes → diastolic abnormal (reduced). Cardiac outflow is destructive.
- CHF:** in late stages due to myocardial fibrosis
- Treatment:** usually with **β-blocker**

③ في حالة الراجنس تحتاجين O₂ ، Blood أكثر د ال heart
 متى تاني الـ بيطي المظلم للـ بيم
 ④ دة كدة الدم الغني الـ heart من coronary arteries
 ما كدة كافي (reduced) كدة بيزر
 الـ HF .

Restrictive Cardiomyopathy

- Characterized by **decrease in ventricular compliance**, resulting in impaired ventricular filling during diastole
- 10% of childhood heart disease in tropical countries

Causes:

- Endomyocardial fibrosis:** (Most common cause, unknown etiology)

- Eosinophilic endomyocardial fibrosis**, or **Löffler syndrome**, due to proteins released from the degranulating eosinophils

- Cardiac amyloidosis**

- Hemochromatosis**

- Radiation injury**

- Endocardial fibroelastosis**

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Restrictive Cardiomyopathy: Clinical features

- In restrictive cardiomyopathy, ventricle is **stiff and inelastic** that can be filled only with **great effort**.

Clinical features:

- fatigue, exertional dyspnea, and chest pain
- systemic emboli may occur
- arrhythmias
- congestive heart failure in later stages

- Treatment:** symptomatic & treatment of the cause

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Restrictive Cardiomyopathy: Morphology

Gross appearance:

- The atria are typically **dilated**
- The ventricles may be of **normal size**
- Mural or valvular thrombi may be present

Microscopic appearance:

- The myocardium may be infiltrated by eosinophils
- Fibroelastic tissue is present in the myocardium

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PERICARDIAL DISEASES

- Pericarditis
- Pericardial effusions

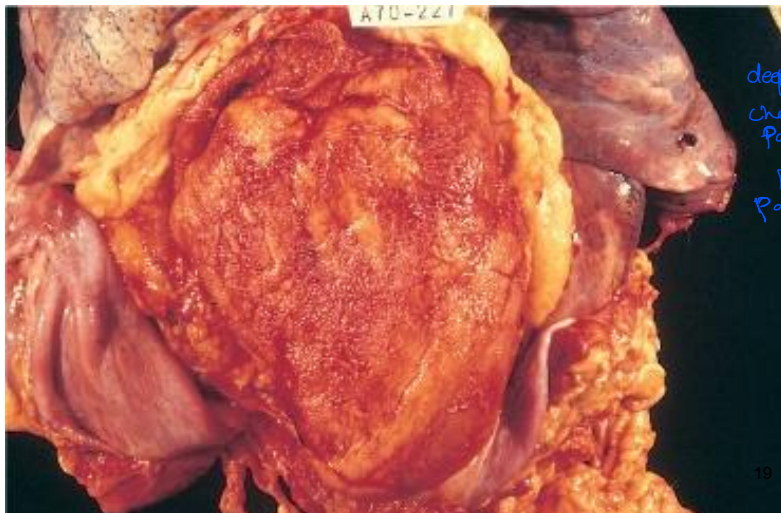
16

Pericarditis

- **Primary pericarditis:** ⇒ most of the time in the infectious → ^{= (due to)} secondary to viral infections.
 - is uncommon and usually infectious in origin
 - Most common cause is **viral infections**
 - Other causes: bacteria, mycobacteria, fungi
- **Secondary pericarditis:** ⇒ ^{متى معروف هو} associated with
 - **Uremia** is the most common ^{Chronic renal failure}
 - Cardiac surgery
 - Radiation
 - Rheumatic fever
 - Systemic lupus erythematosus
 - Metastatic malignancies

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^{سوء الزبدية ، الجينية}
 ("bread and butter" pericarditis): In patients with uremia or acute rheumatic fever



① deep breath increase chest pain
 ② لا يقدر أو يعجز حاله ان الانظار سوف تقل severity في Pain
 ↓ pressure in pericardium

- **Pericarditis outcome:**
 - May cause immediate hemodynamic complications if effusion is significant
 - ① May resolve without significant complications
 - ② May progress to chronic pericarditis
- **Chronic pericarditis:** ^(يعني لما يضر progression)
 - When there is extensive **suppuration**, healing gives rise to chronic pericarditis ^(damage is more severe)
 - The lesion in chronic cases ranges from delicate adhesions to dense **fibrotic** scars that may obliterate the pericardial space
 - In such cases the heart can **not** expand, a condition called **constrictive pericarditis**

abnormal sound
 ↓
 pericardial infarction rub

④ Fibrin is sticky material (adherence to attach other).
 للالتصاق بين ال partial & visceral ال pericardium في هذه الحالة يكون
 ⇒ **constrictive pericarditis** (around the heart).

IVC & SVC له لانه يقل constriction على

Pericarditis

b not normal filling for heart and not normal constriction
 ↓
 restrictive myopathy ⇒

Clinical manifestation:

- **Atypical chest pain:** ⇒ chest pain at is different from chest pain which result ischemic heart disease.
- **a friction rub type of sound on auscultation**
- **cardiac tamponade:** ⇒ ^{emergency → shock} large amount fluid in pericardium cavity. ^{Pericardiocentesis tube drains fluid}
- Distant heart sounds → ^{لانه ما ينفذ مع طرقة} Fluid normally.
- Distended neck veins (SVI) ^{له لانه في constrictive (في انش) يمنع fluid في heart}
- **Declining** cardiac output
- **Shock**

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Pericardial Effusions

- **Serous:** CHF, hypoalbuminemia
water like fluid
- **Serosanguineous:** blunt chest trauma, malignancy
water like fluid + blood
- **Chylous:** mediastinal lymphatic obstruction
lymph
- **Hemopericardium:** rupture aortic aneurysm, or ruptured MI, or penetrating trauma
blood
- **Treatment:** cardiac tamponade is a cardiac emergency. It should be treated by pericardiocentesis

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Cardiac Tumors

- **Secondary tumor:** (Metastatic Neoplasms)
heart tumor (metastatic neoplasms)
lymphoma, melanoma, breast, lung (most common)
– more common than primary cardiac tumors.
- occur in up to 10% of patients with cancer
- Most often, they involve the pericardium
- cause **pericarditis** and **hemorrhagic pericardial effusions**
- The most common primary neoplasms that metastasize to the heart are: **carcinomas of the lung and breast, malignant melanomas, lymphomas and leukemias**
- **Primary tumors:** are rare

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Primary Tumors (rare).

- **Most common tumors in descending order:**

– Myxomas

– Papillomas

– Papillary elastofibroma

elastic, fibrous tissue

– Rhabdomyomas

– Angiosarcomas

Blood vessels tumor

– Rhabdomyosarcomas

– Lipoma → adipose tissue tumor.
epicardium myocardium

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Primary Tumors

المزغزغ
Primary tumors
إما مغلوقات غشاء المشيمة

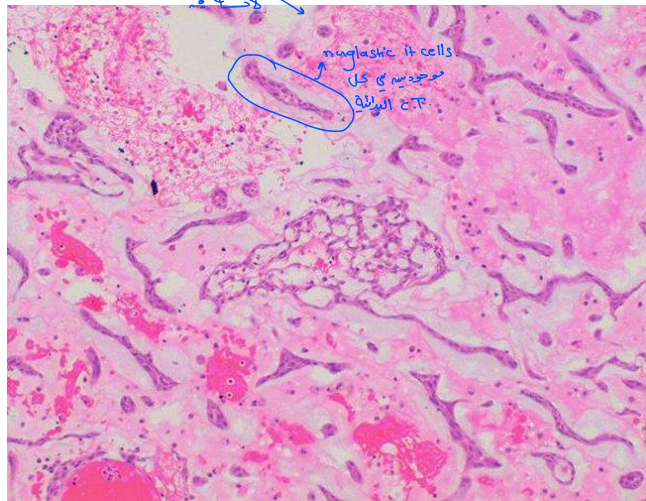
• Myxomas:

(Myxoma)

- Benign tumors
- Arise from left atrium near fossa ovalis
- May be sessile or pedunculated
- Composed of multinucleated stellate cells, smooth muscle cells may be present, the cells are suspended in a mucopolysaccharide rich stroma
- They may obstruct the atrioventricular valves with resultant syncopal episodes or even death
- They may fragment and cause emboli
- Treatment: surgical resection is lifesaving

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Myxoma



25

Primary Tumors

• Cardiac rhabdomyomas:

- The most common primary cardiac tumors of infancy and childhood
- Best known for their association with tuberous sclerosis
- Present as myocardial mass that project into the ventricular lumen
- May be solitary or multiple
- Composed of eosinophilic, polygonal cells, many of which contain large, glycogen rich cytoplasmic granules.
- Myofibrils can be demonstrated in such cells under the microscope

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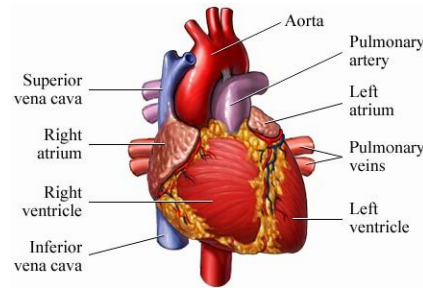
Primary Tumors

• Lipomas:

- May occur anywhere in the heart
- They most likely represent malformation than true neoplasm
- Lipoma like accumulation in the ventricular septum is quite common
- Though morphologically benign, they may be implicated in sudden cardiac death

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Cardiovascular System



Lecture III: CHF and Hypertension

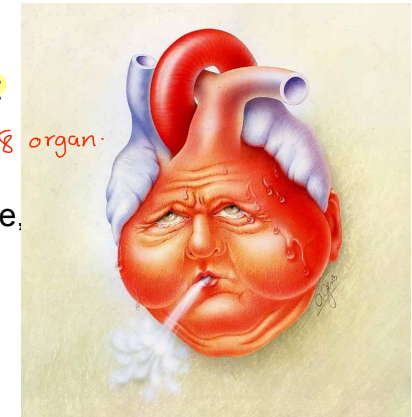
Dr. Marwan Qubaja
Al-Quds University
Faculty of Medicine
Pathology Department



1

Congestive Heart Failure (CHF)

- Definition:** diminished ^{تضاؤل} functional capacity of the heart which is unable to maintain an output sufficient for metabolic needs. of tissue & organ.
- Can involve the heart's left side, right side, or both sides
- Called congestive because of abnormal accumulation of fluid or blood in apart of the body
- pulmonary congestion and peripheral edema (systemic circulation).



2

inadequate ^{بسيطة} for word flow or back up of blood.

CHF: Causes

- Congenital heart disease (valvular problems), *endocarditis, myocarditis*
- Ischemic heart disease
- Rheumatic heart disease and other immune disease :
– E.g., SLE, RA, Scleroderma
- Hypertensive heart disease
- Inflammatory disease of the heart
- Nutritional, endocrine, and metabolic diseases including:
 - Thyrotoxicosis * hyper metabolic rate
 - Myxedema
 - Beriberi (thiamine) → vit B₁ deficiency
 - Carcinoid syndrome
 - Storage disease
 - Amyloidosis
- Cardiomyopathy
 - tumor

3

Types of heart failure

- **High output failure:** inability of the heart to meet the increased demand for blood by tissues ^{even} → Cardiac output is normal and more than normal. ^{ولكن اقل من احتياجات الجسم لانه في عندك زيادة need في الجسم من tissue, organs مثل حالة hyper metabolic state, anemia & pregnancy}
 - Thyrotoxicosis, anemias, arteriovenous shunts
- **Low output failure:** cardiac output is insufficient at rest or at exertion: ^{reduction in output ⇒ ex: any disease in heart}
 - *myo Cardial infarction* MI, cardiomyopathy, valvular disease
 - aortic < stenosis incomp
 - mitral < stenosis incomp
- **Forward failure:** Decreased left ventricular output
 - Cardiac tamponade, aortic stenosis * Filling abnormal * put out → not normal
- **Backward failure:** increased congestion of the venous circulation, because the failing ventricle is unable to eject the normal volume of venous blood delivered to it during diastole

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Types of heart failure

- **Compensated heart failure**: If the **dilated** ventricle is able to maintain cardiac output at a level that meets the needs of the body
- **Decompensated heart failure**: With time, the failing myocardium is no longer able to propel sufficient blood to meet the needs of the body, even at rest.
- **Right-sided cardiac failure**
- **Left-sided cardiac failure**

main type

5

Types of heart failure

- **Systolic heart failure**: is the result of impaired contractile function
 - E.g., MI, Dilated cardiomyopathy
- **Diastolic heart failure**: reduced ventricular compliance in the setting of normal or near normal systolic function
 - E.g., HTN, aortic stenosis

6

CHF: Symptoms

الاعراض

- **Dyspnea on ordinary exertion**
- **Exercise intolerance**
- **Fatigue**
- **Nocturia**
- **Cough (nonproductive)**
- **Orthopnea**
- **Paroxysmal nocturnal dyspnea**

CHF: Signs

congested Blood في ال pulmonary or Systemic circulation

- **Acute pulmonary edema**
- **Cardiomegaly**
- **Laterally displaced apical impulse**
- **Increased central venous pressure**
- **Hepatojugular reflux**
- **Hepatomegaly**
- **Lower extremity edema**
- **Neck vein distention**
- **Pleural effusion**
- **Rales**
- **S3 gallop**
- **Tachycardia**
- **Unexplained weight gain**

7

8

Right-sided cardiac failure

The most common causes:

- **Left sided heart failure** (the most common cause)
Rt. side HF ← R. side HF هو سبب أساسي في أنه يتردى
- **Intrinsic diseases of the lung:** (in the absence of LHF)
 - pulmonary HTN (cor pulmonale)
↓ heart ↓ lung
* لما يكون هناك intrinsic disease في lung
cor pulmonale ← R. side cardiac failure
مرض في ال heart سببه هو مرض في ال lung
 - COPD
 - Pulmonary fibrosis
- **Pulmonic or tricuspid valve disease**
- **Congenital heart diseases** (left-to-right shunt)

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Clinical Features: Right heart failure

Systemic venous congestion:

Congested in the Blood in Systemic circulation

- distended neck veins
- passive congestion of the liver
- generalized venous congestion including jugular veins
- enlarged, sometimes tender liver (hepatomegaly).
- increased frequency of deep venous thrombi & pulmonary embolism

Edema:

- subcutaneous edema
- weight gain
- ascites, pleural effusions
- dependent edema (the feet and lower legs)

له اعتماد على ال gravity

10

Left-sided cardiac failure

The most common causes:

- **systemic hypertension**
- **mitral or aortic valve disease** ← stenosis in competence
- **ischemic heart disease** → part from myocardium will die replaced in fibrous tissue (non-functioning).
- **primary diseases of the myocardium.**
cardio myopathy ←

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Clinical Features: Left heart failure

- **Dyspnea** due to pulmonary congestion and edema:

- **Exertional dyspnea:** during physical activity
- **Orthopnea:** when the person is lying down
- **Paroxysmal nocturnal dyspnea:** sudden, severe dyspnea, with coughing, choking sensation, & wheezing

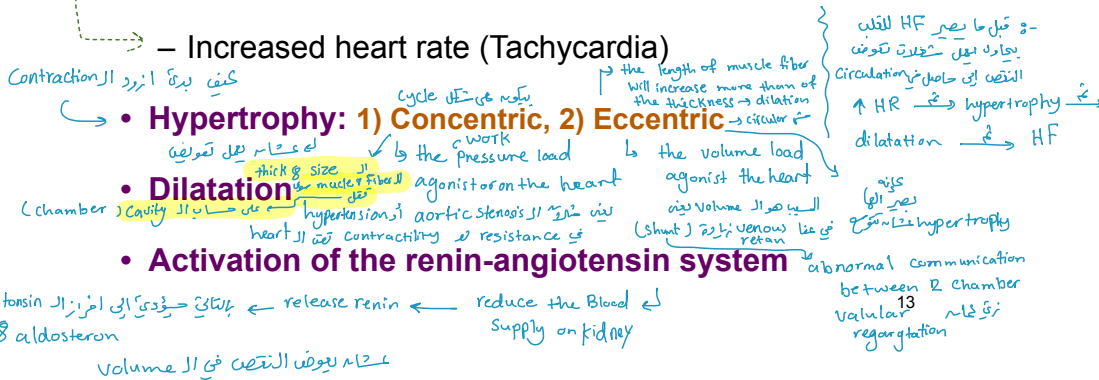
- **muscle fatigue**
- **Enlarged heart, Tachycardia**
- **Third heart sound (S3)**
- **Rales** at the lung bases
- **Mitral regurgitation** with systolic murmur
- **Atrial fibrillation:** "irregularly irregular" heartbeat due to chronic dilation of the left atrium

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Compensated heart failure: adaptive responses

- **Neurohumoral reactions:** release of catecholamines in response to reduced cardiac output, this leads to:

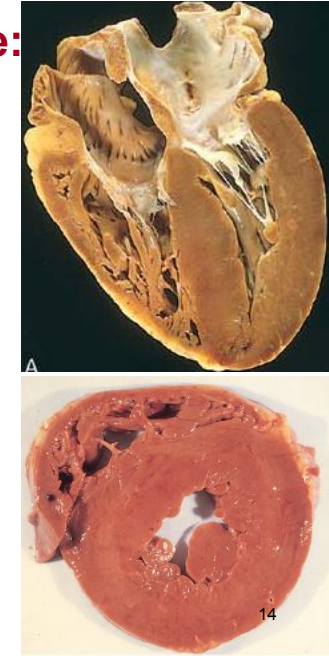
- Increased force of contraction (inotropic effect)
- Increased heart rate (Tachycardia)



Compensated heart failure: adaptive responses

Cardiac hypertrophy:

- **Concentric hypertrophy:** the thickness of the ventricular wall increases **without** increase in the size of the chamber
- Pure **pressure load**
- increase the diameter of individual muscle fibers
- e.g., HTN, valvular stenosis



Compensated heart failure: adaptive responses

Cardiac hypertrophy:

- **Eccentric hypertrophy:**
 - an increase in heart size as well as an increase in ventricular wall thickness
 - pure **volume load**
 - increase in cardiac fiber length → net result is dilatation
 - E.g., valvular regurgitation, abnormal shunts

Handwritten notes: "نتيجة خلية", "end organ damage", "mainly congestive heart failure or renal failure".

Hypertension (HTN) - Introduction

- **"Sustained increase in blood pressure"**

- **Silent Killer** – asymptomatic until late

- **Symptoms:** dizziness, headache, and visual difficulties

- **Risk factor** – MI, DM, Stroke, heart & renal failure

- 25% of population, <35% aware

- **Chronic**, end organ & vascular damage

- **Complications:** ATH, IHD, Renal damage, Stroke

- 95% of HTN is idiopathic, 5% is secondary HTN

Handwritten notes: "Complication ال hypertension", "بكون على cycle ال work", "ال thick size of muscle fiber", "agonist on the heart", "the pressure load", "the volume load", "aortic stenosis", "aortic regurgitation", "shunt", "regurgitation", "abnormal communication between R Chamber & Vascular", "regurgitation", "13", "volume ال نتاج في ال volume", "angiotensin", "aldosterone", "release renin", "reduce the Blood supply on kidney".

Table 12-4. CLASSIFICATION OF BLOOD PRESSURE IN ADULTS

Category	Systolic (mm Hg)	Diastolic (mm Hg)
Normal	<130	<85
High normal	130–139	85–89
Hypertension		
Stage I (mild)	140–159	90–99
Stage 2 (moderate)	160–179	100–109
Stage 3 (severe)	180–209	110–119
Stage 4 (very severe)	>210	>120

المalignant له غالباً يتكون في حالة الـ

Causes of Hypertension

idiopathic

Essential Hypertension (90%-95% of cases)

Secondary Hypertension (5%-10%)

Renal:

- Acute glomerulonephritis
- Chronic renal disease
- Polycystic disease
- Renal artery stenosis
- Renal vasculitis
- Renin-producing tumors

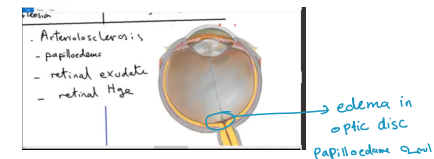
Malignant (Accelerated) Hypertension

- Occurs in 5% of hypertensive persons
- Rapidly rising blood pressure that if untreated leads to death within 1 or 2 years.
- May complicate any type of HTN.
- Severe hypertension (**diastolic > 120 mm Hg**)

قريب من الـ stroke

Characterized by:

- renal failure
- retinal hemorrhages and exudates, with or without papilledema



Renal Causes:

Polycystic Disease



Causes of Hypertension

Endocrine:

- **Adrenocortical hyperfunction** ^{plasma} (Cushing syndrome, primary aldosteronism, congenital adrenal hyperplasia)
- **Exogenous hormones** (glucocorticoids, estrogen [including pregnancy-induced and oral contraceptives], sympathomimetics and tyramine-containing foods, monoamine oxidase inhibitors)
- **Pheochromocytoma** $\Rightarrow$ tumor in ^{supra medulla} and it secretes ^{high level from corticoid amid}
- **Acromegaly**
- **Hypothyroidism** (myxedema)
- **Hyperthyroidism** (thyrotoxicosis)
- **Pregnancy-induced**

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Causes of Hypertension

Cardiovascular:

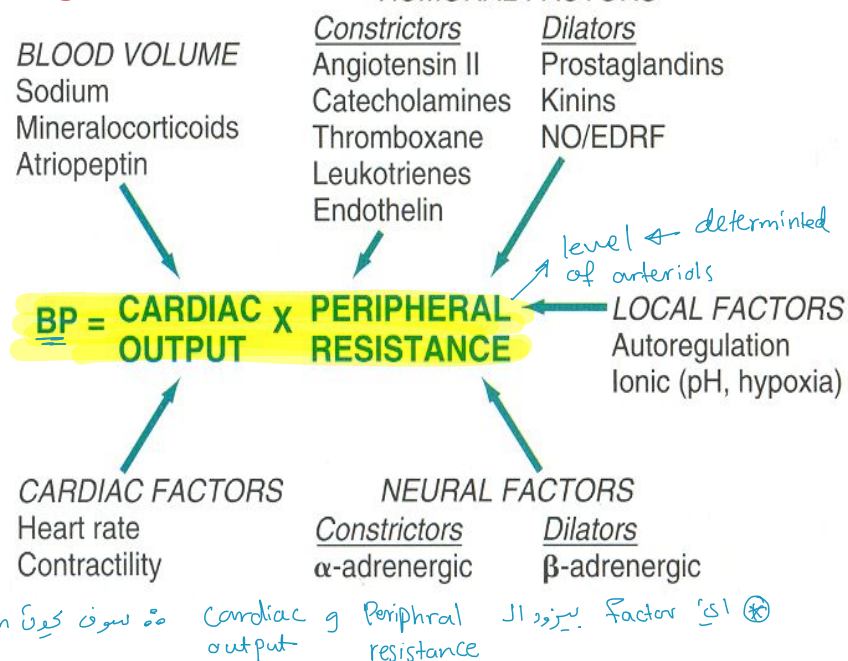
- ^{nerve} Coarctation of aorta
- Polyarteritis nodosa
- Increased intravascular volume
- Increased cardiac output
- ^{not elastic} Rigidity of the aorta

Neurologic:

- Psychogenic
- Increased intracranial pressure
- Sleep apnea $\rightarrow$ usually in obese patient $\rightarrow$ ^{just be!} difficult in breathing sleep.
- Acute stress, including surgery

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Regulation of BP: HUMORAL FACTORS



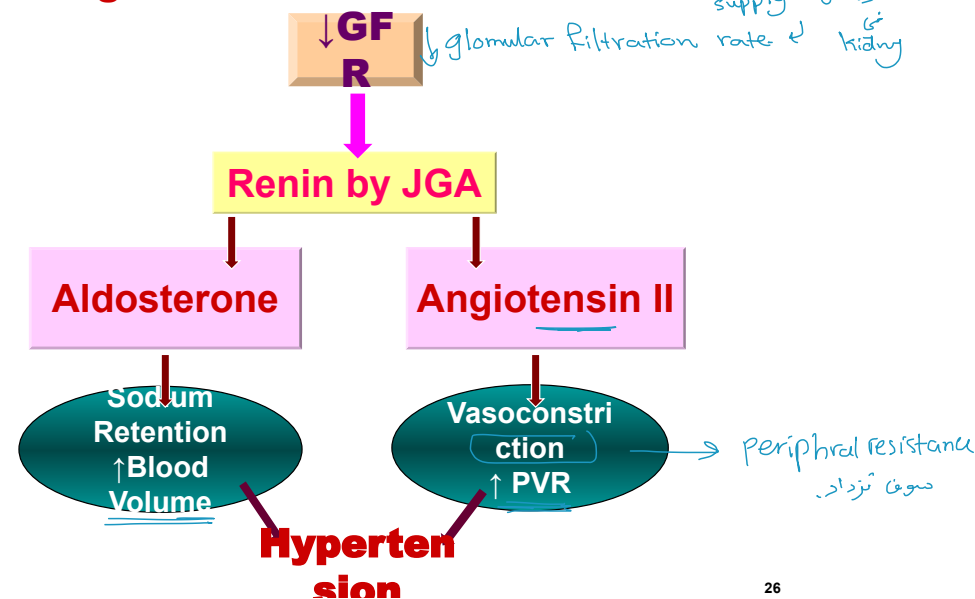
Pathogenesis of HTN

- both increased blood volume and increased peripheral resistance contribute to the increased pressure
- Cardiac output is influenced by blood volume, which is greatly dependent on body sodium
- **Total peripheral resistance is determined at the level of arterioles**, and depends on the effects of the neural and hormonal influences
- Normal vascular tone depends on the competition between vasoconstricting influences and vasodilators

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Peripheral resistance & Cardiac output على B.P ال (*) كذا يحد ال

Pathogenesis of Renovascular HTN



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Pathogenesis of Essential Hypertension

Essential hypertension is a complex **multifactorial disorder**

- **Genetic factors:**
 - Polygenic mutations are more likely
 - Gene defects in some enzymes like:
 - Aldosterone synthase, 11 hydroxylase, 17 hydroxylase
 - Lead to increase in secretion of aldosterone with the result of increased Na and water reabsorption, plasma volume expansion, and HTN
- **Environmental factors**
 - Stress
 - Obesity
 - Physical inactivity
 - Heavy consumption of salt

multiple injuries ال رنل & surface of the kidney rough not smooth

Complications of HTN

- **Large Blood Vessels – Macroangiopathy**

- **Atherosclerosis** and its complications

- **Small Blood Vessels – Microangiopathy**

- **hyaline** and **hyperplastic arteriolosclerosis**

- **Heart:** reduction in lumen & thickening of wall

- **LVH** Lt. vent. hypertrophy

- **Kidney:**

- **Benign nephrosclerosis**

- **Eyes:**

- **Hypertensive retinopathy** → hemorrhage

- **Brain:**

hemorrhage, infarction

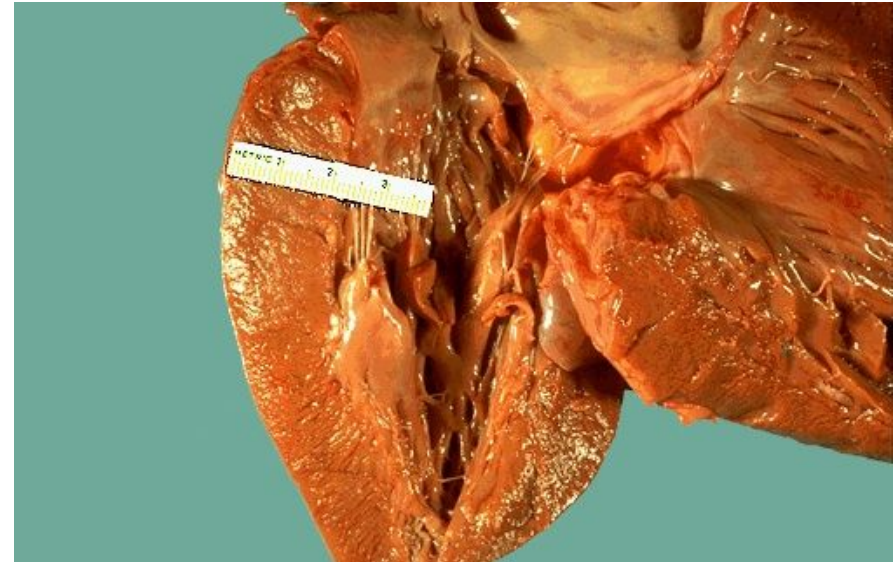
28

Benign Nephrosclerosis

Leathery Granularity
due to minute scarring



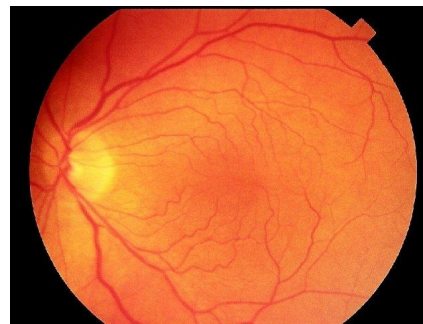
29



LV Hypertrophy secondary to HTN

30

Retinopathy secondary to HTN



Normal retina



retinal hemorrhage

hypertrophy ← mainly Lt ventricle
↓
Consentric
↓
هذا نوع من أنواع التكيف
(adaptation)
↓
بعد مدة يستمر لطول الوقت
مع في البداية حمار hypertrophy
لوقت معين ثم سوف يكون failure

Hypertensive Heart Disease

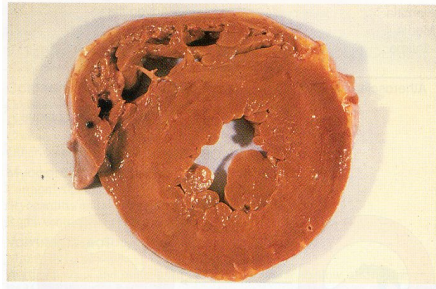
hypertension ← changes due to hypertension
← mainly Lt ventricle hypertrophy

- **Left ventricular hypertrophy** with a history of hypertension
- other causes of ventricular hypertrophy have been excluded.
 - (e.g., aortic stenosis or primary hypertrophic cardiomyopathy)
- **Cause:** sustained pressure load on LV
- with increasing degrees of hypertrophy, the metabolic requirements continue to increase but the ability of the heart to meet these demands decreases.
- hypertrophy decreases diastolic filling and stroke volume
- **Complication:** CHF, MI, arrhythmias.

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Morphology

- LV concentric hypertrophy
- Heart weight > 450 g.
- wall thicknesses > 2.0 cm.
- When LV fails, RV undergoes hypertrophy, and dilation may also develop
- **Histology:** cardiac myocytes enlarge, and contain hyperchromatic, rectangular box-car shaped nuclei



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LV hypertrophy: Clinical features:

- **Initially:** no symptoms
- **Later:** LV may decompensate (fail)
- **Diagnosis:** CXR, echo, ECG
- **Complications:** *outcomes → end organ damage.*
 - heart failure is a poor prognosis
 - progressive renal damage
 - cerebrovascular accidents *CVA or Stroke*
 - sudden cardiac death

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disease in lung *ب* *disease in heart (Rt)* *ع*

Cor Pulmonale (Pulmonary Heart Disease)

- Describe disease of right side chambers of the heart.
- This results from pulmonary hypertension, occurred from pulmonary parenchymal or vascular disease
- Characterized by hypertrophy and/or dilation

Morphology:

- In **acute cor pulmonale:** RV is usually dilated.
- In **chronic cor pulmonale:**
 - RV & right atrium hypertrophy.
 - Thickness of the RV may exceed that of the LV
 - Later: RV failure with RV & right atrium dilation

حالة مرضية حيث يصاب القلب بالاختناق
غير طبيعي أو قوسى خلف له
vertebra

35

DISORDERS THAT PREDISPOSE TO COR PULMONALE ⇒ *association in pulmonary hypertension.*

Diseases of the Lungs:

- Chronic obstructive lung disease (the most common chronic cause)
- Diffuse pulmonary interstitial fibrosis
- Extensive, persistent atelectasis
- Cystic fibrosis

Diseases of Pulmonary Vessels:

- Pulmonary embolism (the most common acute cause)
- Primary pulmonary vascular sclerosis
- Pulmonary arteritis (e.g., Wegener granulomatosis)
- Drug-, toxin-, or radiation-induced vascular sclerosis

Disorders Affecting Chest Movement:

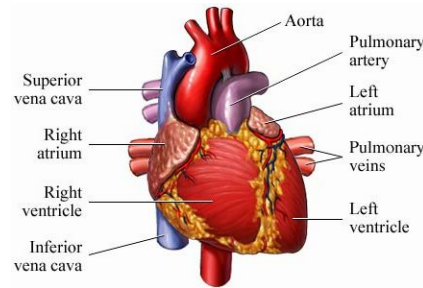
- Kyphoscoliosis *kyphosis abnormal in vertebral column when lying for word.*
- Marked obesity *~ ~ ~ ~ ~ lying laterally → scoliosis*
- Neuromuscular diseases *kyphoscoliosis*

Disorders Inducing Pulmonary Arteriolar Constriction:

- Metabolic acidosis
- Hypoxemia

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Cardiovascular System



Lecture IV: Arteriosclerosis

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Al-Quds University
Faculty of Medicine
Pathology Department



1

VASCULAR DISEASES

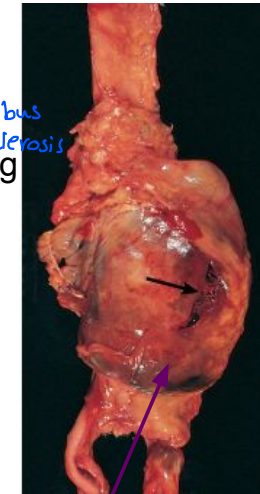
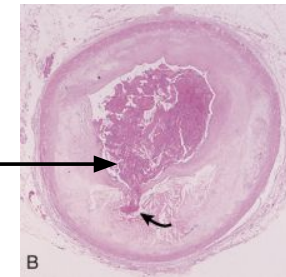
Vascular abnormalities cause

clinical disease by:

- ① **Narrowing** or completely **obstructing** lumen by:
 - by: thrombus
 - by: atherosclerosis
- Weakening of the wall leading to

dilation or **rupture**
abnormal dilation ← aneurysm lead

Obstruction:
thrombosis with atherosclerosis



Dilation:
aneurysm with rupture

2

Atherosclerosis (ATH)

Definition: "Chronic inflammatory disorder

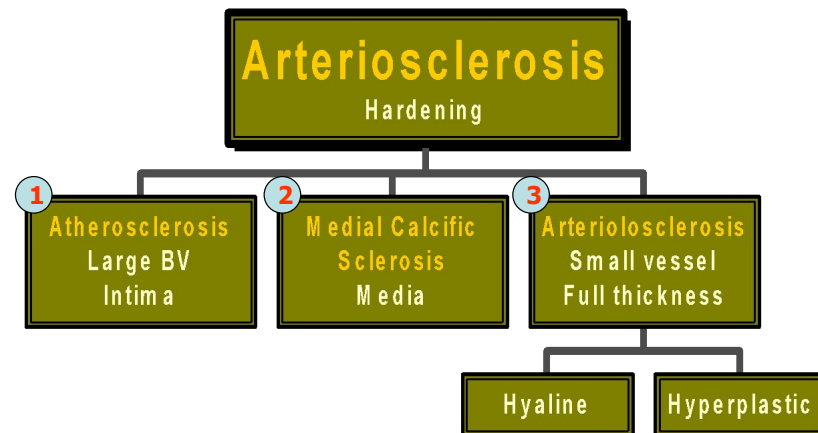
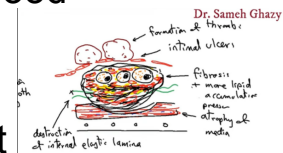
of intima of large and medium sized blood

vessels characterised by formation of

fibrofatty plaques called **atheroma** that protrude into and **obstruct vascular lumen**, **ischemia**.

weaken the underlying **media**, and may

undergo **serious complications**".



Arteriosclerosis "hardening of the arteries": thickening and loss of elasticity of arterial walls

- ⊗ large and media vessels ⇒ atherosclerosis بقول عنه
- ⊗ Small vessel ⇒ arteriolosclerosis بقول عنه
- hyaline
- hyperplastic

3

↳ Fissuring (تجريح)
↳ Ulceration
↳ development of thrombus.

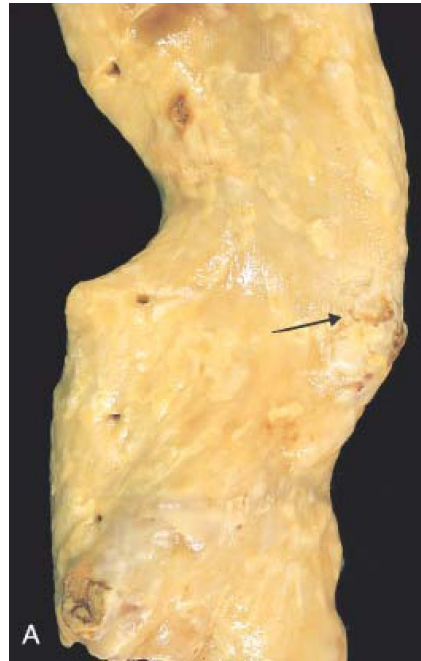
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Atherosclerosis

- **Morphology of the atheroma:** a raised focal lesion **within the intima** that has **yellow core** made from **cholesterol** and other lipids and covered by a **fibrous cap**

Atheroma vary in size from 0.3 to 1.5 cm in diameter

atherosclerosis $\Rightarrow$ 3mm



① intracellular (is side cytoplasm) Endothelial cell
 ② second part from atheroma

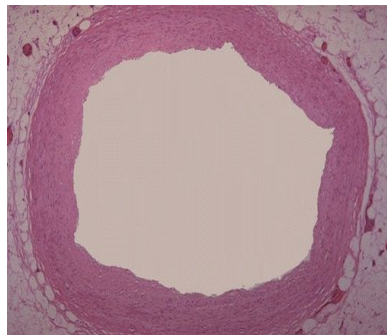
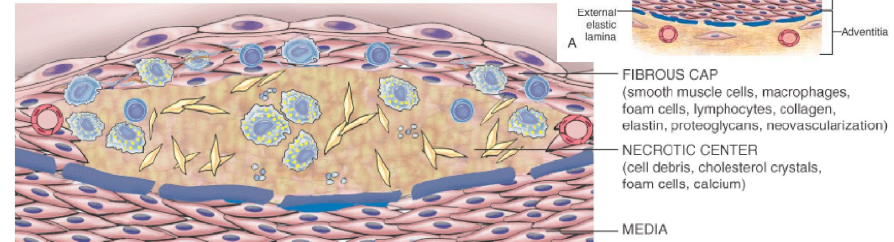
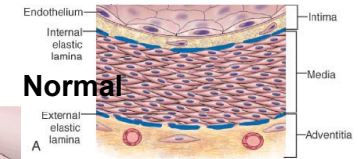
Principal components of atherosclerotic plaque

تكون من 3 compounds

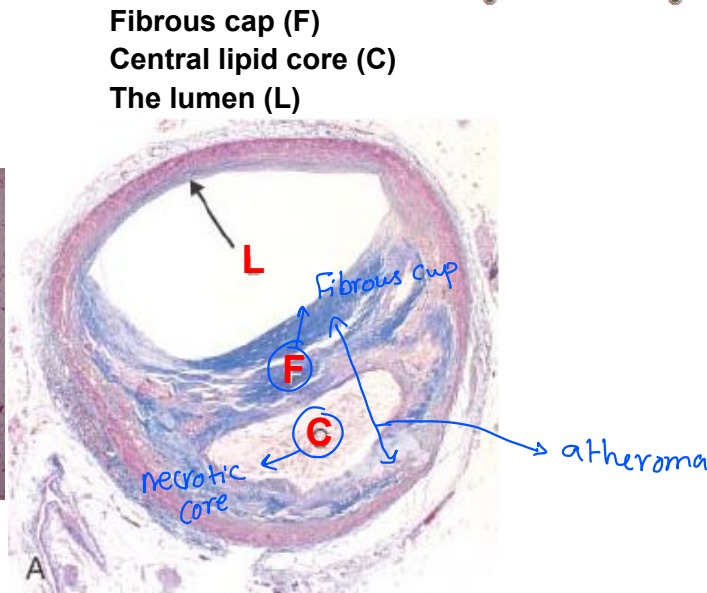
Fibrous cap composed of proliferating **smooth muscle cells**, **macrophages**, **lymphocytes**, **foam cells**, and **extracellular matrix**

Necrotic core consists of cellular debris, extracellular **lipid** with **cholesterol crystals**, and **foamy macrophages**

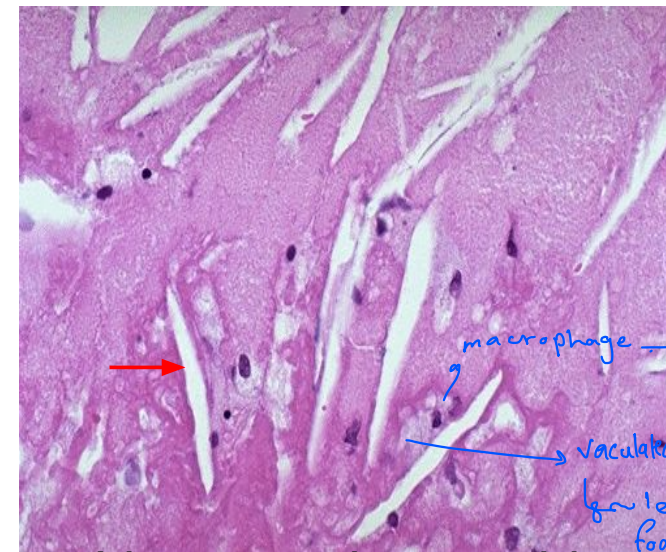
Neovascularization $\rightarrow$ Formation of new vessels



Normal coronary artery



Atherosclerosed coronary artery



Atheromatous plaque containing **cholesterol clefts** and macrophages

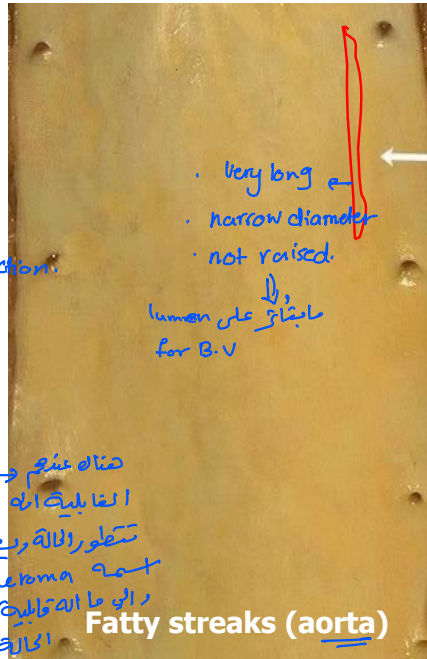
$\rightarrow$ extracellular cholesterol or extracellular lipid which as accumulated atheromatous plaque

Fatty Streak origin for atheroma.

Fatty Streaks

structure

- Composed of **lipid-filled foam cells** → macrophage or smooth muscle cell.
- Not raised** and don't disturb blood flow, not obstruction.
- Start as multiple **yellow fat spots** <1mm in diameter, 1 cm long or longer
- Appear in the aorta of all children **> 10 years** of age
- not all fatty streaks are destined to become advanced atherosclerosis



عنه انه تغير (modifiable) ↓ Controlled

Risk factors for atherosclerosis

Major Risks	Lesser, Uncertain, or Nonquantitated Risks
Nonmodifiable	Obesity
Increasing <u>age</u>	Physical inactivity
Male <u>gender</u>	Stress ("type A" personality) → impatient, competitive, organized, nervous
<u>Family history</u>	Postmenopausal estrogen deficiency
<u>Genetic abnormalities</u>	High carbohydrate intake
Potentially Controllable	Hardened (trans) unsaturated fat intake
Hyperlipidemia → علة غير طبيعية / metabolic / diat	Chlamydia pneumoniae (infection) → له اصابة تكون هي التي في damage or injury in endo thelial. (not all causes).
Hypertension → علة غير طبيعية / anti hypertensive drug	
Cigarette smoking	
Diabetes	

→ Risk factor
لانه يتطور فيه
Fatty streak
↓
atherosclerosis
لتصبح

ATH: Risk factors

modifiable
non-modifiable

- Age:** men >45, women >55 yrs → usually
- Hypertension:** BP >140/90
- Cigarette smoking**
- Low high density lipoprotein cholesterol**

(HDL): < 40mg/dl

↓
good fat.

Good and Bad



Risk factors: Hyperlipidemia

↑ fatty streak → فمكة لثوية
↑ Fatty acid or lipid.
↑ hyperlipidemia
↑ fatty streak لثوية فمكة

diat طرية ال عه طرية ال modifiable
▪ **Hypercholesterolemia** – mainly

▪ Hypertriglyceridemia - less significant

▪ **LDL** – Increased risk

▪ **HDL** – lowers the risk – Reverse transport
↑ ازوده عه طرية
olive oil
↑ عه طرية
excretion
↑ omega-3 fatty acid

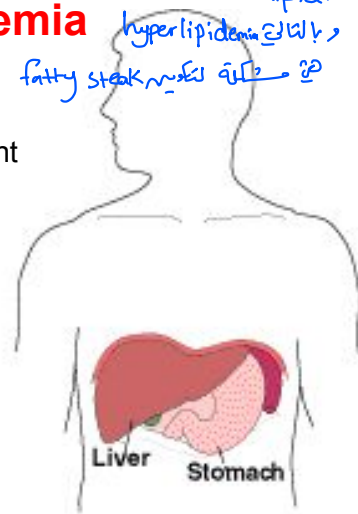
Increase Good Fats?

▪ Lower LDL, Increase HDL

▪ Mono unsaturated fats

▪ Poly unsaturated fats

* omega-3. Fatty acid



ATH: Pathogenesis:

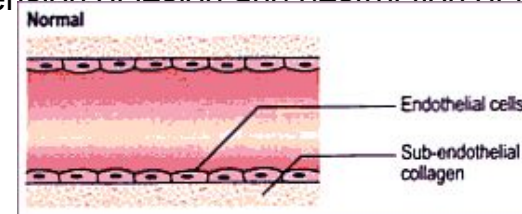
▪ **Intimal injury** (endothelial cell injury) → ① smoking
② stress

▪ **Inflammation and necrosis**

▪ Cholesterol accumulation (**soft atheroma**)

▪ **Fibrosis**, smooth muscle proliferation (**hard atheroma**)

extension of lesion and destruction of vessel
▪ **Extension of lesion and destruction of vessel**



18

Pathogenesis: The response to injury hypothesis

▪ Considers **ATH** to be a chronic inflammatory response of arterial wall initiated by injury to the endothelium

▪ **Central to this theory are the following:**

1. **Chronic endothelial injury:** e.g. (HTN, smoking, stress) injury سبب ال

2. **Endothelial dysfunction:** in set of being of having anti coagulate propensity as normal endothelial.

• Increased permeability, and thrombotic potential

• Accumulation of lipoprotein (LDL) and oxidation

• Adhesion of monocytes (and other leukocytes) to the endothelium, and their migration into the intima and transformation into macrophages & foam cells

• Adhesion of platelets (adhesions of platelets)

↓
formation of the thrombus.
↓
release into
for adhesions of platelets.

Pathogenesis: The response to injury hypothesis

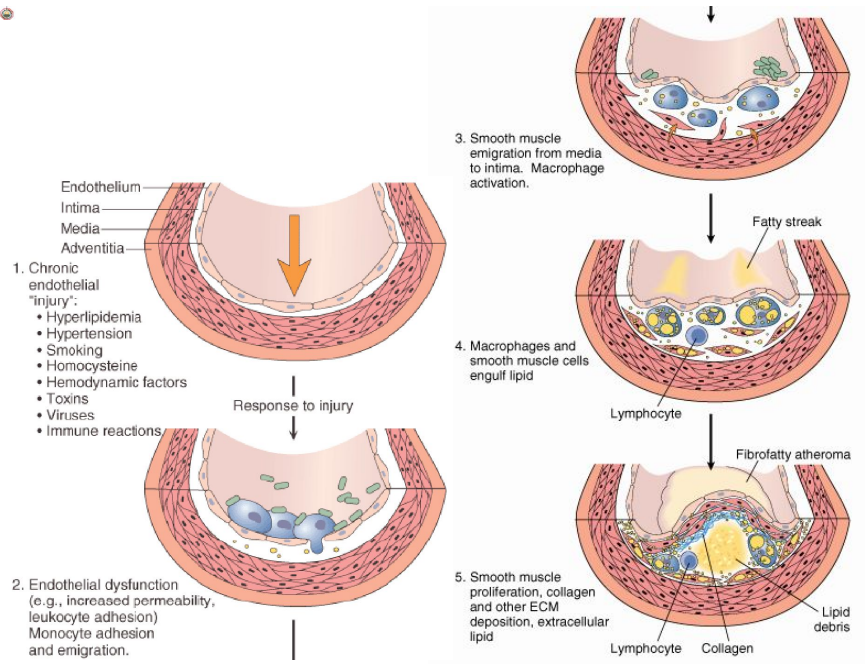
3. **Emigration of SMCs** from media into the intima, due to factors released from activated platelets, macrophages, or vascular cells

4. **Accumulation of lipids** both within cells (engagement to the lipid). (macrophages and SMCs) and extracellularly

5. **Proliferation of SMCs** in the intima, and elaboration of extracellular matrix, leading to accumulation of collagen and proteoglycans.

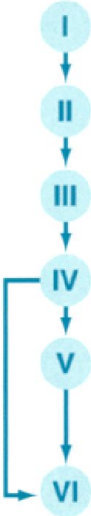
↓
for lipid.
↓
for foam cells

20

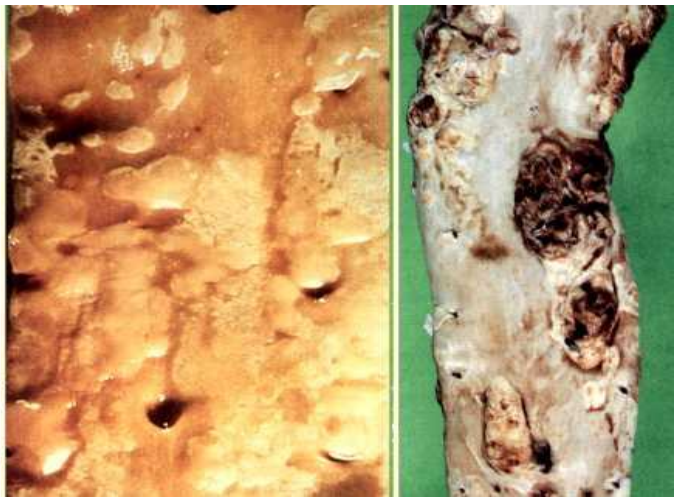


المرحلة 6 مراحل

American Heart Association classification of atherosclerotic lesions

Nomenclature and main histology	Sequences in progression	Main growth mechanism	Earliest onset	Clinical correlation	
Type I (initial) lesion Isolated macrophage foam cells		Growth mainly by lipid accumulation	From first decade	Clinically silent	
Type II (fatty streak) lesion Mainly intracellular lipid accumulation			From third decade		
Type III (intermediate) lesion Type II changes and small extracellular lipid pools				Accelerated smooth muscle and collagen increase	From fourth decade
Type IV (atheroma) lesion Type II changes and core of extracellular lipid			Thrombosis, hematoma		
Type V (fibroatheroma) lesion Lipid core and fibrotic layer, or multiple lipid cores and fibrotic layers, or mainly calcific, or mainly fibrotic					
Type VI (complicated) lesion Surface defect, hematoma-hemorrhage, thrombus					

Morphologic types:



Fibroatheroma Plaques
V

Complicated
VI

كيفية تعديل
modifiable
Risk factor

Prevention of **ATH**

Primary prevention: change in life style

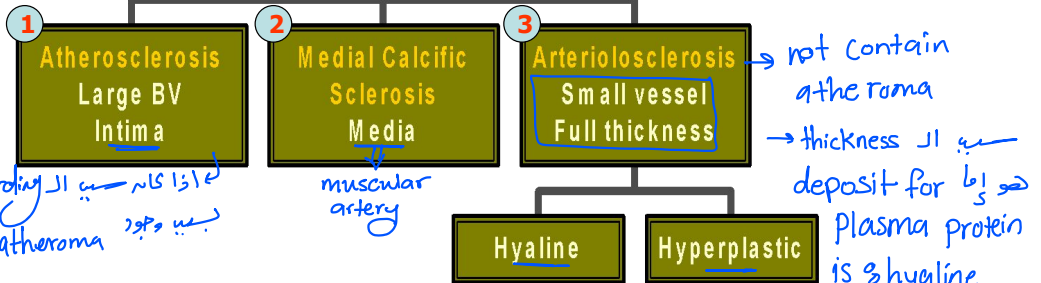
- cessation of cigarette smoking
- control of hypertension
- weight reduction
- increased exercise
- lowering total & LDL cholesterol while increasing HDL

Secondary prevention: to prevent recurrence

- use of lipid-lowering drugs (statins)
- * use of anti-platelet drugs

تعديل Modification على الـ
نوعه وكمية الـ statins و
antiplatelet drugs

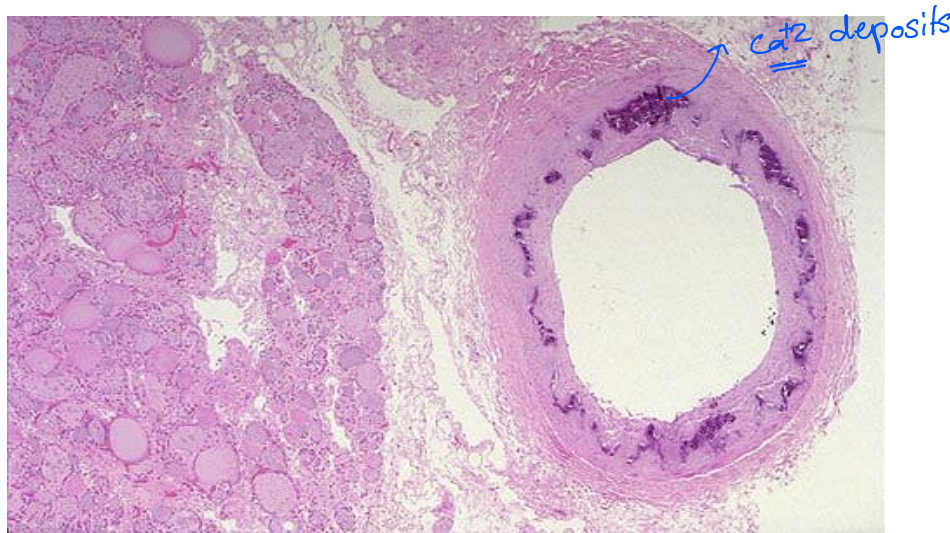
Arteriosclerosis Hardening



Arteriosclerosis "hardening of the arteries": thickening and loss of elasticity of arterial walls

Handwritten notes: increase of the number muscle fibers of layer in the Tunica media. hyaline arteriolosclerosis :: hyperplastic arteriolosclerosis

Mönckeberg medial calcific sclerosis



27

Mönckeberg medial calcific sclerosis

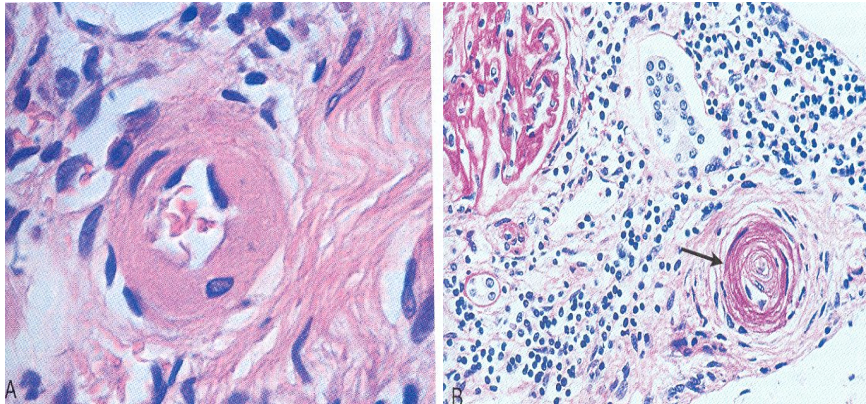
- Calcific deposits (ring-like) in muscular arteries
- Calcifications are **radiographically visible** *B.V. اذا علنا X-ray بنشوف the calcification in wall*
- Calcific deposits are **palpable** *لانه بيكون اذا كانوا على superficial Blood vessels*
- Occurs **after 50 years** of age
- do not invade the vessel lumen or narrow it** *ازله هـ asymptomatic*
- Affects mostly femoral, tibial, radial, ulnar, coronary, and genital arteries *and genital arterieres*

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Arteriolosclerosis (**Hyaline**)

- Pink homogenous thickening of the arterioles**
- Associated with **narrowing of the lumen**
- Occurs in elderly people
- Occurs more in **benign hypertensive & diabetic patients**
- leakage of plasma components across vascular endothelium
- increase production of extracellular matrix by SMCs
- most common in benign nephrosclerosis** *(secondary for hypertension)*
- Renal sclerosis:** arteriolar narrowing causes diffuse renal

28



**Hyaline
Arteriosclerosis**

Hyperplastic → عادة ما
Cancer
بـ hyperplasia
↑ number of muscle layer.
29

Arteriosclerosis (Hyperplastic)

- Related to more acute or **severe elevation of BP (diastolic >120 mm of Hg)** (malignant hypertension)
- Has onion-skin, concentric, laminated thickening of the walls of arterioles with progressive narrowing of the lumen
- The lamination consists of **proliferation of SMC** cells in the vessel walls and reduplication of the basement membranes.
- In malignant hypertension**, associated with **fibrinoid deposits** and **acute necrosis** of the vessel wall, which is referred to as **necrotizing arteriolitis**

30

Hyperplastic Arteriosclerosis:



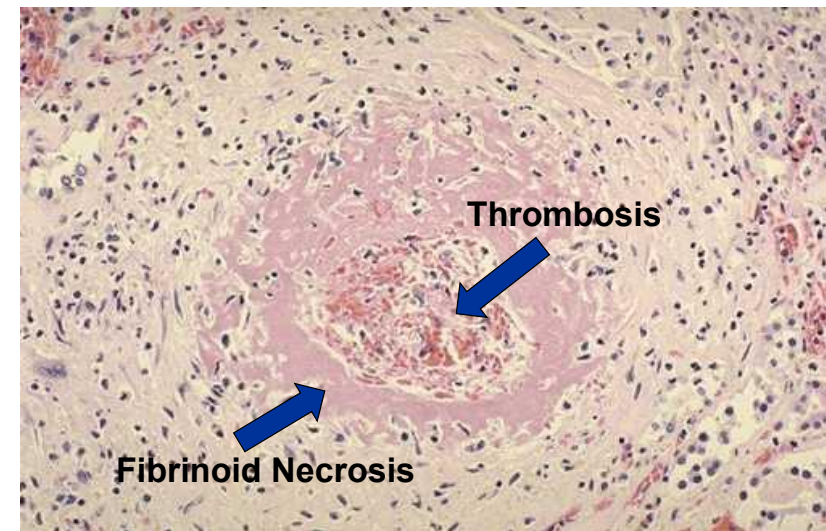
Narrow Lumen

Onion Skin Thickening Of arterioles.

may result → ischemia in the Blood flow.

31

Necrotizing arteriolitis:



Thrombosis

Fibrinoid Necrosis

32

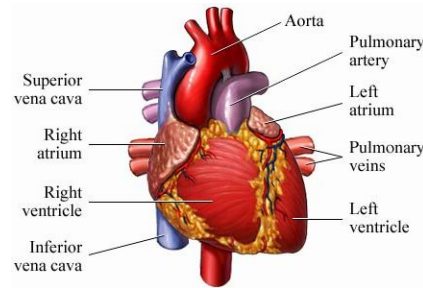
muscle layer
ischemia Blood supply
arteriol = بـ
may result → ischemia in the Blood flow.
ischemia in Wall B.V it self.

injury ال thrombus formation

← غير ال ischemia الي حصر في organ الي هنا ال
arteriol مفرقة =

* necrosis in the B.V wall = Fibrinoid necrosis.

Cardiovascular System



Lecture V: IHD

Dr. Marwan Qubaja
Al-Quds University
Faculty of Medicine
Pathology Department



IHD: Epidemiology

• Peak incidence:

- Above 60 for men
- Above 70 for women

⊗ عند عمر 80 سنة
بشكل فرصة لها
Female = male
تبيّن لـ

• Risk factors:

- HTN
- DM
- Smoking
- High levels of LDL
- Genetic factors

⊗ كل IHDs لها نفس الـ
atherosclerosis لـ R.F
→ very important for IHDs

- ⊗ obesity
- ⊗ low activity

Ischemic Heart Disease (IHD)

- **Definition:** imbalance between myocardial oxygen demand and the blood supply
- also termed **coronary heart disease**
- Most common cause of death in the Western world
- **Four syndromes may develop:** with IHD

– Angina pectoris (chest pain)

– Unstable Angina

– Acute MI

– Sudden cardiac death

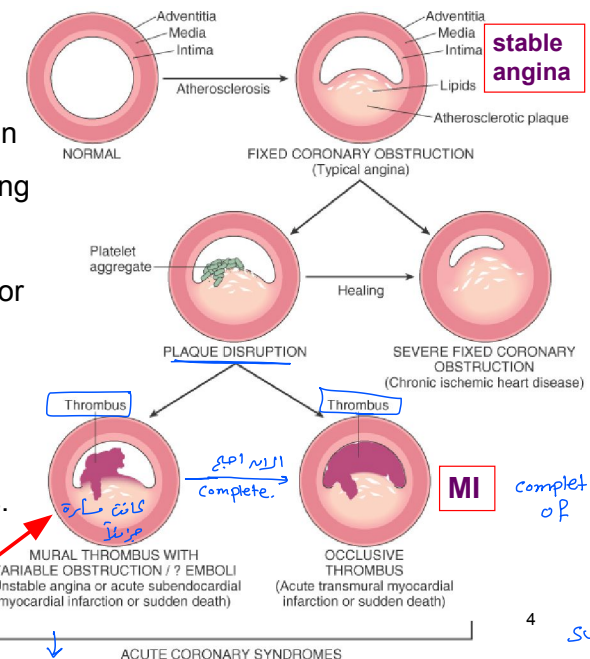
– Chronic ischemic heart disease with CHF

acute
coronary
syndromes

because they result
why? From abnormality change
in the coronary
B.V
التي سوف تؤدي إلى هذه
disease or disorder

Progressive ← congestive heart failure
left ventricular heart
Failure secondary to myocardial infarction

Sequential
progression of
coronary artery lesion
morphology, beginning
with stable chronic
plaque responsible for
typical angina and
leading to
the various acute
coronary syndromes.



Partial obstruction in lumen
is secondary for thrombus
, atherosclerosis.

complete obstruction
of the lumen
↓
MI
↓
sudden cardiac death.

IHD: Pathogenesis

- Most Common
 - Atherosclerosis:** with $\geq 75\%$ reduction in the lumen of one or more major coronary arteries

1. Acute plaque changes:

- Fissuring, hemorrhage, rupture with embolization

2. Coronary artery thrombosis:

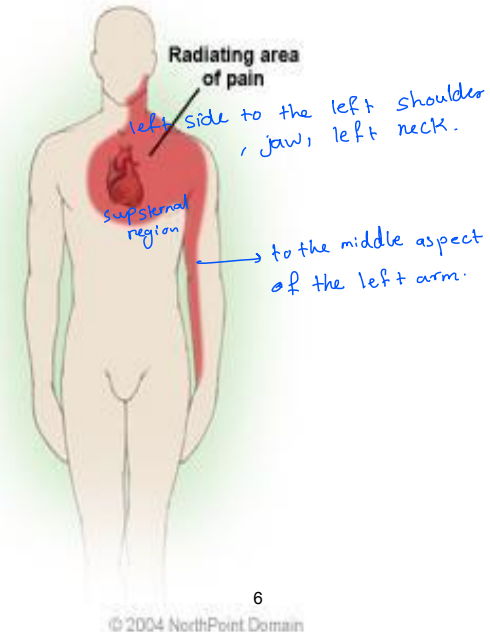
- Thrombus may occlude the vessel fully or partially.

3. Coronary artery vasospasm:

- unclear mechanism
- Emboli** originating from vegetations
 - infective endocarditis
- Coronary vasculitis**
 - inflammation in B.V with involvement the coronary B.V
- Severe systemic hypotension**
 - generalized ischemia and hypo perfusion in tissue

قد تؤدي إلى IHD in younger age. (4 year)

5



6

* pericarditis $\Rightarrow$ atypical chest pain

Angina Pectoris $\Rightarrow$ secondary for Ischemia.

- Definition:** intermittent chest pain caused by transient, reversible myocardial ischemia.

Three major types:

- Typical (stable) angina
- Prinzmetal (variant) angina
- Unstable angina

7

Typical (stable) angina $\rightarrow$ substernal chest pain

- Chest pain is associated with stress or exertion
- Associated with $\geq 75\%$ atherosclerotic narrowing of coronaries
- Pain is substernal crushing or squeezing, or heaviness or tightness $\Rightarrow$ rock in my chest
- Pain may radiate down the left arm.

The pain is usually relieved by:

- Rest** (reducing demand)
- Nitroglycerin** (vasodilation)

* حكايتها transient بين ال stable angina معظم اللاتة طاباخذ 5 دقائق ال attack تاتعيا له فانه يوصل ل 15 min stable angina تاتعيا لانه لايم هذا النوع exertions أو stress

معظم الحالات بتخفف ال attack ببر الهوى مثلاً لمانعة معينة خاصة اذا كان فيها طاباخذ أو انه لم يوصل ال درج

Unstable (crescendo) angina ⇒ very severe.

- increased frequency, duration & intensity of anginal pain
(الفرق بين 4) ^{مفهوم الثلاثة} ^{مصابا بذلك} ^{myocardial infarction (irreversible) ↓ angina}
- attacks tend to occur by less and less exertion, and at rest
at rest ^{مع الأعراض} ^{unstable angina عليه وهو في حالة}
- more serious, referred to as **pre-infarction angina** ^{لأنه مرضه الـ stable}
^{لأنه المرضي تاع الـ} ^{لأنه ضالك بعض المرفه مع الـ infarction وبنفس الوقت مع الـ [unstable angina]}
- induced by **acute plaque change** with partial thrombosis, distal embolization of the thrombus, and/or vasospasm. ^{induced by} ^{acute plaque change} ^{with partial thrombosis,} ^{distal embolization of the thrombus,} ^{and/or vasospasm.} ^{Pain بـ}

unstable & stable ^{الفرق بين الـ}

① severity and intensity of the chest pain -

② more frequent for pain

③ ^{لو المرضي تاع الـ stable يتبعه الـ attack خلاه الـ 24 ساعة 5 مرات}

④ ^{المرضي الي معه unstable يتبعه الـ attack خلاه الـ 24 ساعة من 10 الى 15 مرة}

⑤ most causes the pain continuous for 4-5 min in stable angina.

⑥ ^{في اصلياً توصل الـ 15 min} ^{but, unstable angina most causes is 15 min - 20 min.}

Myocardial Infarction (MI)

"heart attack"

- Definition:** the development of an area of myocardial

(coagulative) ^{the cardiac muscle sensation in the blood supply & oxygen upto 3 min → after duration the cardiac muscle will undergo infarction & die.} ^{لأنه حكي انه unstable اسمها الـ Pre-infarction angina} ^{man > women خاصة في عمر 45-54} ^{the risk becomes the same in both sexes after 80 years} ^{The major risk factors for acute MI are the same as those for} ^{atherosclerosis}

- Most common cause of death in industrialized countries
- Among fatal cases, half die before reaching the hospital

Between ages of 45-54 men are at 4-5 times risk as women

The risk becomes the same in both sexes after 80 years

The major risk factors for acute MI are the same as those for

atherosclerosis

dead part of the cardiac muscle replace by fibrous tissue.

Function of the heart ^{و يؤدي الى} ^{complication}

⑦ Following cell death (necrosis or infarction) ⇒ there are a release creatin cellular content ⇒ that can you detect in the Blood & they can consider is marker irreversible cell injury.

Prinzmetal (variant) angina ⇒ sudden onset in pain.

↳ secondary for vasospasm. in coronary blood vessels.

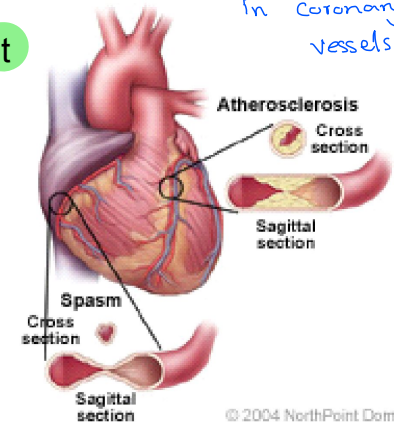
- refers to pain that occur at rest or may awaken patient from sleep

- associated with coronary spasm

- mechanism of spasms is not clear

- respond to vasodilators

⑧ duration is a middle portion between stable & unstable angina



MI: Clinical Features

- severe, crushing substernal chest pain
- may radiate to the neck, jaw, epigastrium, shoulder, or left arm

in 50% of patients: MI is preceded by episodes of angina pectoris (from any type angina).

the pain typically lasts several hours to days (vary long). minimum duration = 20 min

pain is not significantly relieved by nitroglycerin. ^{لأنه استمر الـ pain مع 20 دقيقة وأكثر يعني انه MI}

pulse is rapid and weak

associated symptoms: sweating, dyspnea

“Silent” MI: In (20% to 30%) patients with MI:

- diabetes mellitus ^{لأنه في بعض المرضى ما يكون عنده} ^{MI وهاذا اسمه}
- hypertension ^(silent MI)
- elderly patients. ^{لأنه اذا كان المريض مع diabetes or hypertension.}

death in myocardial muscle. (function: Vaso dilator)

MI: Pathogenesis

- Most common cause is **coronary artery**

occlusion:

- thrombosis due to atherosclerosis → most common
- vasospasm and platelet aggregation
- stenosing coronary atherosclerosis → Complete Obstruction in lumen

MI: Pathogenesis

- Myocardial necrosis **begins within 20-30 min** of coronary artery occlusion.

Blood supply في more distal area
لأنها تقع على
وبالتالي أي نقص في الدم إليها أقل درجة ستأثر.

- MI typically **begins in the subendocardial region**

- The zone of necrosis "wavefront" extends externally to involve the mid- & subepicardial areas of the myocardium.

- The infarct reaches its **full size within 3-6 hrs (transmural infarction)** → more dangerous

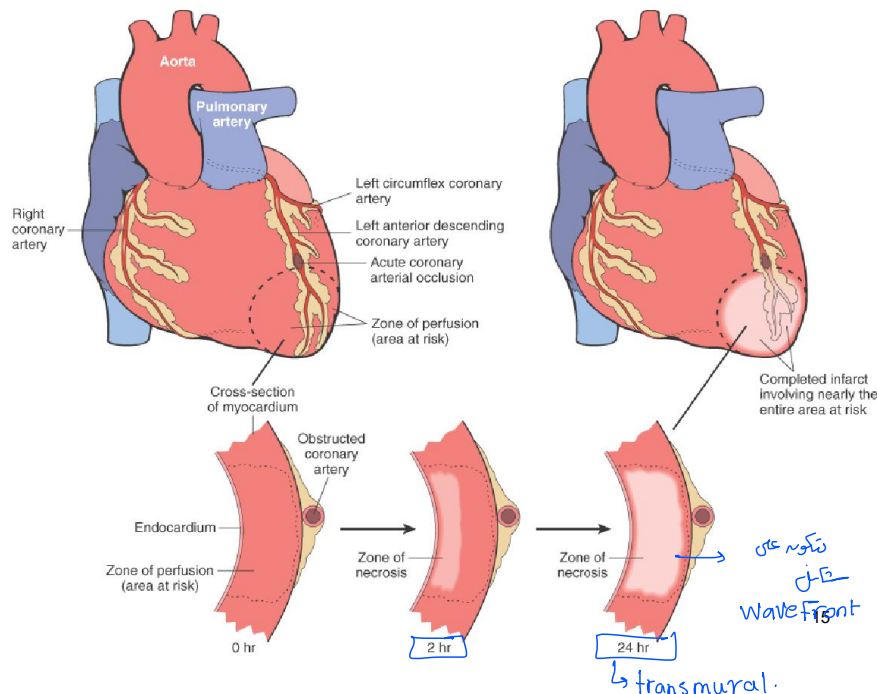
لأنها إذا ما شخنا جراحيا وظل obstruction سوف يكون full thickness in myocardium
كذلك obstruction اسمها أو necrosis

- Lysis of the thrombus by the administration of thrombolytic agents (e.g., streptokinase or tissue plasminogen activator)

may limit the size of the infarct (**nontransmural infarction**)

- * Size and the location of infarction ⇒ in myocardium → myoCardium
① site of the atheromus and occlusion is formed in Proximal part of Coronary B.V → large area MI
but, Formed in adistal part of Coronary B.V → small area MI
many factor على size
من علامات MI region of the Coronary died, necrosis (تفريغ المنطقة التي تفريغها)

Complete obstruction في الشريان
مثل حصى في مجرى الدم
تقلل تدفق الدم
لذلك يحدث infarction
(nontransmural infarction).

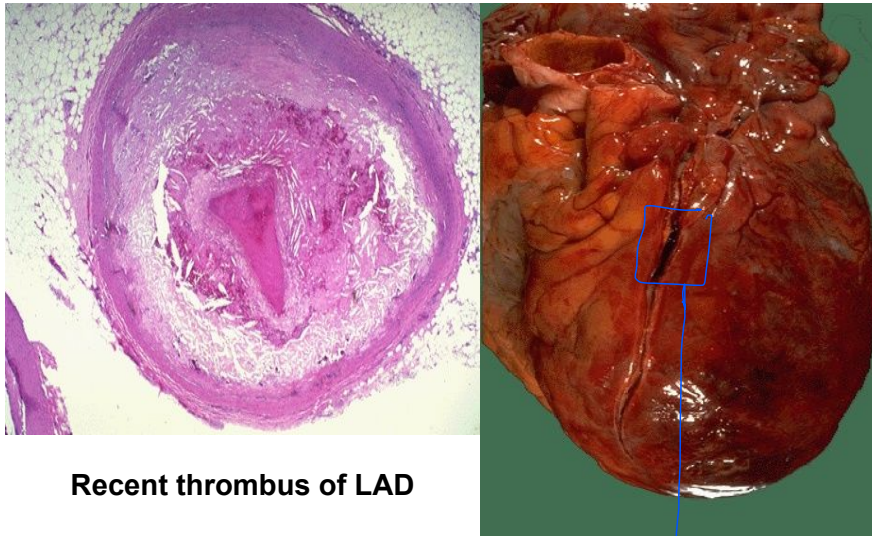


MI: Location

Coronary artery affected	Heart area affected
Left anterior descending coronary artery (LAD) (40% to 50%)	① Anterior and apical left ventricle; anterior two thirds of the interventricular septum ② له هي الامامية التي سوف يكون فيها necrosis او الوبائيات ant. descend.
Right coronary artery (RCA) (30% to 40%)	Posterior wall of the left ventricle; posterior one third of the interventricular septum (in persons with right-dominant coronary circulation)
Left circumflex coronary artery (15% to 20%)	Lateral wall of left ventricle (may also involve the posterior wall in persons with left-dominant coronary circulation) 16

المنطقة التي حدث فيها
infarction سوف
enlargement يكون

* المنطقة التي يكون فيها necrosis يكون affected ب coronary artery



Recent thrombus of LAD

Thrombus in coronary artery.

17

Sequence of changes in MI

Time	Gross	Light Microscope
0-30 min	No change	No change
1-2 hr	No change	Few "wavy" fibers at margin of infarct
4-12 hr	No change	Early coagulation necrosis; edema; occasional neutrophils; minimal hemorrhage
18-24 hr	Slight pallor or mottling	Continuing coagulation necrosis (nuclear pyknosis and disintegration; cytoplasmic eosinophilia); "contraction band" necrosis at periphery of infarct; neutrophilic infiltrate
24-72 hr	Pallor	Complete coagulation necrosis of myofibers; heavy neutrophilic infiltrate with early fragmentation of neutrophil nuclei
4-7 days	Central pallor with hyperemic border	Macrophages appear; early disintegration and phagocytosis of necrotic fibers; granulation tissue visible at edge of infarct
10 days	Maximally yellow, soft, shrunken; purple border	Well-developed phagocytosis; prominent granulation tissue in peripheral areas of infarct
7-8 wk	Firm, gray	Fibrosis

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* When the cell injury and tissues injury irreversible (lethal) usually we will detect before we can see morphological changes

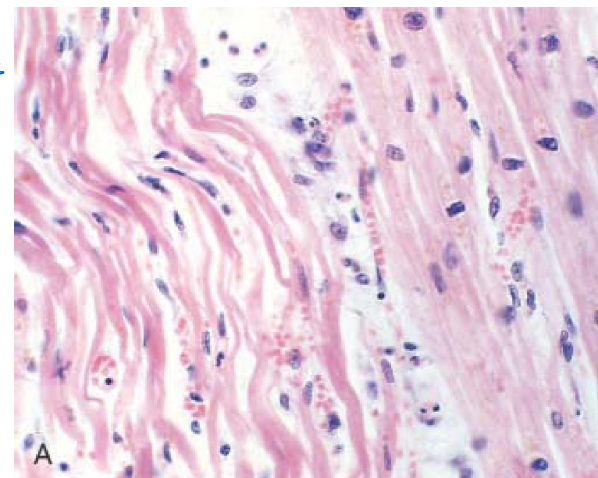
MI: Size

- Occlusion of more proximal segments produces **larger infarcts**, involving the full thickness of the myocardium (**transmural infarcts**)
- MI restricted to the inner one third of the myocardium are called **subendocardial infarcts** ⇒ Blood supply لا يها امد نقطة عبر ال ischemia اذا صار منو منطقة سوف تتأثر حتى
- Thrombi in more distal branches tend to cause **smaller infarcts**
- Size is influenced by the **degree of collateral circulation** that exists at the time of the occlusion.
- In patients with long-standing coronary atherosclerosis, **collateral vessels** may develop over time and may limit the **size of the infarct**.

slow & gradual occlusion in the blood vessels

may development collateral vessels.

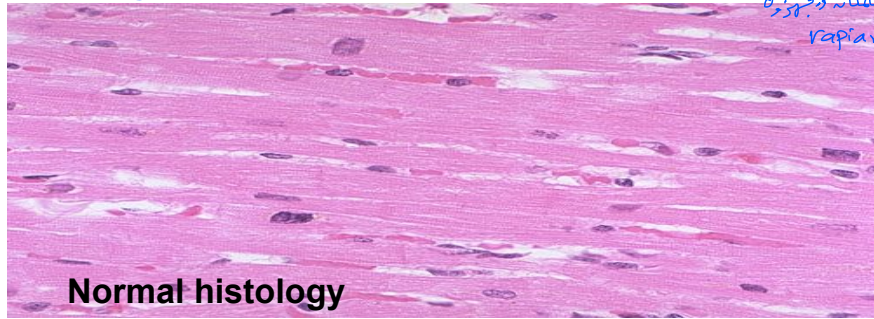
One-day-old infarct showing coagulative necrosis along with **wavy fibers** (elongated and narrow), compared with adjacent normal fibers (at right). Widened spaces between the dead fibers contain edema fluid and scattered neutrophils.



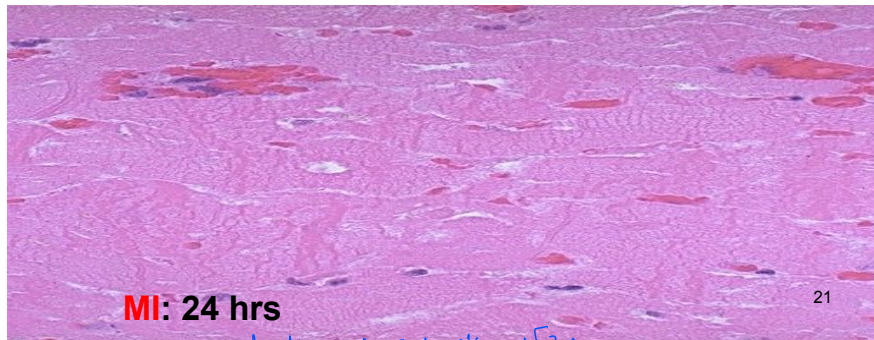
صاروا منتفخة عن بعضهم البعض

20

- * acute inflammation → polymorph nucleolar lymphocytes.
- * chronic inflammation → macrophage & monocyte → تنظيم النسيج و إصلاحه rapidly



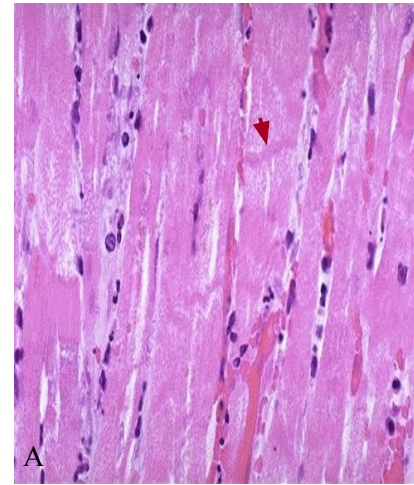
Normal histology



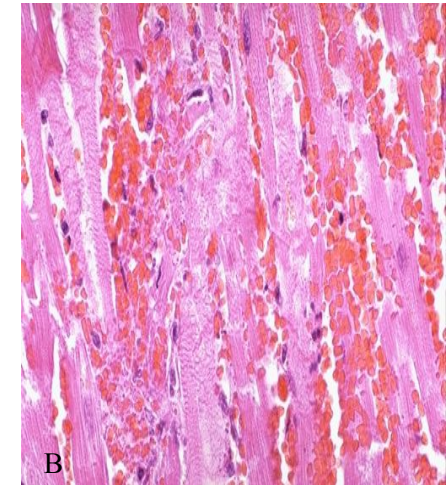
MI: 24 hrs

21

- * intercalated disc ⇒ contraction bands



A

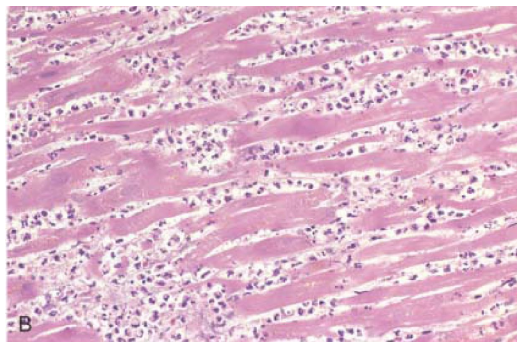


B

MI **1-2 days** contraction bands, loss of nuclei, beginning of inflammation. In B we also see hemorrhage

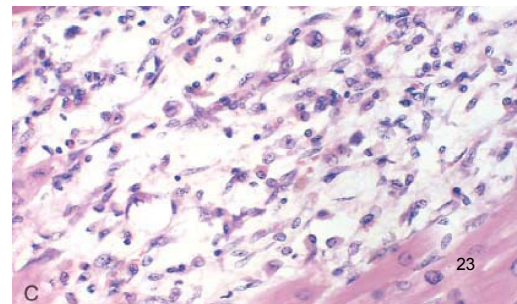
22

3 to 4 days: Heavy polymorphonuclear infiltrate in area of acute MI



B

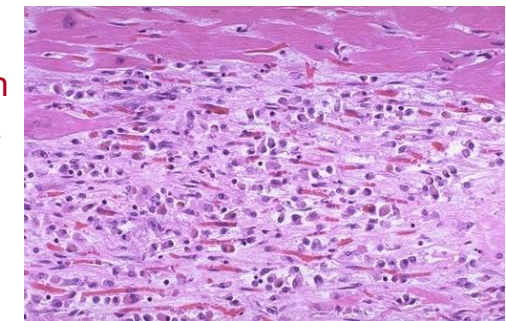
7 to 10 days: Nearly complete removal of necrotic myocytes by phagocytosis



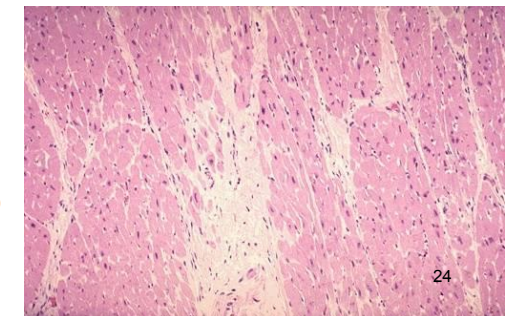
C

23

1-2 weeks: Granulation tissue characterized by loose collagen and abundant capillaries



7-8 weeks: Well-healed MI with replacement of the necrotic fibers by white pale collagen fibrosis

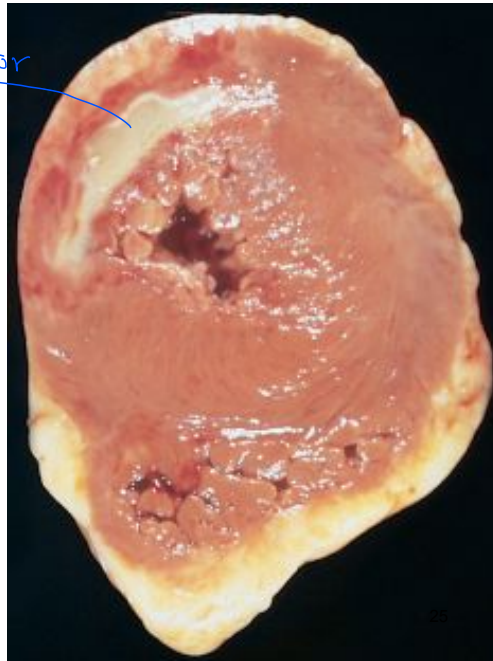


24

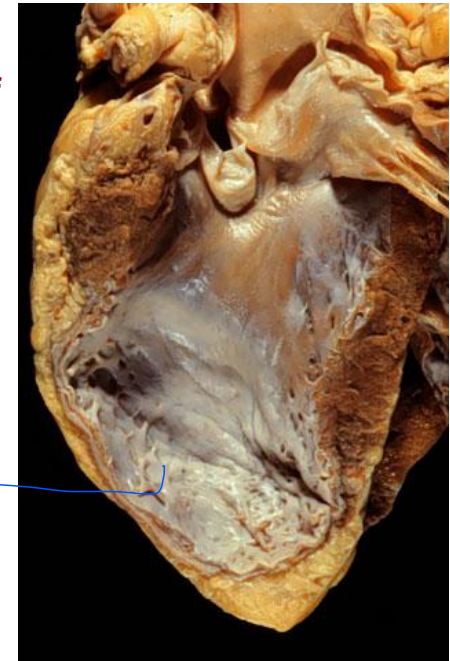
من نرى ان normal myocyte متحلل

وظيفة القلب الطبيعية رابطة في هذا سرور في إلى complications خطيرة

Acute MI, 4 to 7 days
in the posterolateral
region of LV.



The white appearance of
the endocardial surface
indicates the extensive
scarring of LV.



MI: Complications

- most dangerous
- **Sudden cardiac death** from arrhythmia in 25% of patients before hospitalization
↳ death patient after sever chest pain
↳ sudden death without symptoms.

• Of hospitalized patients:

- 10 - 20% experience no complications.
- 80 - 90% develop one or more of the following:

- **Cardiac arrhythmias** (75 to 95%) → most common
- **Left ventricular failure** with **pulmonary edema** (60%)
↳ edema و pulmonary hypertension و قلة الـ circulation
- **Cardiogenic shock** (10%): when > 40% of LV involved
↳ complication

- **Rupture** of free wall, septum, or papillary muscle (4 to 8%) ⇒ ↑ size of infarct
⇒ ↑ complication.
- **Thromboembolism** (15 to 49%)
↳ thrombus formation

27

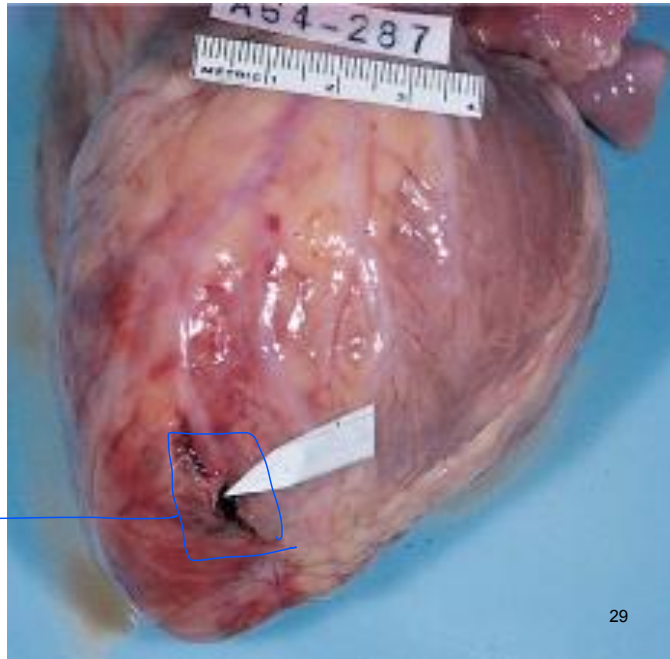
Other Complications:

- **Acute pericarditis** occurs in up to 15% of patients with MI within 2 to 4 days after MI
- **Pericardial effusion**
- **Cardiac tamponade** (sever haemopericarditis)
- **Ventricular aneurysm** ⇒ abnormal dilatation in ventricle
- **Re-infarction** ⇒ infarction in other zones or larger zone in myocardium

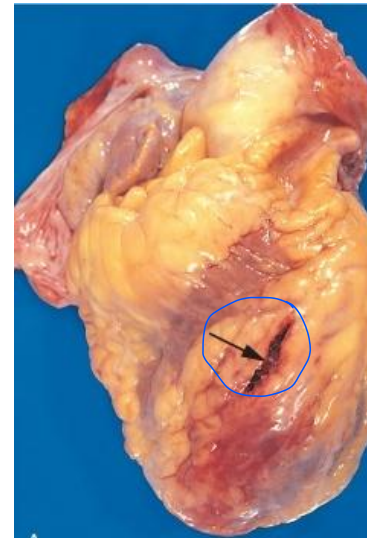
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Myocardial rupture 6 days after a MI

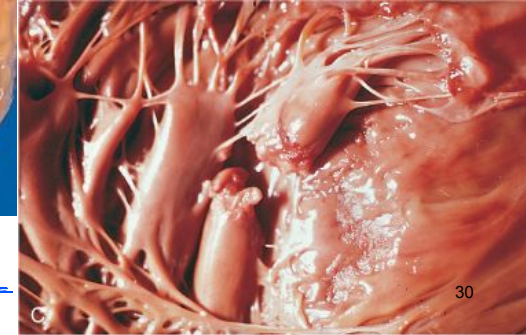
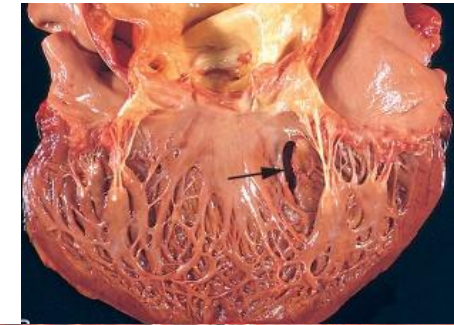
Free border ←
after 6 days.
→ rupture



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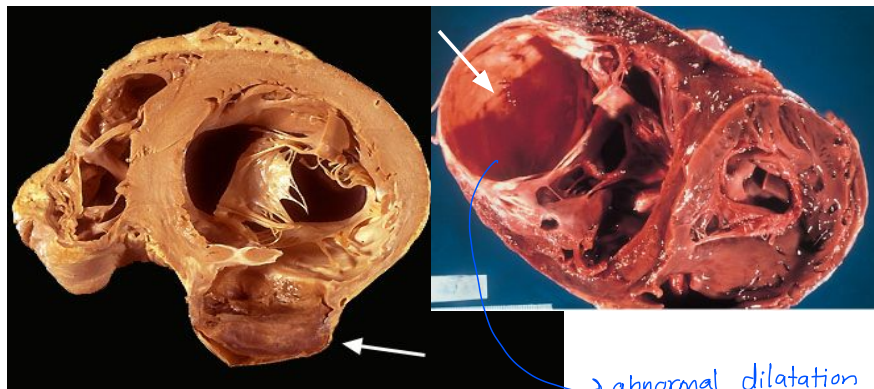


Papillary muscle rupture is most common about 3 days after MI



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rupture in papillary muscle.
بعد 3 أيام من MI



→ abnormal dilatation
of the ventricle wall

Ventricular aneurysms:

- late complication of large transmural MI
- most common in the **anteroapical region** of the heart
- A mural thrombus is often present
- may cause congestive heart failure & recurrent arrhythmias
- Surgical resection is beneficial in some cases.

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MI: Diagnosis

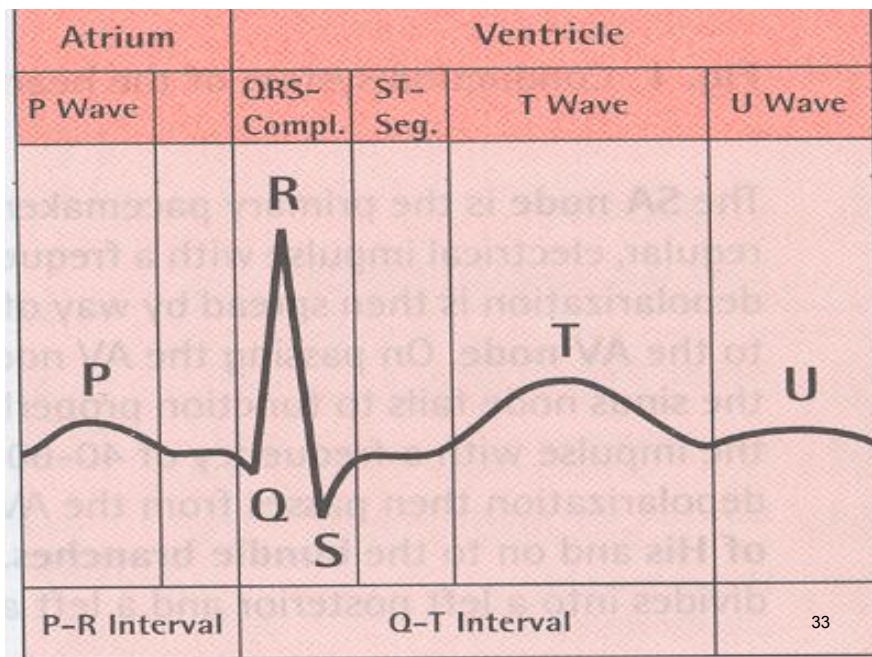
- According to WHO any two of these: 2 criteria.

- 1) classical history of ischemia **>20 min**
- 2) ECG changes on serial tracing
- 3) cardiac enzymes changes

- ECG changes:

- Q wave
- ST segment elevation
- T wave inversion
- Persistent **ST segment** elevation may indicate **ventricular aneurysm**

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MI: cardiac enzymes

- Total CK activity begins to rise within 2 to 4 hours of an MI, peaks at 24 hours, and returns to normal within approximately 72 hours.
- Total CK** activity is **not specific**, because CK is also elevated in other conditions, such as skeletal muscle injury.
- The specificity for the detection of MI is enhanced by measurement of the **CK-MB** fraction.
- CK-MB rises within 2 to 4 hours of the onset of an MI, peaks at 18 hours, and usually **disappears by 48 hours**.

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MI: cardiac enzymes

- Fraction العريضة
- Creatine kinase (CK):** ⇒ cells damage ⇒ irreversible marker for cell injury.
 - CK-MM: skeletal muscle and heart
 - CK-BB: brain, lung, and other tissues
 - CK-MB:** mainly from myocardium, but small amount comes from skeletal muscle (most sensitive for myocardium injury). *specific in CK*
 - Cardiac Troponin:**
 - Troponin-I (TnI):** with high specificity and sensitivity for cardiac muscle
 - Troponin-T (TnT):** found in other tissues in addition to its presence in cardiac muscle
 - Lactate dehydrogenase (LDH), Myoglobin**
- most common fraction the in detect the present myocyte injury.
- باني الانزيمات
تلك تكون
ارتفاع لا سيما
آخرها غير
myocardial
in fraction
- 34

MI: Diagnosis

- Troponins are a group of proteins found in both human skeletal and cardiac muscle.
- They regulate **calcium-mediated contraction** of muscles.
- Cardiac **troponin I** is found only in heart muscle and is thus more specific than **CK-MB**
- Troponin levels remain elevated for **4 to 7 days** after the **acute event**

⊗ بقتل مرتفعة مدة 4 و 7 ايام.

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MI: Diagnosis

• Myoglobin:

- Protein found in **skeletal** and cardiac muscle which binds **oxygen**.
- It is a very sensitive indicator of muscle injury.
- A negative myoglobin can help to rule out myocardial infarction.
- It is elevated even before **CK-MB**.
- It is not specific for cardiac muscle, and can be elevated with any form of injury to skeletal muscle.

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Biomarker	Time to Initial Evaluation	Time to Peak Evaluation	Time to Return to Normal
CK-MB	2-4 hrs	18-24 hrs	±72 hrs
Myoglobin	2-6 hrs	8-10 hrs	24 hrs
LDH	10-12 hrs	48-72 hrs	7-10 days
Troponin-I	4-6 hrs	12 hrs	3-10 days
Troponin-T	4-8 hrs	12-48 hrs	7-10 days

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Conditions Associated with Increased Biomarker Levels

CK-MB	AMI, LV hypertrophy, renal failure, HTN, skeletal muscle injury, hypothyroidism
Myoglobin	AMI, skeletal muscle injury, decreased renal function
LDH	AMI, cardiac injury, renal failure, leukemia
Troponin-I	AMI, cardiac injury, CHF, unstable angina, myocarditis
Troponin-T	AMI, musculoskeletal disease, renal disease, polymyositis

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Chronic Ischemic Heart Disease → Secondary for sudden death.

- Also called **ischemic cardiomyopathy**
- **Definition:** development of **progressive congestive heart failure** as a consequence of long-term ischemic myocardial injury
or secondary
- **Morphology:**
 - coronary arteries show moderate to severe atherosclerosis
 - the heart is enlarged because of hypertrophy
 - dilation of all cardiac chambers
 - myocardial **fibrosis** (transmural **scarring**)
Fibrosis is the scar tissue that forms in the heart after a heart attack. It can lead to heart failure.
 - both atrophic and hypertrophic fibers are present
loss of function
 - **Myocytolysis** (vacuolated cells) is common
heart failure
- **Clinical Features:** progressive heart failure, arrhythmias

ischemic cardiomyopathy

CARDIAC CAUSES OF SUDDEN DEATH

Coronary Artery Diseases

- Coronary atherosclerosis
- Developmental abnormalities
- Coronary artery embolism
- Other (vasculitis, dissection)

Sudden cardiac death

Unexpected death from

cardiac causes usually

within one hour after a

cardiac event or without

the onset of symptoms.

symptom
asymptom.

Myocardial Diseases

- Cardiomyopathies
- Myocarditis
- Right ventricular dysplasia

Valvular Diseases

- Mitral valve prolapse
- Aortic stenosis and other forms of left ventricular outflow obstruction
- Endocarditis

Conduction System Abnormalities