Ischemic heart diseases (IHD:(Group of syndromes caused by an imbalance between the myocardial demand & the blood supply. All these diseases are due to narrowing of coronary artery by atherosclerosis.

-1 Age: IHD mainly after the age of 60 years in men, &after 70 years in women.
-2 Sex: male are more affected by disease than female.
-3 Atherosclerosis. In more than 90% of cases, IHD is a consequence of reduced coronary blood flow secondary to obstructive atherosclerotic vascular disease. %75reduction in the lumen of coronary artery (critical stenosis) will result in clinical symptoms.

HEART FAILURE

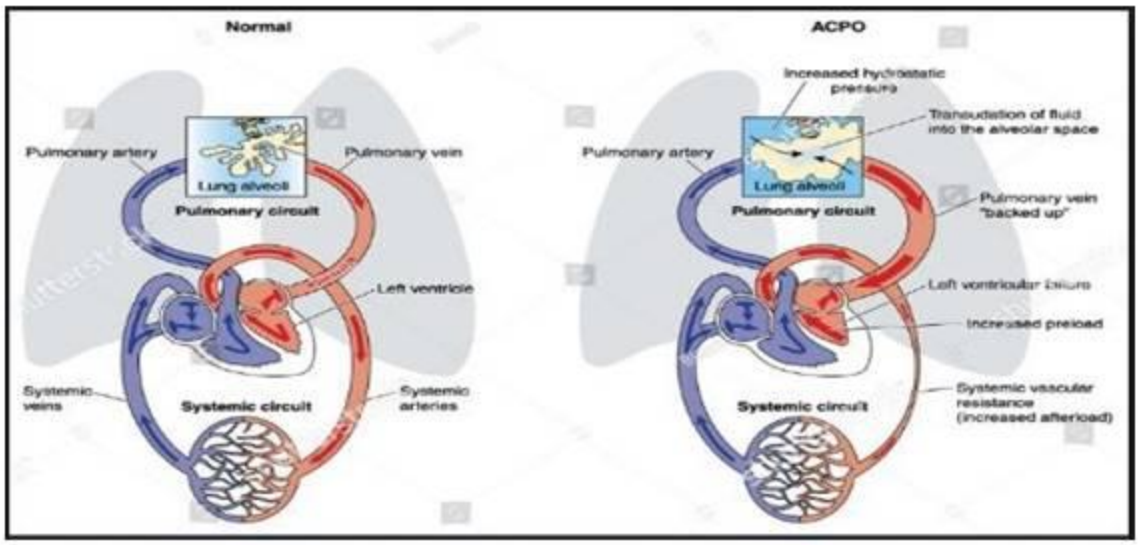
Occurs when the heart is unable to provide adequate perfusion to meet the metabolic demands of peripheral tissues; inadequate cardiac output usually is accompanied by congestion of the venous circulation.

A. causes of left sided heart failure:

.1 Systemic hypertension
.2 Mitral or aortic valve disease .
.3 Ischemic heart disease.
.4 Primary diseases of myocardium.
.5 Congenital heart diseases.

- **Left-sided heart failure:**

i. **Primary Left-sided heart failure of the myocardium;** symptoms are mainly a consequence of pulmonary congestion and edema, although systemic hypo perfusion can cause renal and cerebral dysfunction.
ii. **Secondary Left-sided heart failure** is most commonly to ischemic heart disease, systemic hypertension, mitral or aortic valve disease.



B.Causes Right sided heart failure*:*

.1 The mast common cause of right sided is the left sided heart failure.

.2 Right sided failure can occur in absence of left sided failure, in condition which is called Cor pulmonale (means right sided failure due to intrinsic diseases of the lung parenchyma & or pulmonary vasculature.(

.3 Pulmonic valve disease.

.4 Sometimes in congenital heart diseases.

Angina pectoris:

is referred to intermittent chest pain caused by transient reversible myocardial failure

There are three variants of angina pectoris:

-1 **Typical or stable angina pectoris:** It occurs suddenly and gets worse over time. It may eventually lead to a heart attack. Though stable angina is less serious than unstable angina, it can be painful and uncomfortable."Typical" angina, by contrast, is often triggered by physical exertion or emotional stress.

2- **Prinzmetal's variant angina (PVA**): is characterized by recurrent episodes of chest pain (angina) that usually occur when a person is at rest, between midnight and early morning.

-3 **Unstable angina pectoris:** sometimes referred to as acute coronary syndrome causes unexpected chest pain, and usually occurs while resting. The most common cause is reduced blood flow to the heart muscle because the coronary arteries are narrowed by fatty buildups (atherosclerosis) which can rupture causing injury to the coronary blood vessel resulting in blood clotting which blocks the flow of blood to the heart muscle. Unstable angina should be treated as an emergency,& increased risk for severe cardiac arrhythmias or cardiac arrest, which could lead to sudden death.

The difference between stable and unstable angina, unstable angina doesn't follow a pattern. It may occur more often and be more severe than stable angina. Unstable angina also can occur with or without physical exertion, and rest or medicine may not relieve the pain

Myocardial infarction:

Is referred to develop of an area of myocardial necrosis caused by local ischemia.

Etiology: Most cases of M.I acute are due coronary arteries thrombosis

important notes:

- ✓ Myocardial necrosis begin within 20-30 minutes of coronary occlusion & the first area of myocardium liable for necrosis is subendocardial areas.
- ✓ Frequency of occlusion of coronary arteries: Left anterior descending coronary artery %40to (50%

Types of MI according to thickness of infracted area:

-1Transmural infarcts are referred to involvement of most thickness of myocardium by infarction.

-2Subendocardial infarction are referred to involvement of inner myocardium third of Myocardium.

Complications of M.I:

.1Ventricula rupture
.2Papillary muscle (rupture(
.3Aneurysm formation.
.4Mural thrombus.
.5Arrhythmia
.6Pericarditis
.7Heart Failure

Laboratory tests M.I:

-1the creatine kinase CK is an enzyme that is highly concentrated in brain, heart, (CK-MB mainly from myocardium.(

-2Troponins are a group of proteins found in both human & cardiac muscles. (troponin T, & troponin I(

- ✓ Troponin I is more specific than CK enzyme, because it only present in the heart.

Rheumatic Fever & heart disease:

Rheumatic fever is an acute immunologically mediated multisystem inflammatory disease, that follows an episode of Group A streptococcal pharyngitis after an interval of a weeks

Pathogenesis of RHEUMATIC FEVER: cute rheumatic fever is hypersensitivity reaction & autoimmune disease induced by Group A, Beta hemolytic streptococci. By formation of autoantibodies against the M protein of Group A, Beta hemolytic streptococci that cross react with normal tissue proteins present in the heart, joints& tissues.

Morphology of RHEUMATIC FEEVER:

Acute Rheumatic fever infection: is characterized by discrete inflammatory foci within a variety of tissues involves wide range of organs which (synovium, joints, skin, & the most important site which is the Heart).

Acute Rheumatic Carditis characterized by:

1- Pancarditis: means of inflammation of 3 layers of heart

2- Aschoff bodies this is hallmark of acute rheumatic disease, which is present in connective tissue of the heart. **Aschoff bodies consist of:**

A. Central area of fibrinoid necrosis

B. Mononuclear inflammatory cells surrounding the area of necrosis.

C. Sometimes there are macrophages vasicular nuclei, called Anitschkow cells

Chronic Rheumatic Disease: Characterized by deformity of one or more of cardiac valves, resulting from previous attack of acute rheumatic disease 70% of chronic rheumatic disease affected mitral valve, 25% combined aortic & mitral Valves, the tricuspid valve is less frequently involved; and the pulmonic valve almost always escapes injury.

Clinical features of rheumatic fever:

1- occur after 10 days to 6 weeks after an episode of (Lag Pharyngitis with group A, Beta hemolytic streptococci(leg period)

2- Peak age is between 5-15 years (school age)

3- There are important laboratory tests which are ASOT titer antistreptolysin O), & DNAase B, these tests in diagnosis & follow up of patient with Rheumatic fever.

Infective Endocarditis IEA

Infective endocarditis (IE) is a microbial infection of the heart valves or the mural endocardium that leads to the formation of vegetations composed of thrombotic debris and organisms, often associated with destruction of the underlying cardiac tissues. The aorta, aneurysmal sacs, other blood vessels, and prosthetic devices also may become infected. Although fungi, rickettsiae (agents of Q fever), and chlamydial species can cause endocarditis, the vast majority of cases are caused by extracellular bacteria. **Traditionally divided into:**

.1Acute Endocarditis:	**subacute Endocarditis**
Due to high virulence organisms Staphylococci	Due to low virulence organisms like alpha –hemolytic streptococci
Even involve: normal Rapidly heart valve.	Affect the abnormal valves.
Rapidly progressive infection.	Slowly progressive infection.
little immune reaction of host (depressed immunity(	High immune reaction of host local inflammation & granulation tissue

Morphology of I.E: The hallmark of I.E is the

1- Presence of valvular vegetations containing bacteria.

2- Aortic valve & Mitral valves are the commonest sites of I.E

Laboratory tests:

✓ **Repeated blood cultures:**

- **Is important in evaluation of patient with I.E. :Culture for both aerobic& anaerobic organisms**
- **Sometimes negative cultures, because of either fastidious nature of organisms, or the effects of previous antibiotic treatment.**

Respiratory system disorder

Chronic obstructive pulmonary diseases

-1 Emphysema
-2 Chronic bronchitis
-3 Asthma
-4 Bronchiectasis

❖ **Emphysema:** It is an abnormal permanent enlargement of the air spaces distal to the terminal bronchiole with destruction of their wall accompanied by destruction of their walls without significant fibrosis.

Pathogenesis: The current theory favors emphysema arising as a consequence of two coexisting critical imbalances

1- Protease-antiprotease imbalance.
2- Oxidants & Antioxidant imbalance.

❖ Normally protease is secreted by neutrophils; Proteases are (enzymes which digest the tissue).

❖ Anti- proteases: are the counteracting enzyme action of digestion, important one is antielastase (**Alpha-1 antitrypsin**), which is normally present in serum, tissue fluids, & macrophages.

So the development of emphysema occurs:

1. When there is elastase activity as in smoking
2. When there is anti-elastase activity as in:

❖ Hereditary alpha-1 antitrypsin deficiency.
❖ Acquired as in smokers due to the effect of nicotine, O2 free radicals that inhibit the release of anti-elastase.

❖ **Chronic bronchitis**

it is characterized by (cough +sputum) production for at least 3 months in at least 2 consecutive years.

Complications:

1. It may end up with cor-pulmonale.

2. It causes atypical metaplasia &dysplasia.

Pathogenesis: Two Important things should be present:

1- Chronic irritation which may interfere with the ciliary action of the respiratory epithelium e.g smoking.
2- Microbial infection: which is usually secondary and responsible for maintaining the condition.

These two factors will initiate the earliest which are:

1- Hyper secretion of mucous in the large airways (trachea & bronchus) due to Hypertrophy of mucous gland .
2- Marked in goblet cells of airways (small bronchi and bronchioles).

Smoking → irritation → stimulate mucous secretion → sputum overproduction.

Bronchial asthma

Is characterized by reversible bronchoconstriction caused by airway hyperresponsiveness to a variety of stimuli and a chronic relapsing inflammatory disorder characterized by hyper-reactive airways that causes recurrent episodes of wheezing, breathlessness, chest tightness, and cough, particularly at night and/or early in the morning. The hallmarks of asthma are intermittent, reversible airway obstruction; chronic bronchial inflammation with eosinophils; bronchial smooth muscle cell hypertrophy and hyperreactivity; and increased mucus secretion.

Pathogenesis

- Eosinophils are key inflammatory cells found in almost all subtypes of asthma; eosinophil products)such as major basic protein) are responsible for airwaydamage.
- Airway remodeling (sub-basement membrane thickening and hypertrophy of bronchial glands and smooth muscle) adds an irreversible component to the obstructive disease.

Major factors contributing to the development of asthma include genetic predisposition to type I hypersensitivity (atopy), acute and chronic airway inflammation, and bronchial hyperresponsiveness to a variety of stimuli.

Type of asthma according the causes of it:

Atopic asthma most often is caused by a TH2 and IgE-mediated immunologic reaction to environmental allergens and is characterized by early-phase (immediate) and late-phase reactions. The TH2 cytokines IL-4 IL-5 and IL-13 are important mediators.Non-TH2 inflammation also has roles in atopic asthma.

• Triggers for nonatopic asthma are less clear but include viral infections and inhaled air pollutants, which also can trigger atopic asthma.

.1Extrinsic asthma	.2Intrinsic asthma
Is the type most common type	Less common than extrinsic type
Initiated by type I reaction hypersensitivity	Initiated by non immune mechanism.
Caused by exposure to external allergens)dust, pollens, food.(	aspirin ingestion, pulmonary infection stress, exercise.
It starts at childhood.	Starts at adulthood.
Associated with Atopy (genetic tendency.(	Not associated with Atopy
+ve family history.	-ve family history
Serum IgE levels are usually elevated	Serum Levels are normal

❖ Bronchiectasis:

is chronic necrotizing infection of the bronchi and bronchioles leading to or associated abnormal dilatation of permanent with these airways.

Clinically:

Cough+ fever (when a powerful microorganism present) + copious foul smell+ purulent sputum.

Pathogenesis: Two important factors should be present

1. Obstruction.
2. Infection

So either the condition starts with:

A.Bronchial obstruction ➡ atelectasis ➡ bronchial wall inflammation + accumulated bronchial secretion ➡ dilatation, which is irreversible If:

- The obstruction persist
- There is a superadded infection.

B. It starts with bronchial infection ➡bronchial wall inflammation & weakening ➡ further dilatation.

Grossly:

- Affects the lower lobes bilaterally.
- The affected airways are dilated & may take the shape of tube (cylindroid bronchiectasis). Others may show fusiform.
- The dilatation produce cystic pattern on cut surface.

❖ Pneumonia (pulmonary infection(

Any infection in the lung. It can be caused by: Viral, bacterial, fungal and mycoplasma infection.

Community-Acquired Bacterial Pneumonias:

Bacterial pneumonias often follow a viral upper-respiratory tract infection. **Streptococcus pneumoniae** (i.e., the pneumococcus) is the most common cause Bacterial infection; bacterial invasion of the lung parenchyma will cause an exudative solidification (consolidation) of the lung tissue.

Pathogenesis:

Normal lung is FREE from bacteria due to the presence of defense mechanisms:

.1Nasal clearance: by sneezing, & blowing mucous secretion.
.2Tracheobronchial Clearance: by mucociliary action in which the foreign particles by swallowed or expectorated
.3Lymphatic alveolar clearance: by the alveolar macrophages ➡lymphatic circulation.

Pneumonia results whenever these defense mechanisms are impaired or host resistance get lowered (chronic diseases, deficiency immune, leucopenia.(

Two types of pneumonia

-1bronchopneumonia:

i. Caused by staphylococcus، streptococcus، pneumococcus, hemophilus influenza.
ii. The consolidation is patchy.
iii. occur in infancy and old age groups caused by low resistance
iv. Can complicate long term heart failure

-2Lobar pneumonia:

i. %95-90are caused by pneumococci.
ii. Others are klebsiella pneumonia staphylococcus, strept., Haemophilus influenzae
iii. The consolidation involves a portion of a lobe or the whole lobe.

Morphology of lobar pneumonia: There are four stages of evolvement of lobar pneumonia, they are:

.1Stage of congestion: the lung is heavy, boggy, and red. It is characterized by vascular engorgement، intra alveolar fluid with few neutrophils.

.2Stage of red hepatization: is characterized by massive confluent exudation, as neutrophils, red cells, and fibrin fill the alveolar spaces.

.3Stage of grey hepatization: is marked by progressive disintegration of red cells and the persistence of a fibrinosuppurative exudate.

.4Stage of resolution: the exudate within the alveolar spaces is broken down by enzymatic digestion to produce granular, semifluid debris that is resorbed, organized by fibroblasts growing into it.

Complication:

%90of cases will end up with resolution, otherwise complication includes:

- Abscess formation, specially if the m.o is klebsiella and pneumococcal infection.
- Spread of infection to the pleural cavity ➡ empyema (pus inside the pleural cavity).
- Organization of the exudate ➡ part of the lobe will turn solid
- Bacteremic dissemination to heart valves, brain, pericardium, kidney.

❖ Cystic fibrosis:(CF)

Is an autosomal recessive genetic disorder manifested by chronic lung disease، pancreatic exocrine deficiency, and elevation of sodium chloride in the sweat. The disorder is caused by a mutation of chromosome 7 that codes for the CFTR (protein called the cystic fibrosis transmembrane conductance regulator(which functions in the transepithelial transport of the chloride ion. The defect causes exocrine gland secretions to become exceedingly viscid, and it promotes colonization of the respiratory tract with **Pseudomonas aeruginosa** and other organisms such as *Staphylococcus aureus*. Accumulation of viscid mucus in the bronchi, impaired mucociliary function, and infection contribute to the development of chronic lung disease and a decreased life expectancy.

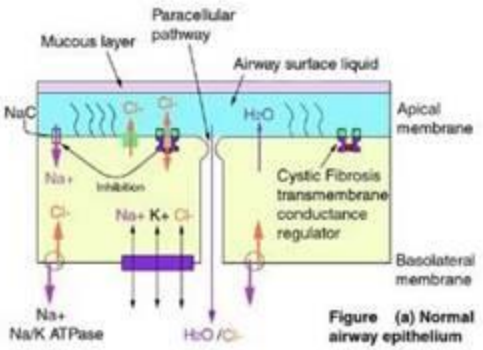


Figure (a) Normal airway epithelium

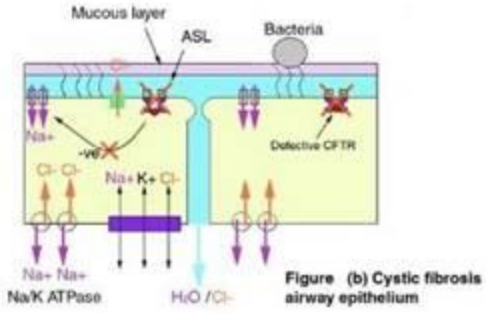


Figure (b) Cystic fibrosis airway epithelium

Pulmonary symptoms of CF: cough، productive of large amounts of tenacious and purulent sputum.

Repeated infectious bronchitis and bronchopneumonia become progressively more frequent, and eventually, shortness of breath develops. Respiratory failure cardiac complications of pulmonary hypertension)cor-pulmonale) are late sequelae.

Fig. (a) and (b) In CF, impairment of CFTR function causes reduced fluid production. Enhanced sodium absorption through epithelial Na+ channels (ENaC) and basolateral Na/K ATPase pumps results in increased fluid absorption leading to drier airways and impaired ciliary clearance.