

RESPIREATORY DISEASES

ASTHMA

- Definition

Asthma is : a chronic inflammatory disorder of the airways which leads to recurrent episodes of airway obstruction, characterized by:

1. Wheezing.
2. Breathlessness
3. chest tightness
4. cough that often is worse at night and in the early morning.
5. Many cells and cellular elements play a role, in particular, mast cells, eosinophil, T lymphocytes, and epithelial cells .
6. These episodes, which usually are reversible either spontaneously or with treatment

- Classification

Asthma can be divided into:

1. **Extrinsic** - implying a definite external cause
2. **Intrinsic or cryptogenic** - when no causative agent can be identified.

- **Extrinsic asthma** : (early onset asthma)

- a. Occurs most frequently in the first two decades of life
- b. Commonly associated with other allergic diseases (eczema is) in the patient and in other family members .
- c. There is elevated blood eosinophil count .
- d. It is episodic and tends to improves in many patients .
- e. Have elevated circulating antibody (IgE) in their serum

- **Intrinsic asthma: (late onset asthma).**

a. Often starts in middle age .

b. Usually no allergic or family history and no demonstrable skin sensitivities .

c. Normal or nearly normal blood eosinophil count

d. Aggravating factors includes aspirin , pulmonary infections , cold, exercise .

e. Have normal circulating antibody (IgE) in their serum

- **Precipitating factors**

1.Cold air : The inhalation of cold, dry air will precipitate an attack

2. Exercise : Exercise-induced asthma occurs in 40% to 90% of persons with bronchial asthma. It has been suggested that during exercise, bronchospasm may be caused by the loss of heat and water from the tracheobronchial tree because of the need for conditioning (i.e., warming and humidification) of large volumes of air. Most asthmatics wheeze after prolonged exercise. the attack does not occur during exercising but after that.

3. Atmospheric pollution and irritant dusts, and fumes

1. cigarette smoke,
2. car exhaust fumes,
3. strong perfumes
4. high concentrations of dust in the atmosphere.

4. Diet: Increased intakes of fresh fruit and vegetables have been shown to be protective possibly owing to the increased intake of antioxidants.

5.Drugs

Non-steroid anti-inflammatory drugs (NSAIDs) particularly aspirin and propionic acid derivatives, e.g. indomethacin, have a major role in the development and precipitation of attacks in approximately 5% of patients with asthma.

Respiratory tract infections,

especially those caused by viruses, may produce their effects by causing epithelial damage and stimulating the production of IgE antibodies directed toward the viral antigens

..6

Pneumonia

Definition : its an inflammation of lung tissue.

Pneumonias caused by infectious agents commonly are classified according to the source of infection into :

1. Community-acquired pneumonia
2. Hospital-acquired pneumonia

Community-acquired pneumonia : results from organisms found .1 in the community

Common causes of community-acquired pneumonia

:A. Bacterial causes

1. The most common pathogen is **Streptococcus pneumonia** and usually the patients is previously healthy
2. Legionella → Institutional outbreaks (hospitals and hotels)
3. Haemophilus influenza → Pre-existing lung disease
4. Staphylococcus aureus → Children, intravenous drug abusers, associated with influenza virus infections
5. Mycobacterium tuberculosis → tuberculous pneumonia
6. Chlamydia → Contact with birds

B. Viral causes :

- **Influenza A virus** → is the **most common cause of** viral pneumonia.
- **Less common causes** are parainfluenza and respiratory syncytial viruses.
- **Other viruses sometimes are implicated**, including the **measles** and **chickenpox viruses**

C. **Chemical causes**, such as in the aspiration of vomit.

D. **Allergic mechanisms** → allergic pneumonia

Streptococcus Pneumoniae

Causes :

- often follows viral infection with influenza or parainfluenza
- Cigarette smoking (the strongest independent risk factor for invasive pneumococcal disease).
- Bronchiectasis (e.g. in cystic fibrosis).
- Bronchial obstruction (e.g. carcinoma)
- Immunosuppression (e.g. AIDS or treatment with cytotoxic agents) - organisms include *Pneumocystis carinii*, , cytomegalovirus.
- Inhalation from oesophageal obstruction - often associated with infection with anaerobes

: Hospital-acquired, or nosocomial, pneumonia .2

is defined as a lower respiratory tract infection that was not present or -
.incubating on admission to the hospital

1. Usually, infections occurring 48 hours or more after admission are considered hospital acquired.
2. Most hospital-acquired pneumonias are bacterial.
3. The organisms are those present in the hospital environment and include
 - a. *Pseudomonas aeruginosa*,
 - b. *S. aureus*,
 - c. *Enterobacter*
 - d. *Klebsiella*
 - e. *Escherichia coli*

The organisms that are responsible for hospital-acquired pneumonias are different from those responsible for community-acquired pneumonia, and many of them have

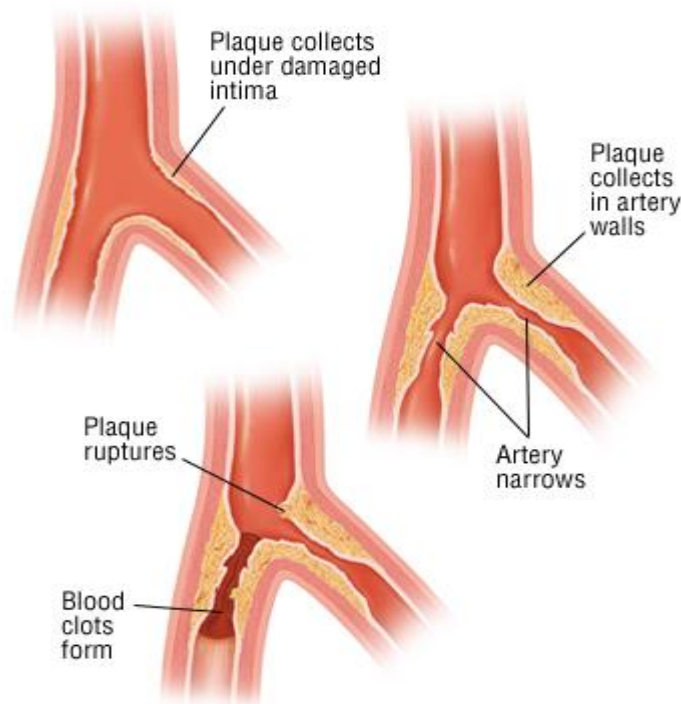
Acquired antibiotic resistance .1

More difficult to treat .2

Atherosclerosis

It means degenerative disease of large and medium sized arteries (but not the vein) characterize by accumulation of lipid rich materials in the inner layer of the arteries and associated with cellular changes leading to wall thickening

The internal plaque is called atheroma which is protruded into the lumen and weakening the underlying layer by a bud of fat leading to narrowing of the arteries caused by a buildup of plaque.



RISK FACTORS FOR ATHEROSCLEROSIS

1- Nonpreventable factors

a- Age: risk increase with age

b- Sex: up to the age of 55y males more than females (2:1) due to the protective effect of estrogen in females. But after the 55y Male = Female

c- Family history: some families with risk factors such as Hypertension, DM and hyperlipidemia

d- Genetic defects in the metabolism of lipid

2- Preventable factors

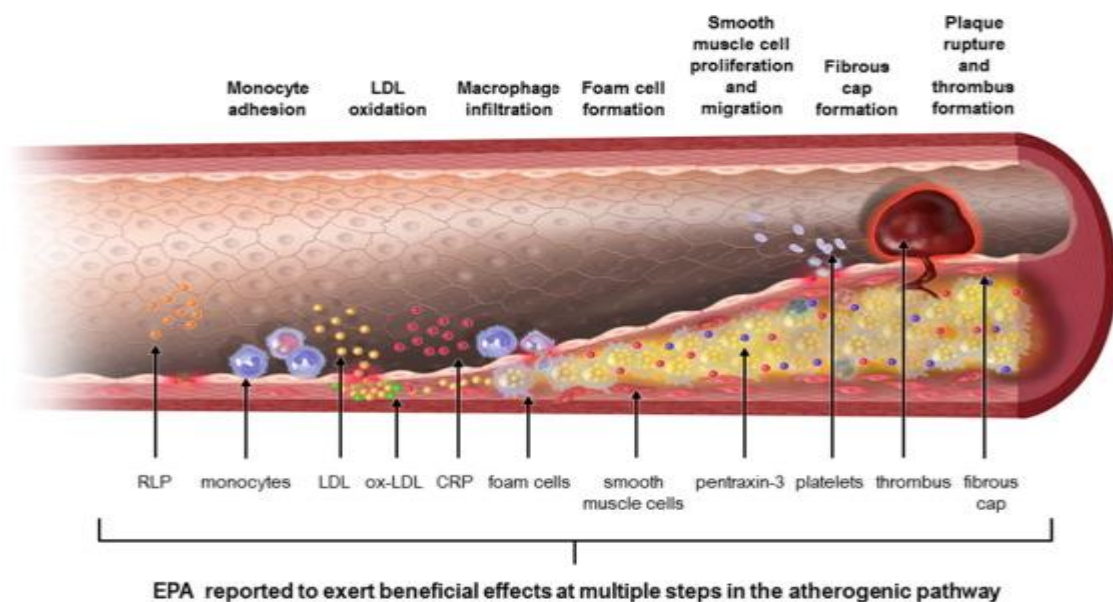
a- Hyperlipidemia (high serum cholesterol) associated with increase IDH especially LDL but HDL decrease the incidences of IHD

b- Hypertension: accelerate atherosclerosis by direct damage to the vessel wall especially after the age of 45y

c- Diabetes mellitus : induce hypercholesterolemia. Myocardial infarction is 2 times more common in diabetics patient

d- obesity

e- Cigarette smoking: more than 20 cigarette per day increase the risk of myocardial infarction



Ischemic Heart Disease(IHD)

Ischemic heart disease (coronary heart disease (CHD) or coronary artery disease):

is defined as inadequate blood and oxygen supply to the heart muscle caused by blockage of (coronary) arteries supplying the local area in the heart .

Ischemia can be caused by :

Reduced coronary blood flow : due to :

a: coronary atherosclerosis

b: vasospasm .

There are four types of ischemic syndrome :

1 : Myocardial infarction:

Ischemia is sufficient to cause death of heart muscle .(complete obstruction)

2 :Angina pectoris :

Ischemia are not sufficient to cause death of heart muscle (partial obstruction)

3: Chronic ischemic heart disease

Is seen typically in elderly patients with moderate to severe multivessel coronary atherosclerosis who gradually developed chronic heart failure .

4 : Sudden cardiac death :

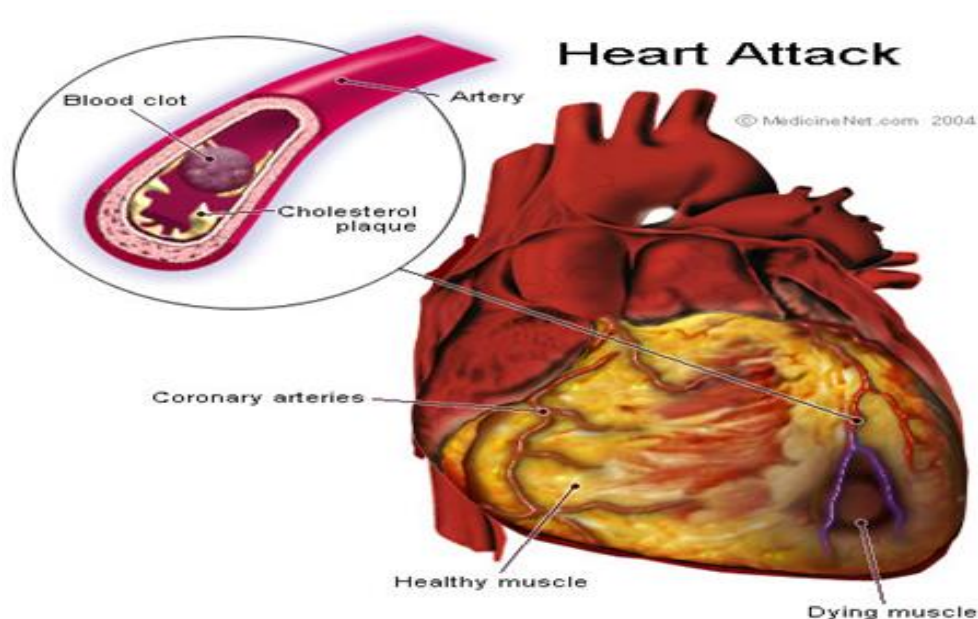
Is defined as unexpected cardiac death within 1 hour of symptom onset .

Acute Myocardial Infarction

Myocardial infarction (MI) is the interruption of blood supply to part of the heart, causing heart cells to die.

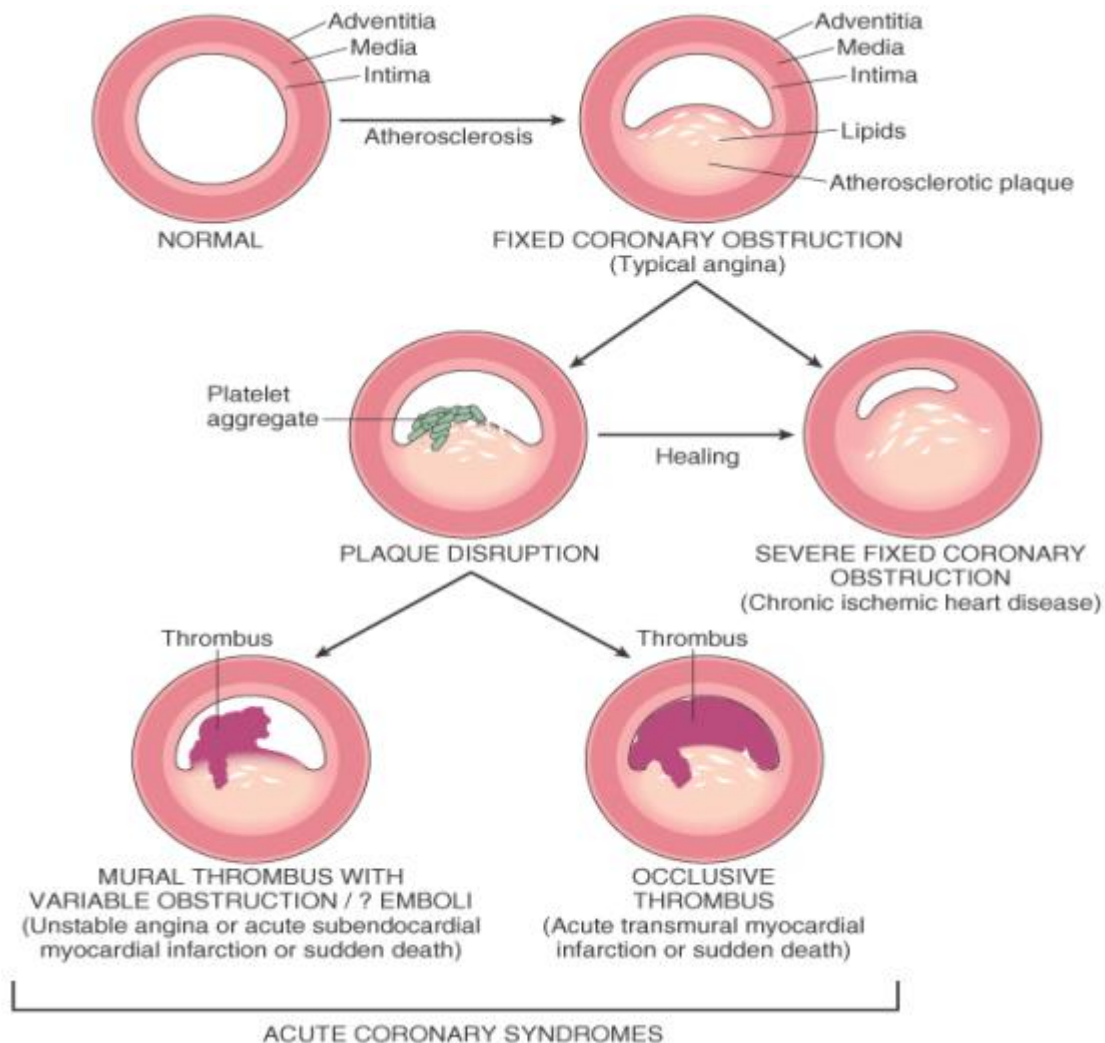
Coronary arteries are blood vessels that supply the heart muscle with blood and oxygen.

If blood flow is not restored to the heart muscle within sufficient time, irreversible death of the heart muscle will begin to occur. Muscle continues to die for six to eight hours at that time the MI usually is "complete." The dead heart muscle is eventually replaced by scar tissue.



Pathophysiology:

Atherosclerotic plaque (collection of lipids + white blood cells (especially macrophages) in the wall of an artery). → ...Rupture .→... Occlusion (blockage) of a coronary artery → ischemia (decrease of blood and oxygen supply) → if left untreated for a sufficient period of time → infarction of heart muscle tissue



Clinical features

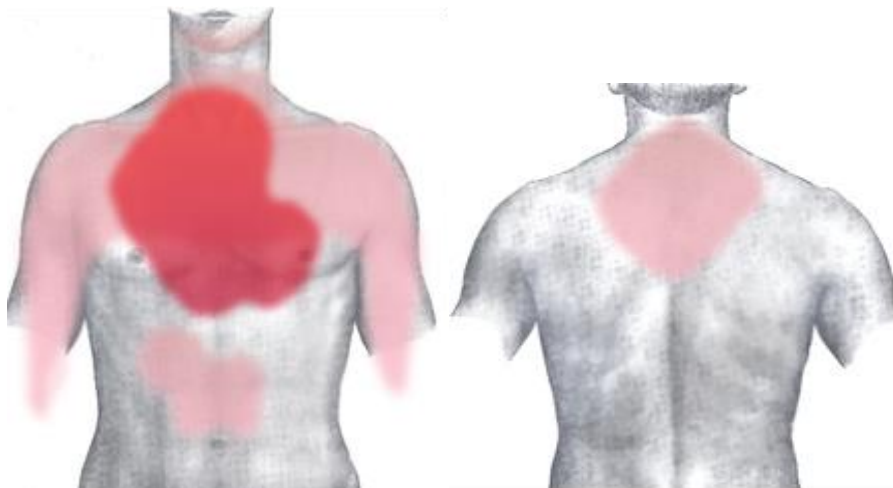
1. The onset of symptoms in (MI) is usually **gradual**, over several minutes .
2. **Chest pain** is the most common symptom and is often described as **a sensation of tightness, pressure, or squeezing, stabbing .**
3. Pain radiates most often to the **left arm, but may also radiate to the lower jaw, neck, right arm, back, and epigastrium,** where it may mimic heartburn.

4. Shortness of breath , excessive sweating , weakness, nausea, vomiting, and palpitations.
5. **Loss of consciousness** (due to inadequate cerebral perfusion and cardiogenic shock)
6. sudden death (frequently due to the development of ventricular fibrillation)

Note: Approximately 25% of all myocardial infarctions are **silent**, without chest pain or other symptoms. These cases can be discovered later on by ECG

A silent course is more common in the

- elderly,
- diabetes mellitus (autonomic neuropathy,)
- after heart transplantation,



Anterior view

Posterior view

Rough diagram of pain zones in myocardial infarction
(dark red = most typical area, light red = other possible)

Complications :

The most common complications of MI are :

1. Arrhythmias – Arrhythmia is the most common complication after an acute MI.

- Ventricular Fibrillation
- A-V block
- sinus bradycardia

2. Embolus formation :

Developed within the first 10 days . stroke is the most common

3. Pericarditis – inflammation developing within the first 1-4 days after MI).

4. Cardiogenic Shock (secondary to acute MI)

Gastrointestinal diseases

Esophagitis

Esophagitis: inflammation of esophagus

Causes of esophagitis

1. Infectious esophagitis

Infectious agents known to cause esophagitis include the following:

a. Fungal infection :

1-. candida species: Candida albicans is the most common cause.

2 -. Non candida fungi (eg, Aspergillus, Histoplasma).

b. **Bacterial species** (eg, Mycobacterium tuberculosis, Staphylococcus, Streptococcus,)

c. Viral infection

- Herpes simplex virus (HSV)
- Cytomegalovirus (CMV)
- Varicella-zoster virus (VZV)
- Epstein-Barr virus (EBV)
- In HIV -infected hosts Mycobacterium avium-intracellulare,
- Human papillomavirus (HPV)
- Poliovirus

d. **Parasitic infections** (eg, Chagas disease , Leishmania donovani)

2. Esophagitis associated with pharmacologic or other therapy

Radiation esophagitis may occur with radiation treatment of cancers located in the chest (lung, esophagus)

3. Metastatic cancer

4. Gastroesophageal reflux disease

Major predisposing factors for Candida esophagitis :

include antibiotic use, radiation therapy or chemotherapy, hematologic malignancies, and AIDS., alcoholism, malnutrition, and advanced age

Peptic ulcer disease **(Duodenal ulcer& gastric ulcer)**

Peptic ulcer : is chronic, solitary (most often), lesion that occur in any portion of GIT exposed to aggressive action of acid juices , there is a break in the superficial epithelial cells penetrating down to the muscular layer.

Gastric ulcers and duodenal ulcers are collectively known as peptic ulcers.

- About 4% of stomach ulcers are caused by a malignant tumor, so multiple biopsies are needed to exclude cancer.
- Duodenal ulcers are generally benign

• Pathogenesis and Causes:

Peptic ulcer are produce by an **imbalance between gastroduodenal mucosal defense mechanism and damaging forces**

1. **H. pylori** : it is gram negative bacillus non spore forming spirochete .
It is colonizes the gastric mucosa particularly the antrum and cardia in a various sites :
 - a. Free in the mucus .
 - b. Surface adhesion
 - c. Intracellular colonization which lead to greatest degree of epithelial damage

H. pylori secretes many substances which lead to epithelial damage :

- a. **Protease and phospholipase** : breakdown glycoprotein and lipid complexes in gastric mucus thus breakdown the first line of mucosal defense .
- b. **Vacuolating toxin -A (Vac A)** → epithelial damage
- c. **Cytotoxin –associated gene A** → attract and activate neutrophil to site of epithelial damage

Infection with **H. pylori** is a major factor in the pathogenesis of peptic ulcer .
It is found in nearly 100 % of patients with DU .
It is found in about 70 % of those with GU

The bacterium can cause a chronic active gastritis, resulting in a defect in the regulation of gastrin hormone production by that part of the stomach,
(Gastrin stimulates the production of gastric acid by parietal cells and, in the presence of H. pylori colonization this will lead to→ increase gastrin production,→ the increase in acid can contribute to the erosion of the mucosa and therefore → ulcer formation)

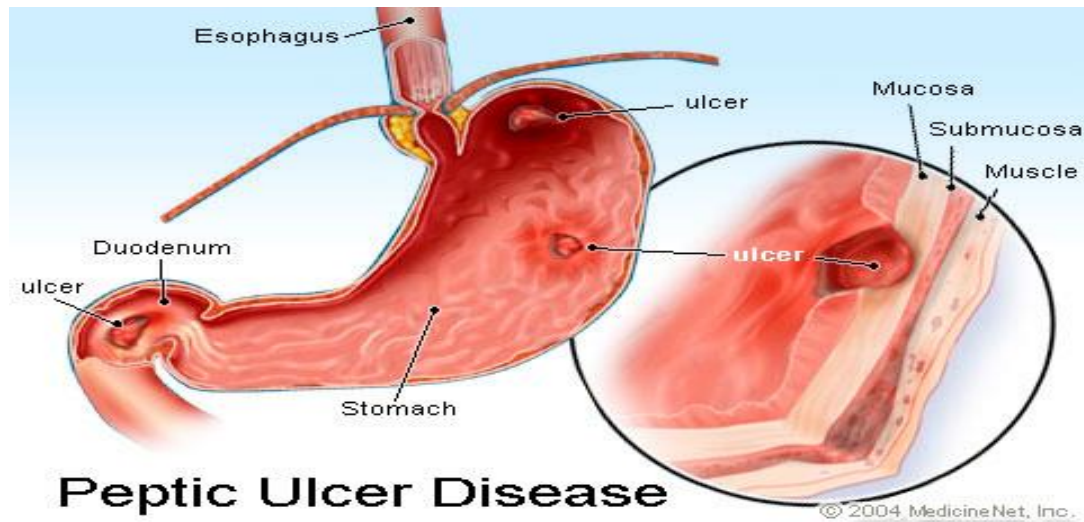
2. Chronic use of NSAIDs(non steroidal anti-inflammatory drugs) NSAIDs are medications for arthritis and other painful inflammatory conditions in the body. Aspirin , naproxen , ibuprofen, indomethacin and diclofinac are a few of the examples of this class of medications . The gastric mucosa protects itself from gastric acid with a layer of mucus and the secretion of mucus is stimulated by certain prostaglandins

Prostaglandins are substances which are important in helping the stomach mucosa to resist corrosive acid damage. NSAIDs cause ulcers by interfering with prostaglandins in the stomach

3. Stress. Researchers also continue to look at stress as a possible cause in the development of ulcers.

Burns , head trauma and stroke,, however, can lead to physiologic stress ulcer

4. Cigarette smoking is also an important cause of ulcer formation and ulcer treatment failure



(There is a break in the superficial epithelial cells penetrating down to the muscular layer)

Appendicitis

Appendicitis : it's an inflammation of appendix

Causes :

acute appendicitis seems to be the end result of a primary obstruction of the appendix lumen (the inside space of a tubular structure). Once this obstruction occurs, the appendix subsequently becomes filled with mucus and swells, increasing pressures within the lumen and the walls of the appendix, resulting in thrombosis and occlusion of the small vessels that supply the appendix. The appendix becomes ischemic and then necrotic with subsequent suppuration. The end result of this events is appendiceal rupture (a 'burst appendix') causing peritonitis, which may lead to septicemia and eventually death.

Rarely, spontaneous recovery can occur at this point.

The causative agents include

1. foreign bodies,
2. trauma,
3. intestinal worms,
4. lymphadenitis
5. most commonly, calcified fecal deposits known as fecaliths

Malabsorption Syndrome

Malabsorption : is a general term used to describe a number of clinical conditions in which one or more important nutrients are inadequately absorbed by the gastrointestinal tract with increased fecal content of intestinal nutrients or their bacterial degradation products.

Mucosal biopsy of the small intestine is essential to confirm and more so to identify the cause of malabsorption in diffuse disease of small intestine.

Malabsorption results from:

1. Pancreatic dysfunction; (pancreatitis or cystic fibrosis).

2. Disaccharidase deficiency- most important is lactase which is essential for sugar absorption .

3. Reduced small intestinal surface area: As in celiac disease

4. Infection: parasitic infestation, bacterial overgrowth.

5. Lymphatic obstruction

Hypermia and Congestion

Definition: Both of them can be defined as a local increase in volume of blood in a particular tissue

Hyperemia -

is an **active process** resulting from an increased inflow of blood into a tissue because of arteriolar vasodilation.

- commonly occurs in **exercising skeletal muscle or acute inflammation.**

.- Affected tissue **becomes red** as there is engorgement with oxygenated blood

Congestion:

is a **passive process** resulting from **impaired outflow of blood from a tissue.** -

- occurs **systemically as in cardiac failure.**

.- Affected tissue **appears blue-red** due to accumulation of deoxygenated blood

In long-standing congestion - poorly oxygenated blood causes hypoxia → results in **cell degeneration or cell death.**

Edema

Definition :

Edema : or oedema :

It is an abnormal accumulation of fluid beneath the skin, interstitial space , and/or in one or more of body cavities that produces swelling. .

Edema is classified according to the distribution of the fluid into :-

a. Generalized edema (anasarca):

In this type the edema involves the whole body (edema in multiple organs and peripherally. For example, severe heart failure can cause pulmonary edema, pleural effusions, ascites and peripheral edema..

b. Localized edema :

The edema here involves one organ or one part of the body.

Examples of localized edema :

- **Hydrothorax:** it is the accumulation of fluid in the pleural cavity.
- **Hydro peritoneum (ascites):** it is an abnormal accumulation of fluid in peritoneal cavity.
- **Hydro pericardium:** it is an abnormal accumulation of fluid in pericardial cavity.
- **Brain edema:** accumulation of fluid in the brain.

Causes of edema:

- a. Increased intravascular hydrostatic pressure
- b. Increased capillary permeability
- c. Decreased oncotic pressure of the plasma
- d. Increased sodium retention
- e. Obstruction of the lymphatic flow

Hydrostatic edema

It results from increased intravascular hydrostatic pressure due to:

- Impaired venous return e.g. heart failure
- Increased influx of arterial blood e.g. inflammation

- Right sided heart failure results in peripheral edema
- left sided heart failure results in pulmonary edema

Oncotic edema

Occurs mainly due to **decrease plasma oncotic pressure** which is depends mainly on the plasma albumin (plasma protein), so it occurs when there is hypoalbuminemia.

Hypoalbuminemia (decreased plasma albumin)occurs due to :

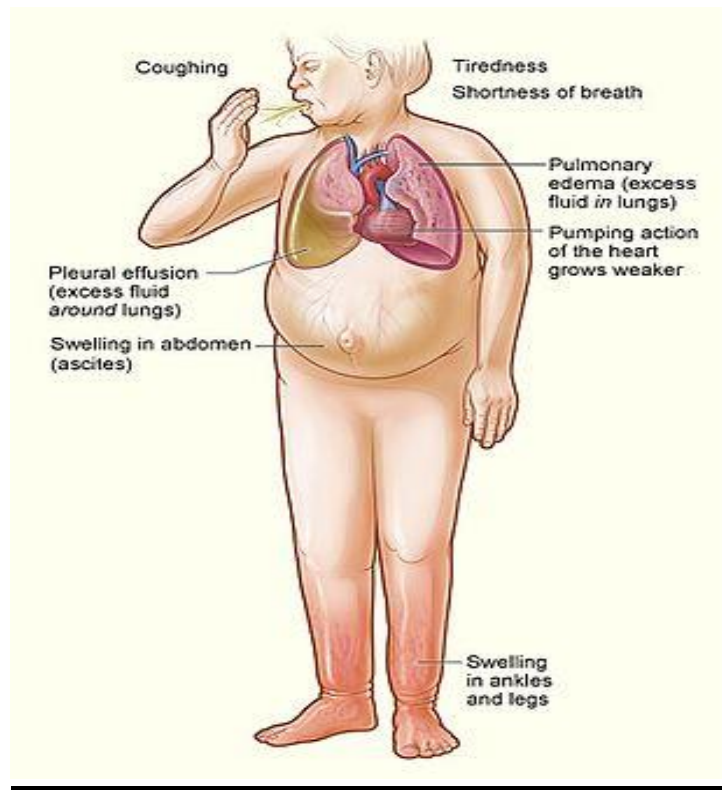
- a. Decreased synthesis of albumin in the liver, this condition seen in liver failure and liver cirrhosis
- b. Increased loss of albumin in urine e.g. proteinuria
- c. Inadequate intake of protein in diet e.g. malnutrition.

What are the differences between transudate and exudate?

	Transudate	Exudate
Appearance	Appear Clear	Appear turbid
Protein content	Protein content less than 3 gm/dl	Protein content more than 3gm/dl
Cell content	Scanty cells	Numerous cells
Examples	Occur in liver cirrhosis, renal failure, heart failure	Occur in malignancy ,tuberculosis



Peripheral edema (swelling of the legs)
(Pitting edema)



SHOCK

Definition :

Shock : It is systemic hypoperfusion resulting from reduction in cardiac output and circulating blood volume.....resulting in hypotension, and cellular hypoxia.

The process of blood entering the tissues is called perfusion, so when perfusion is not happened properly..... this is called a hypoperfusal (hypo = below) state.

Causes of shock:

1. **Decreased cardiac output**, as occurs in hemorrhage
2. **Widespread peripheral vasodilatation**, as occurs in sepsis or severe trauma

Types of shock :

1.Hypovolemic shock -

This is the most common type of shock and result from acute reduction of circulating blood volume.

Its primary causes :

- a. Extensive bleeding, severe burns, c. severe vomiting and diarrhea.

2. Cardiogenic shock -

Caused by the failure of the heart to pump effectively.

Result from :

- . a. Extensive myocardial infarction.
- . b. Arrhythmias
- . c. Congestive heart failure

3. Septic shock :

This is caused by severe infection leading to vasodilatation, such as by Gram negative bacteria, which release an endotoxin and Gram-positive cocci which secrete exotoxin and certain fungi.

4. Anaphylactic shock –

Caused by a severe anaphylactic reaction to an allergen, or drug causing the release of histamine which causes widespread vasodilation, leading to hypotension and increased capillary permeability.

5. Neurogenic shock –

it is often associated with severe trauma, and reactive peripheral vasodilatation resulting in a sudden hypotension

Inflammation

Learning objectives:

1. Understand the definition of inflammation , its aims, types , and their characteristics .
2. Understand the mechanism by which inflammation does it occur
3. Be able to identify the clinical criteria of and laboratory markers and outcome of inflammation .

Inflammation''

It is a local response of living tissue to cell injury and occurs in vascularized tissues and designed to deliver leukocytes to the site of injury .

- The aims of inflammation .

The aim is to eliminate or neutralize the cause of injury and repair its consequences .

-Types of inflammation :

1. Acute inflammation
2. Chronic inflammation

-Acute inflammation characterized by:

1. It is an early and immediate response to injury
2. Short duration (few minutes – few days)
3. Formation of fluid exudate rich in cells and protein .

NOTE :

The causes of acute inflammation are the same causes of cell injury

-Cells of acute inflammation _:

1. Neutrophil
2. Eosinophil
3. Basophil
4. Monocytes

Acute inflammatory response

The main component of acute inflammation are :

Every inflammatory response is based on a coordinated activation and interaction of many components which are :

1. Vascular phase (hemodynamic) : during which

a. blood flow increased : There is vasodilation of the vessels that supply the area , As a result, the area becomes congested, causing the **redness (erythema)** and **hotness** associated with acute inflammation.

b. Capillary permeability are increased :

fluid is moving into the tissues and cause **swelling, pain, and impaired function.** The exudation or movement of the fluid out of the capillaries into the tissue spaces dilutes the causative agent.

2. Cellular phase : during which phagocytic white blood cells move into the area of injury to engulf and degrade the causative agent.

Two types of leukocytes participate in the acute inflammatory response—***the granulocytes and monocytes.***

- **Clinical features of inflammation are :**

1. Generalize malaise
2. Fever
3. Pain often localized to the inflamed area
4. Tachycardia (rapid pulse rate) .

- **Laboratory investigations of acute inflammation :**

1. Increased neutrophil count (↑ WBC count)
2. Increased Erythrocyte sedimentation rate (↑ESR)
- 3 Increased **acute phase proteins** in the blood

Acute phase proteins

Acute-phase proteins are plasma proteins, mostly synthesized in the liver, whose plasma concentrations may increase several hundred-fold as part of the response to inflammatory stimuli

Acute-phase response

It is a systemic effects which usually begins within hours or days of the onset of inflammation or infection, includes changes in the concentrations of plasma proteins, increased erythrocyte sedimentation rate (ESR), fever, increased numbers of leukocytes(WBC) , skeletal muscle catabolism and lethargy. The metabolic changes including skeletal muscle catabolism, provide amino acids that can be used in the immune response and for tissue repair

The most important acute phase proteins are :

1. **C- reactive protein(CRP)**
 2. **Fibrinogen**
 3. **Serum amyloid**
 4. **Hepcidin.**
- **CRP & Serum amyloid** binds to phospholipids on the bacterial cell wall membrane and act to facilitate phagocytosis.
 - **Fibrinogen**: When the liver releases acute phase proteins, the level of fibrinogen in the serum is increased . Fibrinogen coats the surface of RBC which make its aggregation easier and sediment more rapidly than do individual red cells.
 - Another protein whose production is increased in the acute-phase response is the iron-regulating protein **hepcidin.** Chronically elevated plasma concentrations of hepcidin reduce the availability of iron and are responsible for the *anemia* associated with chronic inflammation

A blood test called erythrocyte sedimentation rate (ESR)

provides a simple measure of the level of inflammation .

Thus an elevated ESR indicates the presence of inflammation in the body .

The greater the inflammation ,
The faster the RBC settle to bottom of a test tube
The higher the ESR .

- The ESR is a nonspecific but clinically useful indicator of inflammation .
- Serum CRP activity is also used a nonspecific indicator of inflammation in a manner similar to the ESR .
- Elevated serum levels of CRP have been proposed as a marker for increased risk of myocardial infarction in patients with coronary artery disease .

Outcome of acute inflammation :

1. **Resolution** :in most of cases of acute inflammation all signs disappear without any consequences and occur when the injury is limited and of short duration.
2. **Suppuration** :_with destruction of localized tissues which occur mainly in infection with pyogenic organism. (abscess).
3. **Change to chronic inflammation**
4. **Healing and repair by fibrosis**

Chronic inflammation

Definition:

a prolonged inflammatory process (weeks or months) where an active inflammation, tissue destruction and attempts to repair are proceeding simultaneously

. Chronic inflam. Characterized by :-

1. Long duration (weeks – months)
2. Infiltration with mononuclear chronic inflammatory cells which include (macrophage ,lymphocyte, plasma cell)
3. Tissue destruction largely by inflammatory cells
4. Repair involving new vessels proliferation (angiogenesis) and fibrosis

• Etiology of chronic inflammation :

1. Non healing or persistent acute inflammation for ex. non healing bacterial pneumonia .
2. Persistent infections :
.....Certain microorganisms associated with intracellular infection like T. B. leprosy, certain fungi etc characteristically cause chronic inflammation .
....These organisms are of low toxicity and evoke delayed hypersensitivity reactions
3. Prolonged exposure to nondegradable but partially toxic substances either endogenous lipid components which result in atherosclerosis or exogenous substances such as silica, asbestos .
4. Foreign materials like surgical material left in the wound

Cancer Pathophysiology *(Neoplasia)*

Learning objectives:

At the end of this lecture, the student must

1. Understand the definition of tumor and what are its characteristics.
2. Have idea about the main categories of cancer.
3. Be able to identify the differences between benign and malignant tumors
4. Understand the pathophysiology of tumor development
5. Understand the mechanism of modes of spread of malignant tumor
6. Be able to identify clinical effects of tumors

Cancer Pathology(Neoplasia)

Definition:

Neoplasia means “new growth,” and a new growth is called a *neoplasm*

Neoplasm : it is an abnormal mass of tissue in which abnormal cells divide without control and persists in the same excessive manner after cessation of the stimuli which evoked the change and are able to invade other tissues and spread to other parts of the body .

Oncology (Greek *oncos* = tumor) is the study of tumors or neoplasms.

The growth of body cells is usually controlled and organized by regulatory genes that regulate their growth and proliferation, so any genetic mutation for these genes lead to excessive and unregulated proliferation that becomes autonomous (independent of physiologic growth stimuli), although tumors generally remain dependent on the host for their nutrition and blood supply.

The entire population of neoplastic cells within an individual tumor arises from a single cell that has genetic change, and hence tumors are said to be **clonal**.

The cancer characterize by :

- The growth of this cancer is uncoordinated with that of normal tissue.
- Neoplastic cells are continue to replicate and not controlled by regulatory mechanisms
- Neoplasm behaves as parasites and competes with normal cells for their metabolic needs.

The healthy body is well equipped to defend itself against cancer.

Only when the immune system and other defenses fail , does cancer prevail.

Four classes of normal regulatory genes are the principal targets of genetic damage :

1. **Proto-oncogenes:** are genes found in all cells and have essential roles in regulating the growth and proliferation of normal cells.
 - when activated, stimulate a cell to go through the cell cycle.
 - when this gene is damaged, cellular proliferation can occur without control.
 - Any mutation in these genes cause uncontrolled cell division, at that time they are called oncogenes, or cancer-causing genes
2. **Tumor suppressor genes (TSG) :** prevent or suppress the growth of tumors , it remain dormant unless it lose its function by genetic or acquired mutation resulting in uncontrolled neoplastic cell growth .

TSG can lose their normal function by a variety of mechanisms :

- a. Mutations (hereditary or acquired)
- b. Binding of normal TSG to viral genes .

3. **Genes that regulate programmed cell death (apoptosis),** and
 4. **Genes involved in DNA repair**
-

Pathophysiology of tumor formation :(How does cancer happen ?)

The main concepts of carcinogenesis involves three steps:

- a. Initiation
- b. Promotion
- c. Progression.

a. Initiation

Initiation refers to the **irreversible DNA damage** that occurs when the cell is exposed to a carcinogenic agent during DNA transcription that makes them susceptible to malignant transformation.

The carcinogenic agents can be **chemical**, **physical**, or **biologic**, and produce irreversible changes in the genome of a previously normal cell .

Normally, enzymes detect errors in transcription and remove or repair them.

But sometimes an error is missed ----then we two possibilities:

- a. If regulatory proteins **recognize** the error and block further division, then the error may be repaired or the cell may self-destruct.

b. If regulatory proteins miss the error again, it becomes a permanent mutation that is passed on to future generations of cells.

b. Promotion

It involves the exposure of the already initiated cells to factors (promoters) that enhances its unregulated growth. This exposure may occur either shortly after initiation or years later. The latency period varies with the type of agent, and its dosage.

Promotion is reversible if the promoter substance is removed

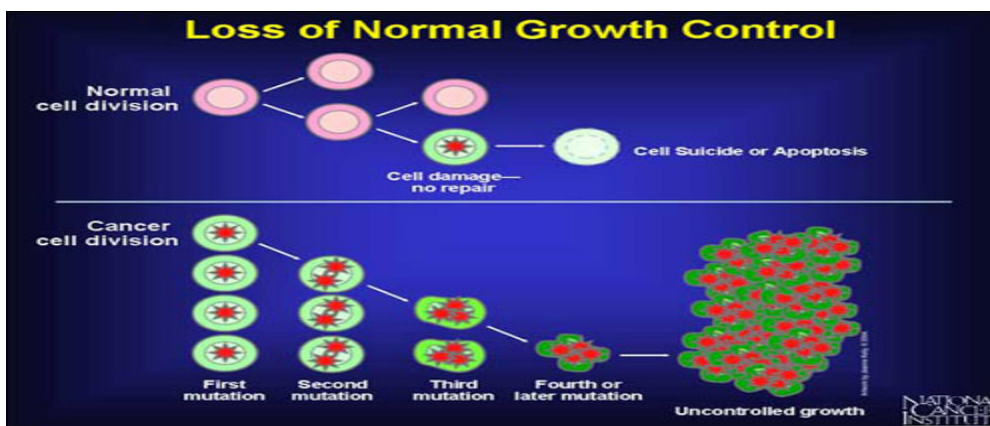
Promoters may be --hormones, such as estrogen;
---food additives, such as nitrates; or
---drugs, such as nicotine.

Promoters can affect the mutated cell by altering function of genes that control cell growth.

Many chemical carcinogens are called complete carcinogens because they can initiate and promote neoplastic transformation.

c. Progression

The progression is actually a late promotion phase in which the cancer invades, metastasizes, and becomes resistant to drugs and have a tendency for autonomous growth. This step is irreversible.



The main categories of cancer include:

1. **Carcinoma** - cancer that begins in the skin or in tissues that line or cover internal organs.
2. **Sarcoma** - cancer that begins in bone, cartilage, fat, muscle, blood vessels, or other connective tissue.
3. **Leukemia**: cancer that starts in the bone marrow(blood-forming tissue) and tend to accumulate in large numbers in the blood stream
4. **Lymphoma** - cancers that begin in the cells of the immune system.

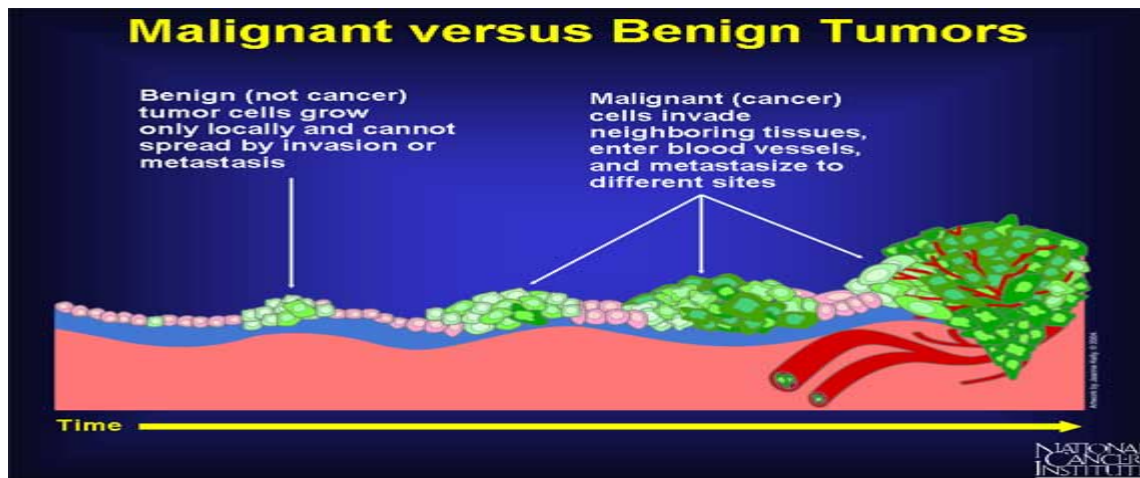
Neoplasm is termed

Well differentiated if it is similar to the original tissue, while it is termed **poorly differentiated** if there is little similarity to the original tissue

Tumor are divided according to their behavior into 2 main groups

- Benign
- Malignant

Feature	Benign tumor	Malignant tumor
Mode of growth	Remain local	Infiltration and metastasis
Rate of growth	Slow	Rapid
Histological feature	Similar to the tissue of origin	Differ from tissue of origin
Clinical effect	Local (pressure effect)	Local and destructive effect



Causes of tumor:-

1. **Persistent irritation** : bladder carcinoma may result from bladder stone
2. **Radiation**: radiation in the form of ultraviolet or ionization radiation can cause cancer:-
 - ultraviolet rays :natural UV radiation is derived from the sun can cause skin cancer specially those people with fair skin, the exposed skin to sun light is more liable to tumor
 - Ionization radiation (electromagnetic radiation) is carcinogenic.
ex. like what occur in Hiroshima and Nagasaki(Japan) , which result in increase in the incidence of certain types of leukemia

3. Chemical substances:

- Aromatic amines (present in tobacco smoking) → bladder carcinoma
- Inorganic substances → lung carcinoma.

4. Viruses :

- DNA viruses: like human Papilloma virus which cause cervical carcinoma in females
- RNA viruses: which associated with some types of leukemia and lymphoma?

5. Hormonal

- Estrogen excess → uterine carcinoma

• Modes of spread of malignant tumor

The spread and metastasis is the most important feature that distinguishes benign from malignant tumors.

Malignant tumor can spread to different parts of body by several ways :-

1. local invasion: -

Malignant tumors invade and destroy normal tissues surrounding them. they do not have well defined capsule so its removal will be difficult or impossible

2. Lymphatic spread: -

This is most often seen in carcinomas The tumor cells will invade the lymphatic vessels, this followed by transport of tumor cells to regional lymph nodes, then to other parts of the body.

3. Vascular spread: -

Most often seen in sarcomas. Because the veins have a thinner wall than arteries so the veins are more frequently invaded than arteries and direction of spread follow the blood flow in the vessel. Lung and liver are the most common sites that involved by this route of spread.

4. Body cavity: -

This occur by seeding the surfaces of body cavities like pleural cavity, abdominal cavity .e.g. carcinoma of ovary spread to the liver and other abdominal organs through the abdominal cavity.