Inflammation;

Definition: it means local vascular and cellular reaction of a living tissue towards an irritant.

Inflammation is designated by adding the suffix " **itis**" to the English, Latin or Greek name of the organ/tissue affected

- Tonsil… tonsillitis.
- Appendix… Appendicitis.
- Colon… Colitis.
- Larynx... Laryngitis.
- Joint…Arthritis.
- Gingiva…Gingivitis.
- Tongue… Glossitis.
- Mouth (oral cavity)…. Stomatitis.
- Stomach…gastritis.
- Urinary bladder… Cystitis.

Aim of inflammation:

1- localization of the irritant.
2- Removal of the irritant (if possible).
3- Preparing the inflamed area for subsequent healing.

Causes of inflammation:

1) Living irritants: Bacteria, viruses, parasites and fungi.
2) Non- living irritants: acids, alkalis, excess heat or cold.
3) Antigens: causing allergic inflammation.

Types of inflammation:

1- Acute inflammation: it lasts few days when the irritant is of short duration and rapid tissue response as tonsillitis. The main inflammatory cells are neutrophils and macrophages.

2- Chronic inflammation: lasting months or even years as the irritant is of long duration and the tissue response is delayed. As tuberculosis or leprosy .Its cells are mainly lymphocyte and plasma cell and Macrophage.

Pathology of acute inflammation:

Acute inflammatory reaction consists of

1: local tissue damage: that occur in the center of the inflamed area as the irritant is at its maximum action. Characterized by extensive death of the central cells. However, this damage is important as dead cells release chemical substances stimulate vascular and cellular response to inflammation.

2: local vascular reaction:

A) Transient vasoconstriction: caused by direct stimulating action of the irritant on the vascular wall. Vasoconstriction is a protective mechanism which lasts few seconds.

B) Dilation of the blood vessel: vessel dilatation increases blood flow so, the inflamed area become red and hot.

C) Slowing of blood stream (stasis): it is due to: increased viscosity of blood due to formation of inflammatory fluid exudate, also Histamine causes swelling of the vascular endothelium and produce mechanichal resistance to blood flow.

D) Formation of inflammatory exudate: the intravascular contents (plasma and cells) escape to the interstitial tissue spaces forming inflammatory exudate, which consists of fluid component and cellular component.

3: local reaction of tissue histeocytes: later on, the histeocytes already present in the inflamed area become activated to deal with any remaining pathogens.

Acute inflammation: mechanisms and formation of fluid exudate

Inflammatory fluid exudate:

Formation:

1) Increase vascular permeability to plasma and its proteins due to histamine and kinins. Also due to endothelial damage occurring in sever inflammation.
2) Increase capillary hydrostatic pressure. This push fluids outside capillaries.
3) Increase osmotic pressure of interstitial tissue fluid as large protein molecules split into smaller ones in the process of tissue necrosis. This acts as a suction force from the capillaries.
4) In acute inflammation, the tissue ground substances become more fluid in structure. This allow easy accumulation of fluid exudate.

Amount of fluid exudate:

It depends on:

1) Structure of inflamed tissue: it is scanty in solid tissues as bone, excess in soft tissues as serous sacs.
2) Nature of irritant: inflammatory fluid exudate is excess in burns and allergic inflammation.
3) Lymphatic obstruction by inflammation and fibrin thrombi delay drainage of exudate resulting in its accumulation.

Composition of inflammatory fluid exudate:

High protein contents (4-8gm%), fibrinogen is especially increased. Specific gravity above 1018. It is turbid and clot on standing.

Functions of inflammatory fluid exudate:

1) It dilute toxins, chemicals and poisons, so minimize their effects.
2) Brings antibodies from blood to sites of inflammation.
3) Supply nutrition to cells and carry away waste products.
4) Supply fibrinogen which change to fibrin, **fibrin has the following functions:**

- Forms a network upon which neutrophils and macrophages move towards irritant.
- Localize infection by surrounding inflamed area and blocking interstitial tissue spaces and some lymphatics.
- Form a network upon which fibroblasts proliferate and start repair.

Fate: it can not be drained by venules due to high smotic pressure. But it is drained by lymphatics. The drained exudate may carry bacteria and bacterial toxins to the draining lymph nodes causing acute lymphadenitis.

Inflammatory cellular exudate:

Formation:

1) Margination of leucocytes: (pavementing of leucocytes): neutrophils leave axial stream due to stasis and settle on sticky endothelial lining of thecapillaries.
2) Emigration of leucocytes: neutrophils push their way through widened inter-endothelial spaces and pass outside the vessel by pseudopodia.

3) Emigration of monocytes: occur in the same way as neutrophils. Both blood monocytes and tissue histeocytes change to macrophages.
4) Diapedesis of RBCs: the role of RBCs in acute inflammation is unknown.
5) Chemotaxis: It means movement of leucocytes towards the irritant along a chemical reagents. These chemical reagents may be exogenous or endogenous substances. Exogenous chemoattractants as bacterial toxins, endogenous chemoattractants as cytokines, complements and leukotrienes.
   - ♦ The nature of the leucocytic infiltrate varies according to age of inflammatory response and type of stimulus. As regards to the age of the inflammation; in acute inflammation; neutrophils are the dominant cells.
   - ♦ As regards to the type of the stimulus; lymphocytes are the dominant cells in viral infection, esinophiles are dominant cells in parasitic infestation.
6) Recognition of microbes and dead tissues (Phagocytosis):
   - ♦ Phagocytosis: It is ingestion, destruction of bacteria, necrotic depris and foreign particles by phagocytic inflammatory cells. This is done by neutrophils (microphages) and macrophages.
   - ♦ Phagocytosis involves three sequential steps; 1) recognition and attachment of the irritant to the phagocytic cells. 2) engulfment with a subsequent formation of a phagocytic vacuole. 3) killing or degradation of the ingested material.
   - ♦ After a particle is bound to phagocytic cell, extensions of the cytoplasm (pseudopods) flow around it and then the cell membrane pinches off to form a vesicle (phagosome) that encloses the particle. The phagosome then fuse with a lysosomal granule, resulting in discharge of the granules contents into the phagolysosome.

General features in acute inflammation:

Fever, malaise, anorexia. Depending on severity of inflammation.

Also there is increase in number of WBCs above 10,000/cmm (leukocytosis).

Local features of inflamed tissue:

Redness: due to vascular dilatation.

Hotness: also due to dilatation and increase blood flow.

Swelling in the inflamed area: due to vascular permeability.

Pain: as pressure on the sensory nerves and irritation by chemical substances.

Acute suppurative inflammation

Course of acute inflammation:

1- **Resolution:** it means complete restoration of inflamed area to normal one. It occurs when tissue damage is minimal. The products of inflammation are rapidly removed. Resolution is the usual course in acute inflammation caused by mild chemical or physical irritant, many viral infections and lobar pneumonia.

2- **Regression and healing:** the body defense mechanism overcome the irritant. Part of necrotic tissue, fibrin and dead cells are removed by the macrophages. The rest get liquefied and together with inflammatory fluid exudate are drained by lymphatics. Next , healing occurs by regeneration or fibrosis.

3- **Progression and spread:** the bacteria overcomes body defense mechanisms. inflammation spread directly, by lymphatics and by blood causing fatal septicaemia.

4- **Chronicity**: the causative agent is partially overcomed, but the body is unable to get rid of it completely. It remains as a weak irritant acting on the tissues for a long time. Thus acute inflammation change to chronic one.

Types of acute inflammation:

They are classified according to presence or absence of pus into

1- Suppurative inflammation either localized (abscess) or diffuse(cellulitis).
2- Non suppurative: that includes:
    1- Catarrhal as catarrhal rhinitis.
    2- Memberanous as Diphtheria.
    3- Fibrinous inflammation: as lobar pneumonia.
    4- Serous inflammation: as in burns.
    5- Sero-fibrinousinflammation: as inflammation of serous sacs.
    6- Hemorrhagic inflammation: as small box.
    7- Necrotizing inflammation: acute inflammation accompanied by marked tissue necrosis as cancrum oris and Vincent angina.
    8- Allergic inflammation as bronchial asthma.

SUPPURATIVE (PYOGENIC, SEPTIC) INFLAMMATION

Definition: Sever acute inflammation characterized by pus formation. It is caused by pyogenic micro-organisms as staphylococci, streptococci, pneumococci, gonococci and bacillus coli.

Composition of pus:

Living and dead pyogenic bacteria and their toxins, inflammatory cells, plasma proteins and the liquefied dead tissue.

Criteria of pus caused by staph aureus:

It is thick (due to high nuclic acids), yellow (because of many pus cells, yellow pigment by the bacteria), odourless, alkaline, does not clot on standing (as its fibrinogen content is destroyed by proteolytic enzymes.

Types of suppurative inflammation:

1) Localized as abscess, cabuncle, furuncle.
2) Diffuse as cellulitis, acute suppurative appendicitis.

I-Abscess : it is localized form of acute suppurative inflammation. Most commonly in subcutaneous tissue but may occur also in lung, liver, brain.

Pathology:

Early the abscess is formed of two zones; central necrotic zone surrounded by zone of acute inflammation containing large number of polymorphonuclear leucocytes.

Many of these leucocytes die liberating proteolytic enzymes liquefy margins of central necrotic zones with formation of pus.

The abscess is formed of three zones central necrotic zone which diminish until disappear, mid zone of pus called abscess cavity, peripheral zone of inflamed tissue called pyogenic membrane.

The abscess enlarge until staphylococci produce coagulase enzyme which help fibrin formation that localizes inflammation.

The abscess in the subcutaneous tissue appears localized tender swelling covered by oedematous skin with opaque yellow center. The covering skin may ulcerate and pus escape. When the abscess can not evacuate itself spontaneously, surgical incision is needed. An internal abscess as in lung may open in the bronchus.

Complications:

1. Lymphatic spread causing lymphangitis and lymphadenitis.
2. Blood spread of bacteria and its toxins cause bacteraemia, toxaemia or septicaemia.
3. Septic thrombophlebitis causes pyaemia.
4. Inadequate drainage and treatment change abscess to chronic one, it acquire a thick fibrous wall.
5. Complications of healing in the form of chronic ulcer, sinus, fistula and keloid.

II- Cellulitis:

It is acute diffuse suppurative inflammation.

Common in subcutaneous tissue of diabetic people. Caused by Streptococcus haemolyticus. The organism produces two enzymes: fibrinolysin; which dissolve

fibrin. And hyaluronidase (spreading factor); which dissolve hyaluronic acid of the ground substance helping spread of bacteria and its toxins.

Sites of Cellulitis: loose connective tissues as subcutaneous tissue, fascial planes, areolar tissue of the orbit, pelvis, scrotum and wall of the appendix.

Pathology of cellulitis: the basic pathological changes are similar to those od abscess with the following differences:

- Failure of localization because of abscess of fibrin.
- The necrosis is extensive and the separated dead tissues are called sloughs.
- Pus formation is slow, pus is thin in consistency and may contain many RBCs.

Complications of Cellulitis:

- Acute lymphangitis and lymphadenitis.
- Septic thrombophlebitis.
- Septicaemia.

NON-SUPPURATIVE INFLAMMATION

1) Catarrhal inflammation:

Definition: it is mild acute non suppurative inflammation of the mucous membranes characterized by excess mucus secretion as catarrhal rhinitis, catarrhal bronchitis, catarrhal appendicitis.

2) Membranous inflammation:

Definition: it is severe acute non suppurative inflammation characterized by formation of a pseudomembrane on the affected surfaces as diphtheria and bacillary dysentery.

(Membranous Inflammation)

3) Sero-fibrinous inflammation:

Definition: acute non suppurative inflammation characterized by formation of excess fluid exudate rich in fibrinogen as inflammation of serous sacs (pleura, pericardium and peritoneum).

4) Fibrinous inflammation:

Definition: acute non suppurative inflammation characterized by an exudate rich in fibrinogen as lobar pneumonia.

5) **Serous inflammation:**

Definition: acute non suppurative inflammation characterized by excess serous exudate as in mild burns and herpes simplex which show epidermal vesicles full of serous fluid containing few inflammatory cells.

6) **Haemorrhagic inflammation:**

Definition: acute non suppurative inflammation characterized by cellular exudate rich in RBCs due to vascular damage as in smallpox and haemolytic streptococcal infection.

7) **Necrotizing inflammation:**

Definition: acute non suppurative inflammation characterized by marked tissue necrosis as in cancrum oris and Vincent angina.

8) **Allergic inflammation**

As bronchial asthma.

Chronic Inflammation

General features of chronic inflammation

- Irritant is mild and has prolonged action.
- Tissue response is gradual and prolonged.
- Chronic inflammation may follow acute inflammation as chronic abscess or begin chronic from the start as tuberculosis or hepatitis B and C.

- Tissue necrosis and subsequent fibrosis is massive and progressive.

- Vascular dilatation and congestion is mild. Later on the small vascular channels show thickened walls with narrow lumen due to proliferation of subintimal connective tissue (End arteritis obliterans).
- Inflammatory fluid exudate is scanty.
- Inflammatory fluid exudate is formed of lymphocytes, plasma cells, macrophages, fibroblasts and giant cells.
- Chronic inflammation may be specific (that means the pathogen cause inflammatory reaction of specific microscopic picture) as in tuberculosis, bilharziasis. Or nonspecific (different irritants produce inflammatory reaction of the same microscopic type, usually follow acute inflammation)

Granuloma

It is a type of chronic specific inflammation characterized by focal accumulation of chronic inflammatory cells forming tiny granules that may fuse together forming tumor like mass.

Types of granuloma

- Infective granuloma as in tuberculosis, bilharziasis, leprosy.
- Non infective granuloma (forign body granuloma) that form around foreign bodies as piece of wood or talk powder.
- Granuloma of unknown origin: as sarcoidosis or regional enteritis.

Effect of granuloma

- Destruction and organ failure; as T.B.
- Obstruction to a hollow viscuss as intestine or bronchus.
- Source of infection.

- May misdiagnose as tumor.

Effects of Bacterial Infection

- Inflammation
- Cell injury
- **Toxemia**
- Invasion of blood by bacteria (**bacteremia**, **septicemia** and **pyemia**)
- Hypersensitivity

Toxemia

Definition:
Circulation of bacterial toxins in the blood, toxins may be:
- **Exotoxins:** gram +ve bacteria as diphtheria bacilli, cholera
- **Endotoxins:** from bodies of dead gram –ve bacteria as typhoid bacilli, E coli

Types:
- **Acute:** acute abscess, pneumonia, tyhpoid and diphtheria
- **Chronic:** chronic lung abscess and T.B

Effects and complications of acute toxemia
- Constitutional symptoms and signs (fever, rigor, headache and pain all over the body)
- Fatty change of parenchymatous organs
- Bilateral tubular necrosis of the kidney and acute renal failure
- Necrosis of suprarenal cortex (acute adrenal insufficiency and death)
- Toxic myocarditis (acute heart failure)
- Endotoxic (septic) shock

Effects and complications of chronic toxemia
- Loss of weight
- Prolonged low grade fever
- Amyloidosis

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- Bone marrow depression

Bacteremia

Definition:

Transient presence of small number of bacteria in the blood stream without multiplication and without toxic manifestations

Causes:

Infection with *Salmonella typhi*, *Streptococcus viridians* and *E.coli*

Pathogenesis:

- After tooth extraction
- Septic focus as tonsillitis, sinusitis

Effects

- No harmful effects
- May localize in the tissue in the presence of predisposing factor e.g. subacute infective endocarditis on top of rheumatic valvulitis after tooth extraction.

Septicemia

Definition:

Large number of virulent bacteria circulates and multiplies in the blood accompanied by severe toxemia

Causative organisms:

- Pyogenic cocci
- Bacilli of plague

Pathological features:

- Hemolysis of RBCs
- Petechial hemorrhage all over the body

 Acute infective endocarditis

 Serofibrinous pericarditis and pleurisy

 Massive adrenal hemorrhages

 Acute splenic swelling: Spleen is enlarged, soft with semifluid cut surface

Pyemia

Definition:

Circulation of septic emboli derived from septic thrombi resulting in development of multiple small abscesses (pyemic abscesses) within one or more organ.

Pathogenesis

Pyogenic organism as *Staph aureus* in septic focus involves a vein → septic thrombophlebitis → septic thrombi → circulating septic emboli → impaction in small blood vessels of different organs → multiple small pyemic abscesses in peripheral parts of the organs adjacent to small blood vessels

Types and sites of affection

 Systemic pyemia: as in

o Acute hematogenous osteomyelitis

o Puerpural sepsis

o Suppurative otitis media

o Suppurative lung disease

o Acute bacterial endocarditis

 Portal pyemia: as in

o Acute suppurative appendicitis

o Infected piles

o Suppuration of gall bladder

Grossly:

Pyemic abscesses are multiple, small nearly of the same size, superficial with hyperemic wall and yellowish central pus.

Microscopically:

Neutrophils, pus cells, debris, macrophages and congested capillaries.

Clinical picture: Manifestations of toxemia.

Good Luck

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