Pathology

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Inflammation

First and Second Lectures

- Inflammation is a protective response of vascularized living tissue to a local injury.
- Inflammation is a Latin word = To Burn.

Inflammatory Response

Includes :

- ❖ Inflammation.
- ❖ Repair (Healing).

However, Inflammation and Repair may be Harmful to the body, as causing :

- ❖ Hypersensitivity reactions.
- ❖ Progressive organ damage and scarring or fibrosis (e.g. Rheumatoid Arthritis).

Causes of Inflammation

1. Infections: Bacterial, viral, parasitic and fungal infections.
2. Physical agents: Heat, cold (frostbite), radiation, etc.
3. Chemical agents: Acid, alkali, drugs, toxins and alcohols.
4. Hypersensitivity: e.g. Rheumatic fever and Glomerulonephritis.
5. Tissue Necrosis : Infarction (Myocardial Infarction).
6. Trauma and Stress.
7. Foreign body.

Aims and functions of Inflammation

It is essentially a protective- defense mechanism (Innate Immunity):

- ✓ To localize and eliminate causative agents.
- ✓ To isolate and limit tissue injury.
- ✓ To destroy invading microorganism (M.O.).
- ✓ To dilute, inactivate and neutralize toxins.
- ✓ To heal and repair the site of injury.

The inflammatory nature of a lesion is usually indicated by the suffix -itis

- Appendix = Appendicitis
- colon = colitis
- Stomach = gastritis
- Larynx = Laryngitis
- Testis = orchitis
- ovary = oophoritis
- Urinary Bladder = cystitis , Gall Bladder = Cholecystitis
- Bone = osteitis
- muscle = myositis
- Bone marrow = osteomyelitis
- Breast = mastitis
- Joint = arthritis and etc.

Exceptions:

- ☒ Lung = pneumonia
- ☒ pleura = pleurisy

Types of Inflammation

1. Acute inflammation
2. Chronic inflammation

Acute Inflammation

Definition: Is of rapid- sudden onset, and of short duration lasting from a few minutes, hours, up to few days.

It is characterized by :

- ❖ Fluid and plasma protein Exudation.
- ❖ Predominantly Neutrophil infiltration.
- ❖ Acute Inflammation may progress into → chronic Inflammation.

The main components of Acute Inflammation are:

- Vascular changes
- Cellular response
- Humoral response

All these responses are induced by (CHEMICAL MEDIATORS).

Vascular changes

- ❖ Transient vasoconstriction.
- ❖ Prolonged vasodilation.
- ❖ Increased blood flow (Active Hyperemia).
- ❖ Increased vascular permeability.
- ❖ Exudation of protein-rich fluid (Plasma).
- ❖ Hemoconcentration and Stasis of blood.
- ❖ Margination or Pavementation and Rolling of WBCs.
- ❖ Transmigration (Diapedesis) of WBCs and passage of RBCs.
- ❖ Migration of WBCs towards sites of injury (Chemotaxis).

What is an exudate?

- ✓ Protein-rich fluid (Plasma) derived from the blood.
- ✓ Accumulates outside of blood vessels.
- ✓ Usually as a result of acute inflammation.

✓ Exudate: is an inflammatory extra- vascular fluid with cellular debris and high protein content, has specific gravity of 1.020 or more.

What is Exudation?

Process leading to the development of an inflammatory exudate.

Inflammatory exudate

Consist of :

1. Fluid (Plasma)
2. Proteins = fibrin + Immunoglobulins (Abs)
3. Cellular debris
4. Cells:
    - Neutrophils
    - Macrophages
    - Eosinophils
    - Few lymphocytes

Fluid Exudation

✓ Due to:

- Increased vascular permeability induced by chemical mediators.
- Direct damage of the vessel wall.

✓ Excessive protein-rich fluid passes to the extra- vascular spaces results in inflammatory exudate and edema.

Mechanisms of Increased Vascular Permeability

(Formation of Inflammatory Exudates)

1. Immediate Transient Vascular Response (Vascular Leakage):
   ❖ most common mechanism of increased vascular permeability.

- ❖ Endothelial cell contraction ➔➔ widening of intercellular gaps.
- ❖ It is caused by vasoactive mediators ➔ Histamine and Serotonin.
- ❖ It occurs rapidly and last for 30 mint.
- ❖ It is a reversible and transient process.
- ❖ It affects venules only (mild injury or mild inflammation).

2. Junctional Retraction:

- ❖ It causes widening of intercellular gaps.
- ❖ It is a reversible process caused by Tumor Necrosis Factor (TNF) and Interleukin-I (IL-1).
- ❖ It affects venules only.
- ❖ Onset of vascular leakage within 4-6hr.

3. Immediate Sustained Vas. Response (Direct Endothelial Cell Injury):

- ❖ Endothelial cell necrosis and detachment caused by severe injury (Burns, Infection, Toxin and Trauma).
- ❖ Leak begins immediately after injury persists for several hours or days.
- ❖ It affects venules, capillaries and arterioles.

Delayed Prolonged Vascular Response (Leakage):

- ✓ Sometime – direct injury to Endothelial Cells begins after a delay of 2-12 hr – lasts for several hours or days.
- ✓ It affects venules and capillaries.
- ✓ Mild – moderate thermal injury, radiation and bacteria toxins.

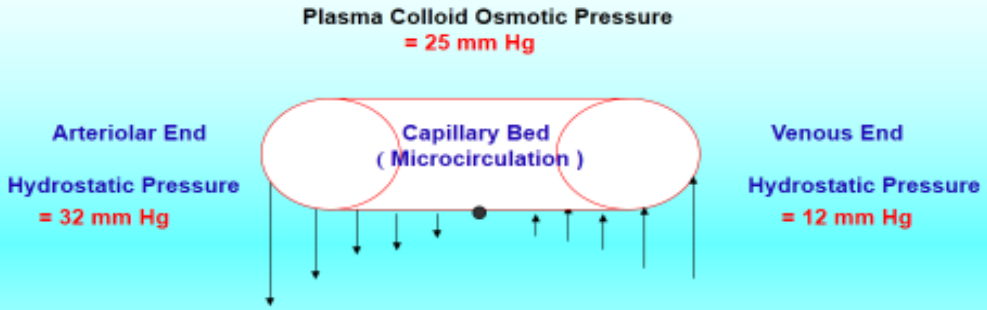
4. Leukocyte - Mediated Endothelial Cell Injury:

- ❖ Late response or leakage.
- ❖ Leukocyte accumulation , activation, and releasing of proteolytic enzymes➔Endothelial cell injury or detachment mostly affect venules.

5. Increased Transcytosis of Protein (venules)

6. Leakage from New Blood Vessels (Angiogenesis):

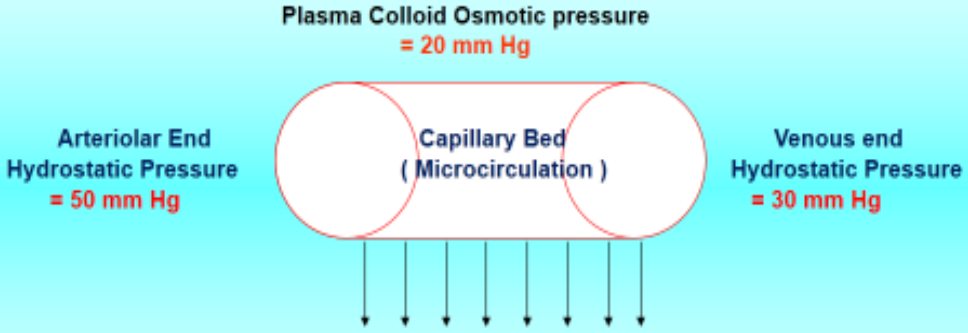
- ❖ New immature blood vessels in tissue repair



Normal

NO Fluid in Extra Vascular Space
OR Interstitial Tissue.

Acute Inflammation



Extra Vascular Space (Interstitial Tissue)

Osmotic Pressure Increases

Fluid Accumulation

In the body, two opposing forces control the normal exchange of body fluids across the wall of blood vessels:

- Hydrostatic pressure causes fluid to move out of the circulation (capillaries).
- Plasma colloid osmotic pressure causes fluid to move into the circulation (capillaries).

Functions of Inflammatory Exudates

A. Beneficial Effects :

1. Dilution of toxins and chemical agents – then removed by lymphatic drainage to lymph nodes.
2. Protective anti-bodies (Abs) in exudates in immune persons help in phagocytosis and neutralization of bacterial toxin by specific anti - toxin.
3. Fibrin meshwork formation - delays bacterial spread and help in phagocytosis.
4. Plasma mediator proteins in exudate.
5. Cellular nutrition (glucose and oxygen) brings with exudate and removed of waste products.
6. Promotion of immunity by stimulation of Immune System to produce anti-bodies (Abs).

B. Harmful Effects :

- Swelling → Mechanical obstruction and Asphyxia as in Acute Laryngitis, especially in children.

Interfere with blood supply → Ischemia of brain tissue as in Meningitis and Encephalitis → ↑ ICP → Coma and Death.

- Ischemic necrosis of bone as in Acute Osteomyelitis.

- Inappropriate Hypersensitivity Reactions (HSR).

What is Transudate ?

(Plasma Ultra-filtrate)

What causes Transudates ?

1. Increased hydrostatic pressure.
2. Decreased plasma osmotic pressure.
3. Impaired removal of interstitial fluid (lymphatic obstruction).

Transudate is an excess extra-vascular fluid (Plasma Ultra-filtrate) with low protein content and Specific gravity of 1.012 or less.

Characters	Transudate Plasma Ultra- filtrate	Exudate Inflammatory fluid
Onset	Early	Late
Appearance	Clear	Turbid
Consistency	Liquid like serum	Viscous like pus
Specific Gravity	1.012	1.020
Protein content	< 3.0 gm/dl	> 3.0 gm/dl
Cell content	Scanty	Numerous Neutrophils
Occurrence (Causes)	Heart & Renal failure Liver diseases	Inflammation

Cellular Changes (Response)

(Emigration of Leukocytes)

-The type of accumulated WBC depends on the type and severity of injury.
-In acute inflammation, mainly Neutrophils pass between endothelial cells to the extra-vascular spaces by its amoeboid movement (transmigration).
-Emigration (Migration) of Leukocytes in interstitial tissues is an active process called Chemotaxis.

Steps of Emigration of Leukocytes (WBCs)

1. Margination and Pavementing of leukocytes (WBCs).
2. Rolling and Transient Loose Adhesion by Selectins.
3. Frim Adhesion by Integrins and Transmigration (Diapedesis).
4. Emigration (Migration) of leukocytes in the interstitial tissue.
5. Chemotaxis, Aggregation and Activation.
6. Phagocytosis.

Chemotaxis :

It is an active directional and controlled movement of the Inflammatory cells (Neutrophils) along a chemical gradient of chemotactic agents to the site of injury or inflammation.

Chemotaxins :

They are chemoattractant substances or chemotactic agents which are able to attract leukocytes toward them. They are of two types:

- ❖ Exogenous Chemotaxins : Bacterial polypeptides.
- ❖ Endogenous Chemotaxins : Chemical mediators such as C5a, Leukotriene-B_4, and certain Cytokines (Chemokine, IL-8).

How do leukocytes kill Bacteria and M.O. ?

The killing of Bacteria or any other M.O. occurs by process called Phagocytosis: Process of engulfment of specific material such as bacteria, M.O, damaged cells, and tissue debris by specialized cells (Phagocytes) which are polymorph nuclear leukocytes (Neutrophils) and Macrophages.

Phagocytosis consists of 3 steps:

Recognition and attachment of bacteria or particles to the surface membrane of phagocytic leukocytes which is mediated by plasma proteins called Opsonins - covering and coating the bacteria or particles and promote their adhesion and binding to specific receptors on cell membranes of phagocytes (Process is called Opsonization).

Phagocytosis of a particle (e.g., a bacterium) involves:

1. Recognition, attachment and binding of the particle or bacterium to receptors on the surface of phagocytes.
2. Engulfment with formation of a phagocytic vacuole within the cytoplasm of the phagocytic cell and then fusion of the phagocytic vacuole with the lysosome within the cytoplasm and formation of phagolysosome.
3. Killing and degradation or destruction of the ingested particle or bacteria by nitric oxide and reactive oxygen species (oxygen free radicals).

Opsonins are 3 types:

1. IgG molecule.
2. C3b and iC3b complement components.
3. Plasma fibronectin (collectins).