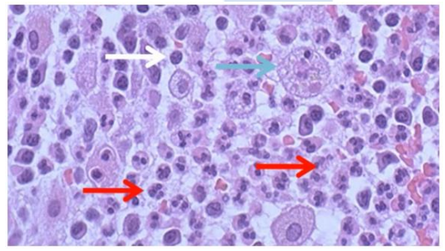
Inflammation

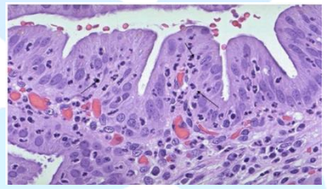
- Is essentially a **protective response** to eliminate both **the initial cause of cell injury (e.g. microbes)** and **to remove necrotic cells and tissue arising as consequence of cell injury.**
- **Inflammatory response** : **dilutes**, **destroys**, or **isolates** the causative agent and arrange for a series of events → healing of the damaged tissues.
- 2 types of inflammation : **Acute** and **Chronic**

➢ Acute Inflammation

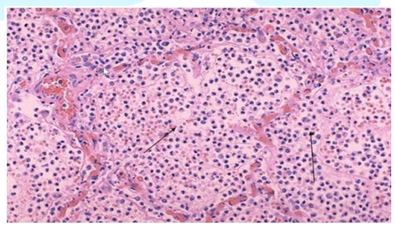
- **immediate** and **rapid** response to injury which is of **short duration (minutes/days).**
- The main characteristics are the **exudation** of fluid and plasma proteins (edema) and the **emigration of leukocytes**, predominantly **Neutrophils** (also called **PMN** leukocytes).



- Various examples of acute inflammation are **Sore Throat**, **Reaction In The Skin To A Scratch** Or **A Burn** or **Insect Bite.**



- The neutrophils are seen infiltrating the **mucosa** and **submucosa** of the gallbladder in this patient with **Acute Cholecystitis.**



- **Neutrophils** fill the alveoli in this case of **Acute** pneumonia.

- Acute inflammatory response has **2 main functions**:
  1.**Eliminating causative agent.**
  2. **Removal of necrotic cells.**

Causes of Acute Inflammation

1. Microbial Infections

- One of the commonest cause of inflammation is microbial infection by producing specific 1- **Exotoxins (Chemicals),** 2- **Endotoxins**, (associated with their cell walls).
- Some organisms cause 3- **Immunologically-Mediated Inflammation** through hypersensitivity reactions.

2. Hypersensitivity Reactions

- occurs when an **altered state** of immunological responsiveness → an **inappropriate** or **excessive immune reaction** → damages the tissues that produce **damage and cell necrotic at site of reaction.**

3. Physical Agents

- Physical trauma (like direct trauma that causes damage of skin or bone)
- Radiation (causing damage of the cells)
- Burns
- Excessive cooling
- Acids, alkalies and oxidizing agents

4.Tissue necrosis

- **Death** of tissues from **lack of oxygen** or **nutrients** resulting from **inadequate blood flow (e.g. infraction).**
- is a **potent** inflammatory stimulus (cell necrosis in living body always associated with inflammatory response)

5. Foreign bodies : sutures ,splinters and dirt

Effects of Inflammation

- The local effects are usually **clearly beneficial** however the destruction of normal tissue on the other hand **may appear to be harmful.**

A. Beneficial effects:

- Both the fluid and cellular exudates may have useful effects, beneficial effects of the fluid and exudate are as the following:

1 - Dilution of toxins:

- such as those produced by bacteria, are carried away by the lymphatics.

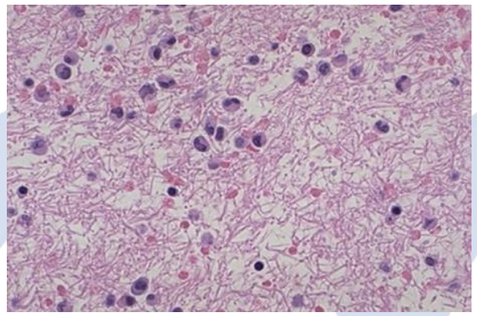
2- Entry of antibodies & drugs

- ↑↑ vascular permeability allows antibodies to enter extra vascular space.

Done by : Dr.Abdullah Alwikhyan

3- Fibrin formation

- Fibrin formation from **exuded fibrinogen** may **impede** the movement of microorganisms trapping them and so **facilitating phagocytosis** .



fibrin mesh in fluid with PMN's (polymorphonuclear) ,that has formed in the area acute inflammation.

4- Delivery of nutrients and oxygen.

- It is essential for the cell. such as neutrophils which have high metabolic activity, is aided by increase fluid flow through the area.

5- Stimulation of immune response.

- The drainage of this fluid exudate into the lymphatics allows particulate and soluble **antigens** to **reach the local lymph nodes** where they may **stimulate the immune response .**

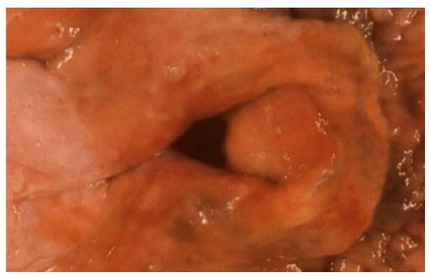
B. Harmful effects

- release of **lysosomal enzymes** by inflammatory cells may also have harmful effects:

I - Digestion Of Normal Tissues.

- Enzymes such as **collagenases** and **proteases** may digest normal tissues, resulting in their destruction.

2- Swelling



- The swelling of acutely inflamed tissues may be harmful: for example the swelling of the **Epiglottis** in **acute epiglottitis** in children due to Haemophilus Influenzae infection may **obstruct the airway,** resulting in death.
- Inflammatory swelling is especially serious when it occurs in an **Enclosed Space** such as the cranial cavity, when intracranial pressure is raised to the point where blood flow into the brain is impaired, resulting in ischemia damage **(e.g. acute meningitis).**

Clinical Aspects of Acute Inflammation

The 5 signs of acute inflammation are:

I - Redness (rubor).

- An acutely inflamed tissue appears red e.g. skin affected by sunburn
- It is due to **dilatation of small blood vessels** within the inflamed area.

2- Heat (calor)

-Increase in temperature is seen **Only** in peripheral parts of the body, such as the skin

- It is due to **increased blood flow (hyperaemia)** → **vascular dilatation** and the **delivery of warm blood** to the area.
- **Systemic fever**, which results from some of the chemical mediators of inflammation, also contributes to the local temperature.

3- Swelling (tumor)

-Swelling results from **edema** (the accumulation of fluid in the extra vascular space as part of the fluid leakage)

- And to a much lesser extent, from the **physical mass of the inflammatory cells migrating into the area.**

4- Pain (dolor)

- For the patient, **Pain is the best known features** of acute inflammation.
- It can be due to :

1. **distortion of tissues** due to inflammatory edema (it making pressure on the nerves) .
2. some of the **chemical mediators** of acute inflammation, including the **prostaglandins** and **serotonin.**

5- Loss of function:

- is a well-known consequence of inflammation, **movement of an inflamed area is consciously inhibited** by pain.

Acute inflammation has two major components

1.Vascular Change

a.vasodilation (Changes in vessel caliber → increase blood flow)

b.increased vascular permeability (**transudate** & **exudate** formation) by leakage of the fluid from inside blood vessel to the outside and accumulation producing swelling and edema .

2. Cellular Events "cellular recruitment & activation".

1.Vascular Changes

1- Changes in Vascular Flow & Vessel Caliber

- These changes occur **quickly** after injury.
- develop at **variable rate** depending on the nature & severity of the injury.
- the following sequential changes take place:

A. Arteriolar vasoconstriction :

- smooth muscle of arterioles contracting as a direct responses to injury. (transient, seconds) occurs early after injury in very short time.

B. Vasodilatation: stasis of blood vessels → increase blood flow, which is the cause of **heat and redness (erythema)** and **local elevation of temperature (warmth)** at the site of inflammation.

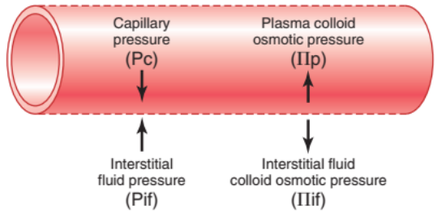
2- Vascular Leakage (Increased vascular permeability)

A. Transudate

- accumulation of ultrafiltrate of blood plasma which contains **little protein in extravascular space** due to **increase of blood hydrostatic pressure.**

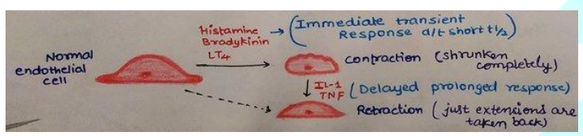
B. Exudate (protein-rich fluid with leukocytes)

- **Accumulation of exudate** in the interstitium → **reduces the intravascular osmotic pressure**, ↑↑ the osmotic pressure of the interstitium.
- The net result is **out-flow of water and ions** → extra-vascular tissues, fluid accumulation is called **edema**.



Mechanism of increased vascular permeability

1 - Endothelial Cell Contraction



- **MCC** of increased vascular permeability, **reversible process.**
- results in **intercellular gaps** in **postcapillary venules .**
- Stimulated by **Histamine**, **Bradykinins** and **leukotrienes**, others mediators.
- occurs rapidly after binding of the **mediators** to **a specific receptors** on the endothelial cells which **line venules 20-60uM**, but **not endothelium in capillaries and arterioles.**
- It is short lived **(15-30 min)** and called **Immediate Transient Response.**

2- Junctional Retraction

- Occur **4-6 hours after initial stimulus** and may persist for **24 hours** or more.
- Induced by a **variety of cytokines mediators** (including **Tumor Necrosis Factor (TNF)** & **Interleukin 1 (IL-1).** → a structural **reorganization of the cytoskeleton**, so that the endothelial cells junctions are disrupted.

3- Direct Endothelial Injury.

A. Immediate sustained response

- Usually **after severe injuries** like **burns**.
- → vascular leakage by causing cell necrosis and detachment, which is usually associated with platelet adhesion and thrombosis.
- Leakage begins **immediately** after injury and persists for **several hours or days** until damaged vessels are repaired.
- **Venules**, **capillaries**, and **arterioles** can **All Be Affected**.

B. Delayed Prolonged Leakage

- Begins after **a delay of 2 - 12 hours**, and last for **several hours to days**.
- Involves **venules** and **capillaries**.

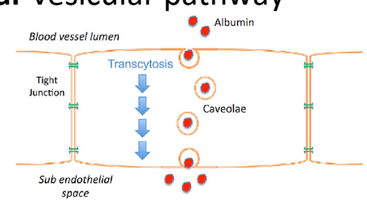
- Caused by:

1. mild to moderate **thermal injury**
2. **X-ray or Ultraviolet irradiation** like late sun-burns.
3. certain **bacterial infection**

4- **Leukocyte - mediated endothelial injury**.

-Occurs as a consequence of the leukocyte accumulation along the vessel wall **releasing many toxic mediators** that may cause endothelial cell injury.

5- **Increased transcytosis of proteins via an intracellular** vesicular pathway (channels formed by fusion of intracellular vesicle.)



- Augments venular permeability
- Modified by **VEGF mediator**

6- Leakage from new blood vessels.

a. **Immaturity** of proliferating endothelial cells

b. **sensitivity** of newly formed endothelial cells to vaso-active mediators as VEGF.

Done by : Dr.Abdullah Alwikhyan