جامعة الانبار

كلية : الصيدلة

قسم : الصيدلة

اسم المادة باللغة العربية: بايولوجيا الانسان

اسم المدة باللغة الإنكليزية: **Human Biology**

المرحلة: الاولى

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عنوان المحاضرة باللغة العربية: الالتهابات

عنوان المحاضرة باللغة الإنكليزية: **Inflammation**

محتوى المحاضرة:

General Feature of Inflammation:

- **In cell injury** – various exogenous and endogenous stimuli can cause cell injury which involves the cells, nuclei and organelles of the cells.

- **In vascularized tissue** – same exogenous and endogenous stimuli produce inflammation.

What is Inflammation?

- **Inflammation** is the reaction of blood vessels, leading to the accumulation of fluid (Serum) and leukocytes in extra vascular tissue.

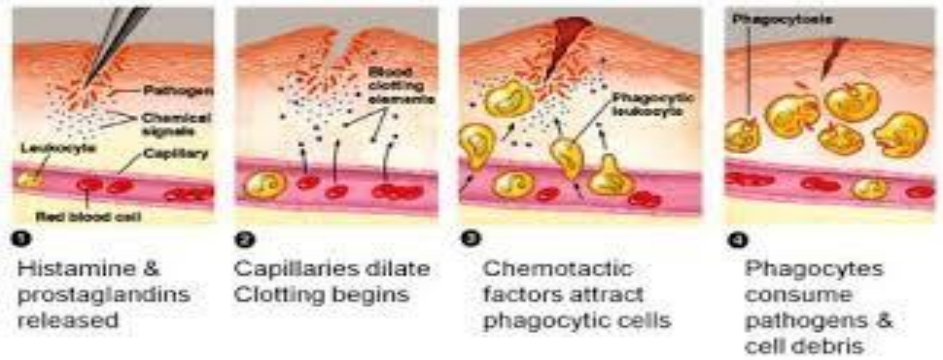
- **"Inflame" - to set fire. Inflammation is** "A dynamic response of vascularised tissue to injury." It is a protective response. It serves to bring defense & healing mechanisms to the site of injury.

- **A reaction** of a living tissue & its micro-circulation to a pathogenic insult. A defense mechanism for survival .

Role of Tissue and Cells in inflammation :

Many tissue and cells are involved in inflammation. The tissue & fluid are:

- The fluid and proteins of plasma.
- Blood vessels.
- Cellular and extra cellular constituents of connective tissue (mast cells & fibroblast).

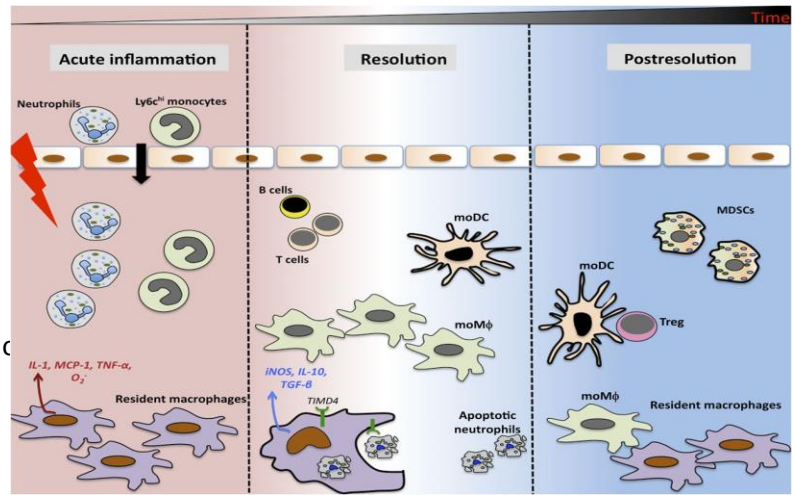


Etiologies of Inflammation:

- Microbial infections: bacterial, viral, fungal, etc.
- Physical agents: burns, trauma--like cuts, radiation
- Chemicals: drugs, toxins, or caustic substances like battery acid.
- Immunologic reactions: rheumatoid arthritis.

Stages of Inflammation

- Vascular stage
- Cellular stage



- Tissue repair

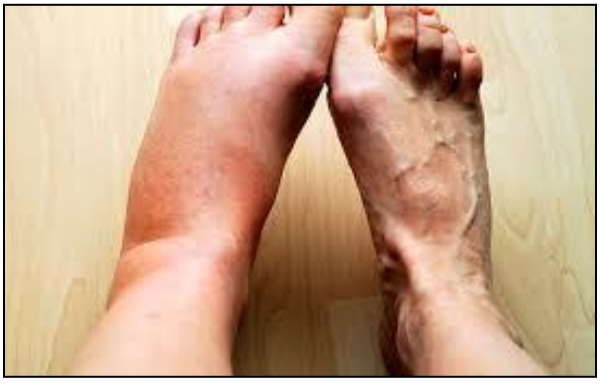
The circulating cells are:

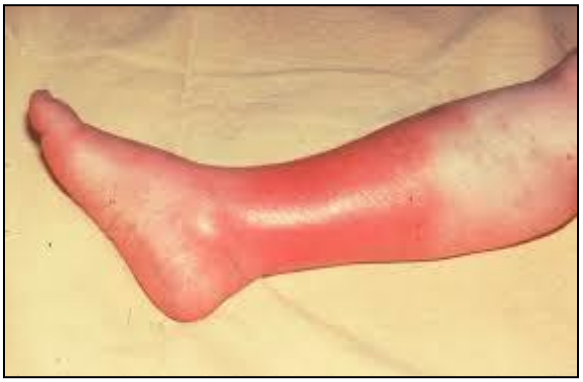
- Neutrophils.
- Monocytes.
- Lymphocytes.
- Basophils.
- Platelets.

Sign & symptoms of Inflammation:

These are:

- Fever, (increase temperature).
- Pain.
- Tissue damage.
- Swelling of tissue.
- Redness of tissue.
- Loss of movements or restricted movement, if near joints.





Pathogenesis of Inflammation:

Three main processes occur at the site of inflammation, due to the release of chemical mediators :

- - Increased blood flow (redness and warmth).
- - Increased vascular permeability (swelling, pain & loss of function).
- - Leukocytic Infiltration.
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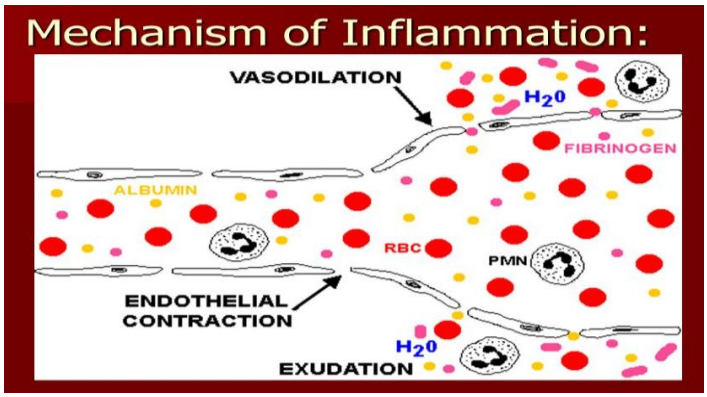
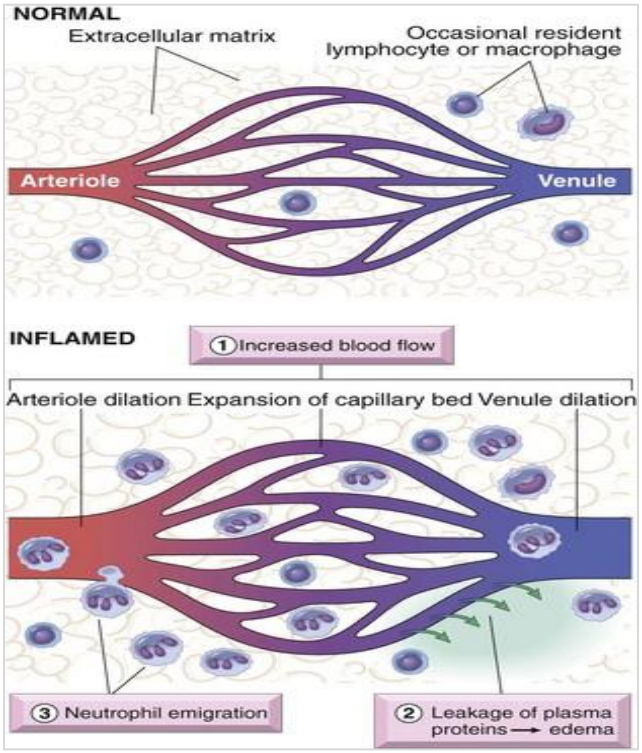
Mechanism of Inflammation

1. Vaso dilatation
2. Exudation - Edema
3. Emigration of cells
4. Chemotaxis



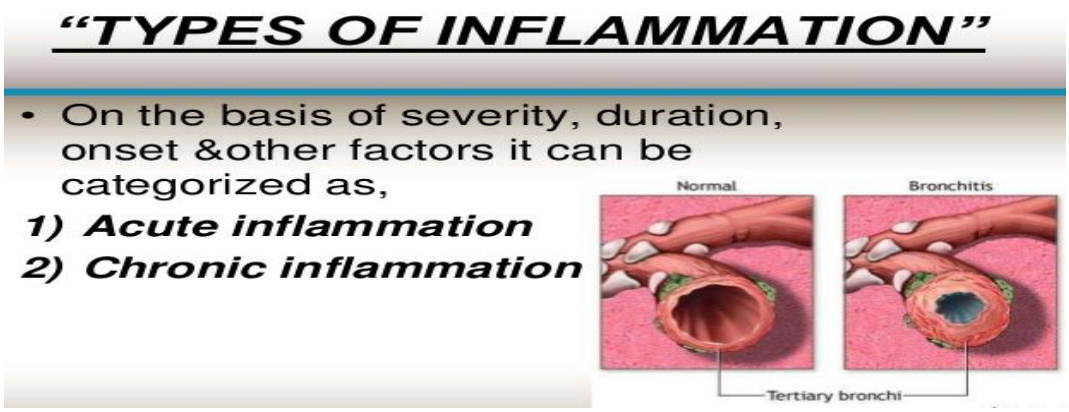


Types of Inflammation:

Inflammation is divided into:

I - Acute inflammation occurs over seconds, minutes, hours and days.

II - Chronic inflammation occurs over longer times, days & months.



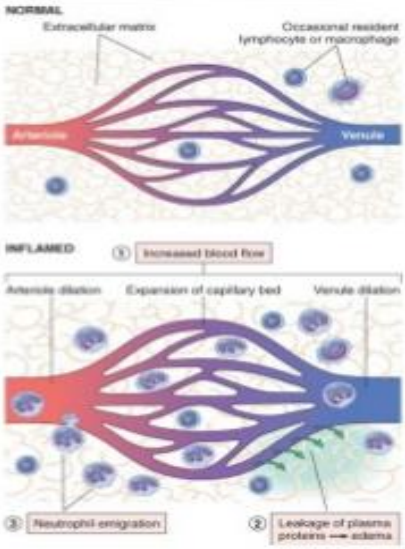
Acute inflammation:

- Acute inflammation begins within seconds to minutes following the injury of tissues.

- The damage may be purely physical, or it may involve the activation

ACUTE INFLAMMATION

- Acute inflammation has 3 major components:
  - Vascular changes:
    - alterations in vessel caliber resulting in increased blood flow (vasodilation) and (increased vascular permeability).
  - Cellular events:
    - emigration of the leukocytes from the microcirculation and accumulation in the focus of injury (cellular recruitment and activation).
  - Mediators, derived from plasma proteins and cells

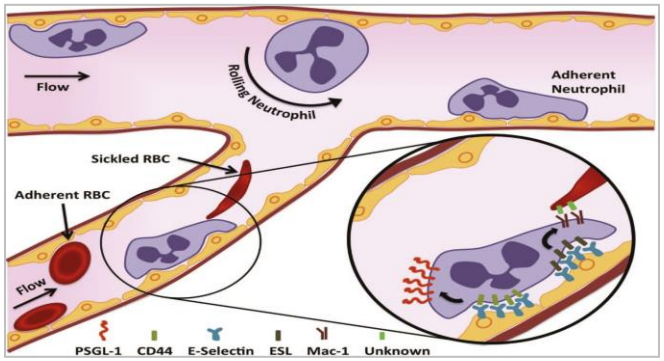


of an immune response.

Chronic inflammation:

- **Chronic inflammation** is of longer duration and is associated histologically with the presence of:
- Lymphocytes and macrophages.
- The proliferation of blood vessels.
- Fibrosis and tissue necrosis.

Response of Inflammation: The main processes are:



I - Increase blood flow.

II - Increased permeability.

III - Migration of neutrophils.

IV - Chemotaxis.

V - Leucocytes recruitment & activation.

I - Increased blood flow: Due to dilation of blood vessels (arterioles) supplying the region.

II - Increased permeability: Increased permeability of the capillaries, allowing fluid and blood proteins to move into the interstitial spaces.

III - Migration of neutrophils (and perhaps a few macrophages) out of the venules and into interstitial spaces.

IV – Chemotaxis

Once outside the blood vessel, a neutrophil is guided towards an infection by various diffusing **chemotactic factors**. Examples include the **chemokines**

and the **complement peptide C5a**, which is released when the complement system is activated either via specific immunity or innate immunity.

V - Leucocytes recruitment & activation.

- This is the first step is the binding of the neutrophils to the endothelium of the blood vessels.
- The binding is due to molecules, called **cell adhesion molecules (CAMs)**, found on the surfaces of neutrophils and on endothelial cells in injured tissue.
- The binding of leukocytes occur in two steps:
- **In the first step**, adhesion molecules called **selectins** tightly gather the neutrophil to the endothelium, so that it begins rolling along the surface

In a second step, a much tighter binding occurs through the interaction of **ICAMs** on the endothelial cells with **integrins** on the neutrophil.

Eosinophils:

However, in some circumstances **eosinophils** rather than neutrophils predominate in acute inflammation. This tends to occur with parasites (worms), against which neutrophils have little success.

Response of Acute Inflammation:

- **Increased Blood Flow, increased permeability and Edema in Inflammation:**
- The increased blood flow & increased permeability are readily visible within a few minutes following a scratch that does not break the skin.
- At first, there is **pale red line** of scratch.
- Later on there is accumulation of inflammatory cells lead swelling, **(inflammation).**
- Finally, there is accumulation of interstitial fluid cause **edema.**

Lymphatics in inflammation: Lymphatics are responsible for draining ***edema***.

Edema: An excess of fluid in the interstitial tissue or serous cavities; either a *transudate* or an *exudate*.

Transudate:

- An ultrafiltrate of blood plasma
  - Permeability of endothelium is usually normal.
  - Low protein content (mostly albumin)

Exudate:

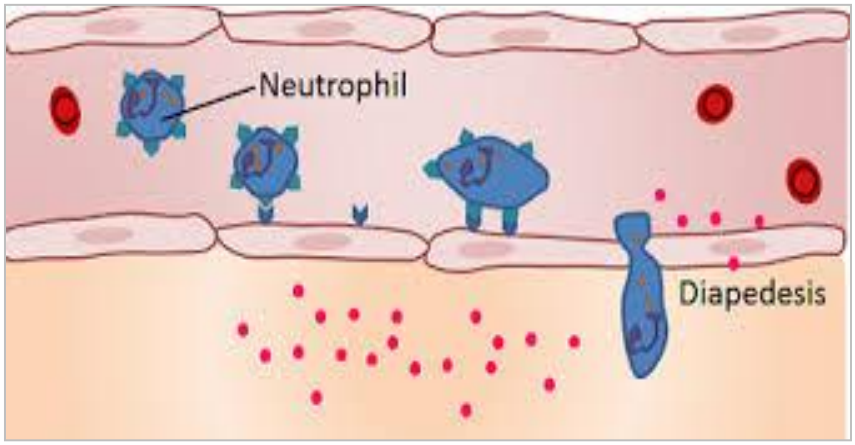
- A filtrate of blood plasma mixed with inflammatory cells and cellular debris.
  - permeability of endothelium is usually altered
  - high protein content.

Pus:

- A purulent exudate: an inflammatory exudate rich in leukocytes (mostly neutrophils) and parenchymal cell debris.

Leukocyte exudation

- **Divided into 4 steps are:**
  - **Margination**, rolling, and adhesion to endothelium
  - **Diapedesis** (trans-migration across the endothelium)
  - **Migration** toward a chemotactic stimuli from the source of tissue injury.
  - **Phagocytosis**



Phagocytosis: 3 distinct steps are:

1- Recognition and attachment
2- Engulfment
3- Killing or degradation

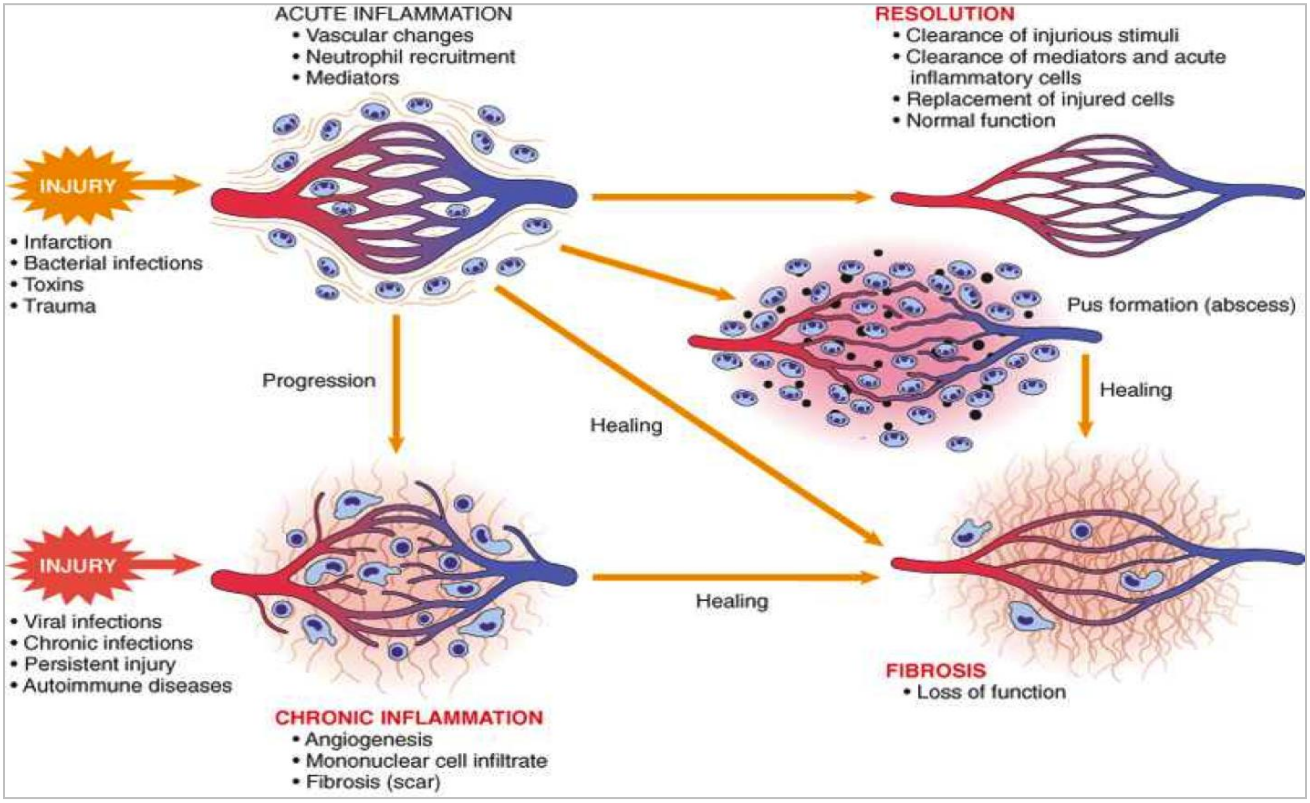
Chronic inflammation

- It is the inflammation of **prolong duration** (weeks or months).

It occurred as:

- Following acute inflammation.
- Occurs, incidentally as active inflammation.
- With tissue destruction.
- With repair process.

Differences between Acute and Chronic Inflammation:



Causes of Chronic inflammation:

I - Persistent infection.

II - Prolonged exposure to potentially toxic agents.

III - Autoimmunity.

I - **Persistent infection:**

- Bacteria.
- Viruses.
- Fungi.
- Parasites

II - **Prolonged exposure to potentially toxic agents:**

- Endogenous, (atherosclerosis).
- Exogenous,(by particulate silica-Silicosis).

III - **Autoimmunity:**

Occurs in:

- Rheumatoid arthritis.
- Lupus erythematosus.
- Lymphocyte, macrophage, plasma cell (mononuclear cell) infiltration
- Tissue destruction by inflammatory cells
- Attempts at repair with fibrosis and angiogenesis (new vessel formation)

- When acute phase cannot be resolved
  - Persistent injury or infection (ulcer, TB)
  - Prolonged toxic agent exposure (silica)
  - Autoimmune disease states (RA, SLE)

Morphological Features of Chronic Inflammation

These are characterized by:

I - Infiltration by mononuclear cells.

II - Tissue destruction.

III - Removal of damaged tissue, (healing).

I - **Infiltration by mononuclear cells:** The mononuclear cells are become predominant after 48 hours. These include;

- Macrophages.
- Lymphocytes.
- Plasma cells.
- Eosinophils.
- Mast cells.

- **Macrophages:**
  - Scattered all over (microglia, Kupffer cells, sinus histiocytes, alveolar macrophages, etc.

- Circulate as monocytes and reach site of injury within 24 – 48 hrs and transform.
- Become activated by T cell-derived cytokines, endotoxins, and other products of inflammation.

- **T and B lymphocytes:**

  - Antigen-activated (via macrophages and dendritic cells)
  - Release macrophage-activating cytokines (in turn, macrophages release lymphocyte-activating cytokines until inflammatory stimulus is removed)

- **Plasma cells:**

  - Terminally differentiated B cells (of lymphocytes).
  - Produce antibodies.

Eosinophils :

- Found especially at sites of parasitic infection, or at allergic (IgE-mediated) sites.
- Eosinophils have highly cationic proteins, which are toxic to parasites.

II - Tissue destruction: Occur due to:

- Inflammatory cells.
- Persistent infecting material.

III - Removal of damaged tissue, (healing):

- Occur by proliferation of small blood vessels, (angiogenesis).

- Proliferation of fibroblast, (fibrosis-repair).

Granulomatous Inflammation:

- Clusters of T cell-activated macrophages, which engulf and surround indigestible foreign bodies (mycobacteria, *H.* capsulatum, silica, suture material)
- Resemble squamous cells, therefore called “epithelioid” granulomas with peripheral lymphocytes, fibrosis & multinucleated giant cells.

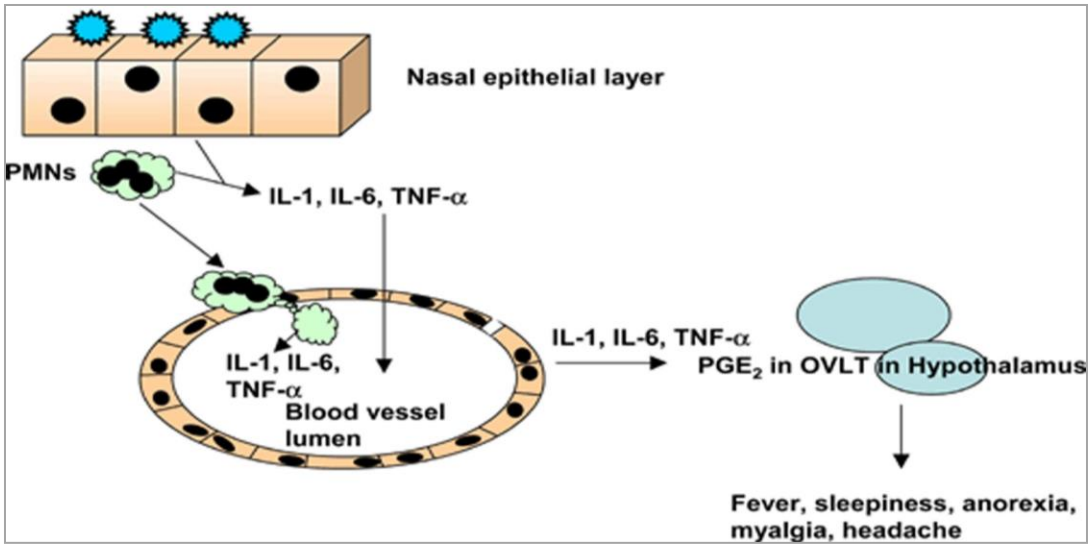
Lymph Nodes and Lymphatics:

- Lymphatics drain tissues
  - Flow increased in inflammation
  - Antigen to the lymph node
  - Toxins, infectious agents also to the node
    - Lymphadenitis, lymphangitis
    - Usually contained there, otherwise bacteremia ensues
    - Tissue-resident macrophages must then prevent overwhelming infection.

Systemic effects

- **Fever**
  - One of the easily recognized cytokine-mediated (esp. IL-1, IL-6, TNF) *acute-phase reactions* including
    - Anorexia
    - Skeletal muscle protein degradation

- Hypotension



- **Leukocytosis**
  - Elevated white blood cell count
  - Bacterial infection (neutrophilia)
  - Parasitic infection (eosinophilia)
  - Viral infection (lymphocytosis)

Leukocytosis: Neutrophilia

- Increased granulocytes:
  - Acute inflammation, Bacterial infections.
- When severe – Leukemoid reaction.
- Clinical features:
  - Infections or Trauma - fever, fatigue.