

Inflammatory cells

- **Leukocytes :**
 - 1. **Granulocytes** : Characterized by their nucleus shape (**lobed** or **polymorphonuclear**) and by their **cytoplasm granules**.
There are four types of granulocytes: Basophils, eosinophils, neutrophils and mast cells.
 - 2. **Agranulocytes** : Characterized by their **round or mononuclear** shaped nucleus and the absence of granules in their cytoplasm. Example: lymphocytes and monocytes.
 - **Leukocytosis** is an increase in the number of leukocytes in the blood whereas **Leukopenia** is a reduction of leukocytes in the blood.

Neutrophils

- Neutrophils are the most abundant type of granulocytes.
- They are formed from stem cells in the bone marrow (myeloblasts).
- The name *neutrophil* derives from staining characteristics of their cytoplasmic granules, neutrophils stain a neutral pink.
- The first leukocytes to gather a sites of acute inflammation, and their speciality is killing microbes.
- Not seen in viral infections
- They are effective in neutral and alkaline environment. The most compatible cells to chemotaxis.

Eosinophils

- These cells are eosinophilic due to their numerous acidophilic cytoplasmic granules, with affinity for acidic dyes such as eosin.
- Eosinophils are recruited from the bloodstream into vascularized connective tissue of most organs in response to eosinophil chemoattractants present in allergic and parasitic diseases.
- They are also seen in the eosinophilic granulomas of domestic species and eosinophilic myositis.

Basophils

- Cytoplasm that is loaded with coarse **granules**, which appear **dark blue** with the usual stains.
- These granules are **histamine and heparin** deposits and are also metachromatic.
- Basophils are the least common of the granulocytes, representing about 0.5 to 1% of circulating white blood cells.

However, they are the largest type of granulocyte.

Agranulocytes

- **Lymphocytes**

- Lymphocyte has a large, **dark-staining nucleus** with **little to no eosinophilic cytoplasm**.
- Lymphocytes are less mobile than neutrophils and **less responsive to chemotaxis**.
- Lymphocytes are frequently encountered in **viral diseases**, in **subacute and chronic inflammations** and in the last stages of acute inflammation.

Lymphocytes include **T lymphocytes** and **B lymphocytes**; both T and B lymphocytes originate from the bone marrow; While B-cells mature in the bone marrow, T-cells travel through the bloodstream to the thymus and mature there.

After maturation T lymphocytes migrate to the spleen and lymph nodes and show a parafollicular localization in the lymph nodes and a periarteriolar localization in the spleen.

As for B lymphocytes, they migrate in the lymph nodes to the center of the follicles and to the subscapular and medullar regions. In the spleen they are localized in the red pulpa.

- ❖ B lymphocytes are responsible for humoral immunity. They differentiate into plasma cells that produce antibody molecules. Life span of B lymphocytes is 3-5 days. During this time, those who do not turn into plasmocytes die.
- ❖ T lymphocytes are involved in cell-mediated immunity. They live for months or years.

T lymphocytes are divided according to their function into 4 types:

- 1. Helper T cells** ; the first to encounter the antigen. They play an important role in the immune system. They help the activity of other immune cells by releasing T cell cytokines. They are essential in B cell antibody class switching, in the activation and growth of cytotoxic T cells, and in maximizing bactericidal activity of phagocytes such as macrophages.
- 2. Cytotoxic T cells** ; Lysis of virally infected cells, tumour cells and allografts
- 3. Suppressor T cells** ; capable of suppressing the functions of both helper and cytotoxic T cells. Function as regulators of the other cells of the immune system
- 4. Memory T cells**; lymphocytes that have previously encountered and responded to the antigen; At a second encounter, they can reproduce to mount a faster and stronger immune response than the first time. They live weeks to several years to a whole lifetime, which is very long compared to other leukocytes.

Natural killer cells or NK cells

- NK cells are defined as large granular lymphocytes (LGL) and constitute the third group of lymphocyte.
- Their origin remains controversial.
- Natural killer (NK) cells are sentinels of the immune system named for lysis of tumor cells and virus-infected cells without previous encounter. These cells enter regions of acute inflammation hours and even days after initiation of the lesion.
- They were named "natural killers" for their ability to kill cells without any priming or prior activation (in contrast to cytotoxic T cells, which need priming by antigen presenting cells).
With these characteristics NK cells are important in non-specific body defenses.

Plasma cells or plasmocytes

- Plasma cells are terminally **differentiated B lymphocytes** that provide protective immunity through the continuous **secretion of antibodies**. Antibody-secreting cells develop in secondary lymphoid tissue following antigen stimulation and may enter a short-lived Plasma cell population that reside primarily in the non lymphoid are of the spleen or lymph nodes, or instead may migrate to the bone marrow where the majority enter a long-lived population of plasma cells
- They have basophilic cytoplasm and an **eccentric nucleus** with heterochromatin in a **characteristic cartwheel or clock face arrangement**.
- Plasma cells are not normally found in the circulation,
but rather located in loose and reticular connective tissues.
- Specially encountered in the organs and chronic inflammations (aktinomycosis, actinobacillosis etc.)

Macrophages

- Macrophages arise from bone marrow–derived monocytes, which circulate hematogenously with some monocytes localizing in tissues physiologically.
- They include:
 - *Monocytes* in circulating blood
 - *Histiocytes* in connective tissue
 - *Kupffer cells* in the liver
 - *Alveolar macrophages* in the lungs
 - *Microglial cells* in the brain
 - *Osteoclasts* in bones
 - *Sinusoidal macrophages* in spleen and lymph nodes
 - *Langerhans cells* in the skin
 - *Mesangial macrophages* kidney

All these cells are part of the **mononuclear phagocytic system (MPS)** (also known as the **reticuloendothelial system**)

- Macrophages are about 10-15 micrometres in diameter. They have a large hypochromatic nucleus and an eosinophilic cytoplasm that contains variable amounts of lysosomes.
- Functionally, macrophages are a component of the innate immune system in terms of their role in phagocytosis and cytokine release during the acute inflammatory response.
- Also macrophages are one of the main triggers of the adaptive immune response because of their ability to process and present antigen and regulate T lymphocyte activity.
- Macrophages are specially present in chronic inflammatory lesions (specially chronic granulomatous lesions) or in the last stages of acute inflammatory lesions.

Epithelioid histiocytes

- Epithelioid histiocytes (**Epithelioid cells**) are activated macrophages resembling epithelial cells.
- Elongated, with pale eosinophilic cytoplasm and hypochromatic oval nuclei. Cell membrane is not clear.
- Epithelioid cells are an essential characteristic of granulomatous inflammatory responses (tuberculosis, paratuberculosis, brucellosis, glanders,..)
- Their main function is phagocytosis.

Mast cells

- Mast cells are morphologically similar to basophils but mast cells are bigger in size. They are recognized by their prominent basophilic cytoplasmic granules.
- Mast cells when stimulated, degranulate to release some proinflammatory mediators. The most prominent of these are histamine and heparin.
- Known for their role in allergy and anaphylaxis. In tissues they are specially found around the blood vessels.

Giant cells

- Multinucleated giant cells syncytial cells formed by the fusion of two or more activated macrophages into one large cell with two or more nuclei.
- They often form in response to foreign bodies or persistent intracellular pathogens. Types of multinucleated giant cells are the following:
 - 1. Langhans type giant cell
 - 2. Foreign body type giant cell
 - 3. Epulis type giant cell
 - 4. Tumor type giant cell
 - 5. Sternberg type giant cell

- ✓ Langhans type giant cells are seen in granulomatous inflammations like tuberculosis, paratuberculosis, brucellosis, sarcoidosis, lepra etc.

1. Langhans type giant cell

- ✓ The nuclei can be arranged in a horseshoe-like semicircle at the periphery of the cell.

2. Foreign body type giant cell

- The nuclei can be distributed in the cell in a haphazard manner or aggregated in the center of the cytoplasm; but in general nuclei are clustered on the opposite side of the foreign body.
- The formation of foreign body type giant cells is induced by endogenous and exogenous foreign bodies and by some living microorganisms.

Cholesterol crystals, a variety of dusts, uric acid and urate crystals, wood and metal splinters, cotton yarns left in surgical sites, necrotic fat tissue, parasites, eggs and larvae, actinomycosis and many fungal infections are conditions that causes the formation of foreign body type giant cells.

3. Epulis type giant cell

- Large cytoplasm with numerous nuclei parallel to each other.
- Seen in conditions like Epulis granulomatosis

4. Tumor type giant cell

- Tumor type giant cells are seen in malignant tumors like carcinomas and sarcomas.
 - This type of giant cell is characterized by numerous large atypical nuclei and a large cytoplasm with various forms.

5. Sternberg type giant cell

- Giant cells found in human with Hodgkin's lymphoma.
- Oval or round cytoplasm with two mirror-image nuclei ("owl eyes").

Fibroblasts and fibrocytes

- Fibroblasts and fibrocytes are connective tissue cells. They are two states of the same cells, fibroblasts being the activated state and fibrocytes the inactive state.
 - **Fibroblasts** are large, flat, elongated cells possessing processes extending out from the ends of the cell body. The cell nucleus is flat and oval.

Fibroblasts produce tropocollagen, which is the forerunner of collagen, and ground substance, an amorphous gel-like matrix that fills the spaces between cells and fibres in connective tissue.

- **Fibrocytes** are spindle shaped cells, smaller and darker than the fibroblasts, with an elongated

Factors affecting the inflammatory response:

- **Phlogistic factors** are the factors that facilitates inflammatory response and **Antiphlogystic factors** are the ones that inhibits the inflammatory response.
 1. Age
 2. The body's defence system
 3. Diabetes mellitus
 4. Blood diseases
 5. Nutrition
 6. Hormones
 7. Blood supply of the organs
 8. Structure of the organs
 9. Pathogenity, quantity and nature of the agent
 10. The pathogen's ability to spread

- ❑ An exudate is an extravascular fluid with a high content of proteins, cellular debris, and leukocytes. It is usually a result of inflammation.
- ❑ In contrast, a transudate is a low-protein fluid that is essentially an ultrafiltrate of the blood plasma consisting primarily of water, small proteins, and dissolved electrolytes.