**Lymphoreticular system**

Lymphocytes are the immunologically competent cells that assist the phagocytes in defence of the body against infection and other foreign invasion.

**Lymphoid Organs:**

* ***The* *primary lymphoid organs*:**

Include the bone marrow and thymus, where lymphocytes develop in the postnatal life.

* ***The* *secondary lymphoid organs***

In which specific immune responses are generated, include the lymph nodes, spleen and lymphoid tissues of the alimentary and respiratory tracts.

**Mucosa-associated lymphoid tissue (MALT)** includes

1. discrete lymphoid structures such as the appendix, Peyer’s patches in the submucosa of the intestine and the tonsils and adenoids (collectively referred to as Waldeyer’s ring) in the pharynx
2. Lymphocytes in the submucosa of various organs.

* **The structure of lymph node:**

Lymph node is divided into:

1. **Cortex**: Within the cortex are primary follicles, which are composed of B lymphocytes and follicular dendritic cells. On antigen exposure, proliferation and maturation of B cells cause the primary follicle to develop into a secondary follicle comprising a germinal center surrounded by a **mantle zone** of small B lymphocytes.

Outside the mantle zone some lymph node germinal center has a **marginal zone**, also composed of B lymphocytes.

1. **Paracortex**: T cells occupy the paracortex, which surrounds and underlies the primary and secondary follicles. It is the zone situated between the cortex and the medulla, which contains the mobile pool of T lymphocytes responsible for cell-mediated immune responses. The paracortex also has abundant dendritic cells.

3. **Medulla:** In the centre of the lymph node, it composed of medullary cords and sinuses. The medullary cords are occupied by B and T lymphocytes, plasma cells and macrophages.

* **The spleen**

Has an important and unique role in the function of the haemopoietic and immune system.

It lies under the left costal margin, has a normal weight of 150-250 g and a length of between 5 and 13 cm. It is normally not palpable but becomes palpable when the size is increased to over 14 cm.

***Extramedullary haemopoiesis***

The spleen is an important site of haemopoiesis *in utero* and retains the ability to reactivate this process after birth.

This can occur:

In severe anaemia, such as chronic haemolysis, megaloblastic anaemia and thalassaemia major, or myelofibrosis or malignant disorders in the bone marrow.

**Causes of splenomegaly**

1. **Leukaemia**
2. **Lymphomas**
3. **myeloproliferative disorders**
4. **haemolytic anaemias**
5. **glandular fever**
6. **portal hypertension**
7. malaria
8. Leishmaniasis
9. schistosomiasis.

**Hypersplenism:**

*Hypersplenism* is a clinical syndrome that can be seen in any form of splenomegaly (it does not imply a specific causal mechanism). It is characterized by:

* Enlargement of the spleen;
* Reduction of at least one cell line in the blood in the presence of normal bone marrow function;
* Evidence of increased release of premature cells, such as reticulocytes or immature platelets, from the bone marrow into the blood.

Normally, only approximately 5% (30-70 mL) of the total red cell mass is present in the spleen and up to half of the total marginating neutrophil pool and 30% of the platelet mass may be located there.

As the spleen enlarges, the proportion of haemopoietic cells within the organ increases such that up to 40% of the red cell mass, and 90% of platelets, may be pooled in an enlarged spleen.

**Hyposplenism:**

Patients with functional hyposplenism have impaired immunity to blood - borne bacterial and protozoal infections, and persistent thrombocytosis.

**Hyposplenism (excluding that induced by medical or surgical intervention) occurs in a wide range of conditions:**

* Sickle cell disease
* Gluten - induced enteropathy (coeliac syndrome).
* Dermatitis herpetiformis.
* Crohn’s disease and ulcerative colitis
* Essential thrombocythaemia
* Congenital absence
* Elderly
* ***Non-Neoplastic Conditions of lymph node:***
* **Reactive Lymphadenitis:** Any immune response against foreign antigens (infectious & noninfectious inflammatory stimuli) is often associated with lymph node enlargement (**lymphadenopathy**). The infections that cause lymphadenitis are numerous and varied, and may be acute or chronic. **In most instances, the histological appearance of the nodes is entirely nonspecific** i.e. different etiologies are associated with similar microscopic changes.

**Causes of Lymphadenopathy:**

|  |  |
| --- | --- |
| Localized | Generalized |
| *local infection*  • pyogenic infection, e.g. pharyngitis,  dental abscess, otitis media,  • viral infection  • cat scratch fever  • lymphogranuloma venereum  • tuberculosis  *Lymphoma*  • Hodgkin's lymphoma  • non-Hodgkin's lymphoma  *Carcinoma (secondary)* | ***Infection***  • viral, e.g. infectious mononucleosis,  measles, rubella, viral hepatitis, HIV  • bacterial, e.g. syphilis, brucellosis, tuberculosis, *Salmonella,*  • fungal, e.g. histoplasmosis  • protozoal, e.g. toxoplasmosis  ***Non-infectious inflammatory diseases***, e.g. sarcoidosis,  rheumatoid arthritis,  SLE,  other connective tissue diseases,  ***Malignant***  • leukaemias, especially CLL, ALL  • lymphoma: non-Hodgkin's lymphoma,  Hodgkin's lymphoma  ***Miscellaneous***  • reaction to drugs and chemicals, e.g. hydantoins, beryllium  • hyperthyroidism |

* ***Acute Nonspecific Lymphadenitis:***

This form of lymphadenitis may be confined to a **local group** of nodes draining a focal infection, or be **generalized,** as in systemic infectious and inflammatory conditions.

The overlying skin is frequently red, and sometimes penetration of the skin can produce draining sinuses.

**Grossly:** inflamed nodes are swollen & congested i.e. gray-red.

**Microscopically:** there are **large germinal centers** containing numerous mitotic figures. When the cause is a pyogenic organism, a neutrophilic infiltrate is seen around the follicles and within the lymphoid sinuses. With severe infections, the centers of follicles can undergo suppurative necrosis.

With control of the infection, the lymph nodes can revert to their ***normal appearance*** or, if damaged by the immune response, undergo ***scarring***.

* **Chronic Nonspecific Lymphadenitis:**

This condition can assume one of three patterns, depending on the causative agent:

1. **Follicular hyperplasia:** is associated with infections or inflammatory processes that activate B cells which migrate into B cell follicles and create the follicular (or germinal center) reaction. The cells in the reactive follicles include:

**-**the activated B cells (called follicular center cells),

**-**scattered phagocytic macrophages containing nuclear debris (tingible body macrophages),

**-**and follicular dendritic cells.

**Causes include**: Rheumatoid arthritis, Toxoplasmosis, and the early stages of HIV infection.

1. **Paracortical hyperplasia:** is caused by immune reactions involving the **T cell regions** of the lymph node, which is reflected microscopically as expanded zones between the cortical follicles.

**Paracortical hyperplasia is encountered in:**

Viral infections (such as EBV), Following certain vaccinations (e.g., smallpox), and in immune reactions induced by certain drugs (especially phenytoin).

1. **Sinus Histiocytosis:** is characterized by distention and prominence of the lymphatic sinusoids, owing to a marked hypertrophy of lining endothelial cells and an infiltrate of macrophages (histiocytes).

**Sinus histiocytosis is often encountered in:** Lymph nodes draining cancers (may represent an immune response to the tumor or its products).

* **Granulomatous lymphadenitis**

Large number of diseases that can result in granulomatous formations in lymph nodes. They include;

A. Various types of infections

B. Foreign body reactions

C. Immunological conditions.

D. Chemical causes; beryllium, zirconium, silica, talc,. Etc.

E. Reaction to malignancy (Lymphoma or metastasis), whether the LN is involved or not by the tumor).

**Infectious causes of granuloma**

1. **Tuberculosis and atypical mycobacteria.**

2. **Sarcoidosis** (unknown etiology; evidences suggest an infectious cause).

3. **Fungal infections**

4. **Brucellosis**

5. Toxoplasmosis

6. Syphilis

7. Leprosy

8. Cat-scratch disease

9. Mesenteric lymphadenitis

10. Leishmaniasis.

11. Bilharziasis.

**Cat-scratch disease:**

-A **self-limited lymphadenitis** caused by the bacterium ***Bartonella henselae*.**

-It is primarily a disease of childhood; 90% of the patients are younger than 18 years of age.

-It presents as **regional lymphadenopathy**, most frequently in the axilla and neck. The nodal enlargement appears approximately 2 weeks after a feline scratch or, less commonly, after a splinter or thorn injury. A raised, inflammatory nodule or vesicle, is sometimes visible at the site of skin injury.

-In most patients the lymph node enlargement regresses over the next 2 to 4 months. Rarely, patients may develop encephalitis, osteomyelitis, or thrombocytopenia

**Morphology:**

Sarcoid-like granulomas are formed; these then undergo central necrosis associated with the accumulation of neutrophils forming **irregular stellate necrotizing granulomas.**

**Glandular fever:**

Is a general term for a disease characterized by: fever, sore throat, lymphadenopathy and atypical lymphocytes in the blood.

**It may be caused by primary infection with Epstein-Barr virus (EBV), cytomegalovirus, human immunodeficiency virus (HIV) or toxoplasma.**

*EBV infection*, otherwise known as infectious mononucleosis, is the most common cause.

* **Infectious mononucleosis**

This is caused by primary infection with EBV.

In developing countries, subclinical infection in childhood is universal. In developed countries, primary infection may be delayed until adolesences or early adult life (mostly result in typical IM)

The virus is usually acquired from asymptomatic excreters via saliva, either by droplet infection or environmental contamination in childhood, or by kissing.

The laboratory diagnosis depends on the Following findings:

In increasing order of specificity:

1. Lymphocytosis with the characteristic atypical lymphocytes in the peripheral blood.
2. A positive heterophil reaction (monospot test).
3. A rising titer of antibodies specific for EBV antigens

Treatment is largely symptomatic (**note:** administration of ampicillin or amoxicillin in this condition commonly causes an itchy macular rash, and should be avoided).