approach for leukocytosis and leukopenia

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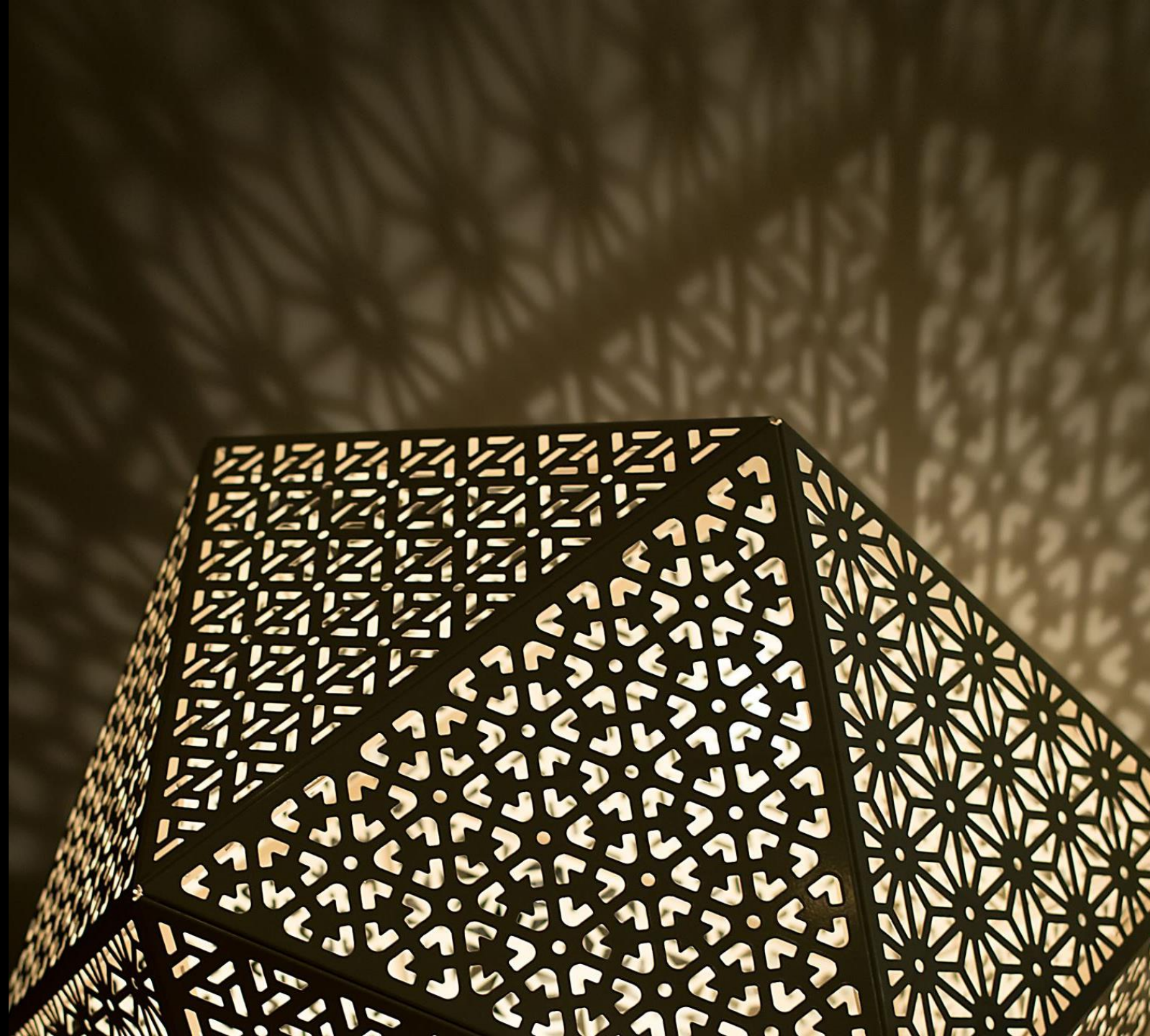


Leukocytes

- **Monocytes**
- **Lymphocytes**
- **Neutrophils** (most count)
- **Eosinophils**
- **Basophils** (rarest)

definitions

Normal leukocyte count is 4.000-11.000/mm3 in adult man

What is leukocytosis ?

Increase in number of leucocytes above 11.000/mm3.

What is leukopenia ?

It means a decrease in the total leucocytic count below 4.000/mm3

Leukocytosis

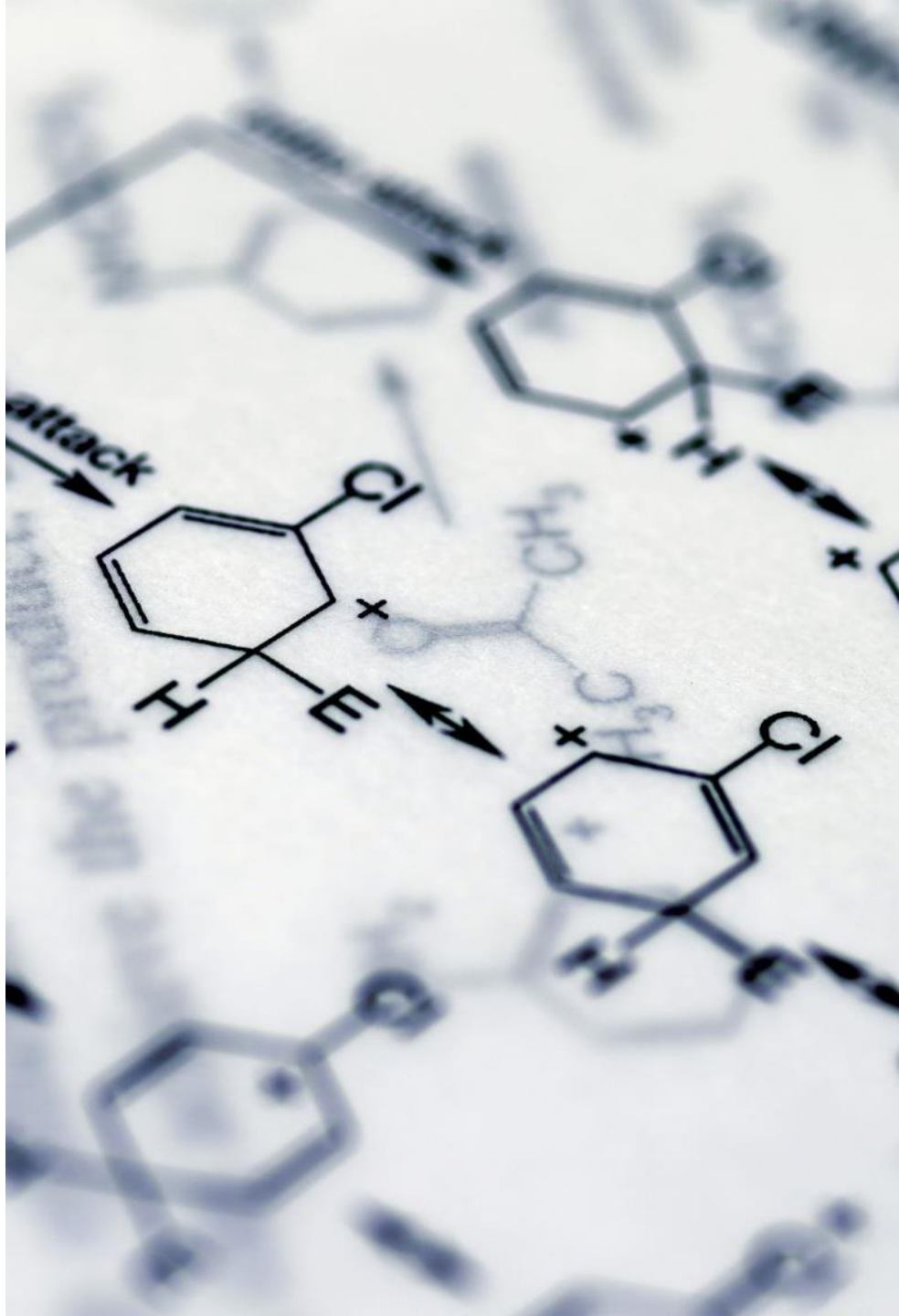
- This condition can occur for various reasons and is often an indication that the body is responding to an infection, inflammation, or other underlying medical conditions. Leukocytosis can be categorized into several types, depending on which specific type of white blood cell is elevated:
- **1) Neutrophilic leukocytosis**
- **2) Monocytic leukocytosis**
- **3) Lymphocytic leukocytosis**
- **4) Eosinophilic leukocytosis**
- **5) Basophilic leukocytosis**
- **6) physiological leukocytosis !**

Neutrophilic leukocytosis:

- **Is an increase number of neutrophil in differential leukocytic count which normally (60-70%).**
- **Causes :**
- **1) Bacterial Infections:** The most common cause of neutrophilic leukocytosis is a bacterial infection.
- **2) Acute inflammation :**
- **3) Tissue Injury:** Trauma, burns, surgery, or other forms of tissue injury can result in neutrophilic leukocytosis as the body works to repair damaged tissue and prevent infection.
- **4) Smoking:** Smoking tobacco products can cause an increase in neutrophils as a response to the inflammation.

Monocytic and lymphocytic leukocytosis

- **Is an increase number of monocyte in differential leukocytic count which normally (3-8%) for monocytic leukocytosis and more than (20-30%) for lymphocytic leukocytosis .**
- **Causes :**
- **1) viral infections:** such as infectious mononucleosis, mumps, and measles .
- **2) Bordetella pertussis infection** - Bacteria produce lymphocytosis-promoting factor, which blocks circulating lymphocytes from leaving the blood to enter the lymph node (lymphocytic leukocytosis) .
- **3) Chronic Infections:** Certain chronic infections, such as tuberculosis (TB), bacterial endocarditis, and fungal infections, can lead to an increase in monocyte counts as part of the immune response to these long-lasting infections. **(**Monocytic leukocytosis) .



Eosinophilic leukocytosis

: Is an increase number of Eosinophiles in differential leukocytic count which normally (1-4%).

Causes :	1) Allergic Reactions	2) Parasitic Infections
3) Asthma	4) Eosinophilic Disorders	5) Hodgkin lymphoma

Basophilic leukocytosis

- **Is an increase number of Basophilis in differential leukocytic count which normally (½-1%)**
- **Causes :**
- **1) Allergic Reactions**
- **2) thyroid :** High basophil levels may also be a sign of low thyroid function, or hypothyroidism. This condition occurs when the body does not produce enough thyroid hormones, which may cause some bodily functions to slow down.

Basophil and Eosinophil in allergy !!

- The immunoglobulin E (IgE) type, has a special tendency to become attached to mast cells and basophils. Then, when the specific antigen for the specific IgE antibody subsequently reacts with the antibody, the resulting attachment of antigen to antibody causes the mast cell or basophil to rupture and release large quantities of histamine and other allergic mediators as serotonin, bradykinin and lysosomal enzymes to mediate allergic manifestation as vasodilatation and tissue reaction
- They increased in allergic conditions by the release of eosinophil chemotactic factor released from the mast cells and basophiles. Eosinophils phagocytose the antigen-antibody complexes and release substances to neutralize the histamine

physiological leukocytosis

Exercise: can cause a temporary increase in WBC count .

Pregnancy: Pregnancy can cause mild leukocytosis as a result of hormonal.

Stress and Emotional Distress

Note : physiological leukocytosis is generally harmless and self-limiting. It does not typically indicate an underlying medical problem.

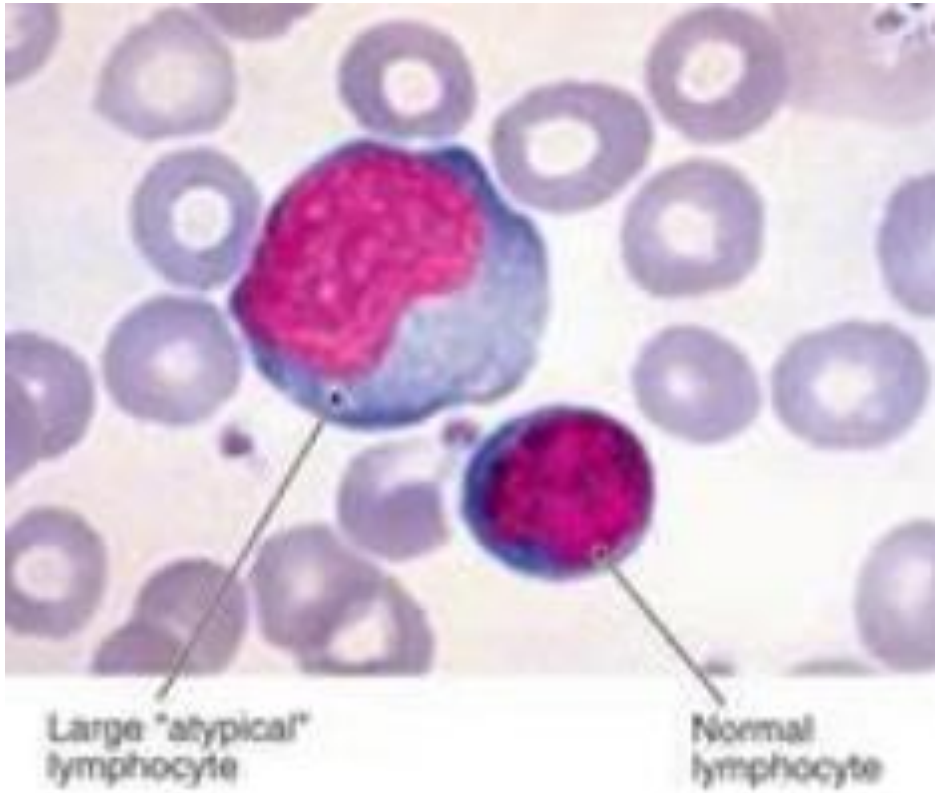
INFECTIOUS MONONUCLEOSIS (IM)

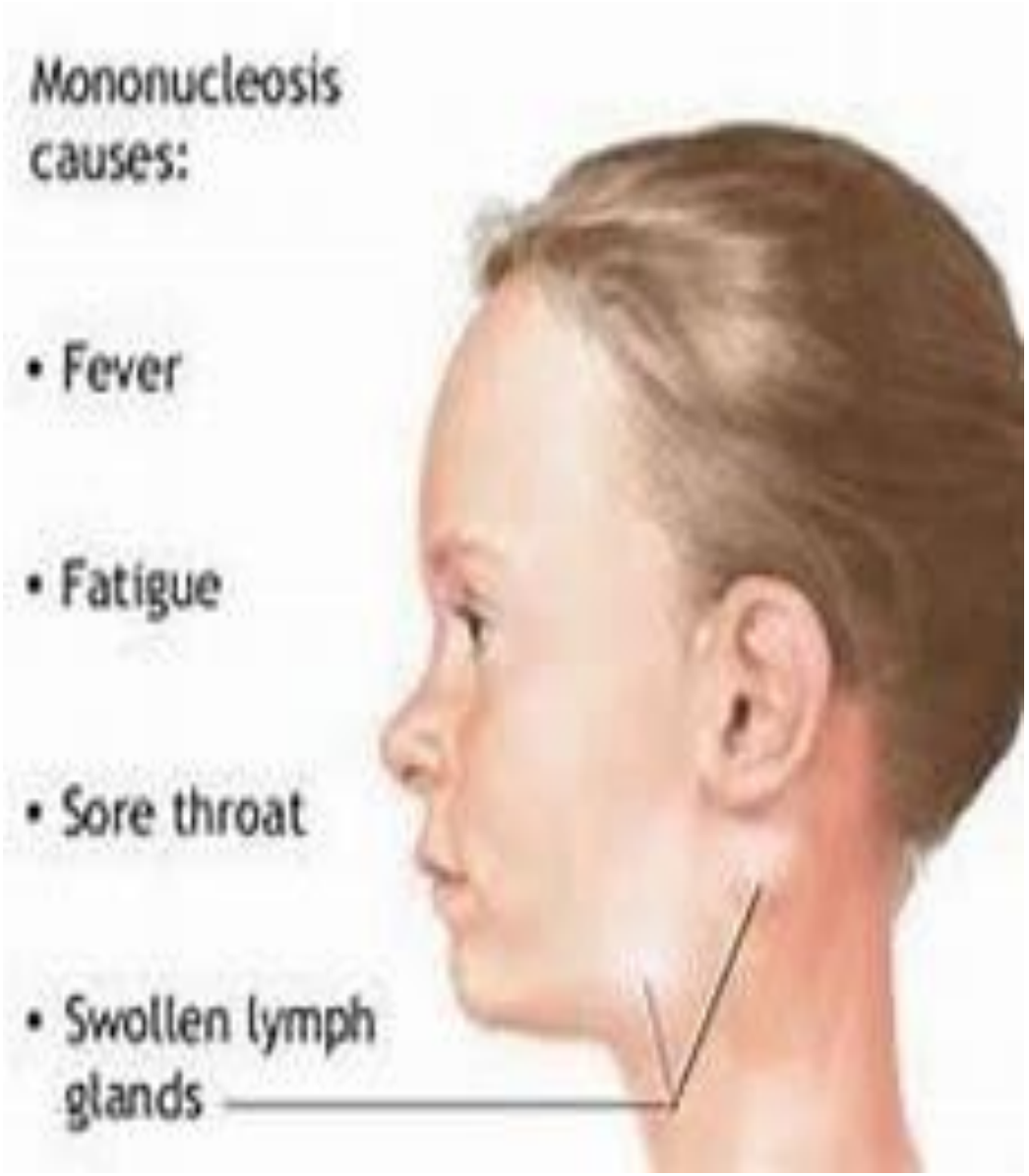
- Presence of Signs and symptoms associated with EBV infection is called **Infectious mononucleosis (IM)** or **Kissing Disease**
- Infections peak in early childhood and late adolescence/young adulthood
- Triad :high fever , oropharyngitis , cervical lymphadenopathy
- Complication : rash / mild splenomegaly / hepatic enlargement / pericarditis/ Guillam-barre syndrome
- Laboratory findings :

  - WBC count is usually elevated **(lymphocytic leukocytosis)**
  - >10% are **atypical lymphocytes** (CD8+ cells are the predominate cells)
  - Low-grade neutropenia and thrombocytopenia are common during the first month
  - Liver function is abnormal in >90% of cases

- Atypical lymphocytes :

enlarged lymphocytes that have abundant cytoplasm, vacuoles, and indentations of the cell membrane.





WBC Neoplastic disorders

leukemia

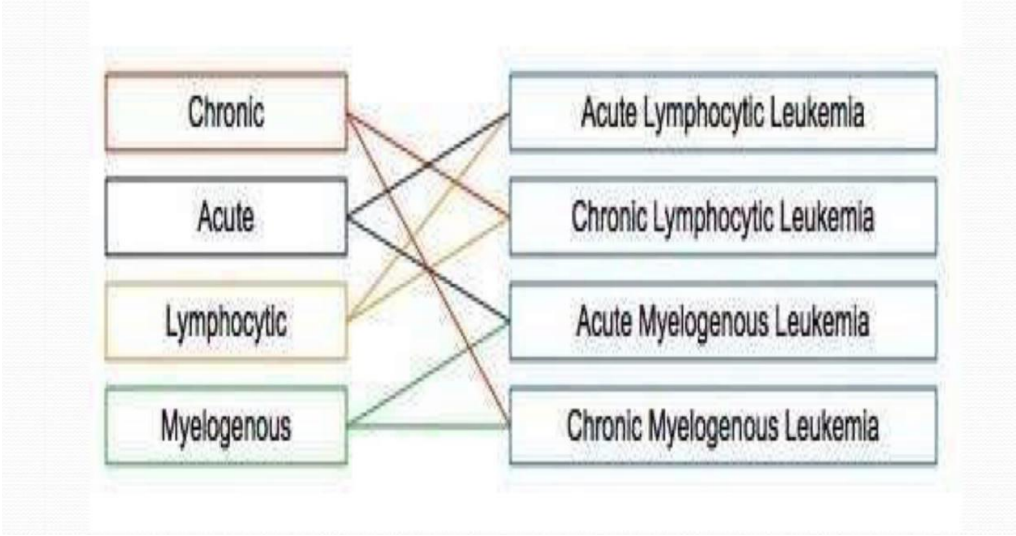
• Leukemias are malignant neoplasms arising from the transformation of a single blood cell line derived from hematopoietic stem cells affecting the blood and blood forming tissue of **the bone marrow**, **lymph system** and **spleen**.

• Because leukemic cells are immature and poorly differentiated, they proliferate rapidly and have a long life span; they do not function normally; they interfere with the maturation of normal blood cells; and they circulate in the bloodstream, cross the blood brain barrier, and infiltrate many body organs.

• Lymphoid stem cells produce either T or B lymphocytes.

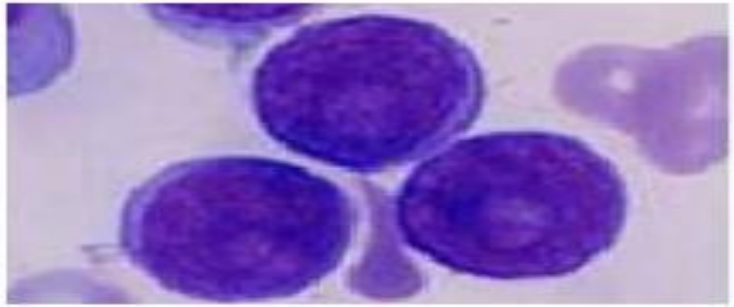
• Myeloid stem cells differentiate into three broad cell types : RBCS, WBCS, and platelets.

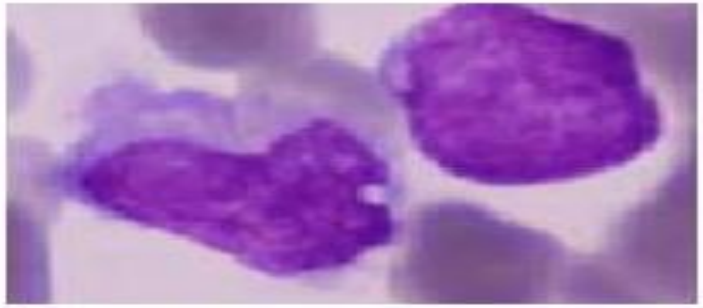
NOTE : It's essential to note that the specific type of leukemia, its stage, and its impact on the bone marrow and peripheral blood counts determine whether **leukocytosis** **or** **leukopenia** occurs

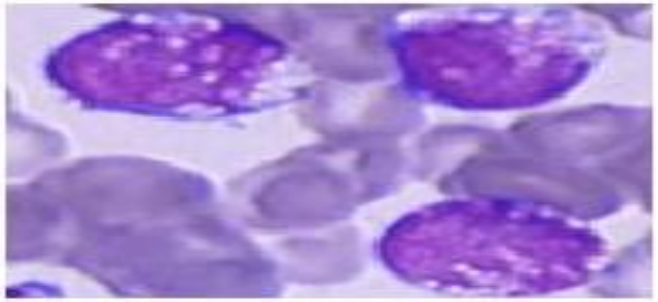


Acute lymphocytic leukemia

- Most common affect male children age between (2-5 years)
- Worse prognosis : T (8:14) Burkitt lymphoma , T (9;22) translocation that forms Philadelphia chromosome , T (4;11) in infant leukemia (age less than 1 or age more than 10) , leukocyte count more than 50,000/mm3 , CNS involvement , Hypodiploidy , T cell ALL
- Children with trisomy 21 have a 15 higher risk of acute leukemia as compared to general population (Journal of Medical Case Reports 2007).
- there's 3 subtypes :
- **L1 morphology:** Lymphoblasts, are the most common subtype of childhood ALL (**80-85%**), have scant cytoplasm and inconspicuous nucleoli; these are associated with a better prognosis
- **L2 category:** accounting for **15%** cases, show large, pleomorphic blasts with abundant cytoplasm and prominent nucleoli.
- **L3 morphology:** Only **1-2%** patients with ALL , cells are large, have deep cytoplasmic basophilia and prominent vacuolation , should be treated as burkitt lymphoma

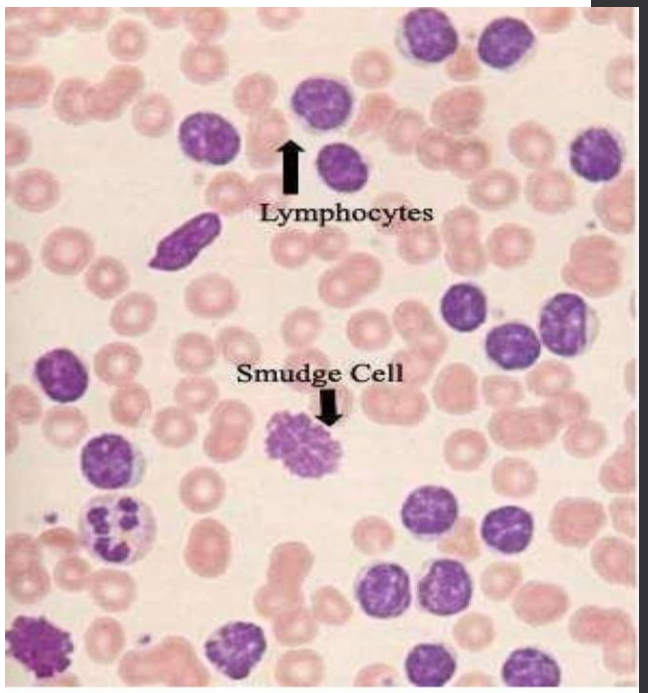

ALL-L1


ALL-L2


ALL-L3

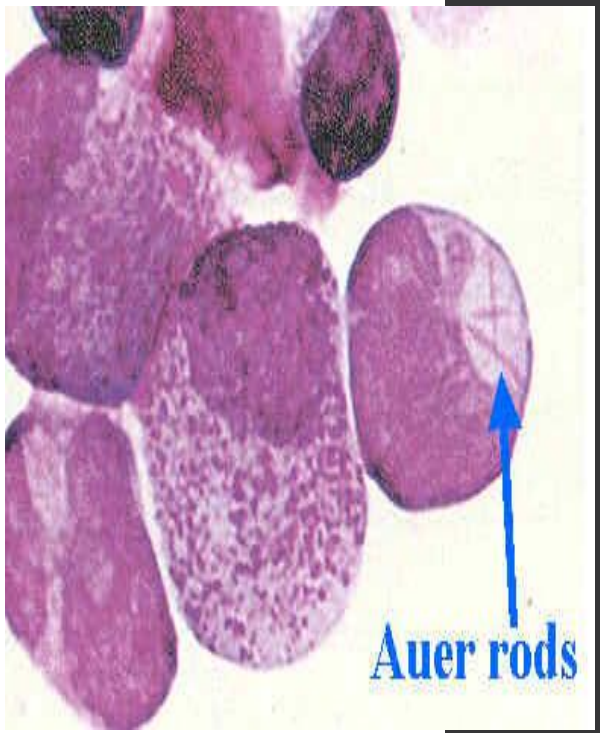
Chronic lymphocytic leukemia

- Most common affect male elderly (age **above 60**)
- Without lymph node involvement we name it CLL
- With lymph node involvement we name it SLL
- **Clinical presentation :** anemia , leukocytosis (20000-100000) ,thrombocytopenia but often asymptomatic
- **Histopathology :** In blood smear it shows : mature B lymphocyte , smudged cell
- **Treatment :** for anemia and thrombocytopenia until severe case developed we use chemotherapy



Acute myeloid leukemia

- Most common affect male elderly
- It may involve PML-RARA gene mutation T(15; 17) which is poor prognosis
- There's more than 8 subtypes but M7 (megakaryocytic subtype) with down syndrome
- **Clinical presentation :** pancytopenia or leukocytosis ,thrombocytopenia , sternal tenderness , Splenomegaly and lymphadenopathy
- **Histopathology :** myeloblast , Auer rods (large, crystalline cytoplasmic inclusion bodies)
- **Treatment :**
  - RARA involved mutation in AML respond to ATRA (all trans retinoic acid)
  - No RARA involved mutation not respond to ATRA
  - ATRA + arsenic trioxide combination is more effective than monotherapy



Chronic myeloid leukemia

- Most common affect elderly
- Its associated with BCR-APL Mutation (Philadelphia chromosome) which is better prognosis in CML because it gives target therapy
- Median survival is 3 years without treatment
- **Clinical presentation** : anemia , thrombocythemia in early stage , thrombocytopenia in late stage , leukocytosis , Massive splenomegaly and often asymptomatic
- **Histopathology :** Bone marrow (blast phase)

  30% have lymphoid blasts

  70% have myeloid blasts
- **Treatment :** The commonly drugs are hydroxyurea and busulfan (monitor of WBC count needed with therapy).

Leukopenia

- Its lowering of WBCS count less than 4.000/mm3
- There are several different types of leukopenia, depending on which type of WBC is low in your blood. The types of WBCs include:
- 1) neutropenia
- 2) lymphocytopenia
- 3) monocytopenia
- 4) eosinopenia

Leukopenia

- Leukopenia can be related to a number of factors including:
- **Aplastic anemia** – A condition where the bone marrow doesn't produce new blood cells
- **Autoimmune disorders** – Conditions that attack the white blood cells or bone marrow cells, such as lupus or rheumatoid arthritis
- **Cancer** or **diseases** of the bone marrow – Such as multiple myeloma
- **Certain medications** – Such as antibiotics , that destroy white blood cells
- **Congenital conditions** – Conditions present at birth that affect the bone marrow
- **Cancer treatments –** Including chemotherapy, radiation and bone marrow transplant

Leukopenia

- Congenital conditions :
- **Kostmann Syndrome :** is a rare, severe, congenital neutropenia disorder characterized by a lack of mature neutrophils , it is caused by disabling mutations in the *HAXI* gene, which encodes *HAX1*, a mitochondrial protein that inhibits apoptosis .
- **Myelokathexis:** is a congenital disorder that causes severe , chronic leukopenia and neutropenia , The disorder is believed to be inherited in an autosomal dominant manner .

Neutropenia

- occurs when you have too few neutrophils , and classified into three degrees :
- **Mild neutropenia** .
- **Moderate neutropenia**.
- **Severe neutropenia**.
- Neutropenia can also be classified as acute (temporary or short-lasting) or chronic (long-lasting), congenital (a condition you’re born with) or acquired (a condition that happens over time) .

Neutropenia

- **There are different causes of neutropenia**
- **Genetic conditions:** Genetic abnormalities that cause neutropenia can be passed from parents to their children. Types of inherited neutropenia include benign ethnic neutropenia (BEN)

- Benign ethnic neutropenia (BEN) is a chronic congenital form of neutropenia that's most common in people of African, Middle Eastern and West Indian descent. Although neutrophil counts are below 1,500 with this type of neutropenia, people with BEN are not at increased risk of infection.

Neutropenia

- **Infections:** Viral, bacterial and parasitic infections can cause neutropenia.

  Common causes include HIV, hepatitis, tuberculosis, sepsis, and Lyme disease, among other infections.

- **Chronic idiopathic neutropenia**: is a specific type of neutropenia that doesn’t have a clear cause.

Leukopenia

- **Treatment Options :**
- treatment options will vary depending on what is causing leukopenia include :

1) Discontinuing treatment that causes low white blood cell counts – Can include medications, chemotherapy or radiation .

2) Growth factor therapy – Treatment derived from bone marrow that can stimulate white blood cell production .

3) Low-bacterial diet – A diet that minimizes your exposure to bacteria found in certain foods, such as raw, unwashed produce or undercooked meat .

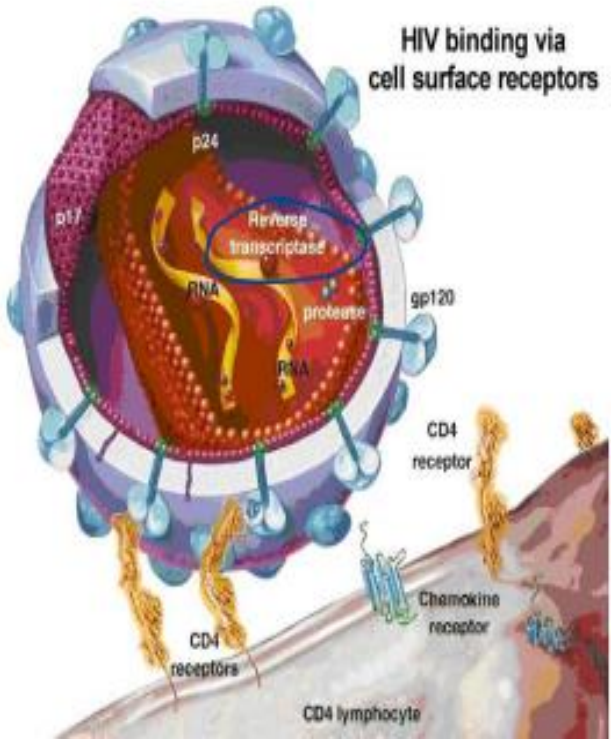
4) Medications – Therapy that helps the body produce more blood cells or that fights the infection that is causing low white blood cell counts .

HIV

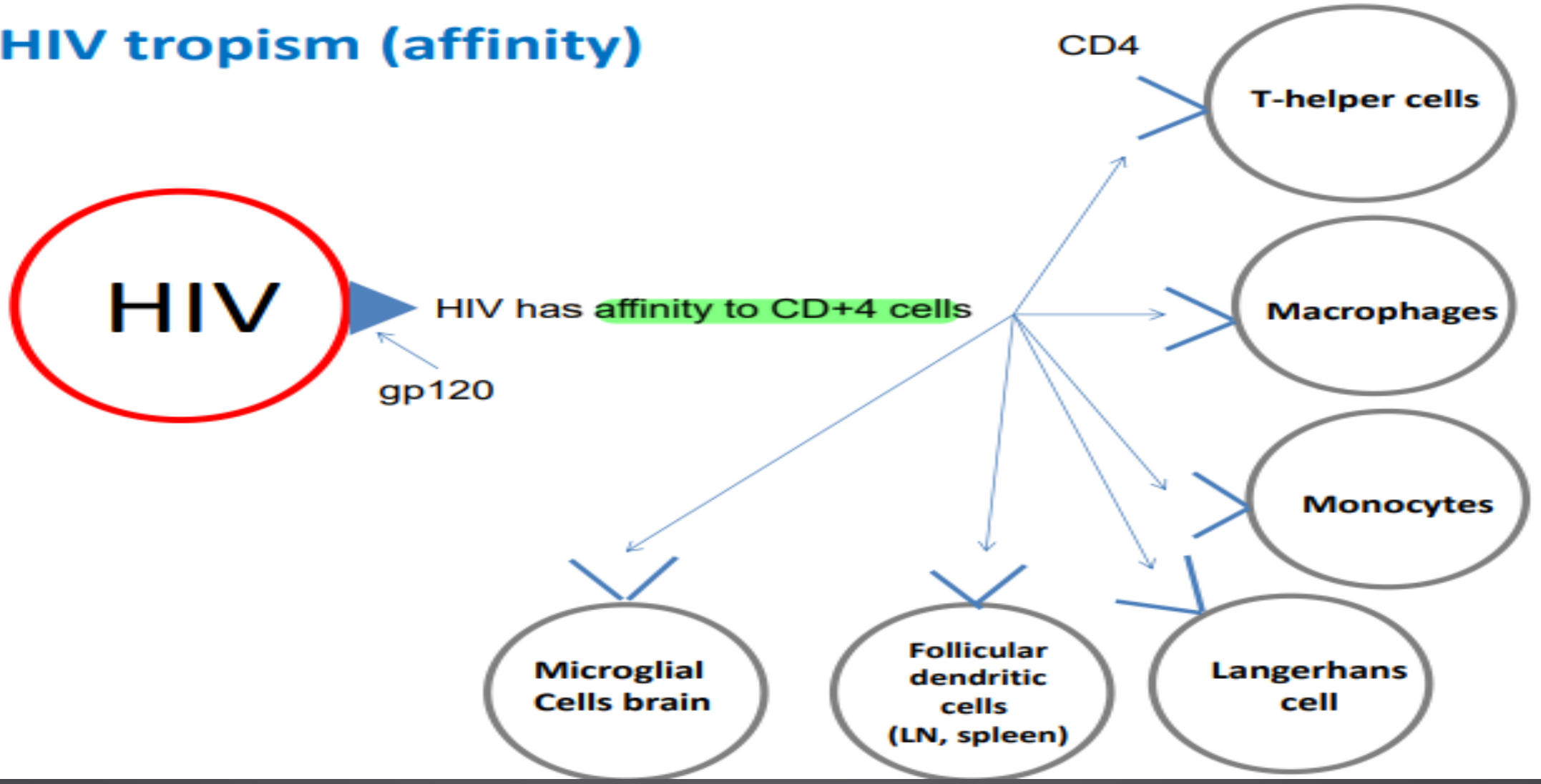
- virus of the lentivirus subfamily of retroviruses
- DsRNA .
- Whith specific viral glycoproteins are imbedded and responsible for binding to target cell they are :

• gp120 protrudes from the surface and interacts with the CD4 receptor

• gp41 is embedded in the envelope and mediates the fusion of the viral envelope with the cell membrane at the time of infection.



HIV tropism (affinity)



Transmission of HIV

- • Direct contact with infected blood
- • Sexual contact (85%)
- • HIV-infected mothers to infants during pregnancy, delivery, or breastfeeding

NOTE : Coughing, sneezing , drinking , eating , Public baths cannot transmit HIV

Stages of HIV Disease

Acute/Early Infection : Following HIV transmission, approximately 50% of individuals will develop a febrile, flu-like illness with non specific symptom

- Onset of illness is generally 1-6 weeks following exposure and can last 1-3 weeks

- Within days, HIV disseminates into lymph nodes, central nervous system where it “hides out” and remains dormant.

- A positive HIV antibody usually develops by 4-6 weeks following transmission so Testing for HIV antibody may be negative at this time.

Intermediate Stage : T cell destruction by HIV begins to weaken the immune system over time

- In general if untreated, there is an 8-10 year period during which an HIV+ individual undergoes a gradual decline in immune function and increase in HIV viral load

- Often no symptoms exhibited during the intermediate disease stag

Stages of HIV Disease

Stage of AIDS : More than 50% of people do not know they are HIV-infected until they become symptomatic (an indicator of advanced disease).

• Hallmarks of this stage of the disease include:

-Leucopenia (Opportunistic and recurrent infections or malignancies)

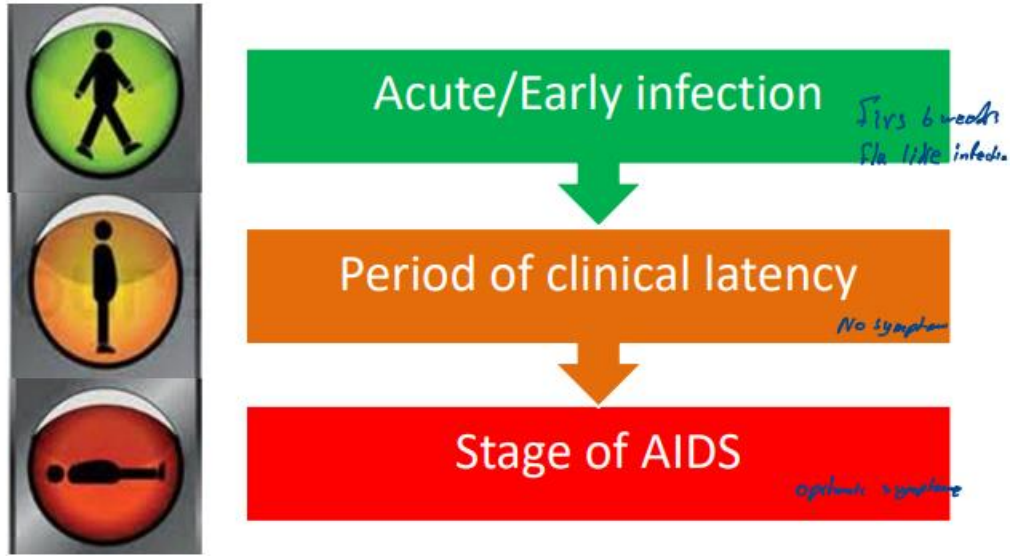
-Rashes

-Vaginal candidiasis

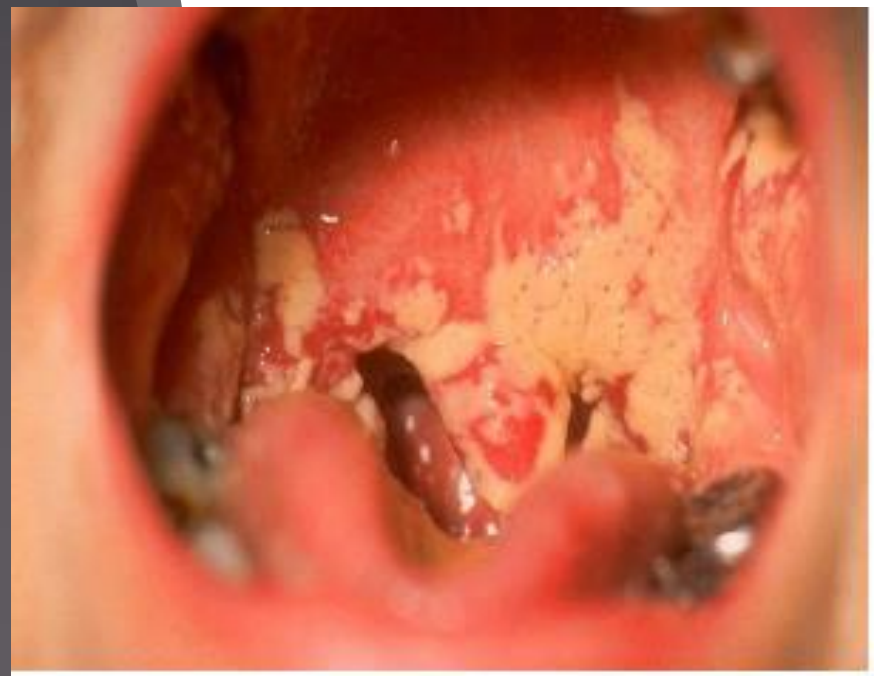
-thrush (oral candidiasis)

-anemia

-Neuropathy

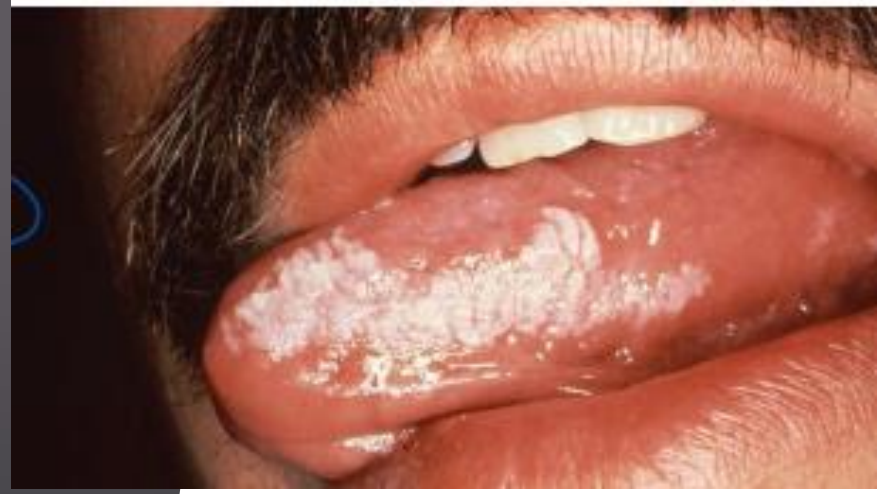


Oral Candidiasis (thrush)



Oral Hairy Leukoplakia

Due to the Epstein-Barr virus under immunosuppressed conditions



Management and diagnosis

- Both leukocytosis and leukopenia are typically detected through routine blood tests
- Their management depends on identifying the underlying condition responsible for the abnormal white blood cell counts.
- Treatment may involve addressing infections, discontinuing medications that contribute to the condition, managing autoimmune diseases, or addressing bone marrow disorders through various medical interventions.

Refrancecses

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- https://www.slideshare.net/MartaGerasymchuk/leucocytosis-leucopenia-leucosis
- First Aid USMLE step 1 book
- Our previous Basic Lectures

THANK YOU