# Approach to Leukocytosis and Leukopenia

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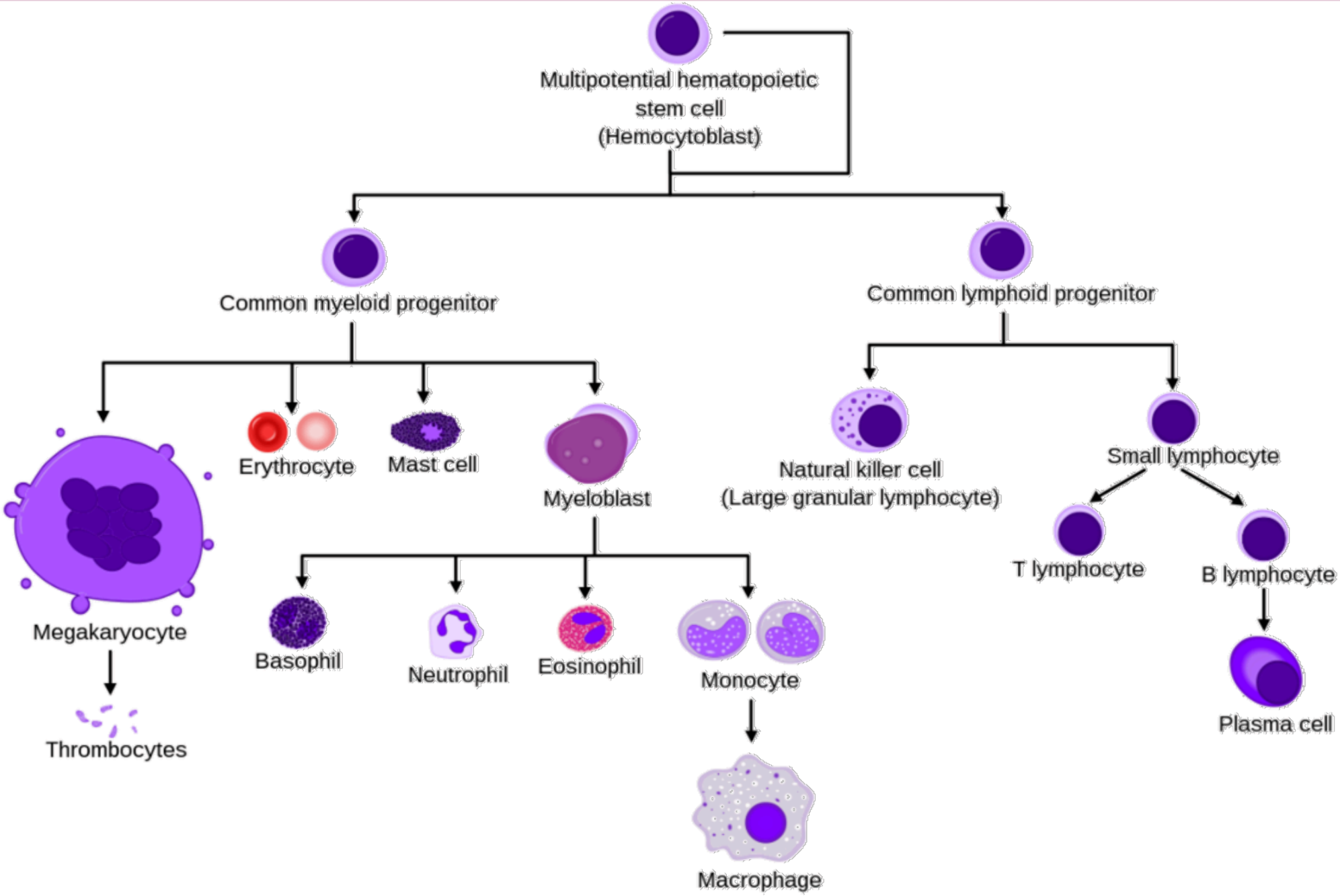
# WBCs

Our body is made up different types of blood cells, including white blood cells (WBC), or leukocytes.

- WBC are important part of our immune system, helping our body to fight off diseases and infections.
- Normal WBC count is 4.500-11.000/mm3 in adult man.
- Normal WBC count ranges vary based on an individual's age, pregnancy status, sex, and ethnicity, and on the laboratory performing the study

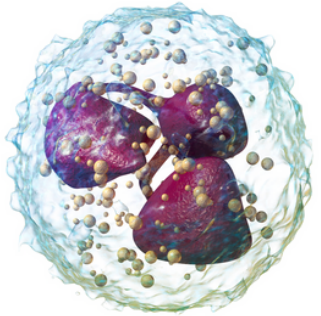

Multipotential hematopoietic stem cell (Hemocytoblast)
Common myeloid progenitor
Common lymphoid progenitor
Megakaryocyte
Erythrocyte
Mast cell
Myeloblast
Natural killer cell (Large granular lymphocyte)
Small lymphocyte
Thrombocytes
Basophil
Neutrophil
Eosinophil
Monocyte
T lymphocyte
B lymphocyte
Plasma cell
Macrophage

# Leukocytosis

- Leukocytosis is an increase in the white blood cell (WBC) count (>11,000/mm3).
- Which can be further characterized by the predominating cell type, e.g., neutrophilia,lymphocytosis, eosinophilia .
- 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

# 1- Neutrophilic leukocytosis:



- Is an increase number of neutrophil in differential leukocytic count which normally (60-70%).

**Common causes of neutrophilia**

- Infection
- Stress response
- Acute myeloid leukemia
- Chronic myeloid leukemia
- Myeloproliferative neoplasm

# • Common causes of neutrophilia :

## Infection

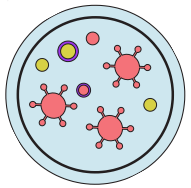
- **clinical features:**

  - Fever
  - Features specific toinfection site, e.g :

Cough, shortness of breath, dysuria , New heart murmur

- **dignostic finding :**

  - Neutrophil left shift
  - Body fluid cultures with bacteria or fungus
  - Imaging (e.g., CXR) consistent with infection



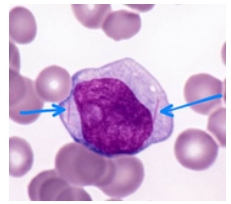
## Acute myeloid leukemia

- **clinical features:**

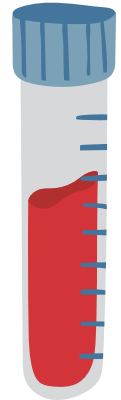
  - Sudden onset and rapid progression of symptoms .
  - Fatigue, pallor, weakness .
  - Epistaxis, bleeding gums,petechiae, purpura

- **dignostic finding :**

  - CBC and blood smear:
  - Anemia
  - Thrombocytopenia
  - > 20% myeloblasts
  - Auer Rods



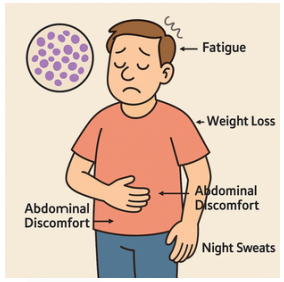
  - Bone marrow aspiration and biopsy

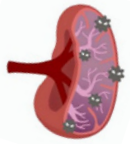


# Common causes of neutrophilia :

## Chronic myeloid leukemia

- **clinical features:**
  - Weight loss, fever, night sweats, fatigue
  - Splenomegaly, LUQ discomfort, infections.



- **dignostic finding :**
  - CBC and blood smear:
  - Sever leukocytosis
  - Thrombocytosis
  - Anemia later stages
  - Bone marrow aspiration and biopsy

## Myeloproliferative neoplasm

- **clinical features:**
  - Constitutional symptoms, especially fatigue
  - Abdominal pain
  - Features of hyperuricemia, e.g., gout

- **dignostic finding :**
  - CBC and blood smear:
  - changes in myeloid cell lines
  - Elevated LDH, uric acid, and/or leukocyte alkaline phosphatase
  - Abdominal imaging (e.g.,CT or ultrasound) with hepatosplenomegaly

- Common causes of neutrophilia :

## Stress response

- **clinical features:**

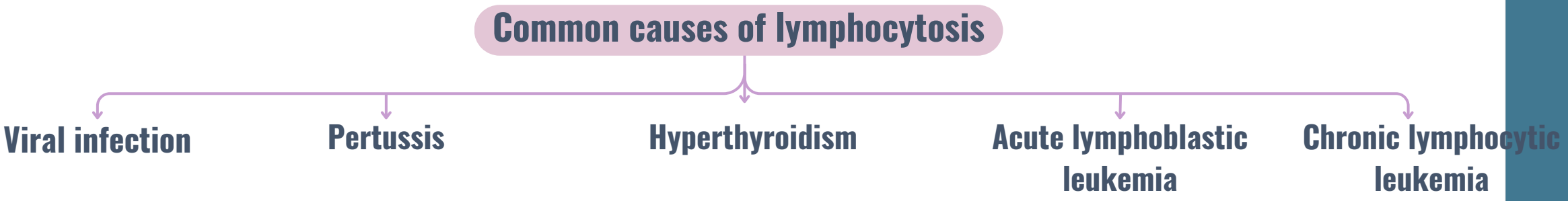
- Recent physical stress (e.g., surgery,seizure,vigorous exercise)
- Recent emotional stress (e.g., panic attack)

- **dignostic finding :**

- Reactive neutrophiliac

# 2-Lymphocytic leukocytosis

- Is an increase in number of lymphocyte in differential leukocytic count which normally more than (20-30%).



# Common causes of lymphocytosis

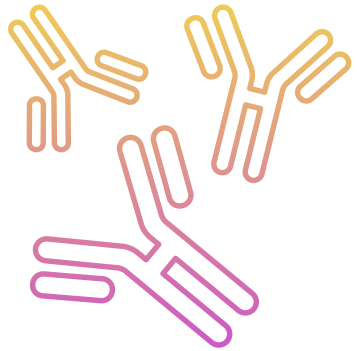
## Viral infectin

- **clinical features:**

- Fever
- Disease -Specific features
- Malaise and/or fatigue,myalgias
- Symptoms ofURTI (e.g.,cough)
- Lymphadenopathy Nausea, vomiting, diarrhea

- **dignostic finding :**

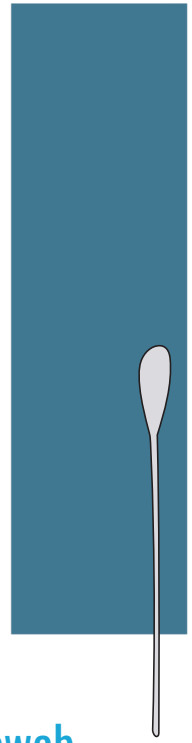
- Often a clinical diagnosis
- Antibody detection and/ or viral PCR
- Imaging (e.g. CXR)consistent with infection.



## Pertussis

- **clinical features:**

- Watery nasal discharge
- Paroxysmal coughing with high- pitched whooping
- Posttussive vomiting
- Low-grade fever (rare)



- **dignostic finding :**

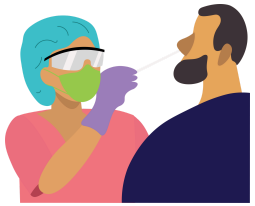
- First 4 weeks of symptoms:

PCR and/or bacterial culture of nasopharyngeal swab or aspirate sample

- > 4 weeks of symptoms:

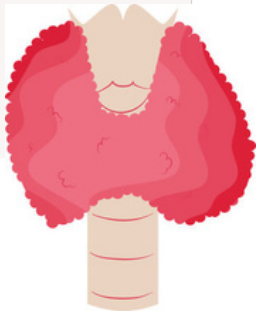
pertussis serology.

CBC: A lymphocyte count of > 20,000 cells/μL is a characteristic Diagnostic finding in infants.



- Common causes of lymphocytosis

# Hyperthyroidism



- **clinical features:**

- Clinical features of thyrotoxicosis
- Fatigue
- Pretibial myxedema
- Graves ophthalmopathy
- Hypertension.

- **dignostic finding :**

- Thyroid function tests:
  Low ↓ TSH, high ↑ free T4

- Imaging of the thyroid gland

# Common causes of lymphocytosis

## Acute lymphoblastic leukemia

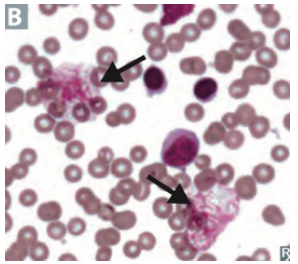
- **clinical features:**
  - **Sudden** onset of symptoms and rapid progression (days to weeks)
  - Fever, night sweats, unexplained weight loss
  - Bone pain
  - Painless lymphadenopathy

- **dignostic finding :**
  - CBC and blood smear:
  - Anemia
  - Thrombocytosis
  - > 20% lymphoblasts
  - Bone marrow aspiration and biopsy

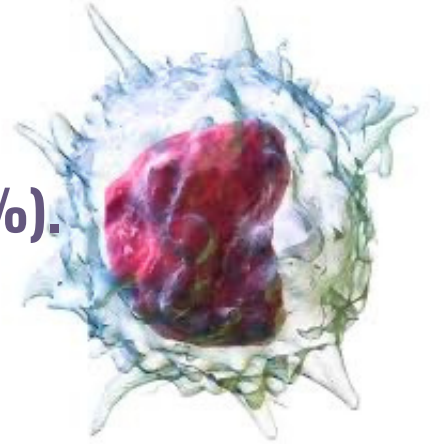
## Chronic lymphocytic leukemia

- **clinical features:**
  - B symptom
  - repeated infections
  - hepatomegaly/ splenomegaly
  - dermatologic symptoms
  - Painless lymphadenopath

- **dignostic finding :**
  - CBC and blood smear:
  - Persistent(>3 months)
  - Smudge cell →
  - Anemia
  - Thrombocytopenia
  - granulocytopenia
  - flow cytometry
  - Bone marrow aspiration and biopsy



# 3-Monocytic leukocytosis:



- **Is an increase number of monocyte in differential leukocytic count which normally (3-8%).**
- Monocytosis is most commonly caused by <u>bacterial infections.</u>

## Causes of monocytosis:

- **Infection:**
  - Bacterial(e.g ,TB)
  - Fungal
  - Viral (e.g , EBV)
  - Protozoal infections (e.g ,malaria)
- **Autoimmune or inflammatory:**
  - IBD
  - Sarcoidosis
  - SLE
- **Malignancy:**
  - Lymphoma
  - Multiple myloma
  - Acute or chronic myelomonocytic leukemia
- **Hematologic :**
  - Recovery from bone marrow suppression
  - Neutropenia
- **Other:**
  - splenectomy

- Question:

- Which of the following best explains why steroids cause a sustained increase in neutrophils?

A) They stimulate the spleen to release WBCs
B) They promote margination of WBCs
C) They increase destruction of aged neutrophils
D) It triggers demargination
E) They enhance antibody production by B cell

# 4- Eosinophilic leukocytosis

- **Is an increase number of eosinophils in differential leukocytic count which normally (1-5%).**

- Causes of Eosinophilia:

- Usually cause by **Infection , Autoimmune or hypersensitivity :**

**# Bacterial (e.g., scarlet fever, leprosy, genitourinary infections, chlamydial infections) and Parasitic infections.**

**#Asthma, Allergic rhinitis, Eosinophilic esophagitis , Rheumatoid arthritis, SLE and Sarcoidosis .**

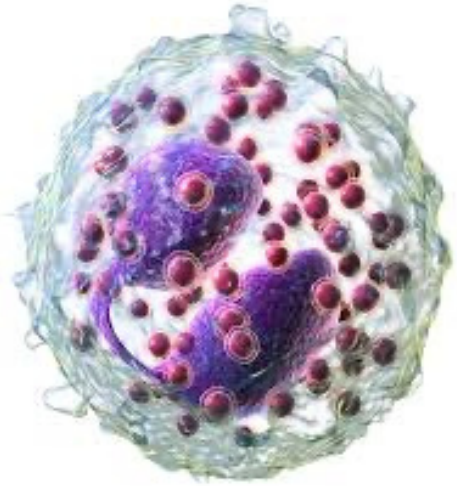
- **Medications: drug hypersensitivity reactions .**

- Other Causes by **Malignancy , Hematologic , or Dermatological diseases :**

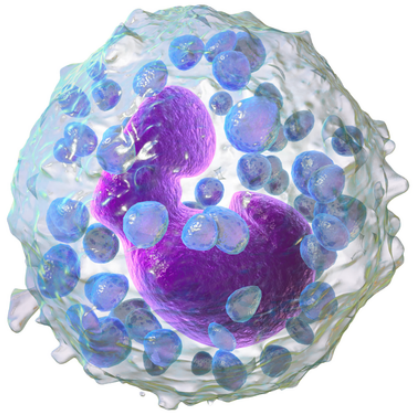
#Non-Hodgkin lymphoma, Hodgkin lymphoma, CML ,T-cell lymphoproliferative disorders

#Polycythemia vera, Myelofibrosis

#Dermatitis herpetiformis and Erythema multiforme



# 5-Basophil leukocytosis



- **Basophilia Is an increase number of eosinophils count which normally (1- .5%)**
- Contain heparin and histamine granules , it is become mast cell in tissue
- Basophilia is most commonly caused by malgnancy(CML)
- Causes of Basophilia:
- The usual cause is a **myeloproliferative or haematological disorder** such as :

chronic myeloid leukemia, Hodgkin lymphoma , polycythaemia vera and Chronic hemolytic anemia

- Reactive basophil increases are sometimes seen during smallpox or chickenpox infection and in ulcerative colitis
- Other Causes such as Allergy , Chronic inflammation of air way or dermatitis , Hypothyroidism , Ovulation and splenectomy

# Leukopenia

- Is a decrease in the white blood cell (WBC) count ( < 4.500/mm3 ).
  - **related to a number of that affect WBCs. Or BM :**
    - Aplastic anemia
    - Autoimmune disorders eg. lupus or rheumatoid arthritis.
    - Cancer or diseases of the bone marrow eg. MM
    - Certain medications eg. antibiotics .
    - Cancer treatments : chemotherapy, radiation and bone marrow transplant
    - Congenital conditions – Conditions present at birth that affect the bone marrow.

- **Kostmann syndrome :** is a rare, severe, congenital neutropenia disorder characterized by a lack of mature neutrophils , it is caused by disabling mutations in the HAX1 gene, which encodes HAX1, a mitochondrial protein that inhibits apoptosis .

- **Myelokathexis (WHIM syndrome) :** is a congenital disorder that causes severe,chronic leukopenia and neutropenia , The disorder is believed to be inherited as autosomal dominant mannerDifferential type of l

# Differential type of leukocytopenia

## 1) Neutropenia :

- **Range:**

- Mild: 1,000–1,500 c/mm3
- Moderate: 500–1,000 c/mm3
- Severe: < 500 c/mm3 (severe infections )

- **cause:**

- Genetic conditions As Benign ethnic neutropenia (BEN)
- Infections: Commoly HIV, hepatitis, TB , sepsis, and Lyme disease
- BM damage/suppression or Drugs e.g.carbimazole, clozapine

## 2) Lymphopenia:

- **Range:**

- Mild: 800–1,000/$mm^3$
- Moderate: 500–800/mm
- Severe: <500/$mm^3$

- **cause:**

- Immunodeficiencies e.g., DiGeorge syndrome, SCID, Wiskott-Aldrich syndrome .
- immunosuppressants: chemotherapy, glucocorticoids, radiation or Drugs (e.g., carbamazepine).
- Infections e.g., sepsis, measles, miliary tuberculosis, HIV.
- Neoplasia Hodgkin some NH. lymphomas).

# Differential type of leukocytopenia

## 1) Neutropenia :

- **Range:**

- Mild: 1,000–1,500 c/mm3
- Moderate: 500–1,000 c/mm3
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- **cause:**

- Genetic conditions As Benign ethnic neutropenia (BEN)
- Infections: Commoly HIV, hepatitis, TB , sepsis, and Lyme disease
- BM damage/suppression or Drugs e.g.carbimazole, clozapine

## 2) Lymphopenia:

- **Range:**

- Lymphocytes : < 25%
- Mild: 800–1,000/$mm^3$
- Moderate: 500–800/mm
- Severe: <500/$mm^3$

- **cause:**

- Immunodeficiencies e.g., DiGeorge syndrome, SCID, Wiskott-Aldrich syndrome .
- immunosuppressants: chemotherapy, glucocorticoids, radiation or Drugs (e.g., carbamazepine).
- Infections e.g., sepsis, measles, miliary tuberculosis, HIV.
- Neoplasia Hodgkin some NH. lymphomas).

# Differential type of leukocytopenia

## 3) Monocytopenia:

- **Range:**
  - Monocytes: < 3%
  - <200/$mm^3$
  - <0.2 × $10^9$/L
- **cause:**
  - Infections (e.g., HIV, EBV).
  - Aplastic anemia or Drugs (e.g., glucocorticoids, chemotherapy ).
  - Malignancy (e.g., hairy cell leukemia, AML)

## 4) Eosinopenia:

- **Range:**
  - Eosinophil: < 1%
  - <50/$mm^3$
  - <0.05 × $10^9$/L
- **cause:**
  - Infections (typhoid fever, paratyphoid fever, sepsis).
  - Cushing syndrome.
  - Glucocorticoids
  - Stress

# Clinical Assessment :

## History:

- Symptoms of infection ( Recent or Recurrent ).
- Symp. Of Malignancies: Night sweats, weight loss, lymphadenopathy suggest leukemia or lymphoma.
- Stress/Physiologic changes: Pregnancy, stress, and exercise can transiently increase WBCs .
- ask about Medications and Autoimmune diseases.

## Physical Examination :

- Fever, signs of infection
- Pallor, bruising, fatigue: Possible bone marrow failure
- Sign Lymphadenopathy or hepatosplenomegaly

## Laboratory investigations:

- Complete Blood Count (CBC)
- Peripheral Blood Smear
- Bone Marrow Aspiration & Biopsy
- Imaging (e.g., CXR in suspected pneumonia).
- Additional Tests Based on Clinical Suspicion

**Table 8.1** White cells: normal blood counts.

| Adults | Blood count |
|---|---|
| *Total leucocytes* | $4.0–11.0 \times 10^9/L^*$ |
| Neutrophils | $1.8–7.5 \times 10^9/L^*$ |
| Eosinophils | $0.04–0.4 \times 10^9/L$ |
| Monocytes | $0.2–0.8 \times 10^9/L$ |
| Basophils | $0.01–0.1 \times 10^9/L$ |
| Lymphocytes | $1.5–3.5 \times 10^9/L$ |

# Peripheral Blood Smear Finding :

- **Morphology:**
  - Monomorphic WBCs are concerning for malignancy.
  - Pleomorphic WBCs suggest reactive leukocytosis
- **Band cells:**
  - are common during the acute phase of bacterial infections and/or inflammation.
- **Platelet clumping:** may be misinterpreted as WBCs.
- **Toxic granulations suggest inflammation:**

- Treatment:

## Supportive Management :

- Hydration.
  IV fluids to reduce blood viscosity, especially in extreme leukocytosis
- Manage Complications.

- then..

**Treat the Underlying Cause.**

- Antibiotic or Antiinflammatory .

**Leukemias & Myeloproliferative Disorders.**

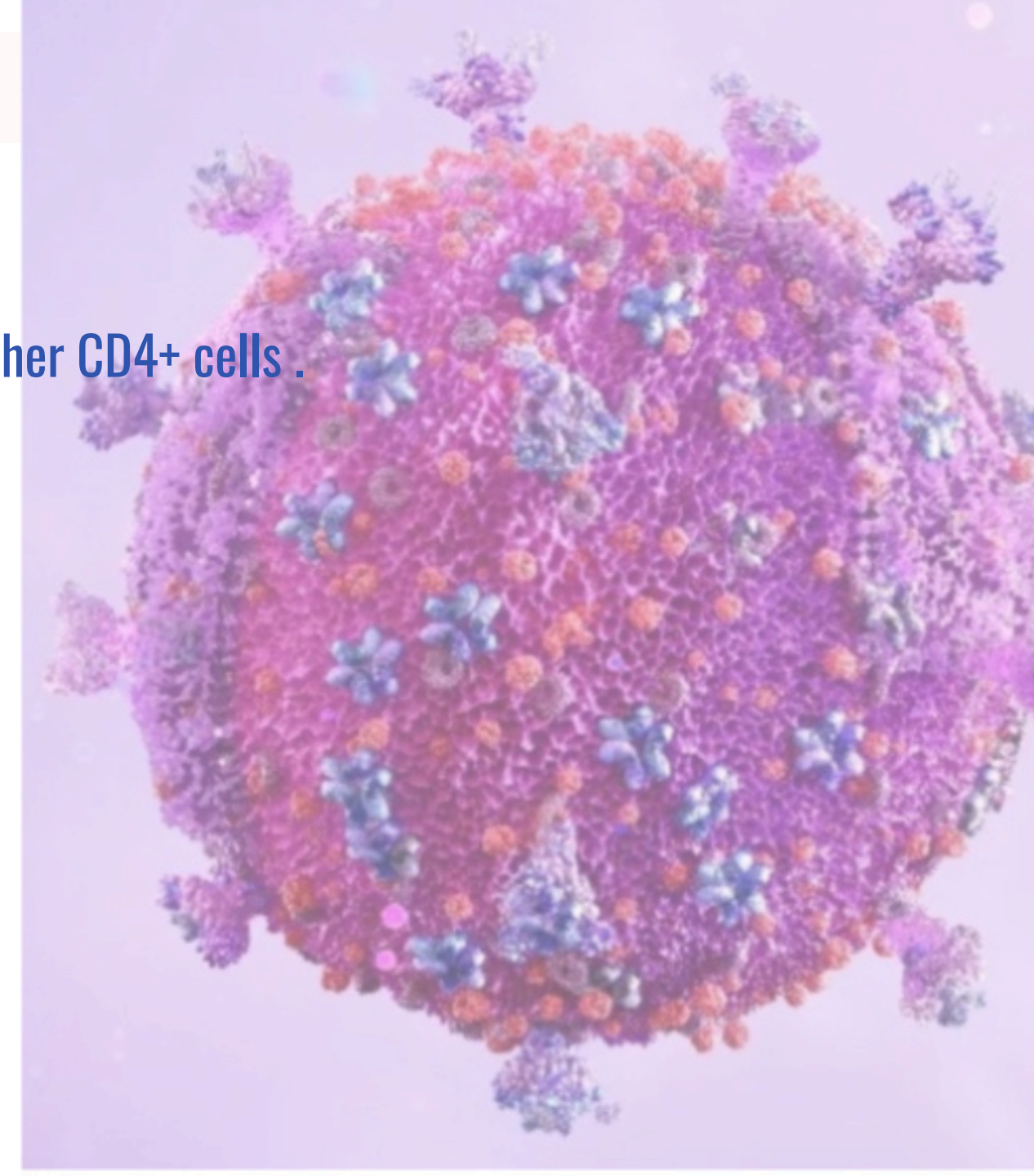
- Hematology consultation.
- Chemotherapy or targeted thera

- HIV:

- Is lipid Enveloped virus of retroviruses subfamily .
- Two viral strands of RNA found in core.
- The virus infects and distrust macrophages and other CD4+ cells .

- **Transmission:**
  - Direct contact with infected blood
  - Sexual contact
  - HIV-infected mothers to infants

- **Treatment by Anti-Retroviral therapy.**



- **Case Scenario:**
- A 45-year-old man presents to the emergency department with a 2-day history of fever, productive cough, and pleuritic chest pain. He appears ill and has a temperature of 38.9°C (102°F), pulse 110 bpm, respiratory rate 24/min, and blood pressure 118/76 mmHg. On examination, there are crackles and bronchial breath sounds in the right lower lung field. A chest X-ray shows a right lower lobe consolidatio

- **Laboratory studies reveal:**
- WBC count: 18,000/$mm^3$ (normal: 4,000–11,000/$mm^3$)
- Neutrophils: 85%
- Bands: 10%
- Hemoglobin: 13.5 g/dL
- Platelets: 250,000/$mm^3$

- **Question**:
- What is the most likely cause of this patient's leukocytosis?

A. Acute bacterial pneumonia
B. Chronic lymphocytic leukemia
C. Viral upper respiratory tract infection
D. Allergic reaction
E. Parasitic infection

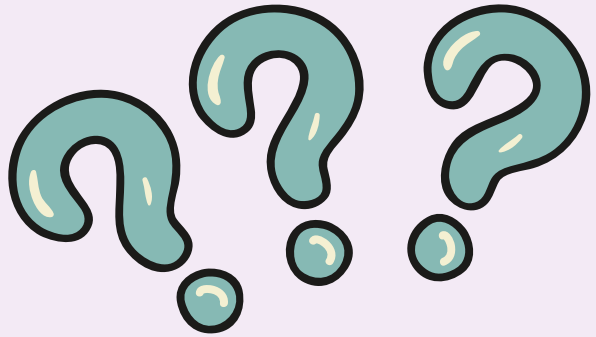
- **Case Scenario:**
- A 25-year-old man with asthma presents for a follow-up. He was recently started on oral prednisone for an acute asthma exacerbation. He feels well. Lab results show:
- WBC count: 14,000/$mm^3$
- Neutrophils: 75%
- No fever, no signs of infection

- **Question**:
- What is the most likely cause of this leukocytosis?

A. Steroid-induced demargination
B. Bacterial infection
C. Leukemoid reaction
D. Viral infection
E. Allergic reaction

- **Case Scenario:**
- A 32-year-old woman presents to the clinic with a 2-week history of fatigue, low-grade fever, and frequent mouth ulcers. She has a history of systemic lupus erythematosus (SLE) and is currently taking hydroxychloroquine. On examination, she appears pale with no lymphadenopathy or splenomegaly.

- **Her labs show:**
- WBC count: 2,400/$mm^3$ (normal: 4,000–11,000/$mm^3$)
- Neutrophils: 50%
- Hemoglobin: 10.5 g/dL
- Platelets: 210,000/$mm^3$
- ANA: positive
- ESR: elevated



- **Question**:
- What is the most likely cause of this patient's leukopenia?

A. Viral infection
B. Aplastic anemia
C. Systemic lupus erythematosus–related bone marrow suppression
D. Drug-induced agranulocytosis
E. Acute myeloid leukemia

# Thanks