

WHITE CELL ABNORMALITIES

MBChB 3 lecture series

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Lecture objective

By the end of the lecture you should be able to:

- Classify the leucocyte disorders
- Explain the causes leukocytosis (benign and neoplastic causes)
- List the causes of leucopenia

LEUCOCYTE DISORDERS

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graph TD; A[LEUCOCYTE DISORDERS] --> B[Quantitative<br/>• Numerical abnormality]; A --> C[Qualitative<br/>• functional/morphologic abnormality]; B --> D[Benign Disorders]; B --> E[Neoplastic Disorders];
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The diagram is a hierarchical flowchart. At the top is a purple box labeled 'LEUCOCYTE DISORDERS'. Two arrows point down from this box to two separate boxes: a pink box on the left and a light green box on the right. The pink box is labeled 'Quantitative' and contains a bullet point 'Numerical abnormality'. The light green box is labeled 'Qualitative' and contains a bullet point 'functional/morphologic abnormality'. From the bottom of the pink box, two arrows point down to two smaller pink boxes: 'Benign Disorders' on the left and 'Neoplastic Disorders' on the right.

Quantitative

- Numerical abnormality

Qualitative

- functional/morphologic abnormality

Benign Disorders

Neoplastic Disorders

Disorders may be inherited or acquired

Quantitative

- Physiologic or pathologic variations in leucocyte counts
- Quantitative
 - Leucopenia
 - Leucocytosis

LEUCOPENIA.

- WBC $<4.0 \times 10^9/L$ (3.5)
- White cell counts below the **lower normal limit**
- May affect any class of the WBC series, singly or in combination
- Physiological
- Pathological

Physiologic leucopenia :

- Most incidences of leucopenia are due to neutropenia (largest Wbc group)
- In Africans low total WBC largely due to low neutrophil counts (constitutional/ethnic neutropenia)
- Hereditary (non-pathologic) causes of leucopenia – eg Benign familial neutropenia

Pathological causes of leucopenia:

- May be due to reduced production in BM or increased destruction
- May be due to reduction in all Wbc or specific group
- Reduced production:
 - As part of pancytopenia eg in BM replacement
 - Agranulocytosis
 - Hereditary causes
- Increased destruction
 - Hypersplenism

Neutropenia causes

Neutrophil counts < $1.5 \times 10^9/L$ ($1.3 \times 10^9/L$)

- **Acute neutropenia** When severe, the risk and severity of bacterial and fungal infections increase
- (occurring over hours to a few days)
 - Rapid neutrophil use or destruction Impaired production
- **Chronic neutropenia** (lasting months to years)
 - Reduced production or Excessive splenic sequestration

Severity

- Relates to the relative risk of infection and is classified as follows:

Category	Levels
Mild	1– 1.5 x 10 ⁹ /L
Moderate	0.5 – 1 x 10 ⁹ /L
Severe	<0.5 x 10 ⁹ /L

Causes of neutropenia

Hereditary

- Cyclic neutropenia
- Severe congenital neutropenia
- Kostmann syndrome
- Chediak-Higashi syndrome

Acquired

- Infections: sepsis, typhoid, some viral infections, granulomatous infection
- Aplastic anaemia
- Myelodysplasia
- Ionizing radiation
- Tumour infiltration
- Drugs
- Immune mediated

Lymphocytopenia

Lymphocyte count of $< 1000 \times 10^9/L$ in adults

Acquired

- Protein energy undernutrition
- AIDS
- Certain viral infections
- Drugs e.g. glucocorticoids, cytotoxics, antilymphocyte globulin
- Immune disorders e.g. SLE, rheumatoid arthritis

Inherited

- Aplasia of lymphopoietic stem cells
- Ataxia-telangiectasia
- Severe combined immunodeficiency
- Immunodeficiency with thymoma

LEUCOCYTOSIS

Increased leucocyte counts to above the upper normal limits ($>11 \times 10^9/L$ or $>10 \times 10^9/L$)

Physiologic

Pathologic

Benign

Neoplastic
(leukaemia)

Any class of leucocytes may be affected , singly or in combination

Causes of leucocytosis

NEUTROPHILIA ($>7.0 \times 10^9/L$)

Physiologic (non pathologic)

- newborn
- Pregnancy
- Exercise
- Stress
- High altitude.

Pathologic causes (reactive)

- Pyogenic infections (abscesses, septicaemia).
- Inflammatory - acute rheumatic fever, burns, thrombosis.
- Chemical poisoning, drugs
- Metabolic e.g. renal and liver failure.
- Malignant disease e.g. cancers
- Burns
- Tumours e.g. cancers of various organs
- Necrosis

LYMPHOCYTOSIS ($>3.0 \times 10^9/L$)

- Viral infections – Many viruses including Infectious mononucleosis, inf. Hepatitis, Acute infectious lymphocytosis.
- Pertussis (*Bordetella pertussis*)
- Chronic infections -T.B., brucellosis.
- Thyrotoxicosis.
- Toxoplasmosis, other Protozoal infections.

MONOCYTOSIS (> 1.0 x 10⁹/L)

- Protozoal infections - malaria, kala-azar, trypanosomiasis.
- Rickettsial infections - typhus
- Some bacterial infections -T.B., bacterial endocarditis, brucellosis, syphilis.
- Collagen vascular diseases –SLE, Rheumatoid arthritis, P.A.N. etc
- Misc. - ulcerative colitis, regional enteritis etc

EOSINOPHILIA (> 0.6 x 10⁹/L)

- Allergic disorders, atopy.
- Parasitic infections.
- Drugs
- Skin disorders.
- Cancer esp. with necrosis or metastasis
- Infectious e.g. scarlet fever.
- Hereditary
- Misc. e.g. radiation, Loeffler's syndrome, hypereosinophilic syndrome, etc.

BASOPHILIA ($> 0.1 \times 10^9/L$)

- Infections - varicella, chronic sinusitis.
- Endocrine - hypothyroidism.
- Drugs.
- Misc. e.g. nephrosis, radiation
- Haematologic/oncologic disorders e.g. Chronic myeloproliferative conditions (CML, MF, Polycythaemia vera)

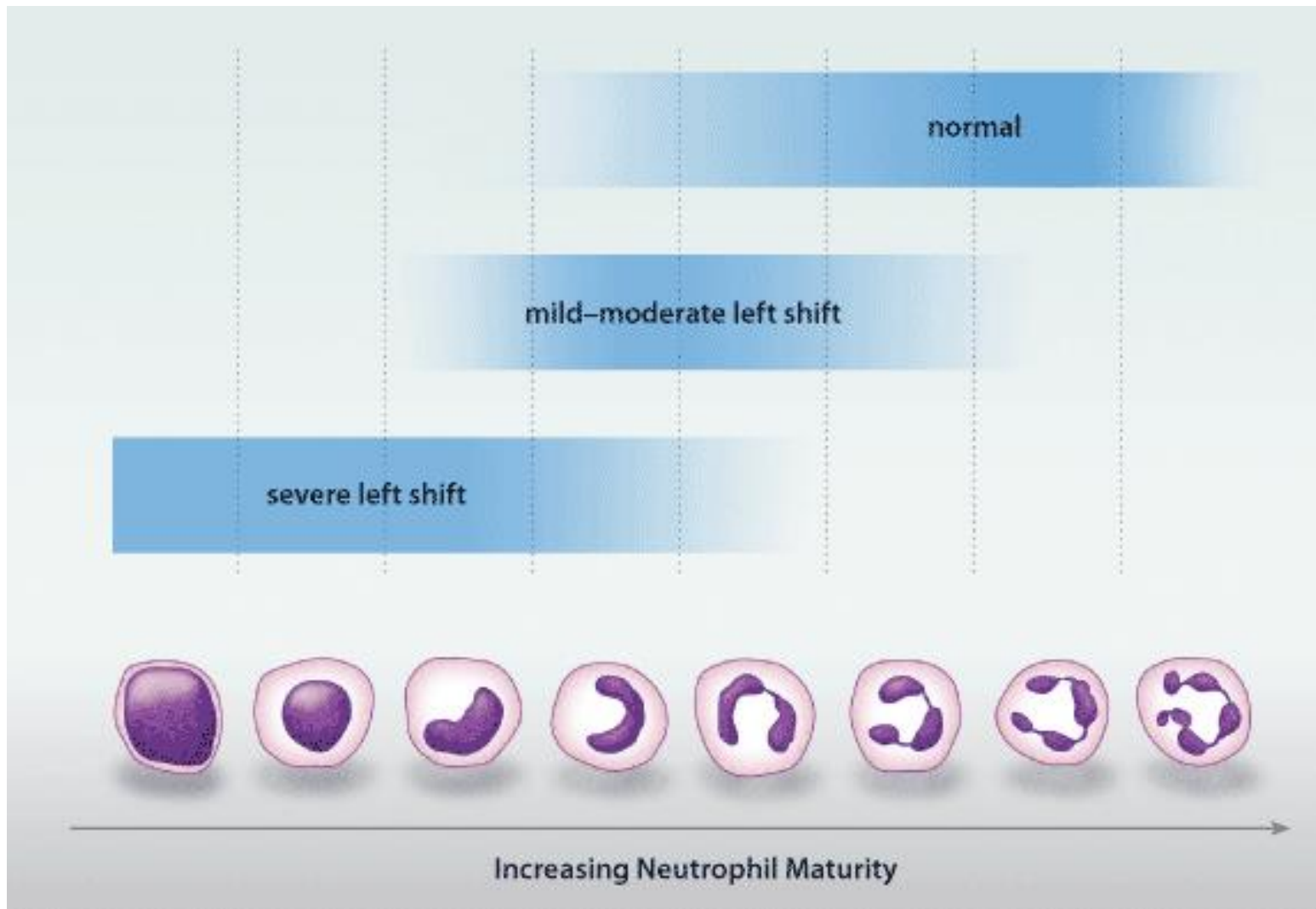
Leukamoid Reaction

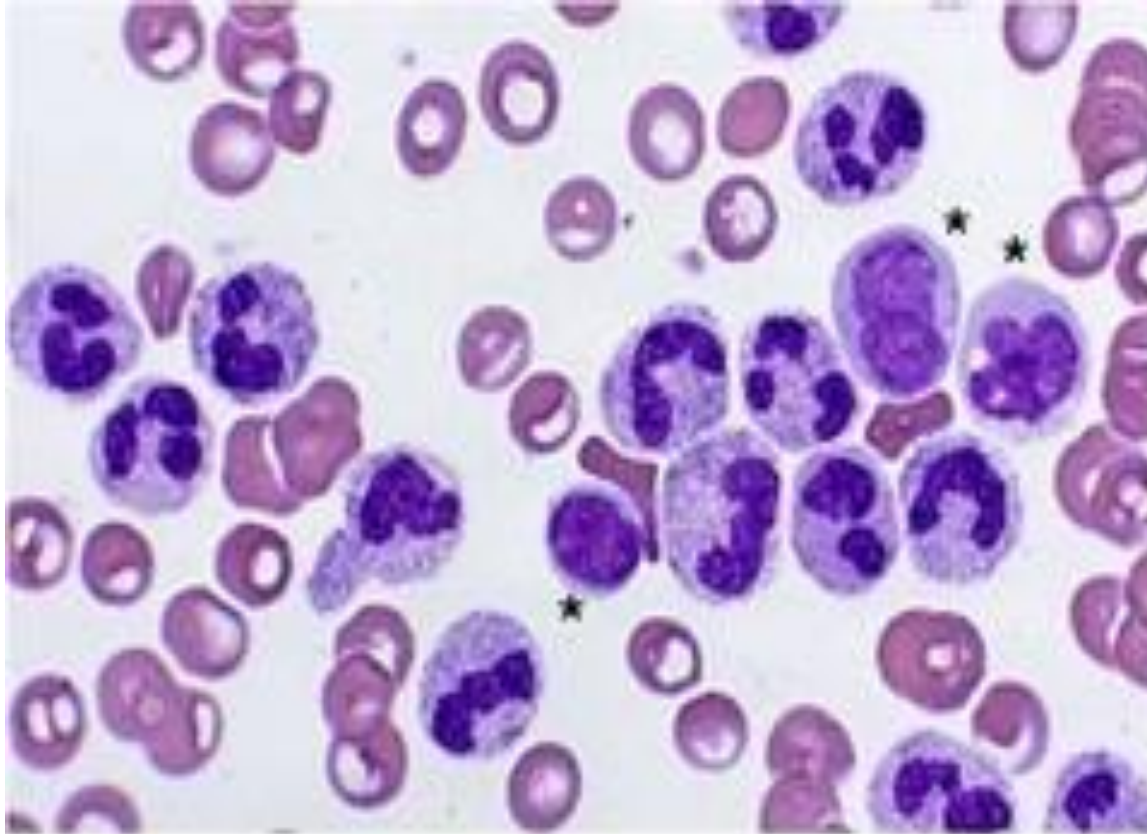
- Extremely high leucocyte counts seen in **non-leukaemic** conditions e.g. in acute infections, intoxications, malignancy
- Various types of leukamoid reaction:
 - Granulocytic (neutrophilic) leukamoid reaction
 - Lymphocytic leukamoid reaction

Leukamoid reaction cont

- Neutrophil leukamoid reaction associated changes seen include:
 - Left shift
 - Toxic granulation
 - Vacuolation
 - Dohle bodies.
 - ↑NAP (LAP)

LEFT SHIFT





Neutrophilia with left shift



Toxic granulation
Of neutrophil
- Left shift (stab cell)



Dohle body

Leucoerythroblastic Reactions.

- Leucoerythroblastic reaction (in PB)
 - Left shift in the granulocyte series associated with nucleated red cells in the peripheral blood.

Is often associated with anaemia

- **Causes:**
 - Marrow invasion by tumour
 - Miliary T.B.
 - Severe haemolysis
 - Multiple myeloma
 - Myelofibrosis

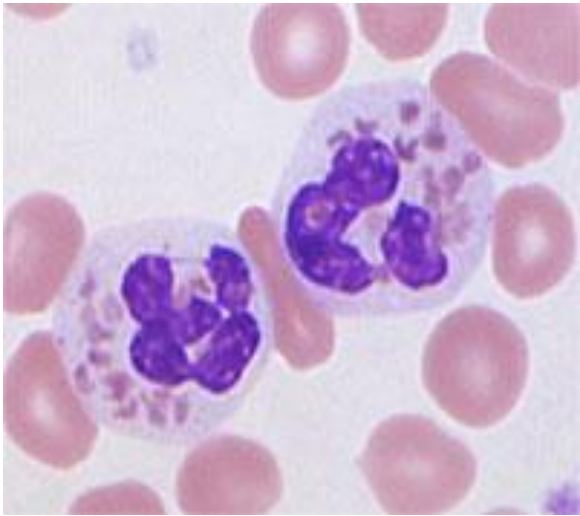
QUALITATIVE DISORDERS.

- Variation in morphology and/or function.
Counts may be normal or abnormal

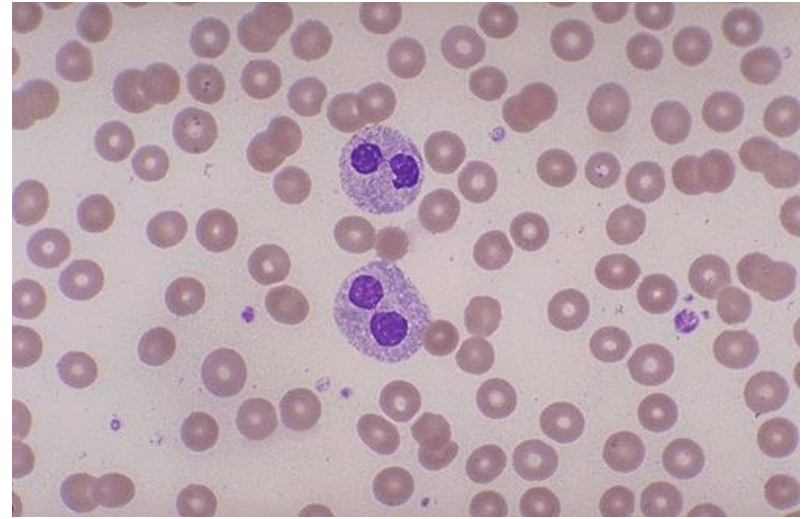
Granulocytes:

- Pelger-Huet forms: Bilobed nucleus
- Chediak-Higashi: Giant leucocyte granules
- Chronic granulomatous disease: Defective neutrophil killing of intracellular bacteria
- May-Hegglin abnormality: Dohle bodies

Qualitative abnormalities



Chediak Higashi



Pelger-Huet anomaly

Lymphocytes.

Abnormalities of function associated with immunodeficiency states e.g.

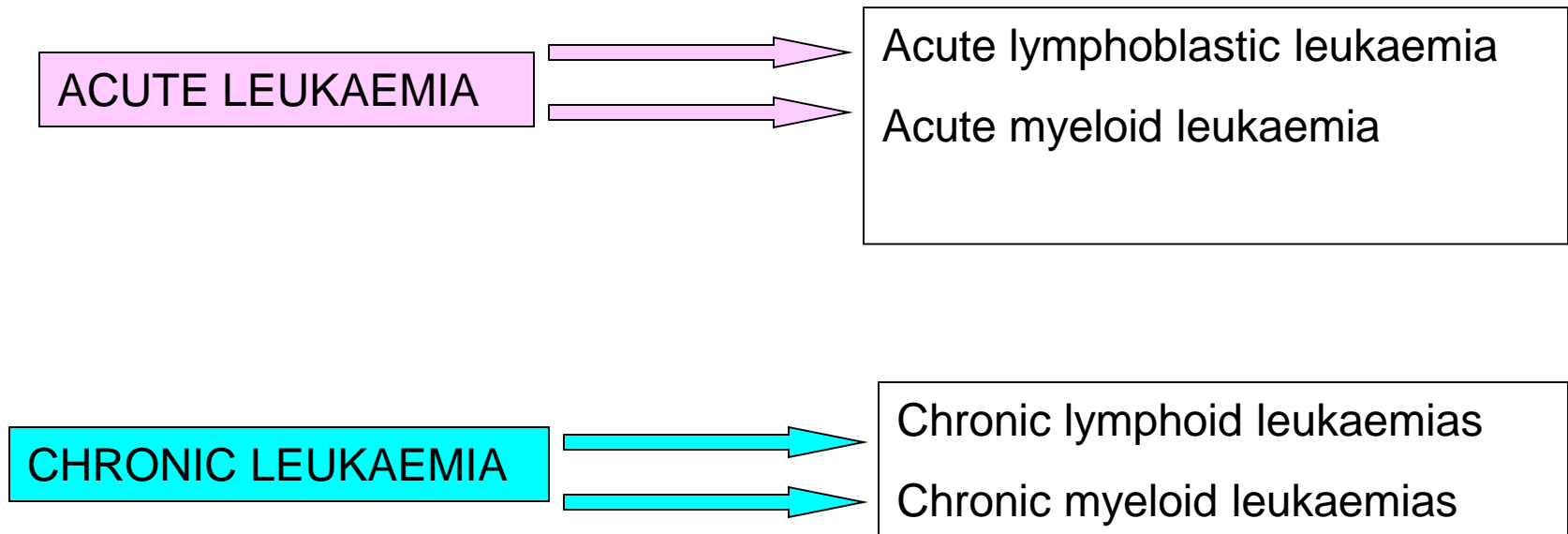
- Congenital hypogammaglobinaemia (B-cell),
- Di George syndrome (T-cell)
- Mucocutaneous candidiasis (T-cell)
- Acquired hypogammaglobinaemia.

Neoplastic Wbc disorders

- **Leukaemia** – one of the neoplastic Wbs disorders
 - A group of disorders characterised by the neoplastic proliferation of haemopoietic cells in the bone marrow with accumulation of the abnormal cells in the BM and peripheral blood

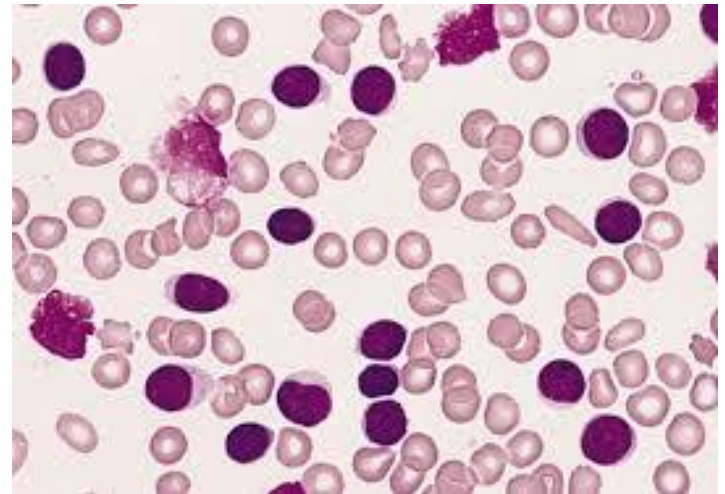
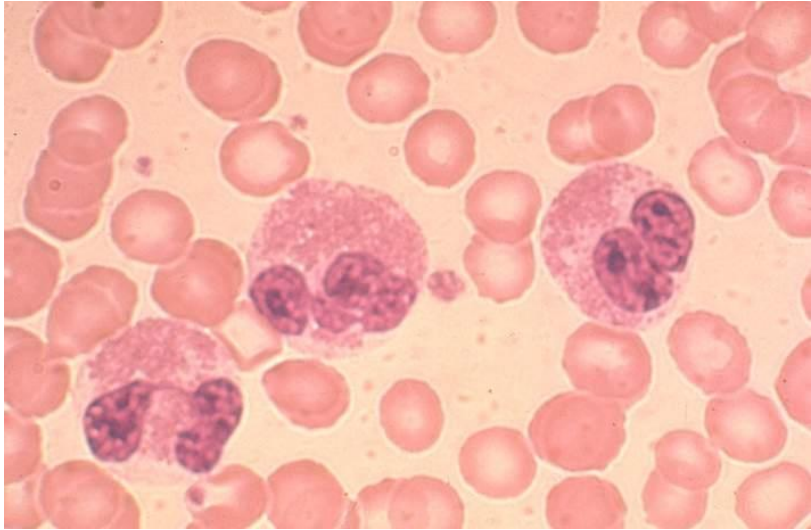
Classification: Leukaemia

- Classified into 4 groups based on the cell of origin and clinical presentation of the disease



Investigations

- TBC
- PBF
- Bone marrow examination
- Other tests: e.g.
 - Genetic tests for hereditary conditions
 - Tests of Wbc function



Thank you!
Questions???