Pathology - Topic 18 - Leukocyte disorders

Leukocytosis

- **Leucocytosis** is a white-cell count above the appropriate reference range, while **leucopenia** is a count below it.

Total and Differential White-cell Counts

- Reference ranges vary with age and laboratory method, and the total count must be interpreted with the differential count.

Absolute Counts

- The **absolute count** of a cell type equals the total white-cell count multiplied by that cell's proportion.
    - An increased percentage does not necessarily mean that the absolute number is increased.

Mechanisms and Reactive-versus-neoplastic Interpretation

- White-cell abnormalities can arise from altered production, release from marrow, redistribution, tissue use or cell survival.
    - A reactive count and a neoplastic count may overlap numerically, so diagnosis requires more than the total number.

Common Reactive Patterns

1. Neutrophilia

- Bacterial infection, tissue injury, acute inflammation and physiological stress commonly increase neutrophils.
- Glucocorticoids can increase the circulating count partly by reducing margination and movement into tissues.
    - The mechanism differs from increased production of immature cells in an infection-driven marrow response.
- A **left shift** means an increased proportion of immature granulocytic forms in blood.
    - Toxic granulation, Döhle bodies and cytoplasmic vacuoles can support a reactive inflammatory process, although none proves a specific organism.

2. Eosinophilia, Basophilia and Monocytosis

A. Eosinophilia

- Allergic disease, drug reactions and tissue-invasive helminths are common causes of eosinophilia.
- Not every parasite causes eosinophilia, and a persistent marked count requires evaluation for other inflammatory or clonal disorders.

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

B. Basophilia

- Basophilia can occur in myeloproliferative neoplasms, especially CML, and should not be dismissed when persistent.

C. Monocytosis

- Monocytosis can accompany chronic infection, inflammation and recovery from marrow suppression.
- A persistent clonal monocytic disorder requires a different assessment from transient reactive monocytosis.

Interpreting the Differential Count

- A typical adult total white-cell reference interval is approximately **4–11 × 10^9/L**, but the reporting laboratory and age-specific range take precedence.
  - For example, 60% lymphocytes with a total count of 3 × 10^9/L gives an absolute lymphocyte count of 1.8 × 10^9/L and does not establish absolute lymphocytosis.
- Neutrophilia may reflect marrow stimulation by cytokines, release from the marrow storage pool or demargination of circulating neutrophils.
  - An acute stress response can therefore raise the count before new cells have been produced.

Lymphocytosis

- Lymphocytosis is an increase in the absolute number of circulating lymphocytes above the appropriate reference range.
- Many viral infections produce lymphocytosis, while pertussis can cause a marked lymphocytic response.
- Reactive lymphocytes may have abundant blue cytoplasm that spreads around adjacent red cells.
  - A varied reactive population differs from a monotonous population of similar lymphocytes, which raises concern for a clonal disorder.
- Persistent unexplained lymphocytosis may require flow cytometry and additional assessment.

Reactive Lymphocytes and Clonal Lymphocytosis

1. Reactive Lymphocyte Populations

- In infectious mononucleosis, many atypical circulating cells are activated cytotoxic T cells responding to EBV-infected B cells.

2. Clonal Lymphocyte Populations

- Flow cytometry evaluates lineage, abnormal antigen combinations and B-cell light-chain restriction when a clonal process is suspected.

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

Leucopenia and Neutropenia

- Leucopenia is a reduced total white-cell count, whereas neutropenia specifically means a reduced absolute neutrophil count.
- The risk of infection depends on the depth and duration of neutropenia and the integrity of skin and mucosal barriers.
    - Fever during severe neutropenia requires prompt assessment because serious infection may produce little pus or local inflammation.
- Some constitutional or ancestry-associated neutrophil-count patterns are lower without the same infection risk as acquired marrow failure.
    - Use the person's history and appropriate reference context instead of diagnosing disease from one isolated value.

Reduced Production, Destruction and Sequestration

- Reduced neutrophil production follows cytotoxic drugs, marrow aplasia, megaloblastic change, marrow infiltration, some viral infections and congenital disorders.
- Peripheral destruction occurs with autoimmune disease and certain drugs, while overwhelming infection increases consumption.
- Splenic sequestration may contribute in hypersplenism.

Severe Neutropenia and Marrow Assessment

- An **absolute neutrophil count below 0.5×10^9/L** is severe neutropenia and substantially increases infection risk.
- Marrow examination distinguishes reduced granulopoiesis, maturation arrest and compensatory proliferation when clinically indicated.

Lymphopenia

- Lymphopenia occurs in HIV infection, glucocorticoid exposure, cytotoxic therapy and some inherited immune disorders.

Leukemoid Reaction

- A **leukemoid reaction** is a marked reactive leucocytosis that can resemble leukaemia.
    - Severe infection, major tissue injury and some cytokine-producing tumours can produce it.
- The smear often shows a reactive left shift and toxic changes, while the clinical cause and response over time support a reactive process.
- Leucocyte alkaline phosphatase is classically high in a reactive neutrophilia and low in untreated CML.
    - This historical test has limitations, and demonstration of BCR::ABL1 is more decisive when CML is suspected.

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

Leukaemia: Principles and Classification

- **Leukaemia** is a clonal malignant disorder of blood-forming cells that involves marrow and commonly blood.

Clonal Disease and Tissue Involvement

- Tumour cells disrupt normal blood formation and may infiltrate the spleen, liver, nodes and other tissues.

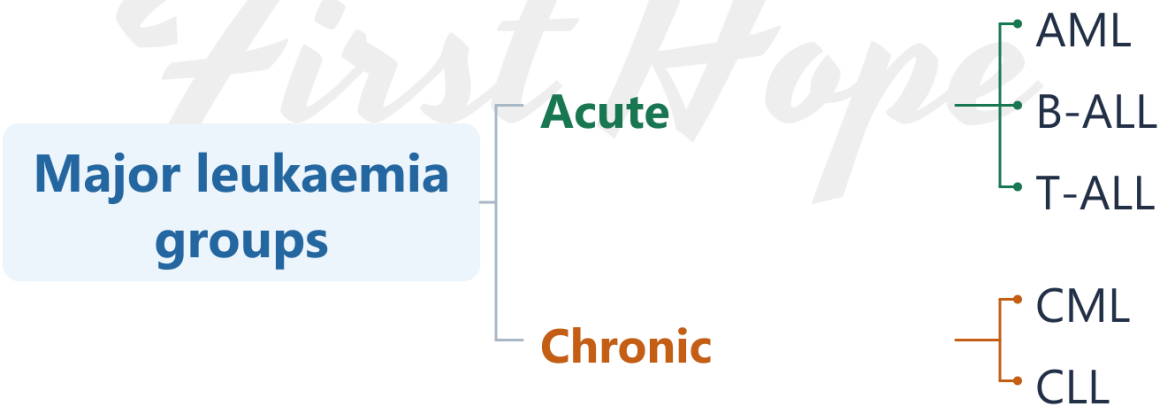
Genetic Mechanisms and Disease Diversity

- Genetic abnormalities can increase proliferation, impair maturation or promote survival.
    - Different combinations produce biologically distinct diseases even when the cells look similar.

Predisposing Exposures and Their Limits

- Radiation, selected chemicals, previous cytotoxic treatment and inherited predisposition increase risk in some cases.
    - Most patients do not have an identifiable preventable exposure.

Broad Clinical Categories



1. Acute Leukaemias

- Acute leukaemias show an accumulation of immature **blasts** and usually progress rapidly without treatment.
    - AML is myeloid, while ALL is a precursor B-cell or T-cell malignancy.

2. Chronic Leukaemias

- Chronic leukaemias usually show more mature-appearing cells and may have a slower initial course.
    - CML is a BCR::ABL1-positive myeloproliferative neoplasm, while CLL is a mature B-cell neoplasm.
- Acute and chronic describe biology and maturation patterns rather than simply the number of months that symptoms have been present.

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

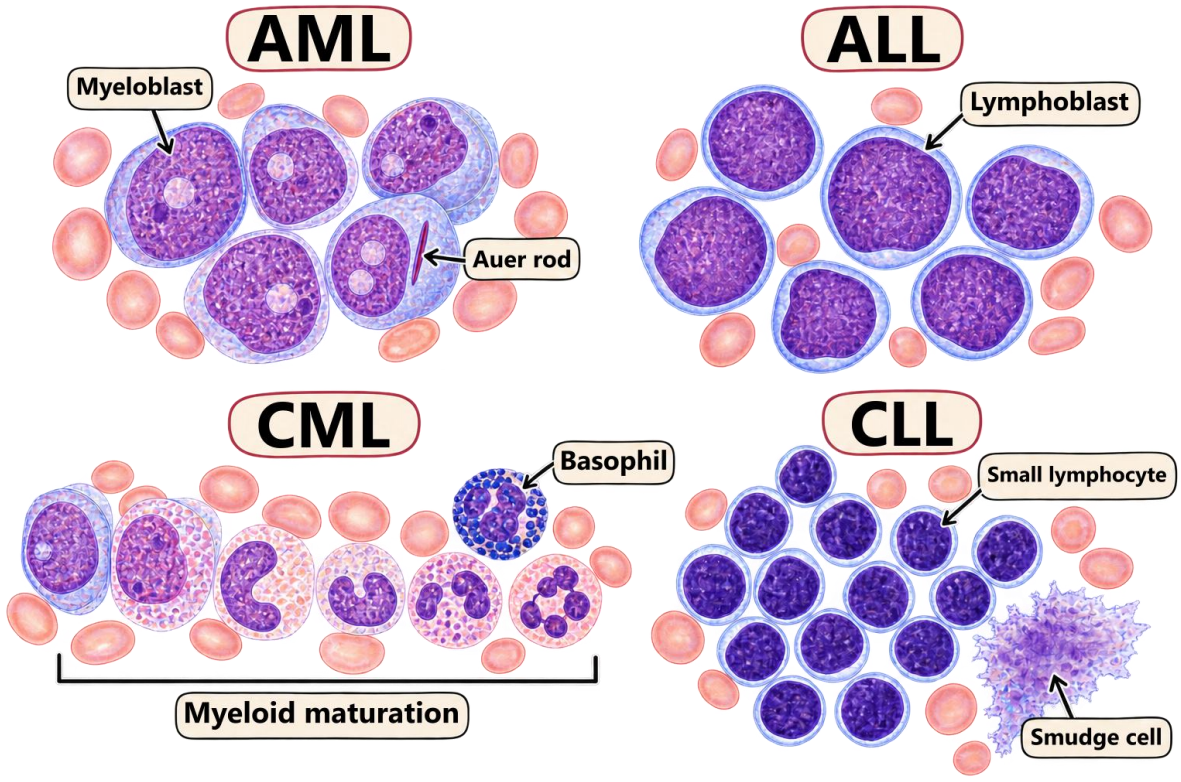
Modern Diagnostic Integration

- Diagnosis combines morphology, flow-cytometric immunophenotyping, chromosome studies and molecular tests.
    - The historical FAB system is useful for learning morphology but is not sufficient as the final modern classification.
- A marrow or blood blast proportion of 20% is an important general threshold for many acute myeloid leukaemias.
    - Some genetically defined AML entities can be diagnosed below this level, and exact requirements depend on the classification system and genetic lesion.
- Report the established entity and supporting findings rather than applying one blast cutoff to every leukaemia.

Historical FAB Morphological Groups

- The historical AML groups are M0, minimally differentiated; M1, without maturation; M2, with maturation; M3, promyelocytic; M4, myelomonocytic; M5, monoblastic or monocytic; M6, erythroid; and M7, megakaryoblastic.
- These labels describe differentiation and remain useful when interpreting older examination terminology, but modern integrated entities and genetic criteria take precedence.
- The old ALL labels L1, L2 and L3 describe blast appearances; L3-type morphology usually directs assessment towards a mature B-cell process such as Burkitt lymphoma/leukaemia rather than ordinary precursor ALL.

Typical Blood-Cell Appearances



Blood-cell appearances in acute leukaemia, CML and CLL

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

FREE PREVIEW

Click here to visit our website

MBBS PREMIUM NOTES

Complete MBBS notes for every subject and year are available only in the FirstHope app.

Scan or click here

Click here to get the app >

Available on Google Play

Browse MBBS notes by year

firsthope.co.in/mbbs

Click here to explore MBBS >

Scan or click here

FirstHope Medical on Instagram

@firsthope.medical

Click here to follow

App and notes help

Find answers about access and downloads

Click here for help

YEAR 1 / YEAR 2 / YEAR 3 / YEAR 4