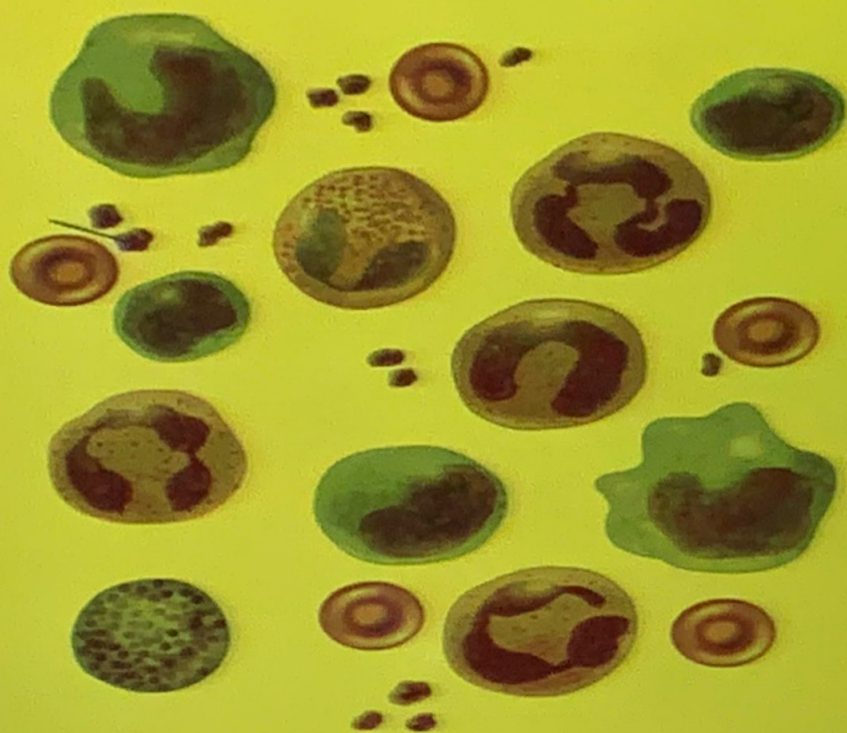


WHITE CELLS: Introduction

MBChB III Lecture Series
11th April 2019



Lecture objectives



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



Provide the reference levels of the different types of leucocytes



Describe the functions of the leucocytes



Classify the leucocyte disorders



Outline the investigation of leucocyte disorders

Classes of white cells

- Normal reference range $4 - 11 \times 10^9/L$
(Locally: $3.5 - 10 \times 10^9/L$)
- Granulocytes (Polymorphonuclear cells)
 - Neutrophils
 - Eosinophils
 - Basophils
- Agranulocytes (mononuclear cells)
 - Monocytes
 - Lymphocytes

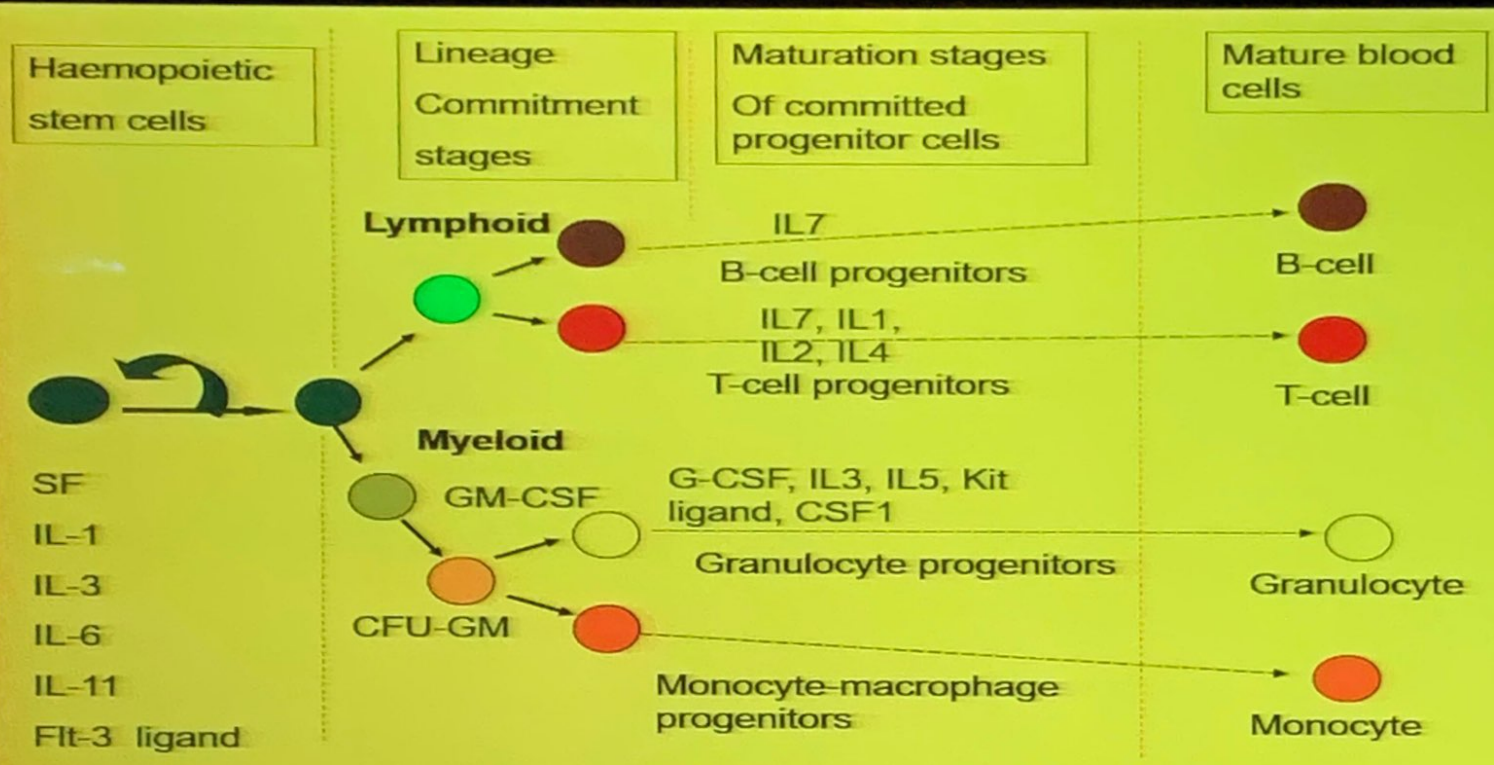


FIG 1 Leucopoiesis



PHAGOCYTES

Granulocytes + macrophages:

Bone marrow derived cells that engulf & digest particulate matter

Essential for host response to infection, inflammation.

Secrete cytokines, digest senescent cells, debris.

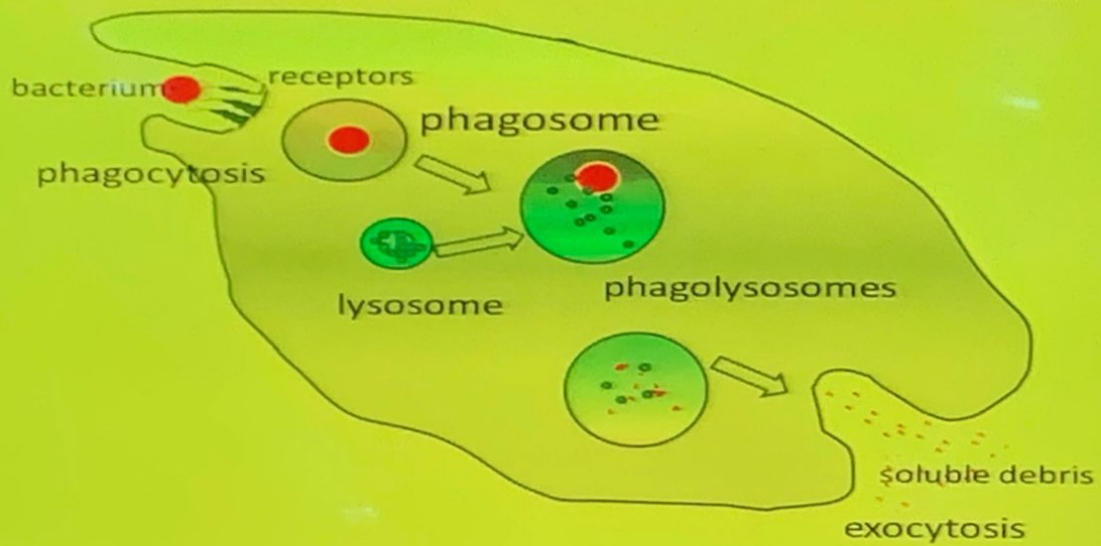
Phagocytosis

- **Phagocytosis** is mediated by macrophages and polymorphonuclear leucocytes
- It involves the ingestion and digestion of the following:
 - microorganisms
 - insoluble particles
 - damaged or dead host cells
 - cell debris
 - activated clotting factors

There are several stages of phagocytosis:

- Chemotaxis
- Adherence
- Pseudopodium formation
- Phagosome formation
- Phago-lysosome formation
 - Lysosome contains hydrogen peroxide, active oxygen species (free radicals), peroxidase, lysozyme and hydrolytic enzymes
 - **Oxidative burst** - leads to digestion of the phagolysosomal contents, and later elimination by exocytosis.

Phagocytosis



Neutrophils

- $2 - 7 \times 10^9/L$; (40 – 80%)
- 14 days to maturation
- “Storage” pool in marrow
- Circulating pool – $t_{1/2}$ is 6-10 hours
- Major role is to protect host against infectious agents

Neutrophil function

Respond to chemotactic signals and leave capillaries by margination, following which they emigrate between the endothelial cells (diapedesis/extravasation)

Phagocytosis

Regulation of neutrophil function

- Cytokines are basic regulators of all neutrophil functions
- Neutrophils also synthesize and secrete small amounts of some cytokines including IL-1, IL-6, IL-8, TNF-, and GM-CSF
- These are pyrogenic, pro-inflammatory and neutrophil activating
- Cytokines also increase the microbistatic and killing capacities of neutrophils against bacteria, protozoa and fungi.

Eosinophils

- $0.02 - 0.6 \times 10^9/L$ (1 – 6%)
- Produced in BM
- “Storage” pool in BM
- IL-5 key role in proliferation and differentiation
- T $\frac{1}{2}$ in circulation similar to neutrophils
- Life span in tissues up to several weeks
- Localise to areas exposed to external environment
- Charcot-Leyden crystals seen in areas of eosinophil degeneration

Functions of eosinophils

- Defense against helminths
- Immunosuppression of immediate hypersensitivity reaction
- Response to certain tumours
- Activation via chemotaxis leads to phagocytosis and degranulation

Basophils

- $<0.1 \times 10^9/L$ ($< 1-2\%$)
- Mature in 7 days in marrow
- Have vasoactive & immunomodulatory chemicals in granules
 - Histamine, released by circulating basophils and tissue mast cells causes capillary and venular dilatation
- Are effector cells in certain hypersensitivity reactions (possess membrane receptors for IgE & C¹)

Monocytes

- $0.2 - 1.0 \times 10^9/L$ (2-10%)
- Monocytes circulate in the peripheral blood prior to emigration into the tissues to become tissue macrophages
 - Kupfer cells (liver)
 - Microglia (brain)
 - Mesangial cells (kidney)
 - Osteoclasts (bone)
- Phagocytosis is mediated by macrophages and polymorphonuclear leucocytes.

Lymphocytes

- $1.0 - 4.0 \times 10^9/L$ (20 – 40 %)
- Two broad categories of lymphocytes:
 - Small lymphocytes – T and B-cells
 - Large granular lymphocytes - Natural killer cells
- B-lymphocytes are produced within bone marrow (a primary lymphoid organ)
- T-lymphocytes are produced in the thymus (also a primary lymphoid organ)
- Secondary lymphoid tissue – Spleen, lymph nodes, adenoids, tonsils and mucosa associated tissue (MALT).



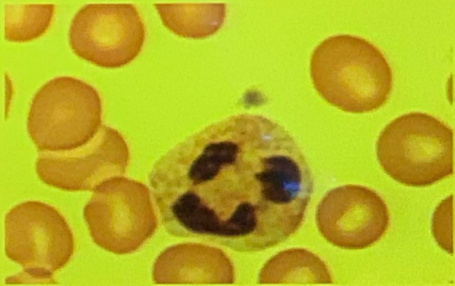
Lymphocyte function

- Lymphocytes respond to presented antigens by production of:
 - **Antibodies** (B cells)
 - **Lymphokines** (T and B cells)
 - Control of the adaptive immune response by secondary action on the participating cells
 - Killing virally-infected host cells (cytolytic T cells)
 - **T cells** - cell-mediated immunity
 - **B cells** -humoral immunity (antibodies)

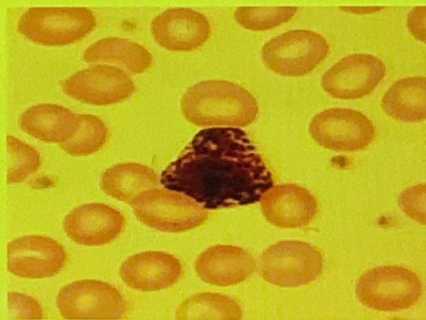
Natural Killer cells

- **NK cells** - Part of cell-mediated immunity (CMI) and act during the innate immune response
- Attack host cells displaying a foreign (e.g. viral) peptide on particular cell surface

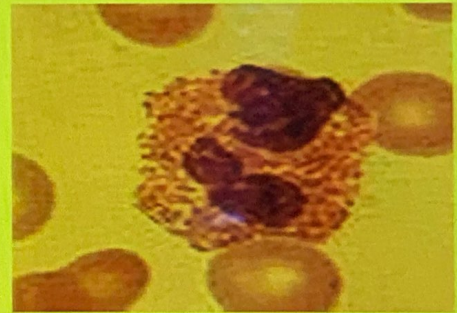
Granulocytes/polymorphonuclear cells



Neutrophil

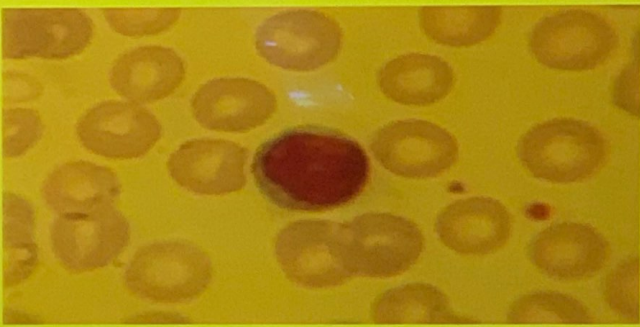


Basophil

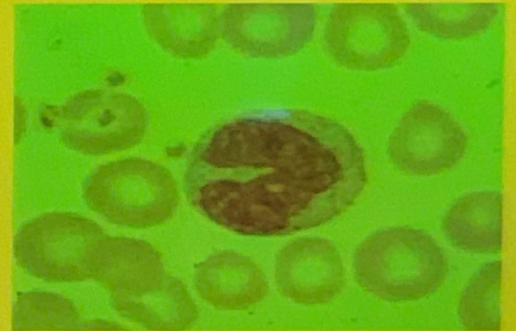


Eosinophil

Mononuclear cells



Lymphocyte



Monocyte

Classification of Leucocyte disorders

Quantitative
= Numerical
abnormality

Qualitative
= functional/morphologic
abnormality

Leucopenia

Leucocytosis

Benign

Neoplastic

Tests for white cells

- Blood counts: WBC – Total/differentials
- Peripheral smear
- Bone marrow
- Cytochemistry (Special cellular chemistry)
- Functional tests
- Molecular biology
- Cytogenetics

Investigation for white cell disorders

- TBC
 - WBC – Total/differentials
 - Other parameters: HB, RBC, Plats, RBC indices
- Peripheral smear
 - Morphologic assessment of cells
- Bone marrow examination
- Cytochemistry
 - Special cellular chemical staining
- Functional tests
- Cytogenetics and Molecular biology