

# ANAT1006

## Lecture 13 - Blood

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**Web:** <http://anatomy.med.unsw.edu.au/cbl/cbl.htm>

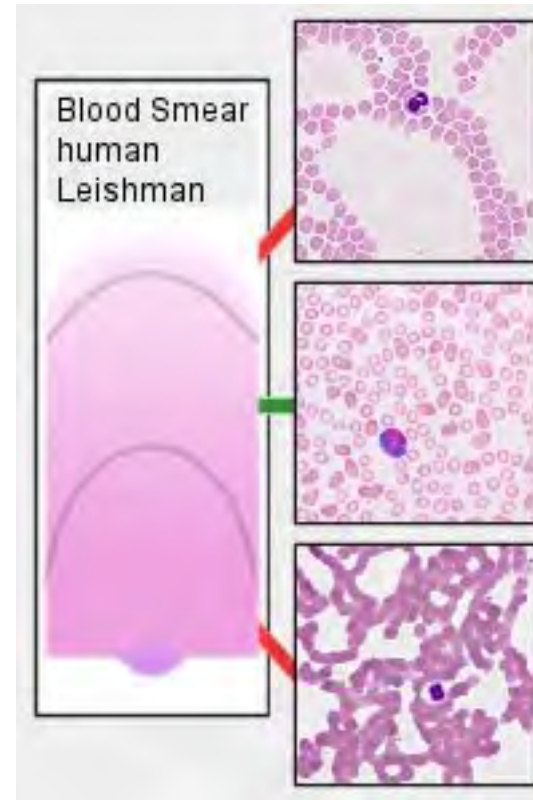
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# Textbook Reference

- Ross, Romrell & Kaye
  - Chapter 9 p188-212
- Bone Marrow
  - will be covered in detail in Med 2

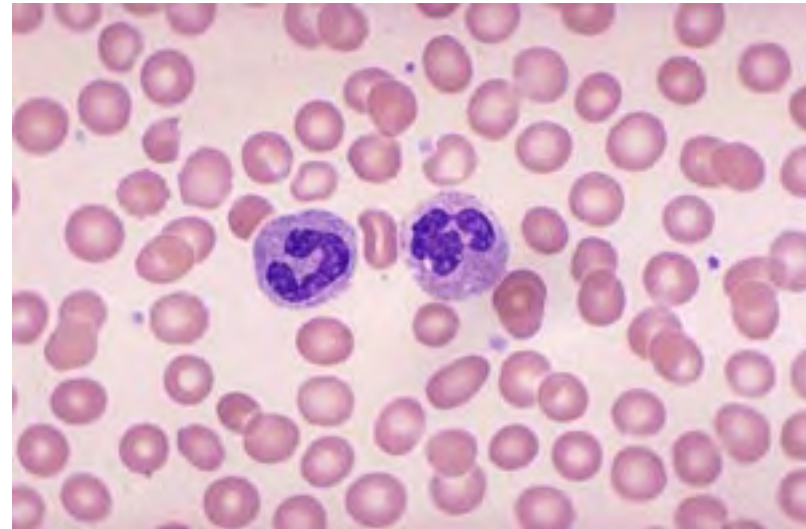
# Lecture Overview

- Development
- Haemopoiesis
- Bone Marrow
- Blood Cell types
- Abnormal examples



# Blood

- mesenchymal origin
- fluid connective tissue
  - low ratio of cells to liquid intercellular substance
    - plasma
- human adults
  - 5 litres of blood
  - 7-8 % to the body weight

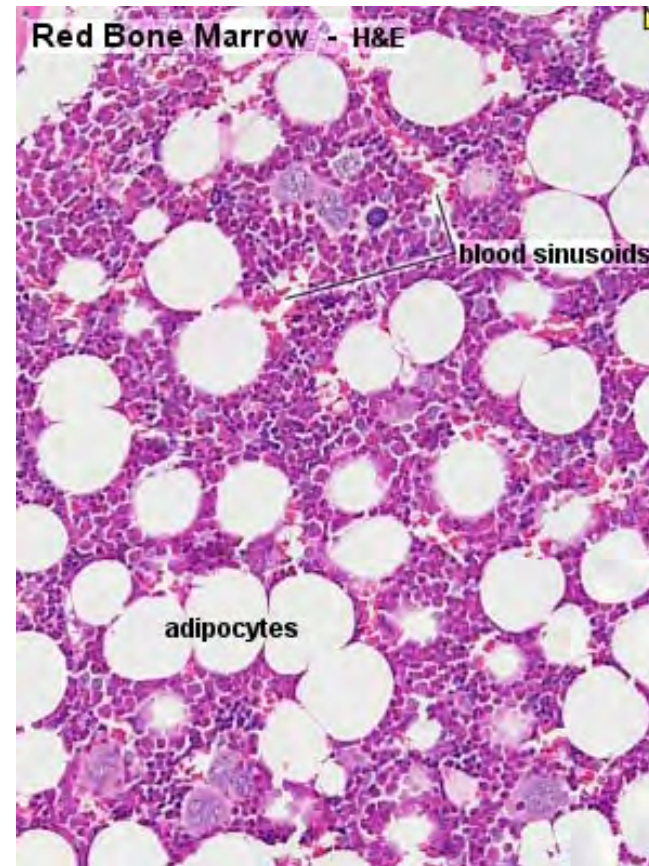


# Haemopoiesis

- Begins
  - in wall of the yolk sac
- 2nd month
  - the liver
  - then spleen, thymus
- 6th-7th month onwards
  - occurs in bone marrow
  - major site in normal adult humans

# Bone Marrow

- Adult Long Bones
  - Yellow bone marrow
    - mainly adipocytes
    - Dominates the hollow diaphysis
  - red bone marrow
    - Where haemopoiesis occurs
    - between trabeculae of spongy bone of epiphysis
- Relative amounts
  - Set by age
  - haemopoietic demand



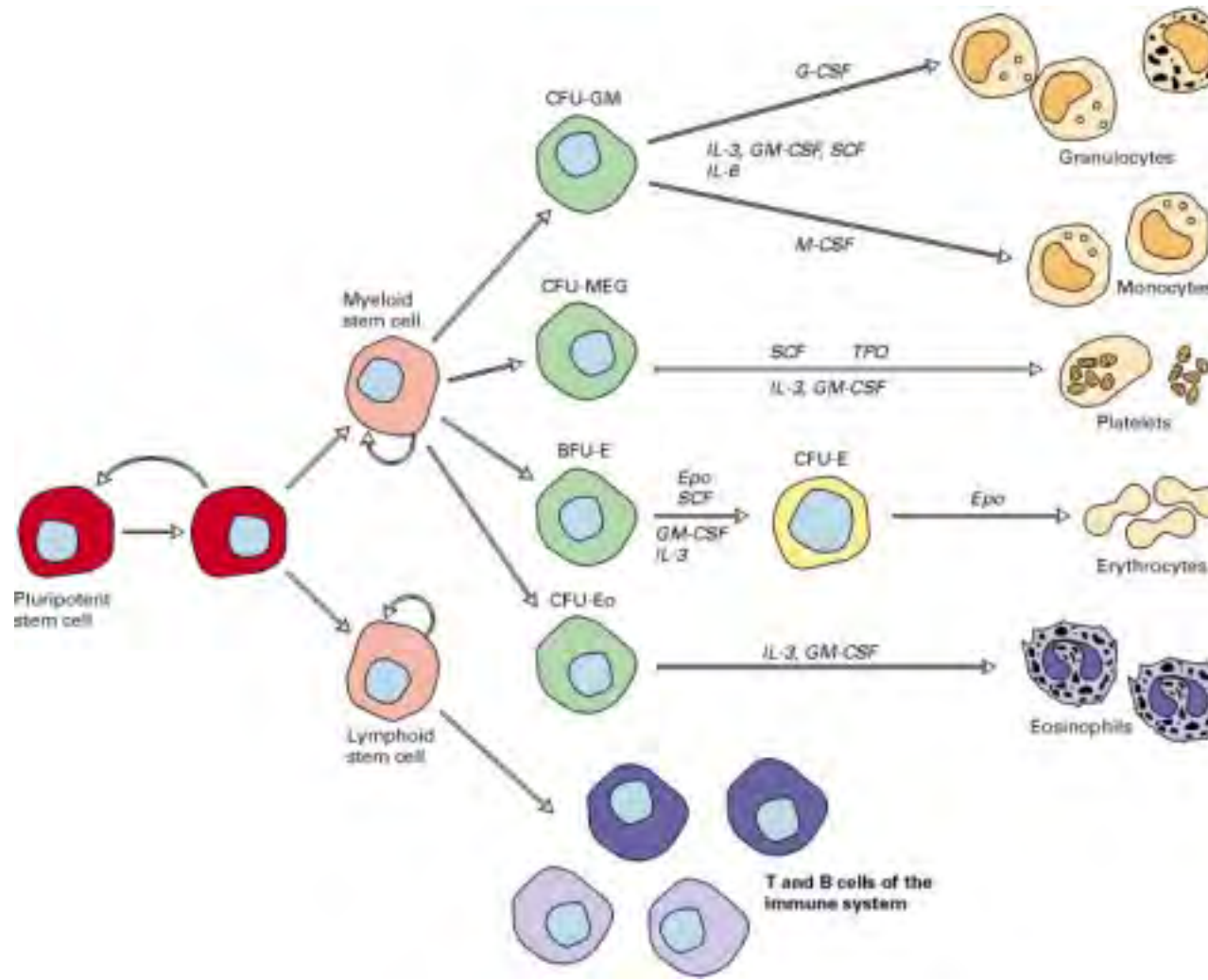
# Bone Marrow

- Haemopoietic cells
  - surround the vascular sinusoids
  - supported by reticular connective tissue
- endothelial cells of the sinusoids
- reticulocytes of the connective tissue
- Macrophages
  - frequent in red bone marrow

# Haemopoietic Cells

- small population stem cells
  - generate all types of blood cells
- Progeny develop into either
  - lymphocytic stem cells
  - pluripotent haemal stem cells
    - colony-forming unit - stem cell - CFU-S
    - generate stem cells which form the major groups of blood cells other than lymphocytes

# Stem Cell Differentiation



# Blood Cells

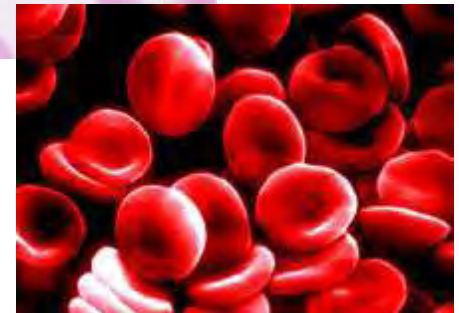
- red blood cells (erythrocytes)
  - total volume of the blood (haematocrit) is about 43%.
  - 99% of cells in the blood
- White blood cells (leukocytes)
- blood platelets
  - These cells also called “formed elements” of blood
- Location
  - Erythrocytes and blood platelets perform their functions exclusively in the blood stream
  - Leukocytes can leave the blood stream through the walls of capillaries and venules
    - enter either connective or lymphoid tissues

# Erythrocyte Function

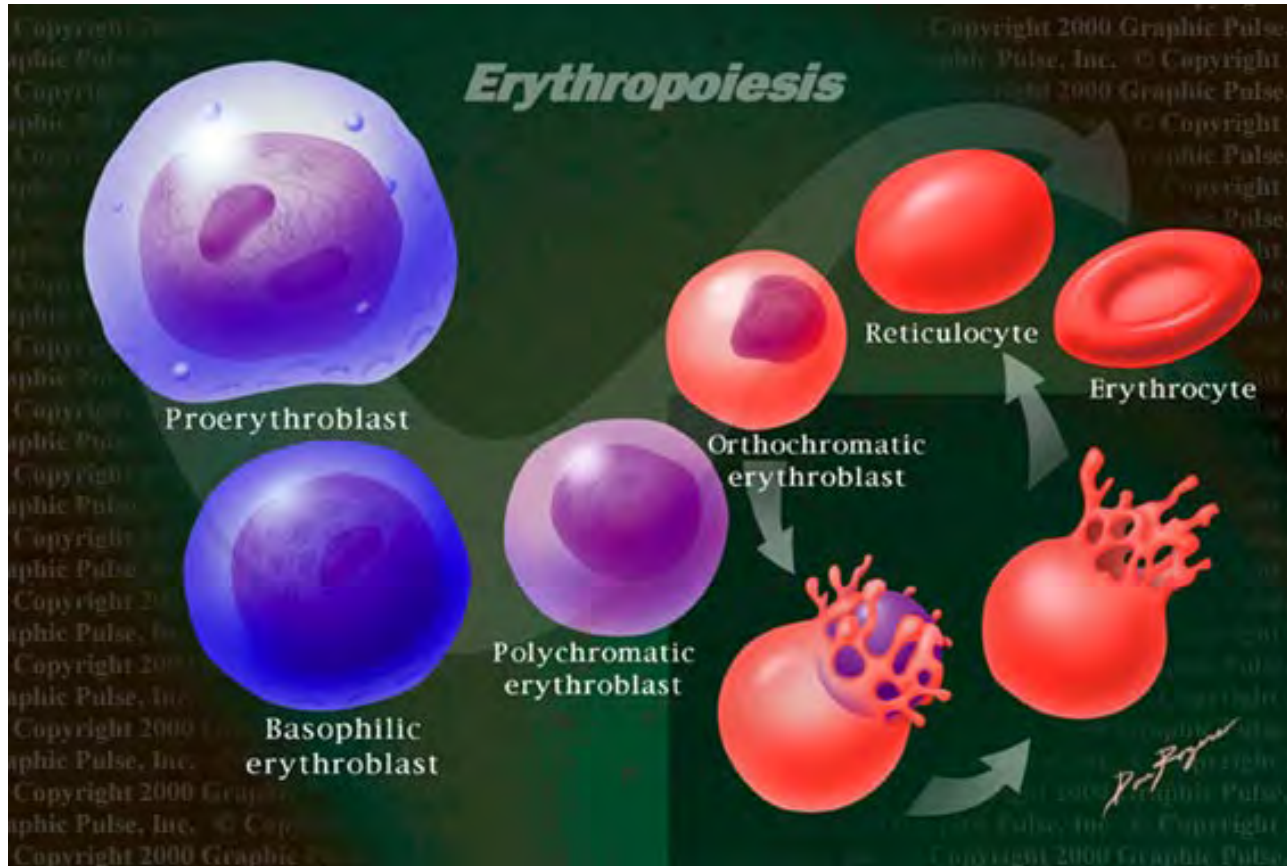
- transport of oxygen
- Haemoglobin
  - the oxygen binding protein
  - contributes 30% of cell mass
- lifespan is 100-120 days
- 4-5 million /mm<sup>3</sup>
  - Compared with 6-9,000 leukocytes mm<sup>3</sup>
- approx  $5 \times 10^{11}$  erythrocytes formed/destroyed each day

# Erythrocyte

- do not contain a nucleus
  - no active movement
  - elastic and can withstand deformation
- typically biconcave disks
  - shape is influenced by osmotic forces
- diameter of the disk is  $\sim 7 \mu\text{m}$ 
  - allow us to estimate the size of other structures or cells
- Mature cells do not contain organelles
- cytoplasm looks homogenous



# Erythropoiesis

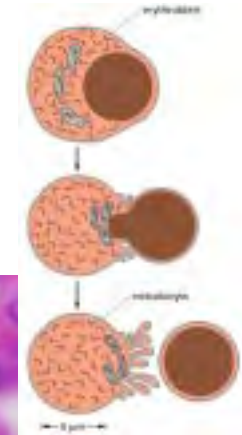
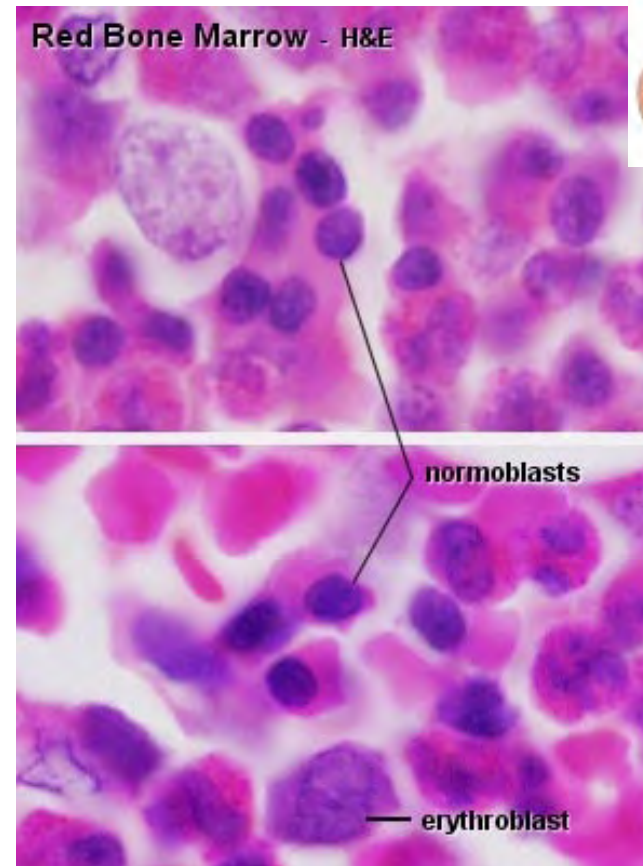


# Erythropoiesis

- Proerythroblast
  - large, slightly basophilic cell
  - contains a large lightly stained nucleus
  - proliferate to generate a sequence of cells
    - which show a gradual decrease in size
    - condensation of chromatin
  - named after changes in the staining characteristic of the cytoplasm
    - basophilic erythroblast
    - polychromatophilic
    - orthochromic normoblasts

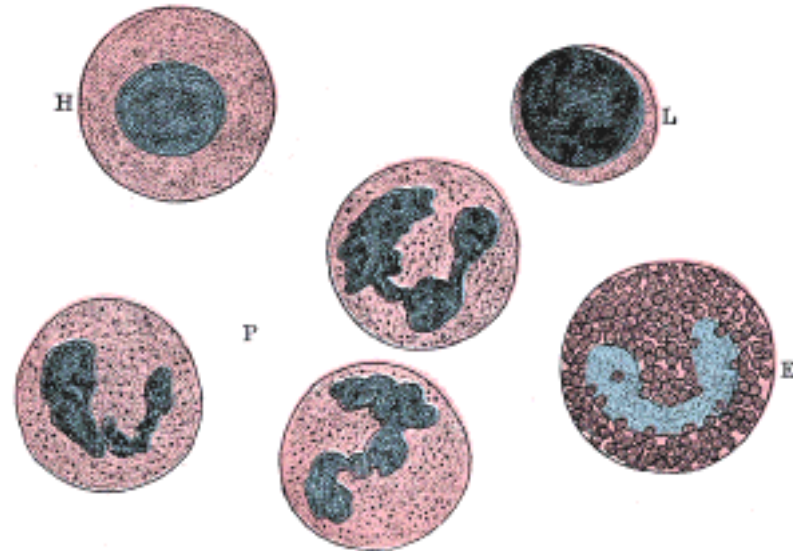
# Erythropoiesis

- Normoblast
  - Loose their nucleus
- Reticulocyte
  - which still contains some organelles
  - remain for a few days in either the bone marrow or the spleen
  - mature to erythrocytes



# Leukocytes

- Granular leukocytes
  - Neutrophils
  - Basophils
  - Eosinophils
- Non-granular leukocytes
  - Monocytes
  - Lymphocytes



# Leukocytes

- In healthy individuals
  - the relative numbers of circulating leukocyte types stable
- Something abnormal
  - changes in relative numbers
  - acute or chronic infection
    - increased neutrophils
      - Neutrophilia
  - allergic disorders
    - Increased basophils and eosinophils
      - Basophilia, eosinophilia

# Leukocyte

- Approx percentage by type
  - 60% neutrophils (50% - 70%)
  - 3% eosinophils (>0% - 5%)
  - 0.5% basophils (>0% - 2%)
  - 5% monocytes (1% - 9%)
  - 30% lymphocytes (20% - 40%)

# Granular Leukocytes

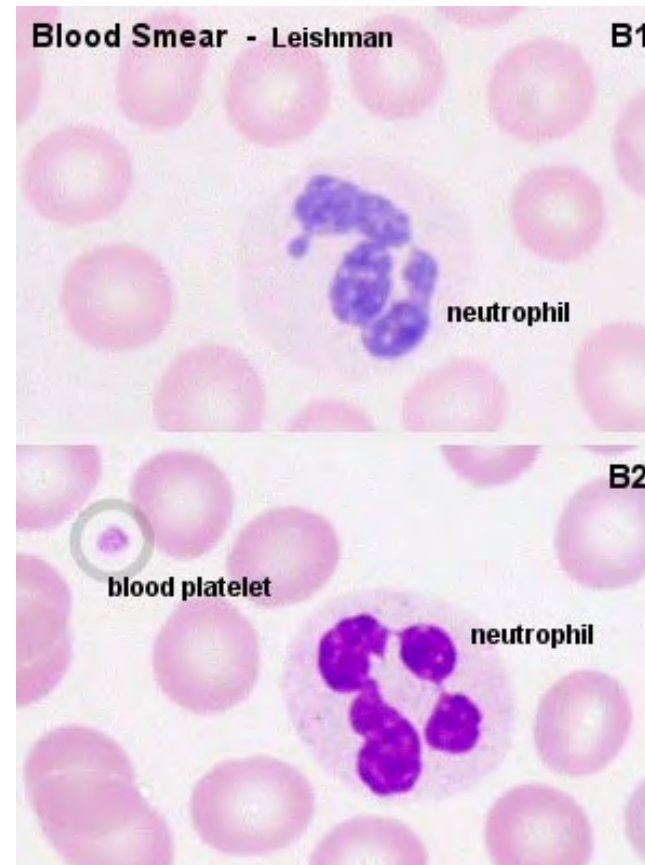
- Cell Size
  - 12-15  $\mu\text{m}$  in diameter
  - All granulocytes are motile
- Nuclei
  - form lobes
  - number of lobes varies by cell type
  - nucleoli cannot be seen
- Cytoplasm
  - contains granules
  - granules are secretory vesicles and lysosomes
    - Specific to particular type of granulocytes

# Neutrophils

- role in inflammatory processes
- invade sites of infection
  - first wave of cells invading sites of infection
- phagocytose tissue debris and foreign bodies
  - bacteria
- cannot replenish their store of granules
- die once their supply of granules has been exhausted
- Dead neutrophils and tissue debris are the major components of pus
  - normal lifespan about one week

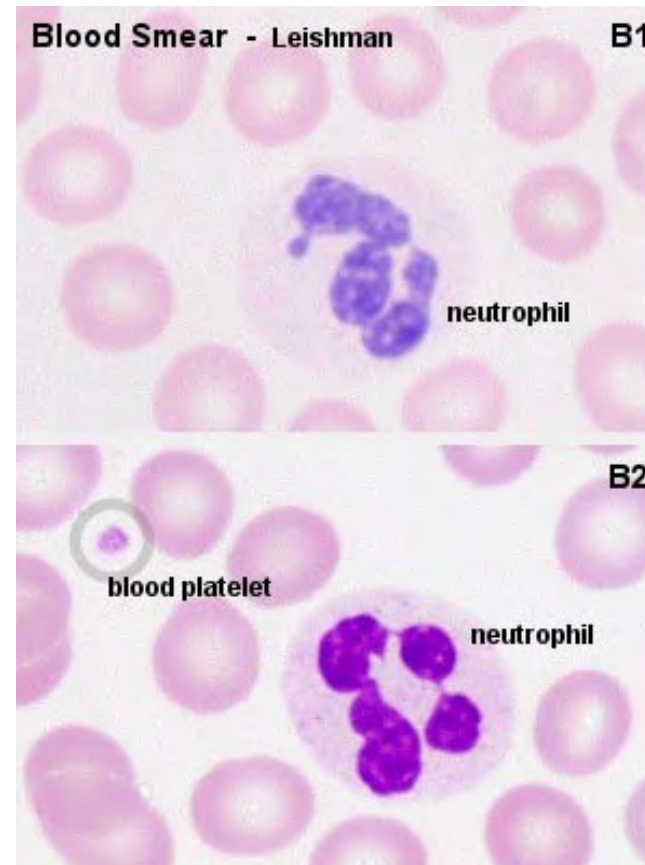
# Neutrophils

- Nucleus
  - divided into 3-5 lobes which are connected by thin strands of chromatin
  - number of lobes increases with cell age
    - Up to 7 lobes can be found in very old neutrophils



# Neutrophils

- Cytoplasm
  - 2 types of granules
    - Primary granules
      - A granules
      - contain lysosomal enzymes (primary lysosomes)
    - Secondary granules
      - B granules
      - the specific granules of the neutrophils
      - contain strong bactericidal enzymes
      - stain only weakly if at all

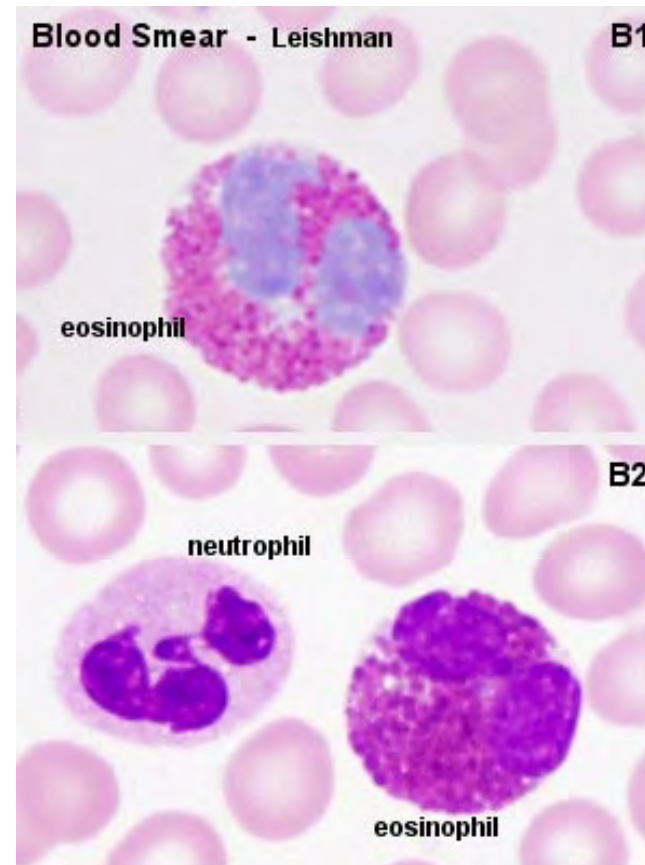


# Eosinophils

- Immune system is stimulated by antibody-antigen complexes
  - Eosinophils phagocytose these complexes
  - prevent the immune system overation
- Granules
  - contain the enzymes histaminase and arylsuphatase
    - enzymes that break down histamine and leukotrienes
  - which again may dampen the effects of their release by basophils or mast cells
  - MBP, which can also function as a cytotoxin, and its release by eosinophils may be involved in the response of the body against parasitic infections, which are accompanied by an increase in the

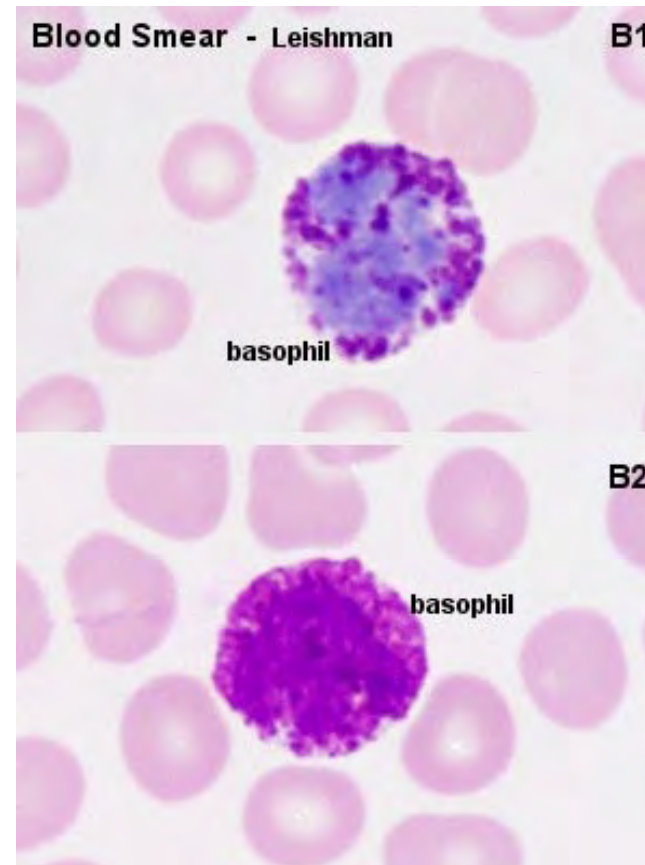
# Eosinophils

- Nucleus
  - usually has only two lobes
- Cytoplasm
  - granules stain red or pink with eosin
  - contain some large rounded vesicles (up to 1  $\mu\text{m}$ )
    - these granules correspond to the eosinophilic grains seen by light microscope
- Contain
  - lysosomal enzymes
  - major basic protein (MBP)
    - Cytotoxin released in the response to parasitic infections



# Basophils

- Nucleus
  - 2 or 3 lobes
  - may appear S-shaped
    - lobes not as well defined as in neutrophils
- Cytoplasm
  - granules stained deeply bluish or reddish-violet
    - matches colour of the nucleus
  - Not as many granules as eosinophils
  - granules about 0.5  $\mu\text{m}$  appear dark in EM
- Contain
  - heparin, histamine lysosomal enzymes and leukotrienes

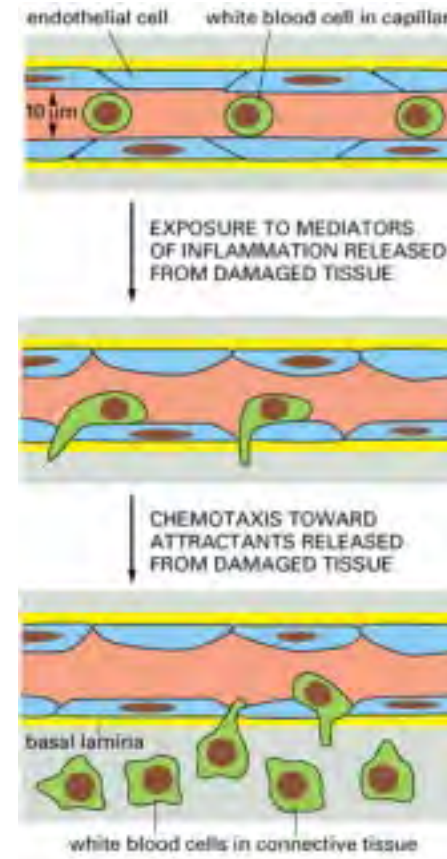


# Basophils

- Heparin and histamine
  - vasoactive
    - dilate the blood vessels
    - make vessel walls more permeable
    - prevent blood coagulation
    - facilitate access of other lymphocytes and antibodies to a site of infection
  - The release of the contents of the granules of basophils is receptor-mediated
  - Basophils do not produce antibodies
    - but they bind antibodies produced by plasma cells (activated B-lymphocytes) on their surface
    - these antibodies contact their antigens, then induce the release basophil granules

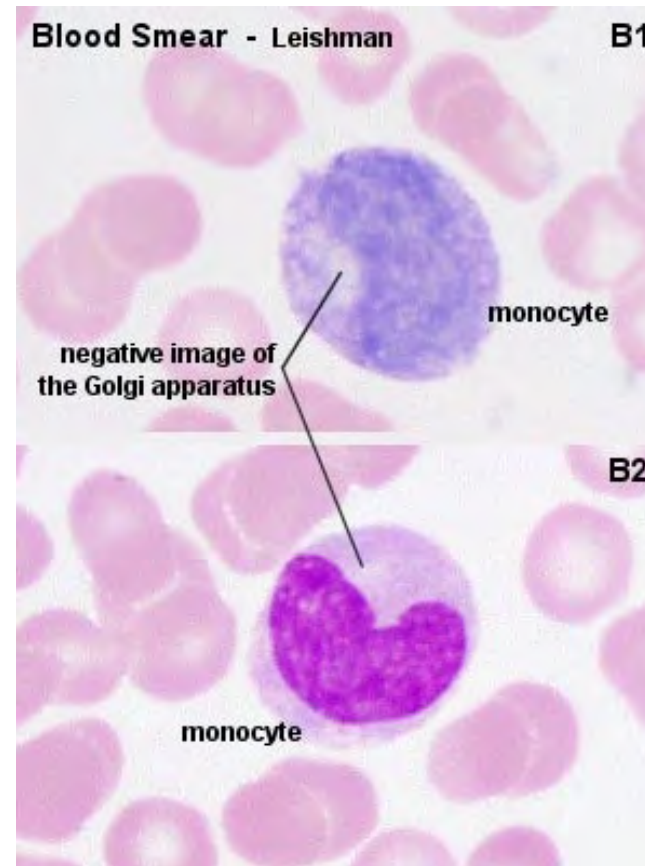
# Monocytes

- Leave circulation
  - enter the connective tissue
  - differentiate into macrophages
- Sites of infection
  - macrophages are the dominant cell type
    - after the death of the invading neutrophils
- Phagocytose
  - micro-organisms, tissue debris and the dead neutrophils
- Osteoclasts
  - dissolve and remodel bone



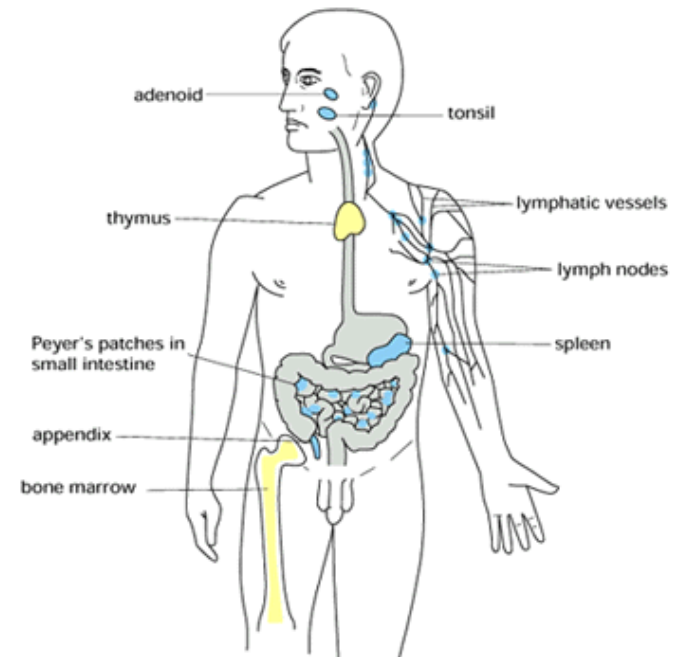
# Monocytes

- Cell size
  - about 12-18  $\mu\text{m}$  in diameter
  - slightly larger than granulocytes
- Nucleus
  - C-shaped nucleus
- Cytoplasm
  - stains stronger than that of granulocytes
  - light microscope
    - no structures visible
  - electron microscope
    - Lysosomes visible as granules



# Lymphocytes

- Two Types
  - B-lymphocytes (~5%)
  - T-lymphocytes (~90%)
  - Cannot distinguish by light or electron microscopy

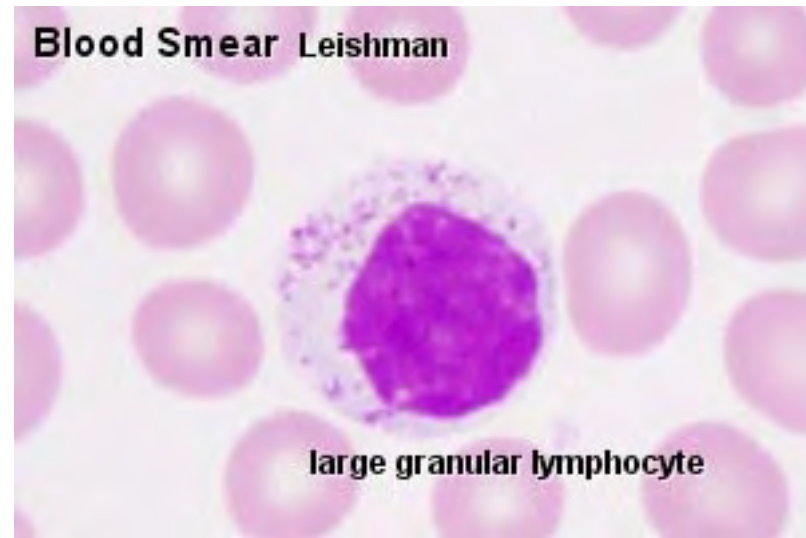


# B- Lymphocyte Function

- Exposure to antigens by antigen-presenting cells
  - Macrophages
  - T-helper cells
    - special group of T-lymphocytes
- B-lymphocytes differentiate into antibody producing plasma cells
  - cytoplasm and RER increases

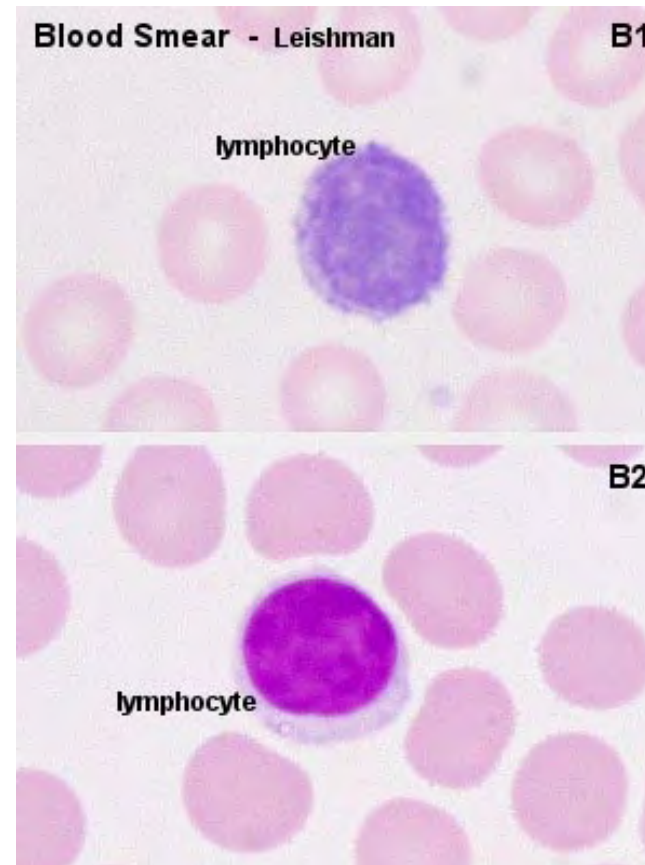
# T- Lymphocyte Function

- Cell immunity
  - immune response (cytotoxic T cells)
- Attack
  - foreign cells
  - cancer cells
  - Virus infected cells

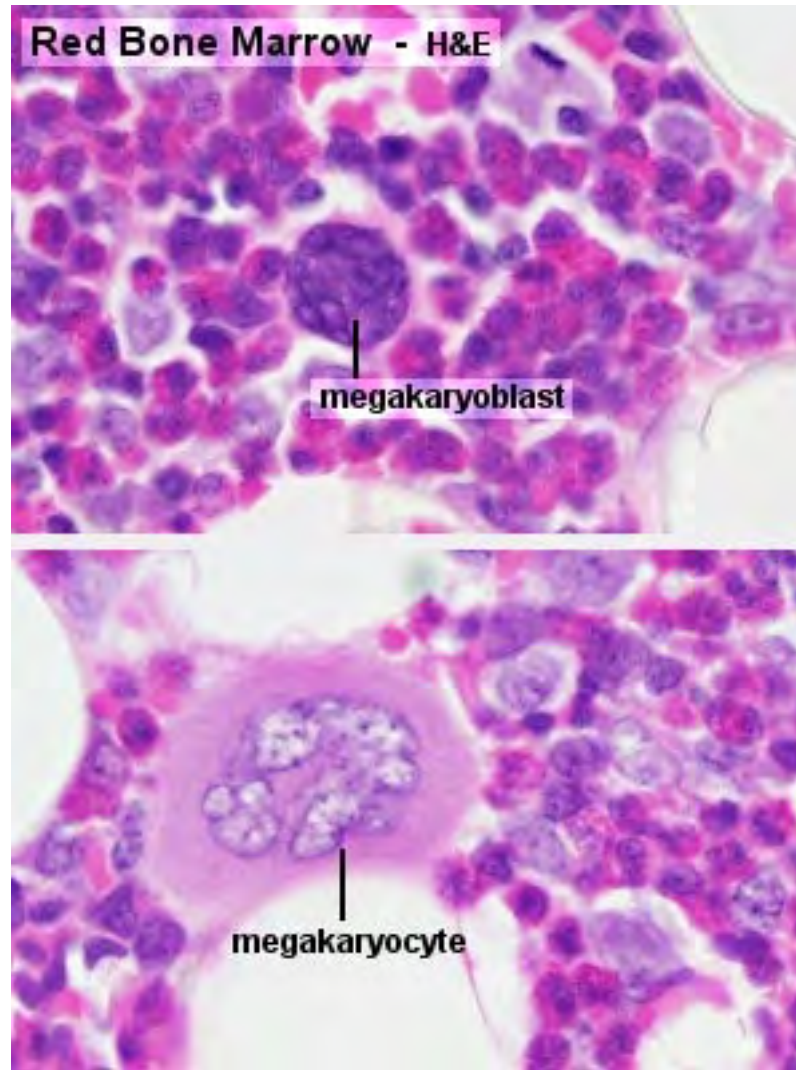


# Lymphocytes

- Cell Size
  - Variable ~5  $\mu\text{m}$  up to 15  $\mu\text{m}$  in diameter
- Nucleus
  - appears to fill the entire cell
- Cytoplasm
  - Small cells are most of lymphocytes in the blood
  - Large cells have a wider rim of cytoplasm
  - Both nucleus and the cytoplasm stain blue
  - appearance changes when activated

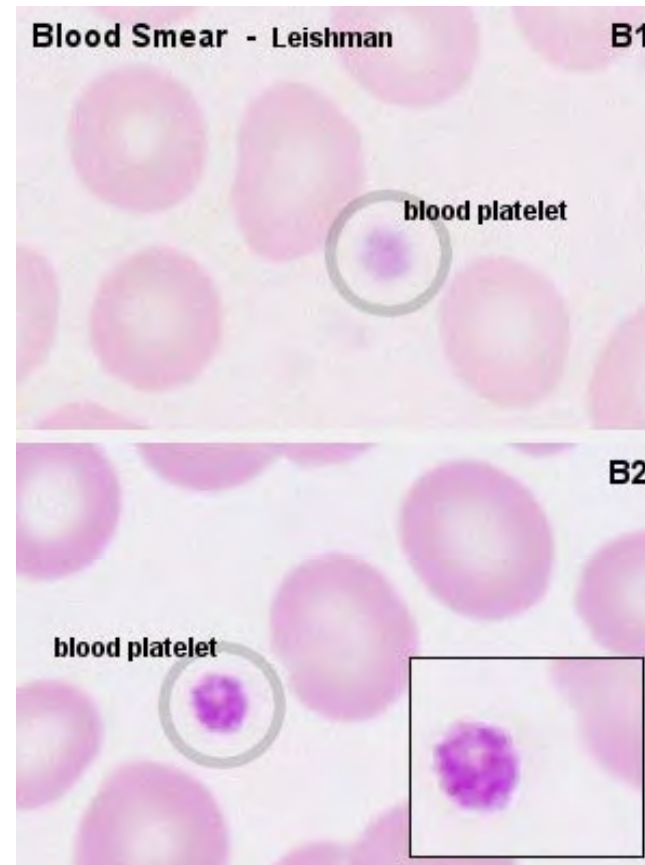


# Megakaryocyte



# Blood Platelets (thrombocytes)

- Size
  - About 3  $\mu\text{m}$  long fragments of the cytoplasm of large precursor
  - Megakaryocytes
    - very large cells (160  $\mu\text{m}$  in diameter) in bone marrow
    - large lobulated nuclei
- Nucleus
  - do not contain a nucleus
    - never been nucleated
- Cytoplasm
  - Hyalomere, outer hardly stains
  - Granulomere, inner bluish staining granules



# Platelet Granules

- Granulomere
  - Light microscope, not individually visible
  - appears homogeneously blue
  - Contain
    - serotonin (delta granules)
    - blood coagulation factors (alpha granules)
    - platelet-derived growth factor (PDGF)
      - repair of damaged tissue
- Hyalomere
  - contains cytoskeletal fibres
    - actin and myosin

# Platelet Functions

- Haemostasis- arrest of bleeding
  - Blood coagulation
  - Vessel constriction

# Platelet Functions

- Platelets adhere to damaged vessel walls
  - Exposure to collagen fibers in the damaged wall
  - Swell
  - become sticky
  - activate other platelets to undergo the same transformation
  - cascade of events results in the formation of a
- Platelet Plug

# Platelet Functions

- Activating substances
  - released from damaged vessel walls and from platelets
  - mediate conversion of prothrombin into thrombin
- Thrombin
  - catalyzes conversion of fibrinogen into fibrin
  - polymerize into fibrils
  - forms a fibrous meshwork in the arising blood clot
- Clot Retraction
  - Platelets captured in the fibrin meshwork contract
  - leads to clot retraction

# Platelets

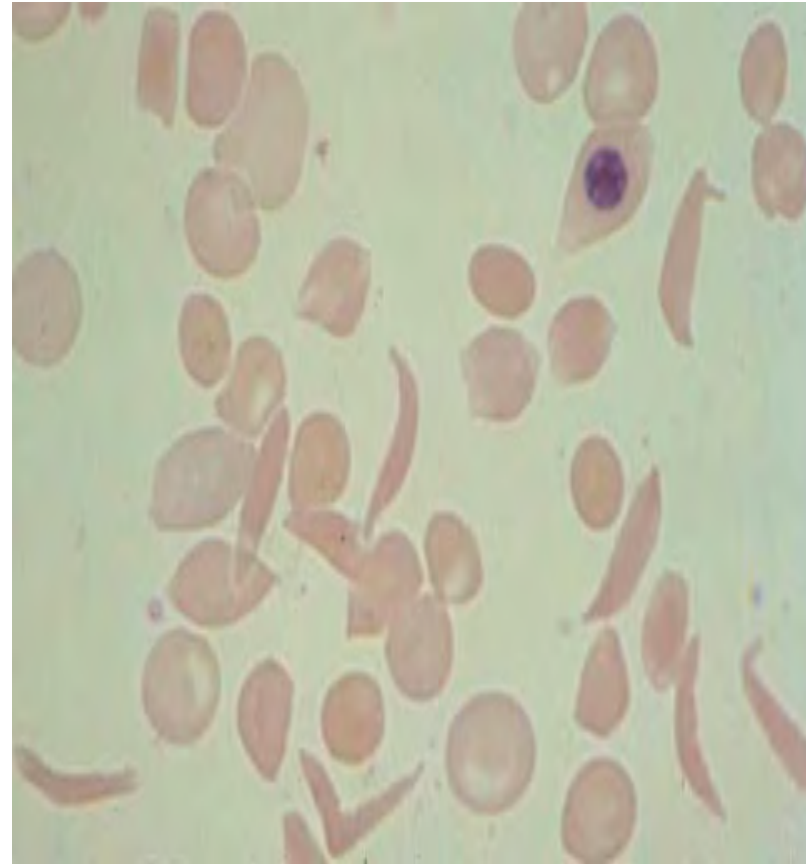
- Blood coagulation
  - complex process
  - involves a large number of other proteins
- Impaired by a deficiency in any factor
  - Inherited
  - acquired

# Abnormal

- pathological conditions
  - lead to presence of blood precursors in peripheral blood
- Erythroblastosis fetalis
  - If a Rh-negative mother has been immunised by erythrocytes of a Rh-positive foetus
  - condition develops during subsequent pregnancies
    - presence of erythrocyte precursors in peripheral blood
- Chronic myeloid leukemia
  - presence of all types of granulocyte precursors in peripheral blood

# Sickle Cell Disease

- genetic disorder
  - mutation in beta globin-chain
  - intermolecular bonding of adjacent haemoglobin molecules when the oxygen tension drops
  - formation of long polymers (tactoids) of deoxy-HbS, which distort the red cell
  - cells obstruct the microvasculature leading to tissue infarction
- The disease is common in individuals of African, Saudi Arabian, and Indian descent.



# References Online

- Histology
  - Duke University
    - <http://pathology.mc.duke.edu/research/PTH225.html>
  - Lumen
    - <http://www.meddean.luc.edu/lumen/MedEd/Histo/frames/Histo19.html>
  - UWA
    - <http://www.lab.anhb.uwa.edu.au/mb140/CorePages/Blood/blood.htm#labneuro>
  - Other
    - <http://www-micro.msb.le.ac.uk/MBChB/2a.html>