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| **Lec-1 Hematology د.حسن سالم**  **Introduction**  **Haematopoiesis** |

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| Haematopoiesis describes the formation of blood cells, an active process that must maintain normal numbers of circulating cells and be able to respond rapidly to increased demands such as bleeding or infection |

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| **Stem cells** |

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| All blood cells are derived from pluripotent stem cells. These comprise only 0.01% of the total marrow cells, but they can self-renew (i.e. make more stem cells) or differentiate to produce lineage-committed stem cells. The resulting primitive progenitor cells cannot be identified morphologically, so they are named according to the types of cell or colony.CFU-GM (colony-forming unit-granulocyte, monocyte) is a stem cell that produces granulocytic and monocytic lines, CFU-E produces erythroid cells, and CFU-Meg produces megakaryocytes   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | Recent evidence suggests that the bone marrow contains stem cells which can differentiate into non-haematological cells, such as nerve, skeletal muscle, cardiac muscle, liver and blood vessel endothelium. This is termed stem-cell plasticity  C:\Users\jannat\Desktop\11.jpg   |  | | --- | | ***Blood cells and their functions*** |  |  | | --- | | **Red cells** |  |  | | --- | | Red cell precursors formed in the bone marrow from the erythroid (CFU-E) progenitor cells are called erythroblasts or normoblasts. |   Mature red cells circulate for about 120 days. They are 8 μm biconcave discs lacking a nucleus but filled with haemoglobin, which delivers oxygen to the tissues from the lungs. In order to pass through the smallest capillaries the red cell membrane is adapted to be deformable.   |  | | --- | | ***Haemoglobin*** is a protein specially adapted for oxygen transport. It is composed of four globin chains, each surrounding an iron-containing porphyrin pigment molecule termed haem. Globin chains are a combination of two alpha and two non-alpha chains;  1- haemoglobin A (αα/ββ) represents over 97% of adult haemoglobin,  2- haemoglobin A2 (2alpha 2delta), present in 2.5%of people  3- haemoglobin F (2 alpha 2gama) is the predominant type in the fetus.  Each haem molecule contains a ferrous ion (Fe2+) to which oxygen reversibly binds |  |  | | --- | | Genetic mutations affecting the haem-binding pockets of globin chains or the 'hinge' interactions between globin chains result in haemoglobinopathies or unstable haemoglobins. Alpha globin chains are produced by two genes on chromosome 16 and beta globin chains by a single gene on chromosome 11; imbalance in the production of globin chains produces the thalassaemias. C:\Users\jannat\Desktop\hemoglobin1.jpg |      |  | | --- | | **White cells** |  |  | | --- | | White cells or leucocytes in the blood consist of granulocytes (neutrophils, eosinophils and basophils), monocytes and lymphocytes .Granulocytes and monocytes are formed from bone marrow CFU-GM progenitor cells. The first recognisable granulocyte in the marrow is the myeloblast,. As the cells divide and mature, the nucleus segments and the cytoplasm acquires specific neutrophilic, eosinophilic or basophilic granules. This takes about 14 days. |  |  | | --- | | Myelocytes or metamyelocytes are normally only found in the marrow but may appear in the circulation in infection or toxic states. The appearance of more primitive myeloid precursors in the blood is often associated with the presence of nucleated red cells and is termed a 'leucoerythroblastic' picture; this indicates a serious disturbance of marrow function. |  |  | | --- | | Neutrophils |  |  | | --- | | Neutrophils, the most common white blood cells in the blood of adults, are 10-14 μm in diameter with a multilobular nucleus containing 2-5 segments and granules in their cytoplasm. Their main function is to recognise, ingest and destroy foreign particles and microorganisms.. Neutrophils spend 6-10 hours in the circulation before being removed, principally by the spleen. Alternatively, they pass into the tissues and either are consumed in the inflammatory process or undergo apoptotic cell death and phagocytosis by macrophages. |  |  | | --- | | Eosinophils |  |  | | --- | | Eosinophils represent 1-6% of the circulating white cells. They are a similar size to neutrophils but have a bilobed nucleus and prominent orange granules on Romanowsky staining. Eosinophils are phagocytic and their granules contain a peroxidase capable of generating reactive oxygen species and proteins involved in the intracellular killing of protozoa and helminths . They are also involved in allergic reactions (e.g. atopic asthma). |  |  | | --- | | Basophils |  |  | | --- | | These cells are less common than eosinophils, representing less than 1% of circulating white cells. They contain dense black granules which obscure the nucleus. Mast cells resemble basophils but are only found in the tissues. These cells are involved in hypersensitivity reactions . |  |  | | --- | | Monocytes |  |  | | --- | | Monocytes are the largest of the white cells, with a diameter of 12-20 μm and an irregular nucleus in abundant pale blue cytoplasm containing occasional cytoplasmic vacuoles. These cells circulate for a few hours and then migrate into the tissue where they become macrophages, Kupffer cells or antigen-presenting dendritic cells. The former phagocytose debris, apoptotic cells and microorganisms . |  |  | | --- | | Lymphocytes |  |  | | --- | | Lymphocytes are derived from pluripotent haematopoietic stem cells in the bone marrow. There are two main types: T cells (which mediate cellular immunity) and B cells (which mediate humoral immunity) . Lymphoid cells which migrate to the thymus develop into T cells, whereas B cells develop in the bone marrow. |  |  |  |  | | --- | --- | --- | | The majority of lymphocytes (approximately 80%) in the circulation are T cells.   |  | | --- | | ***Platelets*** are formed in the bone marrow from megakaryocytes. The formation and maturation of megakaryocytes are stimulated by thrombopoietin produced in the liver. Platelets circulate for 8-10 days before they are destroyed in the reticulo-endothelial system. Some 30% of peripheral platelets are normally pooled in the spleen and do not circulate. |  |  | | --- | | Under normal conditions platelets are discoid, with a diameter of 2-4 μm . | | | | |
| Neutrophilia | |

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| * Infection: bacterial, fungal * Trauma: surgery, burns * Infarction: myocardial infarct, pulmonary embolus, sickle-cell crisis * Inflammation: gout, rheumatoid arthritis, ulcerative colitis, Crohn's disease * Malignancy: solid tumours, Hodgkin lymphoma * Myeloproliferative disease: polycythaemia, chronic myeloid leukaemia (CML) * Physiological: exercise, pregnancy |

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Neutropenia

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| * Infection: viral, bacterial (e.g. *Salmonella*), protozoal (e.g. malaria) * Drugs: * Autoimmune: connective tissue disease * Alcohol * Bone marrow infiltration: leukaemia, myelodysplasia  |  | | --- | | Drugs which can induce neutropenia |      |  |  | | --- | --- | | Group | Examples | | Analgesics/anti-inflammatory agents | Gold, penicillamine, naproxen | | Antithyroid drugs | Carbimazole, propylthiouracil | | Anti-arrhythmics | Quinidine, procainamide | | Antihypertensives | Captopril, enalapril, nifedipine | | Antidepressants/psychotropics | Amitriptyline, , mianserin | | Antimalarials | Pyrimethamine, dapsone, sulfadoxine, chloroquine | | Anticonvulsants | Phenytoin, sodium valproate, carbamazepine | | Antibiotics | Sulphonamides, penicillins, cephalosporins | | Miscellaneous | Cimetidine, ranitidine, chlorpropamide, zidovudine | |

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Eosinophils   
Eosinophilia

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| * Allergy: hay fever, asthma, eczema ,ABPA * Infection: parasitic =schistosomiasis,nematode=ascaris,stongyloidosis * Drug hypersensitivity: e.g. gold, sulphonamides.nitrofurntoin * Skin disease –psoriasis ,eczyma * Connective tissue disease: polyarteritis nodosa.Churg-strauss syndrome * Malignancy: solid tumours, lymphomas * Primary bone marrow disorders: myeloproliferative disorders, hypereosinophilia syndrome (HES), acute myeloid leukaemia |

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Basophils   
Basophilia

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| * Myeloproliferative disease: polycythaemia, chronic myeloid leukaemia * Inflammation: acute hypersensitivity, ulcerative colitis, Crohn's disease * Iron deficiency |

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Monocytes   
Monocytosis

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| * Infection: bacterial (e.g. tuberculosis) * Inflammation: connective tissue disease, ulcerative colitis, Crohn's disease * Malignancy: solid tumours |

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Lymphocytes   
Lymphocytosis

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| * Infection: viral, bacterial (e.g. *Bordetella pertussis*) * Lymphoproliferative disease: chronic lymphocytic leukaemia (CLL), lymphoma * Post-splenectomy |

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Lymphopenia

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| * Inflammation: connective tissue disease * Lymphoma * Renal failure * Sarcoidosis * Drugs: corticosteroids, cytotoxics * Congenital: severe combined immunodeficiency |

