1st lecture in hematology by Dr.Alaa Fadhil Alwan

Introduction to hematology

The average person has approximately 70 mL of blood /kg, or ~5 L total for a 70-kg man. Approximately 50-60% of the blood volume is liquid; the remainder is cells. The liquid component, called plasma, is nearly 90% water. The remaining 10% includes ions, glucose, amino acids. Serum is the liquid remaining after blood clots; it is essentially the same as plasma, except that the clotting factors and fibrinogen have been removed.

ERYTHROCYTES (RED BLOOD CELLS)
The primary function of erythrocytes is gas exchange. Erythrocytes are anucleated cells; a large proportion of their cytoplasm consists of the iron containing oxygen transport molecule hemoglobin. Erythrocytes are shaped like biconcave disks approximately 7 to 8 micron in diameter. The biconcave disk shape gives RBCs the flexibility to squeeze their way through capillaries and other small blood vessels. RBCs look like a circle with a central hole, or central pallor, which is approximately one-third the diameter of the cell. The parameters by which erythrocytes are usually measured are the blood hemoglobin (Hb) in grams per deciliter (g/dL), the hematocrit (Hct) or packed cell volume (volume of RBCs as a percent of total blood volume), and the RBC count (millions of cells/L). The size of red cells is measured as the mean corpuscular volume (MCV), reported in femtoliters (fL; 1 fL = 10^{-15} L). The normal MCV is ~80 to 100 fL. RBCs those are smaller than 80 fL. are called microcytic; those that are larger than 100 fL. are called macrocytic. Red cells have a life span of approximately 120 days; therefore, approximately 1% of red cells are replaced each day. Young red cells can be identified because they contain ribonucleic acid (RNA).With special stains such as new methylene blue, Young RBCs containing RNA are called reticulocytes, and the number of reticulocytes in the peripheral blood (reticulocyte count) is the best estimate of RBC production.

LEUKOCYTES (WHITE BLOOD CELLS)
Several types of leukocytes, or white blood cells (WBCs), are found in the blood. The normal WBC count is ~4,000 to 11,000 x 10^9/L. Leukocytes are usually divided into granulocytes, which have specific granules, and agranulocytes, which lack specific granules. Granulocytes are divided into neutrophils, eosinophils and basophils. Agranulocytes are divided into lymphocytes and monocytes.

Neutrophils
Neutrophils are the most common type of WBCs in adults. Two types are described: segmented neutrophils and band neutrophils; neutrophils are the primary defense against bacterial infection.
Bacteria are killed by antimicrobial agents contained or generated within neutrophil granules. Neutrophils circulate in the blood for ~10 hours and may live 1 to 4 days in the extravascular space. The trip is one way; once neutrophils leave the blood to enter tissues, they cannot return.

Eosinophils
Eosinophils contain large granules that stain reddish-orange (eosinophilic) with usual blood smear stains. The nucleus is segmented (often bi-lobed). Functions of eosinophils include phagocytosis of antigen-antibody complexes and defense against parasitic infection. The normal eosinophil count is ~2 to 4% of total WBC. The number of eosinophils increases with allergic reactions and parasitic infections.

Basophils
Basophils contain large dark blue or purple (basophilic) granules, which often obscure the nucleus. The nucleus is segmented. Basophils are the least common type of leukocytes, normally ≤1% of total WBCs. Basophils appear to be involved in immediate hypersensitivity reactions related to immunoglobulin class E (IgE)

Lymphocytes
Lymphocytes are the second most common type of leukocytes in adults (~20–40% of WBC). The lymphocyte number is higher in children and also increases with viral infections.

Monocytes
Monocytes normally comprise ~3 to 8% of leukocytes. After 8 to 14 hours in the blood, they enter tissue to become tissue macrophages (also called histiocytes). Monocytes are large cells, with abundant light gray to light blue finely granular cytoplasm. The nucleus has very finely granular chromatin and is often folded, bean shaped, or irregular. Monocytes have two functions: Phagocytosis of microorganisms (particularly fungi and mycobacteria) and Antigen processing and presentation.

PLATELETS (THROMBOCYTES)
Platelets, occasionally called thrombocytes, are involved in hemostasis. They adhere to tears in the endothelial lining of blood vessels, forming a platelet plug.
• Platelets are anucleated discs with a diameter of ~1 to 4 micron.
• They are derived from megakaryocytes in the bone marrow by release of fragments of megakaryocyte cytoplasm.
• The normal platelet number is ~150,000 to 350,000 cells/_L.
• Platelets have a life span of approximately 10 days. Senescent platelets are removed by the spleen.
The red cell indices include the mean corpuscular volume (MCV), the mean corpuscular hemoglobin (MCH), and the mean corpuscular hemoglobin concentration (MCHC). The MCV is important in the evaluation of erythrocyte disorders. The MCH and MCHC are generally not of great value.
The red cell distribution width (RDW) is a mathematical description of the variation in RBC sizes; a high RDW indicates greater variation in RBC size.

Morphology of RBCs
Anisocytosis= variation in RBC size occur in various disorders
Microcytosis= Decreased RBC size e.g. Iron deficiency; thalassemia;
Hypochromia= Increased central pallor (> 1/3 to 1/2 the cell diameter) as in Iron deficiency
Macrocytosis= Increased RBC size (MCV > 110 fL.) Megaloblastic anemia; liver disease; reticulocytosis; myelodysplastic syndromes; alcoholism

Target cells (codocytes) =Central thick area surrounded by pale ring as in Liver disease; hemoglobinopathies (thalassemia, sickle cell anemia)
Schistocytes = Fragmented RBCs occur in Mechanical trauma: malfunctioning prosthetic heart valve; thrombotic microangiopathy (TTP/HUS); severe burns; joggers; severe shock or acidosis; severe intravascular hemolytic anemia
Sickle cells ("drepanocytes") =Curved RBCs with pointed ends as in Sickle cell anemia and other sickle cell disease.
Burr cells ("echinocytes") = Cells with relatively even spicules around periphery; central pallor preserved. As in Renal failure; often seen as artifact on blood smears ("crenated cells")
Acanthocytes = Cells with irregular shape a few long projections no central pallor occur in severe liver disease; abetalipoproteinemia; severe starvation
Spherocytes = Small round cells with no central pallor hereditary spherocytosis; immune hemolytic anemia
Bite cells and blister cells =Bite cells: deep rounded notch in side of RBC, Blister cells: clear vacuole along one side of RBC
Teardrop cells ("dacrocytes") = RBCs shaped like teardrops with one pointed end, as in extramedullary hematopoiesis; myelophthisic anemias (myelofibrosis, space-occupying lesions in bone marrow
Polychromasia = RBCs with bluish color on routine stains Young RBCs (reticulocytes); often seen in hemolytic anemias or recovery from blood loss.
Basophilic stippling= RBCs with fine to coarse bluish speckles as in Lead poisoning; Thalassemias; any severe stress on the bone marrow
Rouleaux= RBCs in long lines or stacks
Howell-Jolly body =Small round fragment of nuclear material in RBC occur in Splenectomy;
Hematopoiesis is the process of making blood cells. The term comes from the Greek hema (blood) and poiein (to make). For the average adult, the bone marrow produces ~5×10^{11} cells per day. Production of blood cells is highly regulated and balanced.

PRODUCTION OF SPECIFIC CELL LINES
Erythrocyte Production (Erythropoiesis)
Proerythroblast then Basophilic erythroblast then Polychromatophilic erythroblast then Orthochromatophilic erythoblast followed by Reticulocyte finally Erythrocyte

Granulocytopoiesis
Myeloblast then Promyelocyte then Myelocyte followed by Metamyelocyte then Band neutrophil and Segmented neutrophil

Megakaryocyte and Platelet (Thrombocyte) Production
Platelets are derived from bone marrow megakaryocytes, which are large cells in bone marrow.
Monocyte Maturation
Monocytes are derived from the CFU-GEMM. Monocytes circulate through the blood and then enter the tissues to become either phagocytes (macrophages) or professional antigen presenting cells (Langerhans' cells and dendritic reticulum cells).
Lymphocyte Maturation
Lymphocyte maturation begins in the bone marrow; B cells complete initial development in the marrow and then circulate to peripheral lymphoid tissues (lymph

node, spleen, and mucosal surfaces) to await antigen exposure and final maturation into plasma cells. T-cell maturation also begins in the bone marrow; T-cell precursors then travel to the thymus (initially the cortex of the thymus, progressing down into the medulla of the thymus), where they complete maturation before being released into the blood to travel to tissues.

HEMATOPOIETIC GROWTH FACTORS

Hematopoietic growth factors are proteins or glycoproteins that regulate the production and differentiation of hematopoietic precursors. A large number of growth factors have been identified, including various interleukins (produced by lymphocytes), colony-stimulating factors (CSFs),and others. Erythropoietin and thrombopoietin are produced outside the marrow and reach the marrow through the blood.

Examples of important growth factors:

- Stem Cell Factor: Stem cell factor is critical at the level of pluripotent stem cells. It also has effects on the later maturation stages of several cell lineages.
- Granulocyte Colony-Stimulating Factor (G-CSF, filgrastim, Neupogen): Stimulates granulocyte differentiation and maturation and stimulates the action of mature neutrophils.Available commercially, G-CSF is widely used in bone marrow transplantation, neutropenia induced by chemotherapy, and other conditions to increase the granulocyte count.
- Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF,Leukine): GM-CSF stimulates differentiation and maturation of granulocytes and monocytes, and also the function of mature cells. Commercially available, GM-CSF has clinical uses similar to those of G-CSF.
- Erythropoietin (EPO; Epogen or Procrit): EPO is produced predominantly in the kidney (a small amount is produced in the liver) in response to renal hypoxia. It is required for erythrocyte production and appears relatively specific for erythroid cells. Recombinant human erythropoietin is widely used for the anemia of chronic renal failure and for some cases of anemia of chronic disease, including acquired immunodeficiency syndrome (AIDS).
- Thrombopoietin (TPO, Mk-CSF, megakaryocyte growth and differentiation factor): TPO is critical in megakaryocyte growth and differentiation and is produced predominantly in the liver.