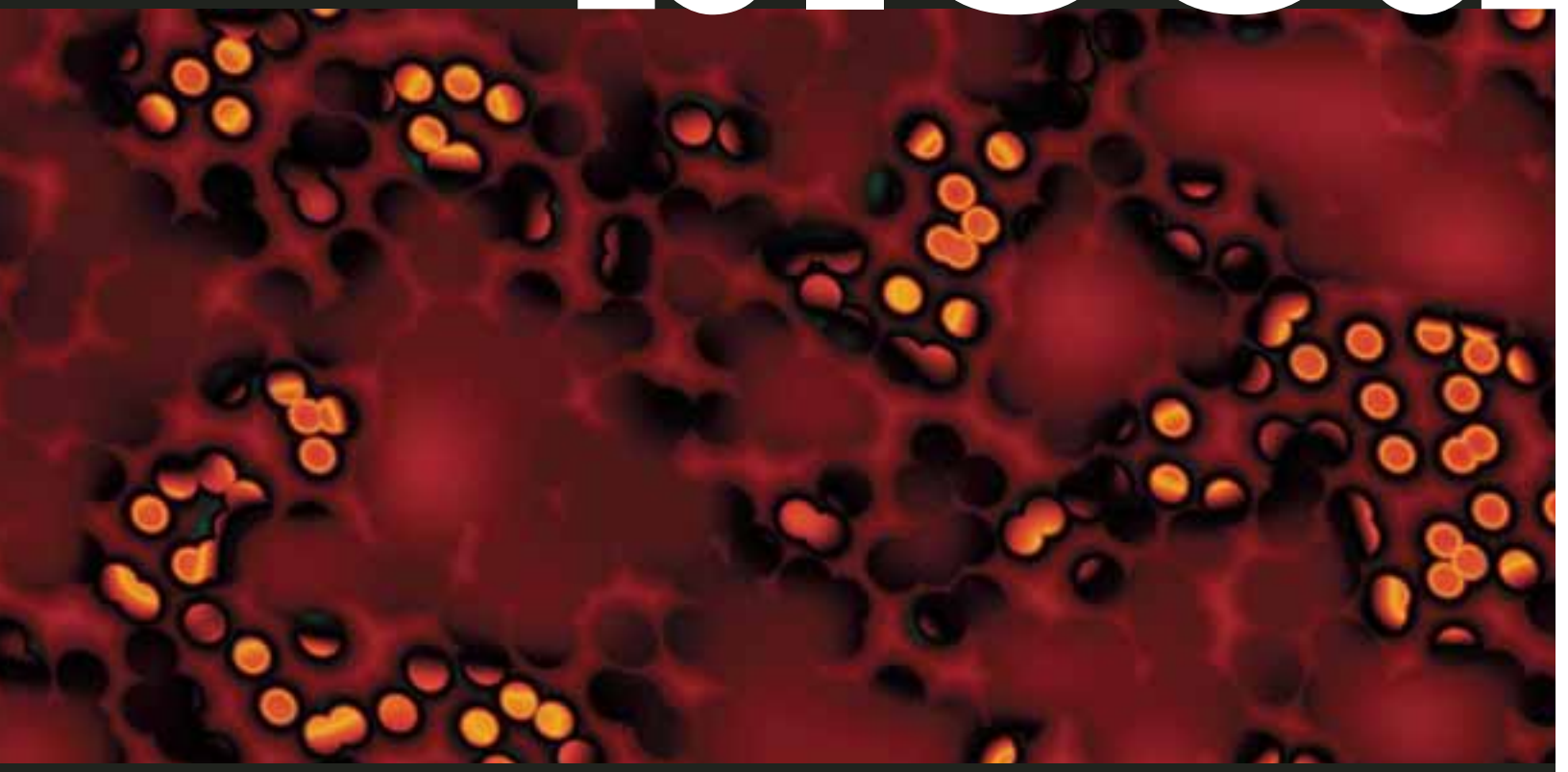
blood



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components

Whole blood consists of two main elements: the formed elements and the liquid element. The formed elements are cell fragments and cells, known as corpuscles, which account for approximately 45% of the total volume of the blood. The liquid element is the intracellular matrix, known as plasma, which accounts for approximately 55% of the total volume of the blood. In the adult, hematopoiesis (blood cell production) occurs in the red bone marrow (myeloid tissue) and all types of blood cells are produced from a single type of pluripotent stem cell (hemocytoblast). Additionally, some leukocytes are produced by the lymphatic system.

Editor's Note: This is part of a review series of short articles about blood. An article on blood basics was published in the January 2003 issue. The attached CE covers the first two articles in this series.

Corpuscles

The formed elements of blood are the erythrocyte (red blood cell, RBC), leukocyte (white blood cell, WBC), and thrombocyte (platelet).

Erythrocytes

Normal mature erythrocytes are red nonnucleated biconcave disks that measure approximately 7.5 microns in diameter. The biconcave shape increases the surface area of the cell and allows flexibility of the cell during passage through the capillaries. Each red blood cell consists of a cell membrane, which encloses the hemoglobin and the cytoplasm. Hemoglobin is the red-pigmented portion of the erythrocyte. Each hemoglobin molecule consists of four polypeptide chains (known as globin) and four nonprotein pigments (known as heme) that contain one ferrous iron atom at the center. This configuration allows four binding sites per hemoglobin molecule. Hemoglobin synthesis depends on the presence of iron and vitamins C, B2, B3, B6, B12, E, and folate (a form of a water-soluble B vitamin). Hemoglobin is responsible for carrying oxygen to the cells (in the form of oxyhemoglobin) and waste products (such as CO_2 in the form of carbaminohemoglobin) away from the cells. Antigens (agglutinogens) contained within the membrane of the erythrocyte determine an individual's blood type (ABO and Rh, positive or negative).

Red blood cell production is triggered by an oxygen sensing (negative feedback) mechanism within the cells of the kidney. A reduced number of erythrocytes results in less oxygen being delivered to the kidney (hypoxia) which in turn causes the kidney cells to release an enzyme capable of converting one of the plasma proteins into a hormone called erythropoietin. Erythropoietin causes the red bone marrow to produce more red blood cells. In turn, the additional red blood cells deliver more oxygen to the kidney cells and the signal to release the enzyme is disrupted. The life span of a red blood cell is 120 days; approximately 2.5 million (1% of the total) red blood cells are replaced per second. Red blood cells are not capable of division.

The process of erythropoiesis (red blood cell production) is as follows:

- The pluripotent stem cell is stimulated by the hormone thrombopoietin (secreted by the liver) to become a blood cell (red blood cell, white blood cell—with the exception of the lymphocyte, or a platelet) in the myeloid tissue (myeloid progenitor).
- The myeloid progenitor is stimulated by erythropoietin to produce the megakaryocyte/erythroid progenitor (proerythroblast), which is the differentiated stem cell that will eventually become the erythrocyte (takes approximately 12 hours) or the thrombocyte.
- As the euchromatic nucleus of the proerythroblast begins to shrink and the cytoplasm darkens with ribosomes, the basophilic erythroblast is formed (takes approximately 19 hours).
- The basophilic erythroblast begins to produce hemoglobin and becomes a polychromatophilic erythroblast (takes approximately 32 hours).
- The polychromatophilic erythroblast becomes an orthochromatic erythroblast (takes approximately 48 hours).
- The reticulocyte forms as the orthochromatic erythroblast shed its nucleus.
- The reticulocyte (marrow reticulocyte) begins to mature in the bone marrow (takes approximately 41 hours).
- The marrow reticulocyte transitions (is extruded) into the blood (blood reticulocyte) where it continues to mature (takes approximately 32 hours).
- The circulating mature red blood cell is functional for approximately 120 days.

Normal destruction of aged, abnormal, or damaged red blood cells takes place primarily in the spleen and liver but can also occur in bone marrow and lymph nodes via phagocy-

tosis. Hemoglobin is divided into globin and heme. Globin is broken down into amino acids that are recycled. The heme is further divided into bilirubin and iron. Iron is recycled to the red bone marrow and bilirubin is sent to the liver and is secreted in bile. The bile is excreted into the intestine where the bilirubin is converted into pigment that is expelled with the feces.

Leukocytes

Leukocytes are round colorless nucleated cells that are part of the body's defense mechanism. White blood cell production is called leukopoiesis. Leukocytes are initially released from the bone marrow into the blood stream; however, they do not remain in the circulating blood. From the blood, the various cells escape through the capillary walls by a process called diapedesis. Leukocytes are mobile cells that migrate to the extravascular tissues using amoeboid motion. Each type of leukocyte performs a different function and has a different life span. Leukocytes are divided into two main categories: granulocytes and agranulocytes.

Granulocytes

The cytoplasm of the granulocyte contains granules. Formation of granulocytes is called granulopoiesis. There are three types of granular leukocytes: neutrophils, eosinophils, and basophils.

Neutrophils

Neutrophils are the most common type of leukocyte accounting for approximately 54%-62% of all leukocytes. Mature neutrophils are released from the bone marrow into the blood. The neutrophils migrate from the blood to the interstitial fluid where they await activation (due to an injury or infection). Neutrophils use phagocytosis to ingest other cells, bacteria, necrotic tissue, and foreign particles and then destroy them with the use of oxidants (expose the cell to destructive oxygen), lysozymes (enzymes destructive to certain bacterial cell membranes), or defensins (antibiotic polypeptides that are destructive to certain bacterial cell membranes).

Neutrophils develop as follows:

- The pluripotent stem cell is stimulated by the hormone thrombopoietin (secreted by the liver) to become a blood cell (red blood cell, white blood cell—with the exception of the lymphocyte, or a platelet) in the myeloid tissue (myeloid progenitor).
- The myeloid progenitor is stimulated by granulocyte monocyte colony stimulating factor to produce the granulocyte macrophage progenitor, which is the differentiated stem cell that will eventually become either a granulocyte or a monocyte.
- The granulocyte macrophage progenitor is stimulated by granulocyte colony stimulating factor to become a neutrophil.

Eosinophils

Eosinophils account for approximately 1%-3% of all leukocytes. Eosinophils use phagocytosis to ingest the undesirable material and destroy it by releasing its cytotoxic granules. Function of the eosinophil is not completely understood. Eosinophils are associated with allergic reactions, inflammation, and the destruction of parasites and certain types of cancer cells.

Eosinophils develop from the granulocyte macrophage progenitor (refer to neutrophil development for the initial developmental stages) when the granulocyte macrophage progenitor that has been stimulated by granulocyte colony stimulating factor to become a neutrophil is additionally

influenced by interleukin-5 to become an eosinophil.

Basophils

Basophils account for less than 1% of all leukocytes. Basophils accumulate at the site of an infection or inflammation, then release their granules that contain mediators (such as heparin, histamine, and serotonin), which increase blood flow to the area. Basophils contribute to (intensify) allergic responses such as hay fever or anaphylaxis related to an insect sting.

Basophils develop from the granulocyte macrophage progenitor (refer to neutrophil development for the initial developmental stages) when the granulocyte macrophage progenitor that has been stimulated by granulocyte colony stimulating factor to become a neutrophil is additionally influenced by interleukin-3 to become a basophil.

Agranulocytes

The cytoplasm of the agranulocyte is relatively clear. Formation of agranulocytes is called agranulopoiesis. There are two types of agranular leukocytes: monocytes and lymphocytes.

Monocytes

Monocytes account for approximately 3%-7% of all leukocytes and are the largest of all leukocytes. Monocytes mature as they enter the blood stream to become macrophages. Macrophages are large phagocytes that migrate to the tissues (especially the liver, lungs, and lymph nodes) and engulf particulate matter such as antigens (foreign material) and dying or dead body cells. Monocytes along with T and B-lymphocytes are important in the immune response system.

Monocytes develop from the granulocyte macrophage progenitor (refer to neutrophil development for the initial developmental stages) when the granulocyte macrophage progenitor is stimulated by macrophage colony stimulating factor to become a monocyte (which eventually matures to become a macrophage).

Lymphocytes

Lymphocytes account for approximately 25%-38% of all leukocytes. There are two main types of lymphocytes: B-lymphocytes (cells) and T-lymphocytes (cells). Lymphocytes mediate the immune response.

Lymphocytes develop as follows:

- The pluripotent stem cell in the bone marrow is stimulated by interleukin-7 to become a lymphoid progenitor.
- Some lymphoid progenitors are released (and transported through the blood) to the thymus where they mature to become T-lymphocytes (hence the name T-cell).
- Other lymphoid progenitors remain in the bone marrow where they are further stimulated by interleukin-6 to become B-lymphocytes (hence the name B-cell).

B-Lymphocytes

B-lymphocytes circulate through the body in the blood, but concentrate in certain tissues (eg, liver), or the lymphoid organs such as the lymph nodes, tonsils, and the spleen. B-cells are specific only to one type of antigen and produce only one type of antibody. B-cells divide mitotically in the bone marrow producing more lymphocytes (clones) containing the genetic material for the same antibody. There are two main types of B-cells: plasma cells and memory cells.

Plasma cells produce and release an antibody specific to a certain type of antigen. Memory cells contain antibody information specific to a certain type of antigen. If the same antigen is encountered again, the memory cells divide rapidly replicating the specific plasma cells and producing more memory cells. Because of the memory cells, the body's second response to the antigen is more rapid.

T-Lymphocytes

T-lymphocytes have specific cell receptors on their surface that are similar to antibodies and are specific to one antigen. T-cells are activated during contact with an antigen. The T-cell with the specific antibody responds by dividing mitotically. There are three main types of T-cells: helper T-cells, killer T-cells, and memory T-cells.

Helper T-cells release cytokines when the receptors on their surface are activated. The cytokines stimulate the related B-cells to divide into plasma cells that make the antibody. The cytokines also stimulate macrophagic phagocytosis.

Killer T-cells (sometimes called natural killer cells) search for and bind to body cells affected by an invader displaying a certain antigen. The killer T-cells kill both the invader and the affected cell by attaching to the cell and secreting a toxin such as hydrogen peroxide.

Memory T-cells are similar to memory B-cells because they initiate a more rapid response if the same antigen is reencountered.

Thrombocytes

Thrombocytes are small nonnucleated cell fragments. Thrombocytes are part of the blood clotting process (cascade). When a vascular injury occurs, thrombocytes are attracted by and adhere to exposed collagen on the blood vessel wall. The clumped (aggregated) thrombocytes swell and release ADP contained in their granules causing more thrombocytes to adhere to the site forming a plug and thereby reducing blood loss. They also release chemicals that cause vascular spasm at a site of injury. The lifespan of a thrombocyte is approximately four days.

The process of thrombopoiesis (platelet production) is as follows:

- The pluripotent stem cell is stimulated by the hormone thrombopoietin (secreted by the liver) to become a blood cell (red blood cell, white blood cell—with the exception of the lymphocyte, or a platelet) in the myeloid tissue (myeloid progenitor).
- The myeloid progenitor is stimulated by erythropoietin to produce the megakaryocyte/erythroid progenitor, which is the differentiated stem cell that will eventually become the erythrocyte or the thrombocyte.
- The megakaryocyte/erythroid progenitor is again stimulated by thrombopoietin as well as interleukin-11 to become the megakaryocyte.
- The megakaryocyte replicates its DNA repeatedly while still in the bone marrow, the cell enlarges but does not divide.
- The megakaryocyte ruptures and fragments of the cytoplasm (thrombocytes) enter the blood.
- Some thrombocytes remain in circulation while others are stored in the spleen and released as needed.

Plasma

Plasma, the straw-colored liquid element of blood, is made up of approximately 90% water. The remaining 10% consists of a variable number of substances such as proteins, nutrients, amino acids, lipids, electrolytes, vitamins, hor-

mones, drugs, and waste products that are either suspended or dissolved in the water. Variations occur as substances are added and removed from the plasma as the blood circulates through the tissues. Proteins account for the largest percentage of material in the plasma. Plasma is the transportation medium for the corpuscles.

> ***Serum***
> Serum is what remains of the plasma when the clotting factors are removed.

Note: Many factors influence hematopoiesis—not all are listed in this brief article.

About the author

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