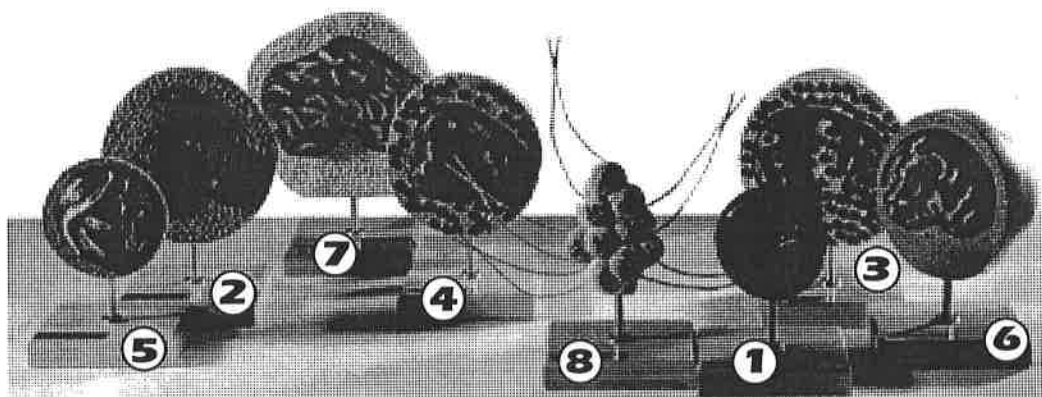


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Human Blood Model Set



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Human Blood Cells

As Illustrated by the Mueller-Ward Models

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Blood is a form of connective tissue in which the intercellular substance is fluid. In vertebrates it consists of liquid *plasma*, which varies from colorless to yellowish in different species, and numerous formed elements or *corpuscles* suspended in the plasma. The term *blood corpuscle* is generally preferable to the term *cell* in dealing with the formed elements of the blood since several of these elements lack a nucleus and therefore are not true cells. The term *cell* is nevertheless widely used in a loose sense when referring to the blood corpuscles.

The blood corpuscles of vertebrates may be classified in the following categories:

1. Red corpuscles:
 - a. Erythrocytes (nucleated, hence true cells); occurring in fish, amphibians, reptiles, and birds.
 - b. Erythroplastids (non-nucleated in their final stage); occurring in mammals.
2. "White" or colorless corpuscles, or leukocytes;
 - a. Granulocytes, or granular leukocytes; including neutrophils, basophils, and eosinophils.
 - b. Agranulocytes, or non-granular leukocytes; including large and small lymphocytes and monocytes. (Both a. and b. in general occur in all classes of vertebrates).
3. Spindle cells, or thrombocytes; occurring in the lower classes of vertebrates, and having a role in inducing clotting.
4. Blood platelets, or thromboplastids; occurring in the blood of mammals. They are small flattened plaques without nuclei, but with mitochondria which stain brilliantly in certain dyes.

In a given quantity of human blood the total volume of the corpuscles in suspension is only slightly less than the volume of the plasma. The color of vertebrate blood is due to the presence in great numbers of a particular type of corpuscle, the red cell, or *erythrocyte* (in mammals sometimes called the *erythroplastid*). The blood circulates through a system of closed vessels, the vascular system, through which it is propelled by a muscular pump—the heart. In the human species the quantity of blood is roughly

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about 7 percent of the body weight. Thus a 170-pound man would have approximately 12 pounds or 6 quarts of blood.

Blood is no isolated tissue, but is associated in the most profound and intimate relationship with all the cells and tissues of the body, and constant exchanges of dissolved substances and cellular elements are occurring between the two. Plasma is constantly escaping through the walls of the vessels into the tissues, where it bathes the cells, and finally returns to the blood stream via the lymphatics as *lymph*. The "white" or colorless corpuscles of the blood represent a heterogeneous community of mixed origin and potentialities. Many of these corpuscles pass through the walls of the capillaries (a process known as *diapedesis*) and wander through the spaces of the connective tissue. Some of these cells remain and reproduce there. Others, as well as the progeny of some of the latter, find their way back to the blood stream via the lymphatic channels. Thus it is that many of the wandering cells of the connective tissue spaces appear to identical with certain of the blood *leukocytes*.

Blood plasma carries the dissolved substances necessary for the nourishment and repair of the tissues and circulates these throughout the body; it carries waste products away from the tissues; it contains *fibrinogen*, the forerunner of *fibrin*, which is necessary for clotting; and the immune substance or antibodies which play such an important part in the resistance of the body to infection and disease. Blood is the medium through which the cells of the body carry on respiration and excretion. The red cells serve chiefly as carriers of oxygen and carbon dioxide in respiration, but the leukocytes are concerned with the defenses of the body against invading foreign organisms, in the disposal of particulate metabolic waste materials, and in the processes of tissue repair following injury, etc. Some kinds of leukocytes exhibit *phagocytosis*—the power of engulfing and digesting foreign materials or invading organisms and thus removing them from the body. The blood is also a pathway of communication in that it carries the hormones from the endocrine glands to distant parts of the body and thus assists in regulating various activities of the organism.

When blood is drawn from the body and allowed to stand it soon solidifies to form a "clot." The clot shrinks over a period of hours, separating as it does so from a quantity of clear fluid, the blood *serum*. The clot contains all of the formed elements of the blood entangled in a meshwork of fibrin fibres, whereas the serum consists of the plasma minus fibrinogen. The clotting property of blood serves a useful purpose in automatically sealing off the vessels after injury and arresting hemorrhage, while shrinkage of the clot serves to approximate the edges of the wound and minimize the task of repair. Failure of clotting leads to a serious condition in which the smallest wound may result in grave hemorrhage, and is characteristic of the hereditary disease known as *hemophilia*, and certain other conditions.

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Fresh red corpuscles in plasma are larger than those seen in dried films, in which some shrinkage occurs. On the other hand the colorless corpuscles, because of their spherical form and consequent deformation in films, appear to have a greater diameter in dried films than when viewed in the fresh suspended state, their exact dimension varying with the degree of flattening they have undergone. Red corpuscles have a rather constant form and size which is more or less characteristic for different species, each species having but a single type. The leukocytes on the other hand, because of ameboid activity, are inconstant in form; hence are distinguished on the basis of nuclear characters, cytoplasmic granules, etc. Every vertebrate has a number of different types of white corpuscles. Red corpuscles never leave the vessels except as a result of injury, whereas the white corpuscles have the power of migrating through the walls of the capillaries and wandering in the tissues under normal conditions (as mentioned above) but particularly in infection and inflammation.

Red corpuscles are highly elastic to permit their bending or squeezing in passing through small capillaries. Immediately the deforming influence is removed their shape is restored. White cells are more or less spherical when floating in the blood stream but when migrating through the tissues they assume ameboid shapes. Blood platelets and thrombocytes have relatively constant forms when floating in the bloodstream, but when blood escapes from the vessels, as in injury, these bodies immediately undergo changes and develop processes at their margins, from which threads of fibrin, precipitated from the plasma, grow outward and entangle the surrounding cells to form a clot.

The process by which new blood cells are formed is known as hematopoiesis and the tissues where this takes place are termed hematopoietic tissues. It is generally accepted that hematopoiesis is maintained when mature cell production equals mature cell loss. The function of the cells of the hematopoietic system are oxygen transport, resistance to infection, antibody production, hemorrhage cessation and reaction to foreign material. All hematopoietic tissue has a similar fundamental framework consisting of loosely anastomosing connective tissue fibres embedded in a network of primitive mesenchymal cells known as *reticular* cells. The blood cells are derived from the reticular cells by a series of transitions which take place in the meshes of the *reticular tissue*. Two general types of reticular tissue are recognized depending upon their location and the cells to which they give rise: (1) the *myeloid tissue* or bone marrow, and (2) the *lymphatic tissue* or lymph glands, Peyer's patches, the spleen, liver and thymus. The red corpuscles and granular leukocytes originate in the former, and are hence known as the *myeloid elements* of the blood; whereas the non-granular leukocytes originate in the latter and are accordingly designated the *lymphoid elements*.

The types and relative numbers of different cells present in the blood are subject to wide variations. In health the numbers of each cell are usually confined within rough limits,

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but these limits are elastic, and the total and relative numbers vary widely in disease, the particular predominant cell involved being in a rough way correlated with the type of disease present. The total and relative numbers of red and white cells are present in the blood are therefore of much clinical interest. A marked reduction in number of red cells is known as *anemia*, of which several different types are recognized depending upon whether there is a failure of production at the source of supply, as in pernicious anemia, or whether the anemia is "secondary." i.e., due to a removal of the cells from the circulation (as in hemorrhage, hookworm disease, etc.) or to their destruction in the blood stream by toxins or parasites (as in malaria). The number of red cells present in the blood may be markedly increased by breathing rarefied air, or by dwelling at high altitudes. A marked reduction in the number of white cells is known as *leukopenia*; a marked rise as *leukocytosis*. In *leukemia*, a cancer of the hematopoietic tissues, there occurs an enormous increase in the number of one or another of the different types of white cells.

Of the large number of stains employed for preparing blood films for study, Wright's stain is probably most widely used, and hence is the one represented in these models. However, many workers prefer Giemsa as yielding more constant results, especially on bird blood.

The Models

These have been made on a scale of 10,000 to 1, hence the diameter of the models in centimeters corresponds to the diameter of the cells in microns. The diameters of the models are based on the apparent diameters of the cells as seen in dried films, the appearance and method of study most familiar to the student; while the form of the models is that observed when the cells are suspended in plasma or isotonic saline solution. The white cells have been completely cut away on one surface in order to show the internal structure as seen in stained films. The red cells are partially cut away to show cell membrane, hemoglobin, and presence or absence of a nucleus.

Models 1 to 8 inclusive represent all of the formed elements found in human blood.

1. *The "RBC" (Red Blood Cell), Erythrocyte, or Erythroplastid of Man*

Although the terms erythrocyte or red cell are not strictly appropriate for the mammalian red corpuscle, since it lacks a nucleus, these terms nevertheless have wide medical usage. There is some justification for this on the ground that during its formative stages the red corpuscle is a true cell and does not lose its nucleus until just before the final stage is reached. It is therefore correct to regard it as a cell which has lost its nucleus.

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The red cell of man is a biconcave disk. Its diameter is usually given for dried film preparations as 7.5 microns, but the diameter of the cell in fresh blood is considerably greater, about 8.8 microns. The greatest thickness is about one quarter of the diameter. Adult healthy males have about 5,000,000 red cells per cubic mm of blood, as opposed to 4,500,000 in the female. The form shown here for man is characteristic of all other mammals except the Camelidae but the size varies greatly with the species from 3.7 microns for the goat (or even less in the musk deer) to 9 microns in the elephant. There is no correlation between the size of an animal and the size of its red blood cells however. It is estimated that the surface of a single human red blood corpuscle is about 128 square microns; that the total number of RBC's in the body is in the neighborhood of 25 quadrillion, and that the total surface area of all the red cells in the blood of a man is about 3500 square meters, or 4200 square yards—approximately half the area of an average city block.

The color of the erythrocyte is due to the hemoglobin which it contains in the form of a colloidal solution. Individual red cells seen by transmitted light are not red but have a straw-colored tinge. Only when in mass do they take on the characteristic red color of blood. Hemoglobin is a protein compound of iron which has the property of absorbing oxygen under conditions of low oxygen tension as in the tissues. Red cells have only a limited life in the blood stream, variously estimated at from 100 to 120 days. Old corpuscles are removed from the blood in the spleen, and to some extent in the bone marrow and liver. (The worn-out hemoglobin is converted into the bile pigments.) During adult life new red cells are constantly being formed in the red bone marrow, particularly in such bones as the ribs and sternum. But before birth blood cells are formed successively in the blood islands of the splanchnic mesoderm of the embryo, in the liver, and finally in the spleen and bone marrow. After birth the bone marrow takes over the function of making new red cells to the exclusion of the other organs.

As noted above, the mature RBC's of mammals are not true cells since they lack a nucleus. During their formative stages, however, they possess a nucleus and at times the penultimate stage in the formation of the erythroplastid—the *normoblast*—a cell resembling a nucleated red cell, is found in the blood stream, as in severe anemias, where the demand for new red cells is so great that the rate of production is inadequate, with the result that immature stages are pushed out into the blood stream. The erythrocyte is surrounded by a thin highly elastic semipermeable membrane, of a lipoid nature which permits water to pass freely while preventing the passage of such ions as sodium and

potassium. Hence when red cells are placed in either hypo- or hypertonic media abnormal swollen or crenated forms are assumed as a result of imbibition or loss of water, as the case may be, through the membrane. Whether the hemoglobin is present in the form of a watery solution or as a jelly is not settled. Red cells have a strong tendency when suspended in the blood plasma to form *rouleaux*—long chains of corpuscles adhering face to face like stacks of coins.

2. *The Neutrophil or Polymorphonuclear Leukocyte*

The white cells number fewer than the red cells, averaging in man about 7,000 to 8,000 per cubic mm of blood, or 1 white cell to about every 600 red cells in the adult. In children and in adults, following exercise, the number is considerably higher. Of the total number present the neutrophils form normally 65 to 70 percent of the total white count. The nucleus is divided into a number of lobes varying with the age of the cell from two to five. Neutrophils usually remain in the blood for four days, then enter the tissues for defense against infectious diseases. This cell can survive for two days in the tissues, but will die sooner if phagocytizing. The granules of the neutrophil contain the enzyme phagocyteen, peroxidase, lipids, glycogen, and acid phosphatase. There is an increase in the number of this cell during severe infection, pneumonia, appendicitis, burns, chemical or drug poisoning, malignant diseases and acute hemorrhage.

All of the granular leukocytes are produced in the bone marrow. Their mother cell is the myeloblast. The granules of the neutrophil are small, ill-defined, and irregular in shape as compared to the large clearly defined granules of the other granular leukocytes and are intermediate in their staining affinities, thus giving the cell a purplish color with Wright's stain.

3. *The Eosinophil*

These cells normally represent 2 to 4 percent of the total leukocyte number, but may rise to as high as 35 percent in certain parasitic diseases such as trichinosis, hookworm, pinworm, schistosomiasis, and toxoplasmosis. The count is also increased in allergic reactions such as hay fever and hypersensitivity to drugs, chronic skin diseases (psoriasis and eczema), and malignancy (Hodgkin's disease). The eosinophil is 10 to 15 microns in diameter. The nucleus is usually divided into 2 or 3 lobes. This cell responds to infection after the neutrophil. The granules of the eosinophil contain histamine (allergic reactions) and the protein arginine (which seems to function in killing parasitic worms). These cells exhibit ameboid activity, but are not phagocytic. Their granules give rise to the Charcot-Leyden crystals which can be seen in the sputum of asthmatics.

4. *The Basophil*

These cells form only about 0.5 percent of the total white cell count and may not be present in a normal blood smear. The basophil is 10-15 microns in diameter. The nucleus may divide into irregular lobes or may be kidney shaped, usually staining lighter than the granules. The granules stain deep blue due to their heparin content. They contain histamine and peroxidase. The basophil is capable of limited ameboid movement and phagocytosis. This cells' number will greatly increase in allergic states, stress reactions, and certain myeloid leukemias. In cutaneous basophil hypersensitivity, basophils constitute the major cell type in an inflammatory site.

5. *The Small Lymphocyte*

Large and small lymphocytes together form 20 to 35 percent of the total white cell count. Large and small lymphocytes are chameleon-like. They are capable of reversible transformation. The adult lymphocyte can change back to a premature state and back again to an adult as long as they do not enter any tissue. Lymphocytes are an essential part of the immune system. Small lymphocytes are 6 to 8 microns in diameter. They are the predominant lymphocyte in the blood. The nucleus is spherical and sometimes has an indentation, the cytoplasm is scanty and in blood smears it appears as a thin rim around the nucleus. A possible reason for the scant rim is that these cells are continually shedding their cytoplasm in the process of antibody production. The cytoplasm may contain azurophilic granules that stain purple, and are associated with chronic infection and virus disease. The life span of this cell varies from a few days to many years.

6. *The Large Lymphocyte*

This Lymphocyte can be up to 18 microns in diameter. This increase is due to the amount of cytoplasm. Large lymphocytes can lead other white cells to inflammatory sites, secrete substances that kill other cells (tumor cells), or that can coat bacteria or other invaders making them more susceptible to phagocytosis. In pre-natal life, primitive cells destined to become lymphocytes enter the blood and are seeded first in the thymus, liver, and spleen. In post-natal life, they are seeded in the bone marrow, lymph nodes, Peyer's Patches of the intestine, and all other organs with the exception of the brain and spinal cord. In older children and adults, lymphocytes originate in the lymphatic system. The large lymphocyte is generally considered less mature than the small. There is an increase of lymphocytes in infectious hepatitis, some bacterial infections, and specific leukemias. Lymphocyte production is repressed in auto-immune diseases.

7. *The Monocytes*

These cells normally represent 2 to 10 percent of the total leukocyte count. Monocytes are the largest of the white cells, 12-20 microns in diameter, but can be as large as 30 microns. The nucleus is very irregular. Usually it is round or kidney-shaped, but may be indented or have two or more lobes. One of the most distinctive features of the monocyte is the superimposed lobes, giving the nucleus a brain-like appearance. Monocytes are derived from stem cells in the bone marrow. The smaller monocyte, the larger wandering macrophages, and tissue macrophages are thought to be capable of reversible transformation from one to the other. Monocytes remove injured and dead cells from the blood, and clear insoluble debris from tissue. They furnish nucleated red cells, the iron needed for the synthesis of heme, and are a first line of defense against foreign invaders. This cell will increase in number when there is a reactivation of tuberculosis, typhus, Rocky Mountain spotted fever, malaria, and acute myelocytic leukemia.

8. *The Blood Platelet or Thrombocyte*

The platelet is a fragment of cytoplasm from giant cells (megakaryocytes) which reside in the bone marrow. Platelets are non-nucleated disk-like cell fragments, 2 to 4 microns in diameter. Platelets promote blood clotting and help repair gaps in the walls of blood vessels to prevent blood loss. In thin portions of a blood smear there are 5 to 25 platelets in an oil-immersion field. No report of a blood smear is complete unless the platelet number is stated and its shape is described. Separate in the blood stream, they clump together when released from the vessels and immediately undergo changes. Small processes appear at their margins and from these threads of fibrin, derived from the plasma, grow outward among the surrounding cells to form a clot. The model represents a clump of platelets with several fibrin strands beginning to form. Darkly staining bodies within the platelets may give the appearance of a nucleus, but are actually mitochondrial in nature.

In mammals, as in man, white blood cells play similar roles. In dogs the number of eosinophils will increase if there is a *dirofilaria immitis* infection (heartworm). In cats with feline leukemia the number of lymphocytes increase and the number of neutrophils decreases. These are the same results in man if there is a parasitic infection and in specific types of leukemia.

The blood platelets also play similar roles in man and mammals.



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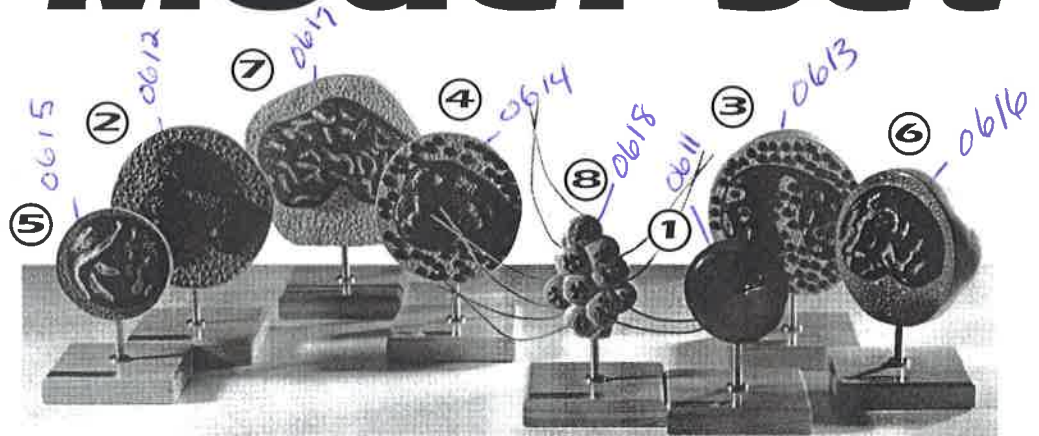
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WARD'STM

User's Guide

Blood Components Model Set



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Blood Components Model Set

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Blood is a form of connective tissue with a fluid intercellular substance. In vertebrates, it consists of liquid plasma, which varies from colorless to yellowish in different species, and numerous formed elements or corpuscles suspended in the plasma. The term "blood corpuscle" is generally preferable to the term "cell" when referring to the formed elements of the blood, since several of these elements lack a nucleus and therefore are not true cells. "Cell" is nevertheless widely used in a loose sense when referring to the blood corpuscles.

The blood corpuscles of vertebrates may be classified in the following categories:

1. Red Corpuscles
 - a. Erythrocytes (nucleated, hence true cells)
 - 1) Occur in fish, amphibians, reptiles, and birds
 - b. Erythroplastids (nonnucleated in their final stage)
 - 1) Occur in mammals
2. "White" or Colorless Corpuscles (Leukocytes)
 - a. Granulocytes, or granular leukocytes
 - 1) Include neutrophils, basophils, and eosinophils
 - b. Agranulocytes, or nongranular leukocytes
 - 1) Include large and small lymphocytes and monocytes
 - c. Both granulocytes and agranulocytes occur in all classes of vertebrates
3. Spindle Cells, or Thrombocytes
 - a. Occur in lower classes of vertebrates
 - b. Induce clotting
4. Blood Platelets, or Thromboplastids
 - a. Occur in blood of mammals
 - b. Small flattened plaques without nuclei, but with mitochondria which stain brilliantly in certain dyes

In any given quantity of human blood, the total volume of the corpuscles in suspension is only slightly less than the volume of the plasma. Vertebrate blood gets its red color from the great numbers of red blood cells (erythrocytes or, in mammals, sometimes called erythroplastids). The blood circulates through a system of closed vessels—the vascular system—propelled by a muscular pump—the heart. The quantity of blood in a human body is roughly 7% of the total body weight. For example, a 170 lb. man would have approximately 12 pounds, or six quarts, of blood.

Blood is not isolated tissue; instead it is associated with all the cells and tissues of the body. Dissolved substances and cellular elements are constantly exchanged between the two. Plasma escapes through the vessel walls into the tissues and finally returns to the bloodstream via the lymphatics, as lymph. The white corpuscles represent a heterogeneous community of mixed origins and potentialities. Many of these corpuscles pass through the capillary walls (a process known as diapedesis) and wander through the spaces of the connective tissue. Some of these cells remain and reproduce there. Others, as well as the reproduced cells, find their way back to the bloodstream via the lymphatic channels. Many of the wandering cells appear identical to certain blood leukocytes.

Blood plasma circulates the dissolved substances necessary for the nourishment and repair of tissues throughout the body, and carries waste products away from the tissues. It contains fibrinogen, the forerunner of fibrin, which is necessary for clotting, and antibodies, which play such an important part in the body's resistance to infection and disease. Blood is the medium through which the cells of the body perform the processes of respiration and excretion. The red cells mainly carry oxygen and carbon dioxide in respiration; the leukocytes are employed defending the body against invading foreign organisms, dispose of particular metabolic waste materials, and repairing tissues harmed due to injury, etc. Some kinds of leukocytes exhibit phagocytosis—engulfing and digesting foreign materials or invading organisms in order to remove them from the body. The blood is also a pathway of communication; it carries hormones from the endocrine glands to distant parts of the body, thereby assisting in regulating various activities of the organism.

When blood is drawn from the body and allowed to stand, it soon solidifies to form a "clot". The clot shrinks over several hours; as it does so it separates from a quantity of clear fluid, the blood serum. The clot contains all of the elements of the blood, entangled in fibrin fibers, whereas the serum consists of plasma without fibrinogen. The clotting property of blood serves a useful purpose; it automatically seals off the vessels after injury, stopping hemorrhaging. The clot shrinking approximates the edges of the wound and minimizes the task of repair. If blood fails to clot, the smallest wound may result in a serious hemorrhage; this is characteristic of the hereditary disease known as hemophilia, as well as other conditions.

Components of Blood

Red Corpuscles

Fresh red corpuscles in plasma are larger than those in dried films because they shrink as they dry. Their form and size are constant, which is more or less characteristic for different species; each species has a single type. Red corpuscles never leave the vessels except as a result of injury. Highly elastic, red corpuscles change shape to bend or squeeze through small capillaries.

White Corpuscles

Because of their spherical form and consequent deformation in films, white corpuscles appear to be larger in diameter when dried than when in the fresh suspended state. Their exact dimensions vary with the degree of flattening they have undergone. Every vertebrate has a number of different types of white corpuscles. They can migrate through capillary walls under normal conditions, but do so particularly in the case of infection or inflammation. White corpuscles are more or less spherical when in the bloodstream, but assume ameboid shapes when migrating through tissues.

Leukocytes

Leukocytes do not have a constant form because of their ameboid activity. They are distinguished on the basis of nuclear characteristics, cytoplasmic granules, etc.

Platelets and Thrombocytes

Both have relatively constant forms when in the bloodstream; however, when blood escapes from the vessels due to injury, etc., these bodies immediately change, developing processes at their margins from which threads of fibrin, precipitated from the plasma, grow outward and entangle the surrounding cells to form a clot.

Formation of New Blood Cells

New blood cells form by a process known as hematopoiesis, which takes place in the hematopoietic tissues. It is generally accepted that hematopoiesis is maintained when mature cell production equals mature cell loss. The functions of the cells of the hematopoietic system are oxygen transport, resistance to infection, antibody production, hemorrhage cessation, and reaction to foreign material. All hematopoietic tissue has a similar fundamental framework consisting of loosely anastomosing connective tissue fibers embedded in a network of primitive mesenchymal cells (reticular cells). The blood cells are derived from the reticular cells by a series of transitions which take place in the reticular tissue.

There are two general types of reticular tissue: the myeloid tissue (bone marrow) and the lymphatic tissue (lymph glands), Peyer's patches, spleen, liver, and thymus. The red corpuscles and granular leukocytes originate in the myeloid tissue and so are known as the myeloid elements of the blood; the nongranular leukocytes originate in the lymphatic tissue and are accordingly called the lymphoid elements.

Number of Blood Cells

The types and relative numbers of different cells in the blood vary greatly. In a healthy body, the numbers of each cell are usually confined within rough limits, but the total and relative number of cells may fluctuate in the presence of disease, the predominant cell depending on the type of disease. Therefore, the total and relative number of red and white cells present in the blood are of clinical interest. A marked reduction in the number of red blood cells is a condition known as anemia; there are several types, depending on whether red blood cells are not produced (pernicious anemia), or whether they are removed from the circulation as in hemorrhaging, hookworm disease, etc., or destroyed in the bloodstream by toxins or parasites (secondary anemia). The number of red blood cells present may be increased by breathing rarefied air or by dwelling at high altitudes. A marked reduction in white blood cells is known as leukopenia; a rise in the number of white blood cells is leukocytosis. In leukemia, a cancer of the hematopoietic tissues, there is a large increase in the number of one of the types of white cells.

Of the large number of stains employed for preparing blood films for study, Wright's stain is probably most widely used; this model presents blood as it would be stained by Wright's stain. Giemsa stain is also used; it yields more constant results, especially on bird blood.

WARD'S Blood Components Models

This set of models represents all the formed elements found in human blood. Enlarged 10,000X, these models' diameters in centimeters correspond to the diameters of the actual cells in microns. The diameters of the models are based on the apparent diameter of the cells in dried films (the form most familiar to the student), while the form of the models is as they appear when suspended in plasma or isotonic saline solution. The white cells have been completely cut away on one surface to show the internal structure as seen in stained films. The red cells are partially cut away to show cell membrane, hemoglobin, and presence or absence of a nucleus.

Model 1: The Red Blood Cell

Also known as the erythrocyte, or erythroplastid in humans. Although the terms "red cell" and "erythrocyte" are not appropriate for the mammalian red corpuscle since it lacks a nucleus, these terms are nevertheless widely used because, during its formative stages, the red corpuscle is a true cell; it does not lose its nucleus until just before the final stage of development. It may be regarded as a cell which has lost its nucleus. At times, in the penultimate stage of their formation—the normoblast—a cell resembling a nucleated red cell is found in the bloodstream. In severe anemia, the demand for new red blood cells is so great that the rate of production is inadequate, resulting in immature red blood cells being pushed into the bloodstream.

The human red cell is a biconcave disk, with a typical diameter of 7.5 microns in a dried film preparation. The diameter of a fresh blood cell is considerably greater—approximately 8.8 microns. The greatest thickness is about one quarter of the diameter. Healthy adult males have approximately 5,000,000 red cells per cubic millimeter of blood; healthy adult females have 4,500,000. This model is characteristic for humans and all other mammals except the Camelidae, but the size varies greatly with the species—from 3.7 microns for a goat (even less in the musk deer) to 9 microns for an elephant. However, there is no correlation between the size of the animal and the size of its red blood cells. It is estimated that the surface of a single human red blood corpuscle is about 128 square microns, the total number of red blood cells in the body is approximately 25 quadrillion, and the total surface area of all the red cells in a male human's blood is about 3,500 square meters, or 4,200 square yards—approximately half the area of an average city block.

Erythrocytes are red due to the hemoglobin which it contains in the form of a colloidal solution. Hemoglobin is a protein compound of iron, which absorbs oxygen under conditions of low oxygen tension as in the tissues. Individual red cells seen by transmitted light are not red; instead they are straw colored. They only appear red in large quantities.

Red cells live from 100 to 120 days in the bloodstream. Old corpuscles are removed from the blood in the spleen and, to some extent, in the bone marrow and liver. The worn-out hemoglobin is converted into the bile pigments. Before birth, blood cells are formed successively in the blood islands of the splanchnic mesoderm of the embryo, in the liver, and in the spleen and bone marrow. After birth, the bone marrow exclusively makes new red cells. During adult life, new red cells are constantly being formed in the red bone marrow, particularly in the ribs and sternum.

The erythrocyte is surrounded by a thin, highly elastic semipermeable membrane of a lipid nature, which permits water to pass freely while preventing ions such as sodium and potassium from passing through. When red cells are placed in either a hypo- or hypertonic medium, abnormal swollen or crenated forms are assumed as a result of inhibition or loss of water through the membrane. Whether the hemoglobin is present in the form of a watery solution or as a jelly has not been determined. When suspended in the blood plasma, red cells have a strong tendency to form rouleaux—long chains of corpuscles adhering face to face like stacks of coins.

Model 2: The Neutrophil

Also known as the polymorphonuclear leukocyte. White cells are fewer than red cells, averaging 7,000 to 8,000 per cubic millimeter of blood, or one white cell to about every 600 red cells in a human adult. In children and in adults, the number is considerably higher after exercise.

Of the total number present, neutrophils are 60 to 70% of the total white count. The granules of the neutrophil contain the enzyme phagocyteen, peroxidase, lipids, glycogen, and acid phosphatase. Its nucleus is divided into a number of lobes that vary from two to five, depending on the age of the cell. Neutrophils usually remain in the blood for four days, then enter the tissues for defense against infectious diseases. This cell can survive for two days in the tissues, but will die sooner if phagocytizing. The number increases in the case of severe infection, pneumonia, appendicitis, burns, chemical or drug poisoning, malignant diseases, and acute hemorrhage.

All granular leukocytes are produced in the bone marrow. Their mother cell is the myeloblast. The granules of the neutrophil are small, ill defined, and irregular in shape as compared to the large clearly defined granules of the other granular leukocytes and are intermediate in their staining affinities, thus giving the cell a purplish color with Wright's stain.

Model 3: The Eosinophil

Eosinophils normally represent 2 to 4% of the total number of leukocytes, but may rise to as high as 35% in the presence of certain parasitic disease such as trichinosis, hookworm, pinworm, schistosomiasis, and toxoplasmosis. The count is also increased in allergic reactions such as hay fever and hypersensitivity to drugs, chronic skin diseases (psoriasis and eczema), and malignancy (Hodgkin's disease). The eosinophil is 10 to 15 microns in diameter; its nucleus is usually divided into two or three lobes.

This cell responds to infection after the neutrophil. The granules of the eosinophil contain histamine (allergic reactions) and the protein arginine (which seems to kill parasitic worms). These cells exhibit ameboid activity, but are not phagocytic. Their granules give rise to the Charcot-Leyden crystals which can be seen in the sputum of asthmatics.

Model 4: The Basophil

These cells form only about 0.5% of the total white cell count; they may not be present in a normal blood smear. The basophil is 10 to 15 microns in diameter. The nucleus may divide into irregular lobes or may be kidney shaped.

The granules stain deep blue due to their heparin content; the nucleus stains lighter than the granules. The granules contain histamine and peroxidase. The basophil is capable of limited amoeboid movement and phagocytosis. This cell's number will greatly increase in allergic states, stress reactions, and certain myeloid leukemias. In cutaneous basophil hypersensitivity, basophils constitute the major cell type in an inflammatory site.

Model 5: The Small Lymphocyte

Large and small lymphocytes, essential parts of the immune system, together form 20 to 35% of the total white cell count; they are the predominant lymphocyte in the blood.

Small lymphocytes are 6 to 8 microns in diameter. The nucleus is spherical and sometimes has an indentation. The cytoplasm is scanty, possibly because these cells are continually shedding their cytoplasm; in blood smears it appears as a thin rim around the nucleus. A possible reason for the scant rim is that these cells are continually shedding their cytoplasm in the process of antibody production. The cytoplasm may contain azurophilic granules that stain purple, and are associated with chronic infection and viral disease. Large and small lymphocytes are capable of reversible transformation: The adult lymphocyte can change from an adult to a premature state and back again, as long as it does not enter any tissue. The life span of this cell varies from a few days to many years.

Model 6: The Large Lymphocyte

This lymphocyte can be up to 18 microns in diameter due to the amount of cytoplasm. Large lymphocytes can lead other white cells to inflammatory sites, secrete substances that kill other cells (tumor cells) or coat bacteria or other invaders to make them more susceptible to phagocytosis. The large lymphocyte is generally considered less mature than the small. In prenatal life, primitive cells destined to become lymphocytes enter the blood and are seeded first in the thymus, liver, and spleen. After birth, they are seeded in the bone marrow, lymph nodes, Peyer's patches of the intestine, and all other organs with the exception of the brain and spinal cord. In older children and adults, lymphocytes originate in the lymphatic system. The number of lymphocytes increases in the presence of infectious hepatitis, some bacterial infections, and specific types of leukemia. Lymphocyte production is repressed in autoimmune diseases.

Model 7: The Monocytes

These cells normally represent 2 to 10% of the total leukocyte count. The largest of the white cells, monocytes are 12 to 20 microns in diameter, but can be as large as 30 microns. The nucleus is very irregular; usually it is round or kidney shaped, but may be indented or have two or more lobes. One of the most distinctive features of the monocyte is superimposed lobes, giving the nucleus a brain-like appearance. Monocytes are derived from stem cells in the bone marrow. The smaller monocyte, the larger wandering macrophages, and tissue macrophages are thought to be capable of reversible transformation from one to the other. Monocytes remove injured and dead cells from the blood and clear insoluble debris from tissue. They furnish nucleated red cells, the iron needed for the synthesis of heme, and are a first line of defense against foreign invaders. This cell will increase in number when there is a reactivation of tuberculosis, typhus, Rocky Mountain spotted fever, malaria, and acute myelocytic leukemia.

Model 8: The Blood Platelet

Also known as the thrombocyte. The platelet is a fragment of cytoplasm from giant cells (megakaryocytes) in the bone marrow. Platelets are non-nucleated disk-like cell fragments, 2 to 4 microns in diameter. No report of a blood smear is complete unless the platelet number is stated and its shape is described. In thin portions of a blood smear there are 5 to 25 platelets in an oil-immersion field. They promote blood clotting and help repair gaps in the walls of blood vessels to prevent blood loss. Separate in the blood stream, they clump together when released from the vessels and immediately undergo changes. Small processes appear at their margins and from these threads of fibrin, derived from the plasma, grow outward among the surrounding cells to form a clot. The model represents a clump of platelets with several fibrin strands beginning to form. Darkly staining bodies within the platelets may give the appearance of a nucleus, but are actually mitochondrial in nature.

In mammals, including humans, white blood cells and platelets play similar roles. In dogs the number of eosinophils will increase if there is a *dirofilaria immitis* infection (heartworm). In cats with feline leukemia, the number of lymphocytes increases and the number of neutrophils decreases. These are the same results in humans if there is a parasitic infection and in specific types of leukemia.

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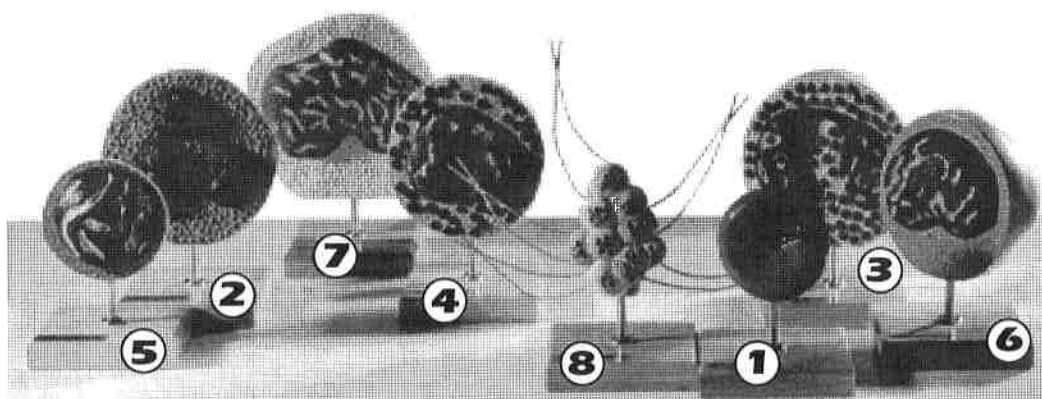
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but these limits are elastic, and the total and relative numbers vary widely in disease, the particular predominant cell involved being in a rough way correlated with the type of disease present. The total and relative numbers of red and white cells are present in the blood are therefore of much clinical interest. A marked reduction in number of red cells is known as *anemia*, of which several different types are recognized depending upon whether there is a failure of production at the source of supply, as in pernicious anemia, or whether the anemia is "secondary," i.e., due to a removal of the cells from the circulation (as in hemorrhage, hookworm disease, etc.) or to their destruction in the blood stream by toxins or parasites (as in malaria). The number of red cells present in the blood may be markedly increased by breathing rarefied air, or by dwelling at high altitudes. A marked reduction in the number of white cells is known as *leukopenia*; a marked rise as *leukocytosis*. In *leukemia*, a cancer of the hematopoietic tissues, there occurs an enormous increase in the number of one or another of the different types of white cells.

Of the large number of stains employed for preparing blood films for study, Wright's stain is probably most widely used, and hence is the one represented in these models. However, many workers prefer Giemsa as yielding more constant results, especially on bird blood.

The Models

These have been made on a scale of 10,000 to 1, hence the diameter of the models in centimeters corresponds to the diameter of the cells in microns. The diameters of the models are based on the apparent diameters of the cells as seen in dried films, the appearance and method of study most familiar to the student; while the form of the models is that observed when the cells are suspended in plasma or isotonic saline solution. The white cells have been completely cut away on one surface in order to show the internal structure as seen in stained films. The red cells are partially cut away to show cell membrane, hemoglobin, and presence or absence of a nucleus.

Models 1 to 8 inclusive represent all of the formed elements found in human blood.

1. *The "RBC" (Red Blood Cell), Erythrocyte, or Erythroplastid of Man*

Although the terms erythrocyte or red cell are not strictly appropriate for the mammalian red corpuscle, since it lacks a nucleus, these terms nevertheless have wide medical usage. There is some justification for this on the ground that during its formative stages the red corpuscle is a true cell and does not lose its nucleus until just before the final stage is reached. It is therefore correct to regard it as a cell which has lost its nucleus.



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The red cell of man is a biconcave disk. Its diameter is usually given for dried film preparations as 7.5 microns, but the diameter of the cell in fresh blood is considerably greater, about 8.8 microns. The greatest thickness is about one quarter of the diameter. Adult healthy males have about 5,000,000 red cells per cubic mm of blood, as opposed to 4,500,000 in the female. The form shown here for man is characteristic of all other mammals except the Camelidae but the size varies greatly with the species from 3.7 microns for the goat (or even less in the musk deer) to 9 microns in the elephant. There is no correlation between the size of an animal and the size of its red blood cells however. It is estimated that the surface of a single human red blood corpuscle is about 128 square microns; that the total number of RBC's in the body is in the neighborhood of 25 quadrillion, and that the total surface area of all the red cells in the blood of a man is about 3500 square meters, or 4200 square yards—approximately half the area of an average city block.

The color of the erythrocyte is due to the hemoglobin which it contains in the form of a colloidal solution. Individual red cells seen by transmitted light are not red but have a straw-colored tinge. Only when in mass do they take on the characteristic red color of blood. Hemoglobin is a protein compound of iron which has the property of absorbing oxygen under conditions of low oxygen tension as in the tissues. Red cells have only a limited life in the blood stream, variously estimated at from 100 to 120 days. Old corpuscles are removed from the blood in the spleen, and to some extent in the bone marrow and liver. (The worn-out hemoglobin is converted into the bile pigments.) During adult life new red cells are constantly being formed in the red bone marrow, particularly in such bones as the ribs and sternum. But before birth blood cells are formed successively in the blood islands of the splanchnic mesoderm of the embryo, in the liver, and finally in the spleen and bone marrow. After birth the bone marrow takes over the function of making new red cells to the exclusion of the other organs.

As noted above, the mature RBC's of mammals are not true cells since they lack a nucleus. During their formative stages, however, they possess a nucleus and at times the penultimate stage in the formation of the erythroplastid—the *normoblast*—a cell resembling a nucleated red cell, is found in the blood stream, as in severe anemias, where the demand for new red cells is so great that the rate of production is inadequate, with the result that immature stages are pushed out into the blood stream. The erythrocyte is surrounded by a thin highly elastic semipermeable membrane, of a lipoid nature which permits water to pass freely while preventing the passage of such ions as sodium and

potassium. Hence when red cells are placed in either hypo- or hypertonic media abnormal swollen or crenated forms are assumed as a result of imbibition or loss of water, as the case may be, through the membrane. Whether the hemoglobin is present in the form of a watery solution or as a jelly is not settled. Red cells have a strong tendency when suspended in the blood plasma to form *rouleaux*—long chains of corpuscles adhering face to face like stacks of coins.

2. *The Neutrophil or Polymorphonuclear Leukocyte*

The white cells number fewer than the red cells, averaging in man about 7,000 to 8,000 per cubic mm of blood, or 1 white cell to about every 600 red cells in the adult. In children and in adults, following exercise, the number is considerably higher. Of the total number present the neutrophils form normally 65 to 70 percent of the total white count. The nucleus is divided into a number of lobes varying with the age of the cell from two to five. Neutrophils usually remain in the blood for four days, then enter the tissues for defense against infectious diseases. This cell can survive for two days in the tissues, but will die sooner if phagocytizing. The granules of the neutrophil contain the enzyme phagocyteen, peroxidase, lipids, glycogen, and acid phosphatase. There is an increase in the number of this cell during severe infection, pneumonia, appendicitis, burns, chemical or drug poisoning, malignant diseases and acute hemorrhage.

All of the granular leukocytes are produced in the bone marrow. Their mother cell is the myeloblast. The granules of the neutrophil are small, ill-defined, and irregular in shape as compared to the large clearly defined granules of the other granular leukocytes and are intermediate in their staining affinities, thus giving the cell a purplish color with Wright's stain.

3. *The Eosinophil*

These cells normally represent 2 to 4 percent of the total leukocyte number, but may rise to as high as 35 percent in certain parasitic diseases such as trichinosis, hookworm, pinworm, schistosomiasis, and toxoplasmosis. The count is also increased in allergic reactions such as hay fever and hypersensitivity to drugs, chronic skin diseases (psoriasis and eczema), and malignancy (Hodgkin's disease). The eosinophil is 10 to 15 microns in diameter. The nucleus is usually divided into 2 or 3 lobes. This cell responds to infection after the neutrophil. The granules of the eosinophil contain histamine (allergic reactions) and the protein arginine (which seems to function in killing parasitic worms). These cells exhibit ameboid activity, but are not phagocytic. Their granules give rise to the Charcot-Leyden crystals which can be seen in the sputum of asthmatics.

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4. *The Basophil*



81-0614

These cells form only about 0.5 percent of the total white cell count and may not be present in a normal blood smear. The basophil is 10-15 microns in diameter. The nucleus may divide into irregular lobes or may be kidney shaped, usually staining lighter than the granules. The granules stain deep blue due to their heparin content. They contain histamine and peroxidase. The basophil is capable of limited ameboid movement and phagocytosis. This cells' number will greatly increase in allergic states, stress reactions, and certain myeloid leukemias. In cutaneous basophil hypersensitivity, basophils constitute the major cell type in an inflammatory site.

5. *The Small Lymphocyte*



81-0615

Large and small lymphocytes together form 20 to 35 percent of the total white cell count. Large and small lymphocytes are chameleon-like. They are capable of reversible transformation. The adult lymphocyte can change back to a premature state and back again to an adult as long as they do not enter any tissue. Lymphocytes are an essential part of the immune system. Small lymphocytes are 6 to 8 microns in diameter. They are the predominant lymphocyte in the blood. The nucleus is spherical and sometimes has an indentation, the cytoplasm is scanty and in blood smears it appears as a thin rim around the nucleus. A possible reason for the scant rim is that these cells are continually shedding their cytoplasm in the process of antibody production. The cytoplasm may contain azurophilic granules that stain purple, and are associated with chronic infection and virus disease. The life span of this cell varies from a few days to many years.

6. *The Large Lymphocyte*



81-0616

This Lymphocyte can be up to 18 microns in diameter. This increase is due to the amount of cytoplasm. Large lymphocytes can lead other white cells to inflammatory sites, secrete substances that kill other cells (tumor cells), or that can coat bacteria or other invaders making them more susceptible to phagocytosis. In pre-natal life, primitive cells destined to become lymphocytes enter the blood and are seeded first in the thymus, liver, and spleen. In post-natal life, they are seeded in the bone marrow, lymph nodes, Peyer's Patches of the intestine, and all other organs with the exception of the brain and spinal cord. In older children and adults, lymphocytes originate in the lymphatic system. The large lymphocyte is generally considered less mature than the small. There is an increase of lymphocytes in infectious hepatitis, some bacterial infections, and specific leukemias. Lymphocyte production is repressed in auto-immune diseases.

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7. *The Monocytes*

These cells normally represent 2 to 10 percent of the total leukocyte count. Monocytes are the largest of the white cells, 12-20 microns in diameter, but can be as large as 30 microns. The nucleus is very irregular. Usually it is round or kidney-shaped, but may be indented or have two or more lobes. One of the most distinctive features of the monocyte is the superimposed lobes, giving the nucleus a brain-like appearance. Monocytes are derived from stem cells in the bone marrow. The smaller monocyte, the larger wandering macrophages, and tissue macrophages are thought to be capable of reversible transformation from one to the other. Monocytes remove injured and dead cells from the blood, and clear insoluble debris from tissue. They furnish nucleated red cells, the iron needed for the synthesis of heme, and are a first line of defense against foreign invaders. This cell will increase in number when there is a reactivation of tuberculosis, typhus, Rocky Mountain spotted fever, malaria, and acute myelocytic leukemia.

8. *The Blood Platelet or Thrombocyte*

The platelet is a fragment of cytoplasm from giant cells (megakaryocytes) which reside in the bone marrow. Platelets are non-nucleated disk-like cell fragments, 2 to 4 microns in diameter. Platelets promote blood clotting and help repair gaps in the walls of blood vessels to prevent blood loss. In thin portions of a blood smear there are 5 to 25 platelets in an oil-immersion field. No report of a blood smear is complete unless the platelet number is stated and its shape is described. Separate in the blood stream, they clump together when released from the vessels and immediately undergo changes. Small processes appear at their margins and from these threads of fibrin, derived from the plasma, grow outward among the surrounding cells to form a clot. The model represents a clump of platelets with several fibrin strands beginning to form. Darkly staining bodies within the platelets may give the appearance of a nucleus, but are actually mitochondrial in nature.

In mammals, as in man, white blood cells play similar roles. In dogs the number of eosinophils will increase if there is a *dirofilaria immitis* infection (heartworm). In cats with feline leukemia the number of lymphocytes increase and the number of neutrophils decreases. These are the same results in man if there is a parasitic infection and in specific types of leukemia.

The blood platelets also play similar roles in man and mammals.

