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BLOOD SUPPLY TO THE HUMAN BODY, VASCULAR ANATOMY AND BLOOD COMPONENTS

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Annotation: **Blood**, fluid that transports oxygen and nutrients to the cells and carries away carbon dioxide and other waste products. Technically, blood is a transport liquid pumped by the heart (or an equivalent structure) to all parts of the body, after which it is returned to the heart to repeat the process. Blood is both a tissue and a fluid. It is a tissue because it is a collection of similar specialized cells that serve particular functions. These cells are suspended in a liquid matrix (plasma), which makes the blood a fluid. If blood flow ceases, death will occur within minutes because of the effects of an unfavourable environment on highly susceptible cells.

Key words: blood, causes, fluid, oxygen, glucose.

The constancy of the composition of the blood is made possible by the circulation, which conveys blood through the organs that regulate the concentrations of its components. In the lungs, blood acquires oxygen and releases carbon dioxide transported from the tissues. The kidneys remove excess water and dissolved waste products. Nutrient substances derived from food reach the bloodstream after absorption by the gastrointestinal tract. Glands of the endocrine system release their secretions into the blood, which transports these hormones to the tissues in which they exert their effects. Many substances are recycled through the blood; for example, iron released during the destruction of old red cells is conveyed by the plasma to sites of new red cell production where it is reused. Each of the numerous components of the blood is kept within appropriate concentration limits by an effective regulatory mechanism. In many instances, feedback control systems are operative; thus, a declining level of blood sugar (glucose) leads to accelerated release of glucose into the blood so that a potentially hazardous depletion of glucose does not occur.

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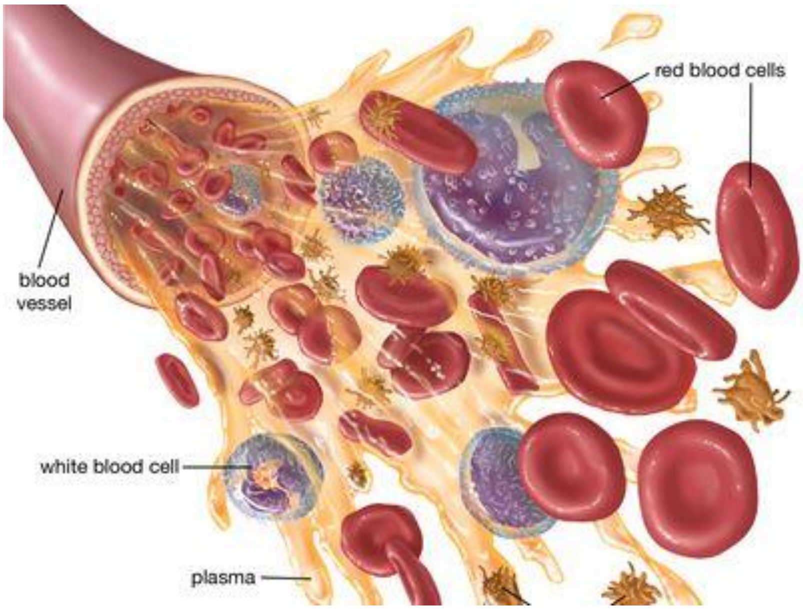

Unicellular organisms, primitive multicellular animals, and the early embryos of higher forms of life lack a circulatory system. Because of their small size, these organisms can absorb oxygen and nutrients and can discharge wastes directly into their surrounding medium by simple diffusion. Sponges and coelenterates (e.g., jellyfish and hydras) also lack a blood system; the means to transport foodstuffs and oxygen to all the cells of these larger multicellular animals is provided by water, sea or fresh, pumped through spaces inside the organisms. In larger and more-complex animals, transport of adequate amounts of oxygen and other substances requires some type of blood circulation. In most such animals the blood passes through a respiratory exchange membrane, which lies in the gills, lungs, or even the skin. There the blood picks up oxygen and disposes of carbon dioxide.

The cellular composition of blood varies from group to group in the animal kingdom. Most invertebrates have various large blood cells capable of amoeboid movement. Some of these aid in transporting substances; other are capable of surrounding and digesting foreign particles or debris (phagocytosis). Compared with vertebrate blood, however, that of the invertebrates has relatively few cells. Among the vertebrates, there are several classes of amoeboid cells (white blood cells, or leukocytes) and cells that help stop bleeding (platelets, or thrombocytes).

Oxygen requirements have played a major role in determining both the composition of blood and the architecture of the circulatory system. In some simple animals, including small worms and mollusks, transported oxygen is merely dissolved in the plasma. Larger and more-complex animals, which have greater oxygen needs, have pigments capable of transporting relatively large amounts of oxygen. The red pigment hemoglobin, which contains iron, is found in all vertebrates and in some invertebrates. In almost all vertebrates, including humans, hemoglobin is contained exclusively within the red cells (erythrocytes). The red cells of the lower vertebrates (e.g., birds) have a nucleus, whereas mammalian red cells lack a

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nucleus. Red cells vary markedly in size among mammals; those of the goat are much smaller than those of humans, but the goat compensates by having many more red cells per unit volume of blood. The concentration of hemoglobin inside the red cell varies little between species. Hemocyanin, a copper-containing protein chemically unlike hemoglobin, is found in some crustaceans. Hemocyanin is blue in colour when oxygenated and colourless when oxygen is removed. Some annelids have the iron-containing green pigment chlorocruorin, others the iron-containing red pigment hemerythrin. In many invertebrates the respiratory pigments are carried in solution in the plasma, but in higher animals, including all vertebrates, the pigments are enclosed in cells; if the pigments were freely in solution, the pigment concentrations required would cause the blood to be so viscous as to impede circulation.

This article focuses on the main components and functions of human blood. For full treatment of blood groups, *see* the article blood group. For information on the organ system that conveys blood to all organs of the body, *see* cardiovascular system. For additional information on blood in general and comparison of the blood and lymph of diverse organisms, *see* circulation. In humans, blood is an opaque red fluid, freely flowing but denser and more viscous than water. The characteristic colour is imparted by hemoglobin, a unique iron-containing protein. Hemoglobin brightens in colour when saturated with oxygen (oxyhemoglobin) and darkens when oxygen is removed (deoxyhemoglobin). For this reason, the partially deoxygenated blood from a vein is darker than oxygenated blood from an artery. The red blood cells (erythrocytes) constitute about 45 percent of the volume of the blood, and the remaining cells (white blood cells, or leukocytes, and platelets, or thrombocytes) less than 1 percent. The fluid portion, plasma, is a clear, slightly sticky, yellowish liquid. After a fatty meal, plasma transiently appears turbid. Within the body the blood is permanently fluid, and turbulent flow assures that cells and plasma are fairly homogeneously mixed. The total amount of blood in humans varies with age, sex, weight, body type, and other factors, but a rough average figure for adults is about 60 millilitres per kilogram of body weight. An average young male has a plasma volume of about 35 millilitres and a red cell volume of about 30 millilitres per kilogram of body weight. There is little variation in the blood volume of a healthy person over long periods, although each component of the blood is in a continuous state of flux. In particular, water rapidly moves in and out of the bloodstream, achieving a balance with the extravascular fluids (those outside the blood vessels) within minutes. The normal volume of blood provides such an adequate reserve that appreciable blood loss is well tolerated. Withdrawal of 500 millilitres (about a pint) of blood from normal blood donors is a harmless procedure. Blood volume is rapidly replaced after blood loss; within hours, plasma volume is restored by movement of extravascular fluid into the circulation. Replacement of red cells is completed within several weeks. The vast area of capillary membrane, through which water passes freely, would permit instantaneous loss of the plasma from the circulation were it not for the plasma proteins—in particular, serum albumin. Capillary membranes are impermeable to serum albumin, the smallest in weight and highest in concentration of the plasma proteins. The osmotic effect of serum albumin retains fluid within the circulation, opposing the hydrostatic

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forces that tend to drive the fluid outward into the tissues. The liquid portion of the blood, the plasma, is a complex solution containing more than 90 percent water. The water of the plasma is freely exchangeable with that of body cells and other extracellular fluids and is available to maintain the normal state of hydration of all tissues. Water, the single largest constituent of the body, is essential to the existence of every living cell.

The major solute of plasma is a heterogeneous group of proteins constituting about 7 percent of the plasma by weight. The principal difference between the plasma and the extracellular fluid of the tissues is the high protein content of the plasma. Plasma protein exerts an osmotic effect by which water tends to move from other extracellular fluid to the plasma. When dietary protein is digested in the gastrointestinal tract, individual amino acids are released from the polypeptide chains and are absorbed. The amino acids are transported through the plasma to all parts of the body, where they are taken up by cells and are assembled in specific ways to form proteins of many types. These plasma proteins are released into the blood from the cells in which they were synthesized. Much of the protein of plasma is produced in the liver.

The major plasma protein is serum albumin, a relatively small molecule, the principal function of which is to retain water in the bloodstream by its osmotic effect. The amount of serum albumin in the blood is a determinant of the total volume of plasma. Depletion of serum albumin permits fluid to leave the circulation and to accumulate and cause swelling of soft tissues (edema). Serum albumin binds certain other substances that are transported in plasma and thus serves as a nonspecific carrier protein. Bilirubin, for example, is bound to serum albumin during its passage through the blood. Serum albumin has physical properties that permit its separation from other plasma proteins, which as a group are called globulins. In fact, the globulins are a heterogeneous array of proteins of widely varying structure and function, only a few of which will be mentioned here. The immunoglobulins, or antibodies, are produced in response to a specific foreign substance, or antigen. For example, administration of polio vaccine, which is made from killed or attenuated (weakened) poliovirus, is followed by the appearance in the plasma of antibodies that react with poliovirus and effectively prevent the onset of disease. Antibodies may be induced by many foreign substances in addition to microorganisms; immunoglobulins are involved in some hypersensitivity and allergic reactions. Other plasma proteins are concerned with the coagulation of the blood.

Many proteins are involved in highly specific ways with the transport function of the blood. Blood lipids are incorporated into protein molecules as lipoproteins, substances important in lipid transport. Iron and copper are transported in plasma by unique metal-binding proteins (transferrin and ceruloplasmin, respectively). Vitamin B_{12}, an essential nutrient, is bound to a specific carrier protein. Although hemoglobin is not normally released into the plasma, a hemoglobin-binding protein (haptoglobin) is available to transport hemoglobin to the reticuloendothelial system should hemolysis (breakdown) of red cells occur. The serum haptoglobin level is raised during inflammation and certain other conditions; it is lowered in hemolytic disease and some types of liver disease.

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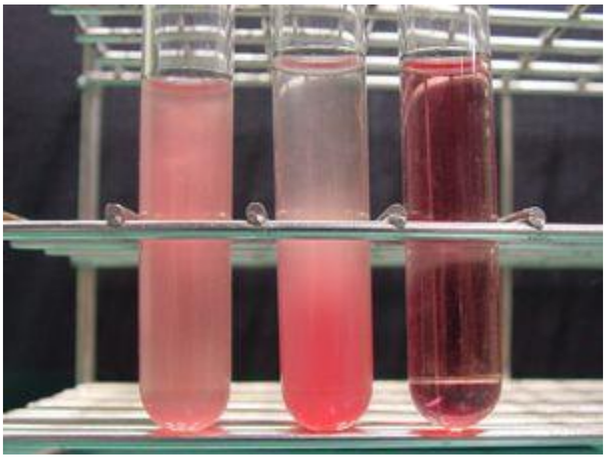
Lipids are present in plasma in suspension and in solution. The concentration of lipids in plasma varies, particularly in relation to meals, but ordinarily does not exceed 1 gram per 100 millilitres. The largest fraction consists of phospholipids, complex molecules containing phosphoric acid and a nitrogen base in addition to fatty acids and glycerol. Triglycerides, or simple fats, are molecules composed only of fatty acids and glycerol. Free fatty acids, lower in concentration than triglycerides, are responsible for a much larger transport of fat. Other lipids include cholesterol, a major fraction of the total plasma lipids. These substances exist in plasma combined with proteins of several types as lipoproteins. The largest lipid particles in the blood are known as chylomicrons and consist largely of triglycerides; after absorption from the intestine, they pass through lymphatic channels and enter the bloodstream through the thoracic lymph duct. The other plasma lipids are derived from food or enter the plasma from tissue sites.



Some plasma constituents occur in plasma in low concentration but have a high turnover rate and great physiological importance. Among these is glucose, or blood sugar. Glucose is absorbed from the gastrointestinal tract or may be released into the circulation from the liver. It provides a source of energy for tissue cells and is the only source for some, including the red cells. Glucose is conserved and used and is not excreted. Amino acids also are so rapidly transported that the plasma level remains low, although they are required for all protein synthesis throughout the body. Urea, an end product of protein metabolism, is rapidly excreted by the kidneys. Other nitrogenous waste products—uric acid and creatinine—are similarly removed.

Several inorganic materials are essential constituents of plasma, and each has special functional attributes. The predominant cation (positively charged ion) of the plasma is sodium, an ion that occurs within cells at a much lower concentration. Because of the effect of sodium on osmotic pressure and fluid movements, the amount of sodium in the body is an influential determinant of the total volume of extracellular fluid. The amount of sodium in plasma is controlled by the kidneys under the influence of the hormone aldosterone, which is secreted by the adrenal gland. If dietary sodium exceeds requirements, the excess is excreted by the kidneys. Potassium, the principal intracellular cation, occurs in plasma at a much lower

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concentration than sodium. The renal excretion of potassium is influenced by aldosterone, which causes retention of sodium and loss of potassium. Calcium in plasma is in part bound to protein and in part ionized. Its concentration is under the control of two hormones: parathyroid hormone, which causes the level to rise, and calcitonin, which causes it to fall. Magnesium, like potassium, is a predominantly intracellular cation and occurs in plasma in low concentration. Variations in the concentrations of these cations may have profound effects on the nervous system, the muscles, and the heart, effects normally prevented by precise regulatory mechanisms. Iron, copper, and zinc are required in trace amounts for synthesis of essential enzymes; much more iron is needed in addition for production of hemoglobin and myoglobin, the oxygen-binding pigment of muscles. These metals occur in plasma in low concentrations. The principal anion (negatively charged ion) of plasma is chloride; sodium chloride is its major salt. Bicarbonate participates in the transport of carbon dioxide and in the regulation of pH. Phosphate also has a buffering effect on the pH of the blood and is vital for chemical reactions of cells and for the metabolism of calcium. Iodide is transported through plasma in trace amounts; it is avidly taken up by the thyroid gland, which incorporates it into thyroid hormone.

The hormones of all the endocrine glands are secreted into the plasma and transported to their target organs, the organs on which they exert their effects. The plasma levels of these agents often reflect the functional activity of the glands that secrete them; in some instances, measurements are possible though concentrations are extremely low. Among the many other constituents of plasma are numerous enzymes. Some of these appear simply to have escaped from tissue cells and have no functional significance in the blood.

There are four major types of blood cells: red blood cells (erythrocytes), platelets (thrombocytes), lymphocytes, and phagocytic cells. Collectively, the lymphocytes and phagocytic cells constitute the white blood cells (leukocytes). Each type of blood cell has a specialized function: red cells take up oxygen from the lungs and deliver it to the tissues; platelets participate in forming blood clots; lymphocytes are involved with immunity; and phagocytic cells occur in two varieties—granulocytes and monocytes—and ingest and break down microorganisms and foreign particles. The circulating blood functions

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as a conduit, bringing the various kinds of cells to the regions of the body in which they are needed: red cells to tissues requiring oxygen, platelets to sites of injury, lymphocytes to areas of infection, and phagocytic cells to sites of microbial invasion and inflammation. Each type of blood cell is described in detail below. The continuous process of blood cell formation (hematopoiesis) takes place in hematopoietic tissue. In the developing embryo, the first site of blood formation is the yolk sac. Later in embryonic life, the liver becomes the most important red blood cell-forming organ, but it is soon succeeded by the bone marrow, which in adult life is the only source of both red cells and the granulocytes. In young children, hematopoietic bone marrow fills most of the skeleton, whereas in adults the marrow is located mainly in the central bones (ribs, sternum, vertebrae, and pelvic bones). Bone marrow is a rich mixture of developing and mature blood cells, as well as fat cells and other cells that provide nutrition and an architectural framework upon which the blood-forming elements arrange themselves. The weight of the marrow of a normal adult is 1,600 to 3,700 grams and contains over 1,000,000,000,000 hematopoietic cells (18×10^9 cells per kilogram). Nourishment of this large mass of cells comes from the blood itself. Arteries pierce the outer walls of the bones, enter the marrow, and divide into fine branches, which ultimately coalesce into large venous sacs (sinusoids) through which blood flows sluggishly. In the surrounding hematopoietic tissue, newly formed blood cells enter the general circulation by penetrating the walls of the sinusoids.

In the adult the bone marrow produces all of the red cells, 60 to 70 percent of the white cells (i.e., the granulocytes), and all of the platelets. The lymphatic tissues, particularly the thymus, the spleen, and the lymph nodes, produce the lymphocytes (comprising 20 to 30 percent of the white cells). The reticuloendothelial tissues of the spleen, liver, lymph nodes, and other organs produce the monocytes (4 to 8 percent of the white cells). The platelets are formed from bits of the cytoplasm of the giant cells (megakaryocytes) of the bone marrow.

Both the red and white cells arise through a series of complex transformations from primitive stem cells, which have the ability to form any of the precursors of a blood cell. Precursor cells are stem cells that have developed to the stage where they are committed to forming a particular type of new blood cell. By dividing and differentiating, precursor cells give rise to the four major blood cell lineages: red cells, phagocytic cells, megakaryocytes, and lymphocytes. The cells of the marrow are under complex controls that regulate their formation and adjust their production to the changing demands of the body. When marrow stem cells are cultured outside the body, they form tiny clusters of cells (colonies), which correspond to red cells, phagocytic cells, and megakaryocytes. The formation of these individual colonies depends on hormonal sugar-containing proteins (glycoproteins), referred to collectively as colony-stimulating factors (CSFs). These factors are produced throughout the body. Even in minute amounts, CSFs can stimulate the division and differentiation of precursor cells into mature blood cells and thus exert powerful regulatory influences over the production of blood cells. A master colony-stimulating factor (multi-CSF), also called interleukin-3, stimulates the most ancestral hematopoietic stem cell. Further differentiation of this stem cell into

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specialized descendants requires particular kinds of CSFs; for example, the CSF erythropoietin is needed for the maturation of red cells, and granulocyte CSF controls the production of granulocytes. These glycoproteins, as well as other CSFs, serve as signals from the tissues to the marrow. For instance, a decrease in the oxygen content of the blood stimulates the kidney to increase its production of erythropoietin, thus ultimately raising the number of oxygen-carrying red cells. Certain bacterial components accelerate the formation of granulocyte CSF, thereby leading to an increased production of phagocytic granulocytes by the bone marrow during infection.

In the normal adult the rate of blood cell formation varies depending on the individual, but a typical production might average 200 billion red cells per day, 10 billion white cells per day, and 400 billion platelets per day.

Red blood cells (erythrocytes)

The red blood cells are highly specialized, well adapted for their primary function of transporting oxygen from the lungs to all of the body tissues. Red cells are approximately 7.8 μm (1 μm = 0.000039 inch) in diameter and have the form of biconcave disks, a shape that provides a large surface-to-volume ratio. When fresh blood is examined with the microscope, red cells appear to be yellow-green disks with pale centres containing no visible internal structures. When blood is centrifuged to cause the cells to settle, the volume of packed red cells (hematocrit value) ranges between 42 and 54 percent of total volume in men and between 37 and 47 percent in women; values are somewhat lower in children. Normal red blood cells are fairly uniform in volume, so that the hematocrit value is determined largely by the number of red cells per unit of blood. The normal red cell count ranges between four million and six million per cubic millimetre.

The red blood cell is enclosed in a thin membrane that is composed of chemically complex lipids, proteins, and carbohydrates in a highly organized structure. Extraordinary distortion of the red cell occurs in its passage through minute blood vessels, many of which have a diameter less than that of the red cell. When the deforming stress is removed, the cell springs back to its original shape. The red cell readily tolerates bending and folding, but, if appreciable stretching of the membrane occurs, the cell is damaged or destroyed. The membrane is freely permeable to water, oxygen, carbon dioxide, glucose, urea, and certain other substances, but it is impermeable to hemoglobin. Within the cell the major cation is potassium; in contrast, in plasma and extracellular fluids the major cation is sodium. A pumping mechanism, driven by enzymes within the red cell, maintains its sodium and potassium concentrations. Red cells are subject to osmotic effects. When they are suspended in very dilute (hypotonic) solutions of sodium chloride, red cells take in water, which causes them to increase in volume and to become more spheroid; in concentrated salt solutions they lose water and shrink.

When red cell membranes are damaged, hemoglobin and other dissolved contents may escape from the cells, leaving the membranous structures as "ghosts." This process, called hemolysis, is produced not only by the osmotic effects of water but also by numerous other mechanisms. These include physical damage to red cells, as when blood is heated, is forced under great

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pressure through a small needle, or is subjected to freezing and thawing; chemical damage to red cells by agents such as bile salts, detergents, and certain snake venoms; and damage caused by immunologic reactions that may occur when antibodies attach to red cells in the presence of complement. When such destruction proceeds at a greater than normal rate, hemolytic anemia results.

The membrane of the red cell has on its surface a group of molecules that confer blood group specificity (i.e., that differentiate blood cells into groups). Most blood group substances are composed of carbohydrate linked to protein, and it is usually the chemical structure of the carbohydrate portion that determines the specific blood type. Blood group substances are antigens capable of inducing the production of antibodies when injected into persons lacking the antigen. Detection and recognition of the blood group antigens are accomplished by the use of blood serum containing these antibodies. The large number of different red cell antigens makes it extremely unlikely that persons other than identical twins will have the same array of blood group substances

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