PEARSON NEW INTERNATIONAL EDITION

Clinical Laboratory Hematology

Shirlyn B. McKenzie

Second Edition

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Pearson New International Edition

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Glossary

A

Abetalipoproteinemia (hereditary acanthocytosis) - rare, autosomal recessive disorder characterized by the absence of serum β-lipoprotein, low serum cholesterol, low triglyceride, and low phospholipid and an increase in the ratio of cholesterol to phospholipid.

Acanthocyte - abnormally shaped erythrocyte with spicules of varying length irregularly distributed over the cell membrane's outer surface; also known as *spur cell*. There is no central area of pallor.

Achlorhydria - absence of hydrochloric acid in stomach gastric secretions.

Acquired aberration - chromosome aberration (either numerical or structural) that occurs at some time after birth and involves only one cell line.

Acquired immune deficiency syndrome (AIDS) - disease caused by infection with human immunodeficiency virus type I (HIV-1). The virus selectively infects helper T lymphocytes (CD4+) causing rapid depletion of these cells. This causes a deficiency in cell-mediated immunity. The patients have repeated infections with multiple opportunistic organisms and an increase in malignancies.

Acquired inhibitors - *See* Circulating anticoagulants.

Acrocentric - description of a chromosome that has the centromere close to the terminal end so that the short arm is much shorter than the long arm. The short arm consists only of a stalk and a small amount of DNA called a *satellite*.

Acrocyanosis - *See* Raynaud's phenomenon.

Activated partial thromboplastin time (APTT) - screening test used to detect deficiencies in the intrinsic and common pathway of the coagulation cascade.

Activated lymphocyte - *See* Reactive lymphocyte.

Activated protein C resistance (APCR) - condition in which activated protein C is not able to inactivate F-V, which may cause or contribute to thrombosis. In most cases, it is due to a mutation in F-V in which Arg 506 is replaced with Gln ($F\text{-}V_{Leiden}$).

Acute leukemia - malignant hematopoietic stem cell disorder characterized by proliferation and accumulation of immature and nonfunctional hematopoietic cells in the bone marrow and other organs.

Acute lymphocytic leukemia (ALL) - malignant lymphoproliferative disorder characterized by proliferation and accumulation of lymphoid cells in the bone marrow. Peripheral blood smear reveals the presence of many undifferentiated or minimally differentiated cells.

Acute myeloid leukemia (AML) - malignant myeloproliferative disorder characterized by proliferation and accumulation of primarily undifferentiated or minimally differentiated myeloid cells in the bone marrow.

Acute phase reactant - plasma protein that rises rapidly in response to inflammation, infection, or tissue injury.

Acute undifferentiated leukemia (AUL) - acute leukemia in which the morphology, cytochemistry, and immunophenotype of the proliferating blasts lack sufficient information to classify them as myeloid or lymphoid origin.

ADAMTS-13 - metalloprotease enzyme responsible for cleavage of the ultralarge multimers of VWF released from endothelial cells into the VWF multimer sizes normally found in the circulation.

Adaptive immune response - interaction of the T lymphocyte, B lymphocyte, and macrophage in a series of events that allows the body to attack and eliminate foreign antigens.

ADCC - antibody-dependent cell cytotoxicity that describes the recognition and lysis of cells by NK cells. This occurs by binding IgG to the NK cell CD 16 receptor. Any target cell coated with IgG can be bound to NK cells and lysed. Monocytes, macrophages, and neutrophils also have this receptor and act in a similar manner.

Adipocyte - cell whose cytoplasm is largely replaced with a single fat vacuole; fat cell.

Adsorbed plasma - platelet-poor plasma that is adsorbed with either barium sulfate or aluminum hydroxide to remove the coagulation factors II, VII, IX, X (the prothrombin group). Factors V, VIII, XI, XII, and fibrinogen (I) are present in adsorbed plasma. This plasma is one of the reagents used in the substitution studies to determine a specific factor deficiency.

Afibrinogenemia - condition in which there is absence of fibrinogen in the peripheral blood. It may be caused by a mutation in the gene controlling the production of fibrinogen or by an acquired condition in which fibrinogen is pathologically converted to fibrin.

Aged serum - serum that lacks coagulation factors fibrinogen (I), prothrombin (II), V, VIII. Aged serum is prepared by incubating normal serum for 24 hours at 37°C. Factors VII, IX, X, XI, and XII are present in aged serum. This serum is one of the reagents used in the substitution studies to determine a specific factor deficiency.

Agglutinate - clumping together of erythrocytes as a result of interactions between membrane antigens and specific antibodies.

Aggregating reagent - chemical substance (agonist) that promotes platelet activation and aggregation by attaching to a receptor on the platelet's surface.

Agonist - chemical substance that can attach to a platelet membrane receptor and activate platelets causing them to aggregate (e.g., collagen, ADP). These agonists are used in the laboratory to test platelet function using a platelet aggregometer or platelet function analyzer.

Agranulocytosis - absence of granulocytes in the peripheral blood.

AIDS related complex (ARC) - second recognized clinical stage of a person infected with the HIV virus. Immune-compromised patients with mild symptoms of weight loss, fever, lymphadenopathy, thrush, chronic rash, or intermittent diarrhea are included in this category.

Alder-Reilly anomaly - benign condition characterized by the presence of leukocytes with large purplish granules in their cytoplasm when stained with a Romanowsky stain. These cells are functionally normal.

Aleukemic leukemia - disorder in which the abnormal malignant cells are found only in the bone marrow.

Allele - one of two or more genes that correspond to the same trait and occupy the same position on paired chromosomes.

Alloantibodies - antibodies produced in one individual in response to the antigens of another individual of the same species.

Allogeneic - pertaining to an allograft in which donor and host belong to the same species but are not genetically identical.

Allogeneic stem cell transplantation - transplantation of stem cells between genetically dissimilar animals of the same species.

Alloimmune hemolytic anemia - hemolytic disorder generated when blood cells from one person are infused into a genetically unrelated person. Antigens on the infused donor cells are recognized as foreign by the recipient's lymphocytes, stimulating the production of antibodies. The antibodies react with donor cells and cause hemolysis.

Alpha granules - platelet storage granules containing a variety of proteins that are released into an area after platelet activation.

Analytical sensitivity - ability to detect small amounts of the analyte.

Analytical specificity - ability to detect only the analyte in question.

Analytical time - period between specimen entry into the test system and the reporting of the result by the instrument.

Anemia - disorder characterized by decrease in the normal concentration of hemoglobin or erythrocytes. This may be caused by increased erythrocyte loss or decreased erythrocyte production. Anemia may result in hypoxia.

Aneuploid - number of chromosomes per cell that does not equal a multiple of the haploid number, n, for example, in human cells a chromosome count of 45, 47, 48, etc.

Anisocytosis - term used to describe a general variation in erythrocyte size.

Antibody - immunoglobulin produced in response to an antigenic substance.

Anticardiolipin antibody (ACA) - autoantibody directed against negatively charged phospholipids. *See* Antiphospholipid antibody.

Anticoagulant - chemical substance added to whole blood to prevent blood from coagulating. Depending on the type of anticoagulant, in vitro coagulation is prevented by the removal of calcium (EDTA) or the inhibition of the serine proteases such as thrombin (heparin).

Antigen - any foreign substance that evokes antibody production (an immune response) and reacts specifically with that antibody.

Antigen-dependent lymphopoiesis - development of immunocompetent lymphocytes into effector T and B lymphocytes that mediate the immune response through production of lymphokines and antibodies. The process is initiated when mature lymphocytes come into contact with an antigen. This process occurs in secondary lymphoid tissue.

Antigen-independent lymphopoiesis - development of lymphoid stem cells into immunocompetent T and B lymphocytes (virgin lymphocytes). This process occurs in the primary lymphoid tissue under the regulation of hematopoietic growth factors.

Antigen presenting cell (APC) - term used to describe the macrophage in the immune response; the macrophage phagocytizes substances foreign to the host and presents its antigenic determinants on its membrane to antigen-dependent T lymphocytes.

Antihuman globulin (AHG) - globulin used in a laboratory procedure that is designed to detect the presence of antibodies directed against erythrocyte antigens on the erythrocyte membrane.

Antioncogene - gene that codes for a normal substance that suppresses tumor formation. Maturation and/or absence of both alleles allows tumor growth. Also called *tumor-suppressor gene*.

Antiphospholipid antibody - autoantibody directed against antigens that consist of a negatively charged phospholipid. Clinically important antiphospholipid antibodies include anticardiolipin antibody (ACA) and lupus anticoagulant (LA). In some individuals, these antibodies are associated with thrombosis and other hemostatic defects.

Antiphospholipid antibody syndrome - clinical condition characterized by the presence of high titers of antiphospholipid antibodies, thrombocytopenia, and recurrent arterial and venous thromboses, often affecting young males.

Aperture - small opening through which blood cells are drawn into an electronic cell counter. Electrodes are located on either side of the aperture, and electrical resistance is detected as the cell passes through the aperture.

Apheresis - separation or removal. Whole blood is withdrawn from the donor or patient and separated into its components. One of the components is retained, and the remaining constituents are recombined and returned to the individual.

Aplasia - failure of hematopoietic cells to generate and develop in the bone marrow.

Aplastic anemia - anemia characterized by peripheral blood pancytopenia and hypoplastic marrow. It is considered a pluripotential stem cell disorder.

Aplastic crisis - abrupt, transient cessation of erythropoiesis that occurs in some hemolytic anemias and infections.

Apoferritin - cellular protein that combines with iron to form ferritin. It is found attached only to iron, not in the free form.

Apoptosis - programmed cell death resulting from activation of a predetermined sequence of intracellular events; "cell suicide."

APSAC - anisoylated plasminogen streptokinase activator complex; a modification of the enzyme streptokinase that is a chemically altered complex of streptokinase and plasminogen and is used as a thrombolytic agent in the treatment of thrombosis.

APTT - laboratory test that measures fibrin-forming ability of coagulation factors in the intrinisic coagulation cascade.

Arachidonic acid (AA) - unsaturated essential fatty acid, usually attached to the second carbon of the glycerol backbone of phospholipids, released by phospholipase A_2 and a precursor of prostaglandins and thromboxanes.

Arachnoid mater - delicate membrane that covers the central nervous system; middle layer of the meninges.

Artificial oxygen carrier (AOC) - two groups of AOCs including hemoglobin-based oxygen carriers (HBOCs) in solution and perfluorocarbons (PFCs). The HBOCs consist of purified human or bovine hemoglobin and recombinant hemoglobin. The oxygen dissociation curve of HBOCs is similar to that of native human blood. Hemoglobin tests based on colorimetric analysis could give erroneous results. PFCs are fluorinated hydrocarbons with high gas-dissolving capacity. They do not mix in aqueous solution and must be emulsified. In contrast to HBOCs, a linear relationship exists between pO_2 and oxygen content in PFCs. Thus, relatively high O_2 partial pressure is required to maximize delivery of O_2 by PFCs.

Ascites - effusion and accumulation of fluid in the peritoneal cavity.

Ascitic fluid - fluid that has abnormally collected in the peritoneal cavity of the abdomen.

Atypical lymphocyte - *See* Reactive lymphocyte.

Auer rods - reddish-blue staining needlelike inclusions within the cytoplasm of leukemic myeloblasts that occur as a result of abnormal cytoplasmic granule formation. Their presence on a Romanowsky-stained smear is helpful in differentiating acute myeloid leukemia from acute lymphoblastic leukemia.

Autoantibodies - antibodies in the blood capable of reacting with the subject's own antigens.

Autohemolysis - lysis of the subject's own erythrocytes by hemolytic agents in the subject's serum.

Autoimmune hemolytic anemia (AIHA) - anemia that results when individuals produce antibodies against their own erythrocytes. The antibodies are usually against high-incidence antigens.

Autologous stem cell transplantation - transplantation or infusion of a person's own stem cells.

Autosome - chromosome that does not contain genes for sex differentiation; in humans, chromosome pairs 1–22.

Autosplenectomy - extensive splenic damage secondary to infarction. This is often seen in older children and adults with sickle cell anemia.

Azurophilic granules - granules (primary granules) within myelocytic leukocytes that have a predilection for the aniline component of a Romanowsky-type stain. These granules appear bluish purple or bluish black when observed microscopically on a stained blood smear. They first appear in the promyelocyte.

▶ B

Backlighting - highlighting a parameter that falls outside its reference interval or a user-defined action limit. Backlighting alerts the clinical laboratory professional of a potential problem or error that requires further investigation.

Band neutrophil - immediate precursor of the mature granulocyte. This cell type can be found in either the bone marrow or peripheral blood. The nucleus is elongated and nuclear chromatin is condensed. The cytoplasm stains pink, and there are many specific granules. The cell is 9–15 μm in diameter. Also called *stab* or *unsegmented neutrophil*.

Basophil - mature granulocytic cell characterized by the presence of large basophilic granules. These granules are purple blue or purple black with Romanowsky stain. The cell is 10–14 μm in diameter, and the nucleus is segmented. Granules are cytochemically positive with periodic acid-schiff (PAS) and peroxidase. The granules contain histamine and heparin peroxidase. Basophils constitute $<0.2 \times 10^9$/L or 0–1% of peripheral blood leukocytes. The basophil functions as a mediator of inflammatory responses. The cell has receptors for IgE.

Basophilia - increased concentration of circulating basophils.

Basophilic normoblast - nucleated precursor of the erythrocyte that is derived from a pronormoblast. The cell is 10–16 μm in diameter. The nuclear chromatin is coarser than the pronormoblast, and nucleoli are usually absent. Cytoplasm is more abundant, and it stains deeply basophilic. The cell matures to a polychromatophilic normoblast. Also called *prorubricyte*.

Basophilic stippling - precipitating ribonucleoproteins and mitochondrial remnants that compose erythrocyte inclusions. Observed on Romanowsky-stained blood smears as diffuse or punctate bluish-black granules in toxic states such as drug (lead) exposure. Diffuse, fine basophilic stippling may occur as an artifact.

B cell ALL - immunologic type of ALL in which the neoplastic cell is a B lymphoid cell. There are subtypes.

B cell receptor (BCR) - specific antigen receptor on the B lymphocyte membrane.

***bcl-2* gene** - gene on chromosome 18 producing bcl-2 protein. The translocation t(14;18) found in follicular lymphoma leads to bcl-2 overexpression and inhibition of lymphocyte cell death.

Beer Lambert's law - law that forms the mathematical basis for colorimetry. The equation is $A = C \times L \times K$. A is absorbance, C is the concentration of the colored substance, L is the depth of the solution through which the light travels, and K is a constant.

Bence-Jones protein - excessive immunoglobulin light chain in the urine.

Benign - Description of tissue that is nonmalignant. Formed from highly organized, differentiated cells that do not spread or invade surrounding tissue.

Bernard-Soulier disease - rare hereditary platelet disorder characterized by a genetic mutation in the gene coding for platelet glycoprotein Ib resulting in platelets' inability to adhere to collagen.

BFU-E - burst forming unit-erythroid; a committed erythroid progenitor cell. It gives rise to the unipotential CFU-E stem cell. It is relatively insensitive to EPO except in high concentrations. GM-CSF stimulates it to enter the cell cycle.

Bilineage leukemia - leukemia that has two separate populations of leukemic cells, one of which phenotypes as lymphoid and the other as myeloid.

Bilirubin - breakdown product of the heme portion of the hemoglobin molecule. Initial steps in the degradation of hemoglobin result in a lipid-soluble form (unconjugated or indirect bilirubin) that travels in the blood stream to the liver, where it is converted into a water-soluble form (conjugated or direct bilirubin) that can be excreted into the bile.

Bioavailability - degree and rate at which a free drug is available to produce its effect.

Biphasic antibody - antibody that binds to erythrocytes at room temperature or below and causes hemolysis when the blood warms to 37°C.

Biphenotypic leukemia - acute leukemia that has myeloid and lymphoid markers on the same population of neoplastic cells.

Birefringent - description of a substance that can change the direction of light rays that are directed at the substance; can be used to identify crystals.

2,3-bisphosphoglycerate (2,3-BPG) - product of the glycolytic pathway that affects the oxygen affinity of hemoglobin. It serves in the biochemical feedback system that regulates the amount of oxygen released to the tissues. As the concentration of 2,3-BPG increases, hemoglobin's affinity for oxygen decreases and more oxygen is released to the tissue. Also referred to as 2,3-*diphosphoglycerate* (*2,3-DPG*).

Bite cells - erythrocytes with a portion of the cell missing; seen in G6PD deficiency and drug-induced oxidant hemolysis.

Bleeding time and PFA 100 - screening test that measures platelet function.

Blinded preanalyzed samples - previously analyzed samples that are integrated randomly into a specimen run and possess no identifying feature (e.g., number or designation) to indicate that they are different from current patient specimens. These samples used as a part of a quality control program can be identified only by the individual who selected and relabeled them.

Blister cell - cell with a clear area next to the membrane on one side of the cell. It is thought to be formed when the phagocyte removes a Heinz body in the cell and is seen in G6PD deficiency.

Blood coagulation - formation of a blood clot, usually considered a normal process.

Bohr effect - effect of pH on hemoglobin-oxygen affinity. This is one of the most important buffer systems in the body. As the H^+ concentration in tissues increases, the affinity of hemoglobin for oxygen is decreased, permitting unloading of oxygen.

Bone marrow aspirate - fluid withdrawn from the bone marrow by aspiration using a special needle (e.g., Jamshidi needle) and syringe. It represents the specialized soft tissue that fills the medullary cavities between the bone trabeculae. Examination of the bone marrow aspirate is useful in evaluating hematopoietic cellular morphology, distribution, and development; observing for presence of abnormal cells; and estimating cellularity.

Bone marrow trephine biopsy - removal of a small piece of the bone marrow core that contains marrow, fat, and trabeula. Examination of the trephine biopsy is useful in observing the bone marrow architecture and cellularity and allows interpreting the spatial relationships of bone, fat, and marrow cellularity.

Bordetella pertussis - gram-negative aerobic coccobacilli that is the cause of whooping cough. The hematologic picture in whooping cough is leukocytosis with lymphocytosis. The lymphocytes are small cells with folded nuclei.

Buffy coat - layer of white blood cells and platelets that lies between the plasma and erythrocytes in centrifuged blood sample.

Burkitt cell - lymphoblast that is found in Burkitt's lymphoma.

Butt cell - circulating neoplastic lymphocyte with a deep indentation (cleft) of the nuclear membrane. Butt cells may be seen when follicular lymphoma involves the peripheral blood.

▶ C

Cabot ring - reddish-violet erythrocyte inclusion resembling the figure 8 on Romanowsky-stained blood smears that can be found in some cases of severe anemia.

Capitated payment - reimbursement method for health care by third-party payers in which the insurer contracts with certain health care providers who agree to provide services for a defined population on a per-member fee schedule. The insurer determines who the providers will be.

Carboxyhemoglobin - compound formed when hemoglobin is exposed to carbon monoxide; it is incapable of oxygen transport.

Carboxylation - addition of a carboxyl group to a coagulation factor (II, VII, IX, X, Proteins C, S, Z). This occurs in the liver. The factor is not functional until it is carboxylated. Vitamin K is required for this reaction.

Cardiac tamponade - critical clinical condition in which the pericardial sac fills with fluid and restricts the heartbeat and venous return to the heart.

Caspase - cysteine protease responsible for cell alterations in apoptosis.

Catalytic domain - molecular area of a molecule that is common to all serine proteases involved in blood clotting. Cleavage of a peptide bond occurs here and converts the proenzyme to its active form.

CD designation - cluster of differentiation; refers to a group of monoclonal antibodies recognizing the same protein marker antigen on a cell. The antibodies are used to classify cell types and stages of maturation.

Cell cycle - biochemical and morphological stages a cell passes through leading up to cell division; includes G1, S, G2, and M phases.

Cell cycle checkpoint - point in the cell cycle at which progress through the cycle can be halted until conditions are suitable for the cell to proceed to the next stage.

Cell-mediated immunity - immune response mediated by T lymphocytes. The event requires interaction between histocompatible T lymphocytes and macrophages with antigen. At least three important T lymphocyte subsets are involved: helper, suppressor, and cytotoxic.

Cellular hemoglobin concentration mean (CHCM) - erythrocyte index that represents the average hemoglobin concentration of the individual cells analyzed. CHCM is derived from the hemoglobin histogram. Interference with the hemoglobin determination due to turbidity or lipemia can be identified by comparing the CHCM to the MCHC.

Central nervous system (CNS) - part of the nervous sytem that consists of the brain and spinal cord.

Centriole - cytoplasmic organelle that is the point of origin for the contractile protein known as *spindle fiber.*

Centromere - primary constriction that attaches sister chromatids in a chromosome, dividing the chromatids into long and short arms.

Cerebrospinal fluid (CSF) - fluid that is normally produced to protect the brain and spinal cord. Produced by the choroid plexus cells and absorbed by the arachnoid pia, it circulates in the subarachnoid space.

CFU-E - colony-forming unit–erythroid; unipotential stem cell derived from the BFU-E. It has a high concentration of EPO membrane receptors and with EPO stimulation transforms into the earliest recognizable erythroid precursor, the pronormoblast.

CH50 - functional hemolytic titration assay to measure lysis, the endpoint of complement activation. It measures the amount of patient serum required to lyse 50% of a standardized concentration of antibody-sensitized SRBC. Because all complement proteins are required for lysis to occur, any single complement factor deficiency causes a negative reaction (no lysis).

Charcot-Leyden crystals - crystals formed from eosinophil granules; found in tissues with large numbers of eosinophils.

Cheidak-Higashi anomaly - multisystem disorder inherited in an autosomal recessive fashion and characterized by recurrent infections, hepatospleomegaly, partial albinism, and CNS abnormalities; neutrophil chemotaxis and killing of organisms is impaired. There are giant cytoplasmic granular inclusions in leukocytes and platelets.

Chemotaxins - chemical messengers that cause migration of cells in one direction. Also called *chemokines*.

Chimerism - state of being of cells from two different zygotes expressed in one individual.

Chloride shift - phenomenon in which a plasma Cl- diffuses into the erythrocyte when a free bicarbonate iron diffuses out of the erythrocyte into the plasma.

Cholecystitis - inflammation of the gallbladder.

Cholelithiasis - formation of calculi or bilestones in the gallbladder or bile duct.

Chromatid - structure of DNA during G_0 and G_1 of the cell cycle. After S-phase, DNA has replicated, and the chromosome consists of two parallel, identical chromatids held together at the centromere.

Chromogenic assay - spectrophotometric measurement of an enzyme's activity based on the release of a colored pigment following enzymatic cleavage of the pigment-producing substrate (chromogen).

Chromosome - nuclear structure seen during mitosis and meiosis consisting of supercoiled DNA with histone and nonhistone proteins. It consists of two identical (sister) chromatids attached at the centromere.

Chronic basophilic leukemia - rare myeloproliferative disease (MPD), also referred to as *atypical MPD*. There is an extreme increase in basophils in the peripheral blood. Cell of origin is a bipotential progenitor cell capable of differentiation into either basophil or eosinophil lineages or differentiation into basophil or mast cell lineages

Chronic eosinophilic leukemia - clonal eosinophilia with an HES phenotype. It is Ph chromosome and has a persistent eosinophilia of $>1.5 \times 10^9$/L. There is no evidence of clonality or $>2\%$ blasts in the peripheral blood.

Chronic idiopathic thrombocytopenic purpura (ITP) - immune form of thromboyctopenia that occurs most often in young adults and lasts longer than 6 months.

Chronic lymphocytic leukemia (CLL) - lymphoproliferative disorder characterized by a neoplastic growth of lymphoid cells in the bone marrow and an extreme elevation of these cells in the peripheral blood. It is characterized by leukocytosis, $<20\%$ blasts, and a predominance of mature lymphoid cells.

Chronic idiopathic myelofibrosis (CIMF) - myeloproliferative disorder characterized by excessive proliferation of all cell lines as well as progressive bone marrow fibrosis and blood cell production at sites other than the bone marrow, such as the liver and spleen. Also called *agnogenic myeloid metaplasia, myelofibrosis with myeloid metaplasia, and primary myelofibrosis*.

Chronic myelogenous leukemia (CML) - myeloproliferative disorder characterized by a neoplastic growth of primarily myeloid cells in the bone marrow and an extreme elevation of these cells in the peripheral blood. There are two phases to the disease: chronic and blast crisis. In the chronic phase, there are less than 20% blasts in the bone marrow or peripheral blood, whereas in the blast crisis phase, there are more than 20% blasts. Individuals with this disease have the BCR/ABL translocation, which codes for a unique P210 protein. Also referred to as *chronic granulocytic leukemia* (*CGL*).

Chronic myelomonocytic leukemia (CMML) - subgroup of the myelodysplastic syndromes. There is anemia and a variable total leukocyte count. An absolute monocytosis ($>1 \times 10^9$/L) is present; immature erythrocytes and granulocytes may also be present. There are less than 5% blasts in the peripheral blood. The bone marrow is hypercellular with proliferation of abnormal myelocytes, promonocytes, and monoblasts, and there are $<20\%$ blasts.

Chronic neutrophilic leukemia - myeloproliferative disorder (MPD) characterized by a sustained increase in neutrophils in the peripheral blood with a slight shift to the left. The Ph chromosome and BCR/ABL translocation are absent.

Chronic nonspherocytic hemolytic anemia - group of chronic anemias characterized by premature erythrocyte destruction. Spherocytes are not readily found when differentiating these anemias from hereditary spherocytosis.

Chylous - body effusion that has a milky, opaque appearance due to the presence of lymph fluid and chylomicrons.

Circulating inhibitor (anticoagulant) - acquired pathologic protein, primarily immunoglobulins (IgG or IgM) with antibody specificity toward a factor involved in fibrin formation. Circulating inhibitors interfere with the activity of the factor. The inhibitors are associated with a number of conditions, such as hemophilia, autoimmune diseases, malignancies, certain drugs, and viral infections.

Circulating leukocyte pool - population of neutrophils actively circulating within the peripheral blood stream.

Clinical Laboratory Improvement Amendments (CLIA) - regulations that mandate standards in clinical laboratory operations and testing signed into federal law in 1988.

Clonality - presence of identical cells derived from a single progenitor. It can be detected by the identification of only one of the immunoglobulin light chains (kappa or lambda) on B cells or the presence of a population of cells with a common phenotype.

Clonogenic - giving rise to a clone of cells.

Clot - extravascular coagulation whether occurring in vitro or in blood shed into the tissues or body cavities.

Clot retraction - cohesion of a fibrin clot that requires adequate, functionally normal platelets. Retraction of the clot occurs over a period of time and results in the expression of serum and a firm mass of cells and fibrin.

Cluster analysis - analysis in which floating thresholds cluster specific cell populations together based on size and staining or absorption characteristics. With cluster analysis, an instrument is able to accommodate for shifts in abnormal cell populations from one sample to another sample.

CLSI - organization whose mission is "to develop best practices in clinical and laboratory testing and promote their use throughout the world using a consensus-driven process that balances the viewpoints of industry, government, and the healthcare professions." (http://www.clsi.org/Content/NavigationMenu/AboutCLSI/Vision-MissionandValues/Vision_Mission_Value.htm)

Coagulation factors - soluble inert plasma proteins that interact to form fibrin after an injury.

Cobalamin - cobalt-containing complex that is common to all subgroups of the vitamin B_{12} group.

Codocytes - *See* Target cell.

Codon - sequence of three nucleotides that encodes a particular amino acid.

Coefficient of determination (r^2) - statistic that represents the square of the correlation coefficient. It is a measure of the strength of the relationship between two data sets.

Coefficient of variation - relative standard deviation or standard deviation expressed as a percentage of the mean for a set of data.

Cofactor - a substance of coagulation factors V and VII that function as cofactors. It is required for the conversion of specific zymogens to the active enzyme form.

Coincidence - in an electronic cell counter, a phenomenon of two or more cells crossing the sensing zone at the same time and evaluated as only one cell.

Cold agglutinin disease - condition associated with the presence of cold-reacting autoantibodies (IgM) directed against erythrocyte surface antigens. This causes clumping of the red cells at room or lower temperatures.

Colony-forming unit - visible aggregation (seen in vitro) of cells that developed from a single stem cell.

Colony-stimulating factor - cytokine that stimulates the growth of immature leukocytes in the bone marrow.

Column chromatography - laboratory separation method based on the differential distribution of a liquid or gaseous sample (mobile phase) that flows through a column of specific substance (stationary phase). Depending on the chemical characteristics of the stationary phase, the substance of interest may bind to the stationary phase and remain in the column or directly pass through the column and remain in the mobile phase. If the substance remains in the column, a second mobile phase (elution buffer) is used to release the substance from the stationary phase and allow it to pass through the column.

Committed/progenitor cells - parent or ancestor cells that differentiate into one cell line.

Common coagulation pathway - one of the three interacting pathways in the coagulation cascade. The common pathway includes three rate-limiting steps: (1) activation of factor X by the intrinsic and extrinsic pathways, (2) conversion of prothrombin to thrombin by activated factor X, and (3) cleavage of fibrinogen to fibrin.

Comparative genomic hybridization (CGH) - assay that can be used for the analysis of changes in chromosome copy number (copy number variants); also designed to analyze critical regions of the DNA for well-defined genetic abnormalities.

Compensated hemolytic disease - disorder in which the erythrocyte life span is decreased but the bone marrow is able to increase erythropoiesis enough to compensate for the decreased erythrocyte life span; anemia does not develop.

Compensation - process of adjusting the settings on the flow cytometer or performing a mathematical correction for overlap of light emitted by several fluorchromes. The is done either before or after the data are collected.

Competency assessment - mechanism of assessing the requisite ability of testing personnel to perform a given laboratory procedure. This includes recognition of specimen collection errors, interpretation of test results to detect possible instrument or specimen problems, interpretation of quality control results, troubleshooting of instrument or specimen problems, and proper reporting of results.

Complement - any of the 11 serum proteins that causes lysis of the cell membrane when sequentially activated.

Complementary DNA - synthetic DNA transcribed from an RNA template by the enzyme reverse transcriptase. Also known as *cDNA*.

Complete blood count (CBC) - hematology screening test that includes the white blood cell (WBC) count, red blood cell (RBC) count, hemoglobin, hematocrit, and, often, platelet count. It may also include red cell indices.

Compression syndrome - altered physiological function of an organ or tissue due to impingement by an abnormal mass.

Compound heterozygote - individual possessing two different abnormal alleles of a gene.

Conditioning regimen - high-dose chemotherapy and/or irradiation given to the patient before stem cell transplantation.

Congenital - present at birth.

Congenital aberration - chromosome aberration (either numerical or structural) that is present at the time of birth in all cell lines or in several cell lines in the case of mosaicism.

Congenital amegakaryocytic thrombocytopenia (CAMT) - condition present at birth with decreased marrow megakaryocytes and peripheral blood thrombocytopenia, which eventually converts into bone marrow failure and aplastic anemia. Most cases are caused by mutations of the gene for the thrombopoietin receptor (c-*mpl*).

Congenital Heinz body hemolytic anemia - inherited disorder characterized by anemia due to decreased erythrocyte life span. Erythrocyte hemolysis results from the precipitation of hemoglobin in the form of Heinz bodies, which damage the cell membrane and causes cell rigidity.

Congenital thrombocytopenia with radioulnar synostosis (CTRUS) - congenital disorder presenting with decreased marrow megakaryocytes and peripheral blood thrombocytopenia, which eventually converts into bone marrow failure and aplastic anemia. Most cases caused by mutations within the *HOXA11* gene (which codes for a regulatory protein involved in the development of hematopoietic and bone tissue).

Consolidation therapy - second phase of cancer chemotherapy whose function is to damage or kill those malignant cells that were not destroyed during the induction phase.

Constitutional aberrations - genetic aberrations present in every cell in a patient's body.

Consumption coagulopathy - *See* Disseminated intravascular coagulation

Contact group - group of coagulation factors in the intrinsic pathway involved with the initial activation of the coagulation system. It requires contact with a negatively charged surface for activity. These factors include factors XII, XI, prekallikrein, and high-molecular-weight kininogen.

Continuous flow analysis - automated method of analyzing blood cells that allows measurement of cellular characteristics as the individual cells flow singly through a laser beam.

Contour gating - subclassification of cell populations based on two characteristics such as size (x-axis) and nuclear density (y-axis) and the frequency (z-axis) of that characterized cell type. This information is used to create a three-dimensional plot. A line is drawn along the valley between two peaks to separate two cell populations.

Correlation coefficient (r) - determines the distribution of data about the estimated linear regression line.

Coverglass smear - blood smear prepared by placing a drop of blood in the center of one cove glass, then placing a second cover glass on top of the blood at a 45° angle to the first cover glass. The two cover glasses are pulled apart, creating two cover glass smears.

CRM– - cross-reacting material negative; a clotting factor that is defective and can be identified both by abnormal functional and immunologic tests.

CRM+ - cross-reacting material positive; a functionally defective clotting factor that can, however, be identified by immunologic means.

Crossover - reciprocal exchange of genetic material between chromatids that normally occurs in meiosis to increase the diversity of the species.

Cryoprecipitate - preparation of proteins containing fibrinogen, von Willebrand factor, and factor VIII prepared by freezing and thawing plasma and used for replacement therapy in patients with hemophilia A and von Willebrand disease.

Cryopreservation - maintenance of the viability of cells by storing them at very low temperatures.

Cryosupernatant - product that lacks large VWF multimers that are present in fresh frozen plasma yet still contains the VWF cleaving protease missing in thrombotic thrombocytopenic purpura (TTP) patients.

Culling - filtering and destroying senescent/damaged red cells by the spleen.

Cyanosis - bluish color of the skin and mucous membranes that develops as a result of excess deoxygenated hemoglobin in the blood.

Cyclins/Cdks - kinase proteins that regulate the transition between the various phases of the cell cycle.

Cytochemistry - chemical staining procedures used to identify various constituents (enzymes and proteins) within white blood cells. It is useful in differentiating blasts in acute leukemia, especially when morphologic differentiation on Romanowsky-stained smears is impossible.

Cytogenetic remission - absence of recognized cytogenetic abnormalities associated with a given neoplastic disease (previously identified in a patient) after therapy.

Cytokine - protein produced by many cell types that modulates the function of other cell types. The group includes interleukins, colony-stimulating factors, and interferons.

Cytomegalovirus (CMV) - herpes virus that replicates only in human cells. The virus has a widespread distribution and is spread by close contact with an infected person.

Cytoplasm - protoplasm of a cell outside the nucleus.

▶ D

DcytB - duodenal cytochrome –B reductase; ferric reductase that reduces ferric iron to the ferrous state at the enterocyte brush border.

D-dimer - cross-linked fibrin degradation product that is the result of plasmin's proteolytic activity on a fibrin clot. The presence of D-dimers is specific for fibrinolysis.

Decay accelerating factor - regulating complement protein found on cell membranes that accelerates decay (dissociation) of membrane bound complement (C3bBb). An absence of this factor leads to excessive sensitivity of these cells to complement lysis.

Deep vein thrombosis (DVT) - formation of a thrombus, or blood clot, in the deep veins (usually a leg vein).

Delayed bleeding - symptom of severe coagulation factor disorders in which a wound bleeds a second time after initial stoppage of bleeding. This occurs because the primary hemostatic plug is not adequately stabilized by the formation of fibrin.

Delta check - comparison of current hematology results to the most recently reported previous result for a given patient. This check helps detect certain random errors.

Delta (δ) storage pool disease - autosomal dominant disease characterized by a decrease in dense granules in the platelets.

Demarcation membrane system - cytoplasmic membrane system in the megakaryocyte that separates small areas of the cell's cytoplasm. These areas eventually become the platelets.

Demyelination - destruction, removal, or loss of the lipid substance that forms a myelin sheath around the axons of nerve fibers. It is a characteristic finding in vitamin B_{12} deficiency.

Dense bodies - platelet storage granules containing nonmetabolic ADP, calcium, and serotonin along with other compounds that are released from activated platelets.

Dense tubular system (DTS) - membrane in the platelet that originates from the smooth endoplasmic reticulum of the megakaryocyte. It is one of the storage sites for calcium ions within platelets. The channels of the DTS do not connect with the surface of the platelet.

Densitometry - laboratory testing method that determines the pattern and concentration of protein fractions separated by electrophoresis. It measures the amount of light absorbed by each dye-bound protein fraction as the fraction passes a slit through which light is transmitted. The amount of light absorbed (optical density) is directly proportional to the protein's concentration.

Deoxyhemoglobin - hemoglobin without oxygen.

Diamond-Blackfan anemia - congenital, progressive erythrocyte hypoplasia that occurs in very young children. There is no leukopenia or thrombocytopenia.

Diapedese - passage of blood cells through the unruptured capillary wall. For leukocytes, this involves active locomotion.

Differentiation - appearance of different properties in cells that were initially equivalent.

2,3-diphosphoglycerate (2,3-DPG) - product of the glycolytic pathway that affects the oxygen affinity of hemoglobin. It serves in the biochemical feedback system that regulates the amount of oxygen released to the tissues. As the concentration of 2,3-DPG increases, hemoglobin's affinity for oxygen decreases and more oxygen is released to the tissue. See *2,3-bisphosphoglycerate* (*2,3-BPG*).

Diploid - number of chromosomes in somatic cells that is 2n. For human cells, 2n = 46.

Direct antiglobulin test (DAT) - laboratory test used to detect the presence of antibody and/or complement that is attached to the erythrocyte. The test uses antibody directed against human immunoglobulin and/or complement. Also called the antihuman globulin (AHG) test.

Disseminated intravascular coagulation (DIC) - complex condition in which the normal coagulation process is altered (resulting in systemic rather than localized activation) by an underlying condition. Resulting complications may include thrombotic occlusion of vessels, bleeding, and ultimately organ failure. DIC is initiated by multiple triggers, most involving damage to the endothelial lining of vessels.

DMT1 - integral membrane protein that transports ferrous iron across the apical enterocyte plasma membrane.

DNA (deoxyribonucleic acid) - blueprint that cells use to catalog, express, and propagate information. DNA is the fundamental substance of heredity that is carried from one generation to the next. It is a double-stranded molecule composed of complementary nucleotide sequences. The two strands of DNA are held together by hydrogen bonds formed according to the following rules of complementary nucleotide pairing: G bonds with C; A bonds with T; other combinations cannot bond.

DNA index (DI) - DNA content of tumor cells relative to a diploid population of cells. It is calculated as the DNA content of cells in the tumor in the G0/G1 phase of the cell cycle relative to the DNA content of G0/G1 cells in a diploid control.

DNA sequencing - Determining the nucleotide sequence in a segment of DNA by replicating the DNA strands and monitoring the order in which labeled nucleotides are added to the new strands.

Döhle bodies - oval aggregates of rough endoplasmic reticulum that stains light gray blue (with Romanowsky stain) found within the cytoplasm of neutophils and eosinophils. It is associated with severe bacterial infection, pregnancy, burns, cancer, aplastic anemia, and toxic states.

Donath-Landsteiner antibody - biphasic IgG antibody associated with paroxysmal cold hemoglobinuria. The antibody reacts with erythrocytes in capillaries at temperatures below 15°C and fixes complement to the cell membrane. Upon warming, the terminal complement components on erythrocytes are activated, causing cell hemolysis.

Downey cell - outdated term used to describe morphologic variations of the reactive lymphocyte.

Drug-induced hemolytic anemia - hemolytic anemia precipitated by ingestion of certain drugs. The process may be immune mediated or nonimmune mediated.

Dry tap - description of situation when bone marrow cannot be aspirated. This can be caused by inadequate technique or alterations in the bone marrow architecture such as extensive fibrosis or very increased cellularity.

Dura mater - dense membrane covering the central nervous system; outermost layer of the meninges.

Dutcher bodies - intranuclear membrane-bound inclusion bodies found in plasma cells. The body stains with periodic acid-Schiff (PAS) indicating it contains glycogen or glycoprotein. The appearance is finely distributed chromatin, nucleoli, or intranuclear inclusions.

Dysfibrinogenemia - hereditary condition in which the fibrinogen molecule has a structural alteration.

Dyshematopoiesis - abnormal formation and/or development of blood cells within the bone marrow.

Dyspepsia - symptoms due to abnormalities in the process of digestion.

Dysplasia - abnormal cell development.

Dyspoiesis - abnormal development of blood cells frequently characterized by asynchrony in nuclear to cytoplasmic maturation and/or abnormal granule development.

▶ E

Ecchymosis - bruise (bluish-black discoloration of the skin) that is larger than 3mm in diameter caused by bleeding from arterioles into subcutaneous tissues without disruption of intact skin.

Echinocyte - spiculated erythrocyte with short, equally spaced projections over the entire outer surface of the cell.

Edematous - the swelling of body tissues due to the accumulation of tissue fluid.

Effector lymphocytes - antigen-stimulated lymphocytes that mediate the efferent arm of the immune response.

Efficacy - ability to produce the desired effect (e.g., anticoagulation).

Effusion - abnormal accumulation of fluid.

Egress - act of going out or exiting. The term is used to describe the exit of blood cells from the blood to the tissue.

ELISA (Enzyme linked immunosorbent assay) - immunological examination that employs an enzyme linked to an antibody or antigen as a marker for the detection of a specific protein. When a substrate specific for the enzyme label is added to the test system, the colored product that results is proportional to the concentration of the protein in the test sample.

Elliptocyte - abnormally shaped erythrocyte. The cell is an oval to elongated ellipsoid with a central area of pallor and hemoglobin at both ends. Also known as *ovalocyte, pencil cell,* and *cigar cell*.

Embolism - blockage of an artery by embolus, usually by a portion of blood clot but can be other foreign matter, resulting in obstruction of blood flow to the tissues.

Embolus - piece of blood clot or other foreign matter that circulates in the blood stream and usually becomes lodged in a small vessel obstructing blood flow.

Endomitosis - rounds of nuclear DNA synthesis without nuclear or cytoplasmic division.

Endoplasmic reticulum (ER) - cytoplasmic organelle in eukaryocytic cells that consists of a network of interconnected tubes and flattened membranous sacs. If the ER has ribosomes attached, it is known as *granular* or *rough endoplasmic reticulum* (*RER*), and if ribosomes are not attached, it is known as *smooth endoplasmic reticulum* (*SER*).

Endosteum - membrane that lines the bone medullary cavity that contains the bone marrow.

Endothelial cells - flat cells that line the cavities of the blood and lymphatic vessels, heart, and other related body cavities.

Endothelial cell protein C receptor (EPCR) - receiver on the membrane of endothelial cells of larger vessels that binds and immobilizes protein C, augmenting the activation of protein C by the thrombin:thrombomodulin complex.

Engraftment - homing of infused stem cells into the bone marrow microenvironment resulting in hematopoietic recovery.

Enzyme - protein that catalyzes a specific biochemical reaction but is not itself altered in the process.

Eosinophil - mature granulocyte cell characterized by the presence of large acidophilic granules. These granules are pink to orange pink

with Romanowsky stains. The cell is 12–17 μm in diameter, and the nucleus has 2–3 lobes. Granules contain acid phosphatase, glycuronidase cathepsins, ribonuclease, arylsulfatase, peroxidase, phospholipids, and basic proteins. Eosinophils have a concentration of less than 0.45×10^9/L in the peripheral blood. The cell membrane has receptors for IgE and histamine.

Eosinophilia - increase in the concentration of eosinophils in the peripheral blood ($>0.5 \times 10^9$/L). It is associated with parasitic infection, allergic conditions, hypersensitivity reactions, cancer, and chronic inflammatory states.

Epigenetics - heritable changes in gene expression not due to changes in DNA sequence.

Epistaxis - hemorrhage from the nose.

Epitope - structural portion of an antigen that reacts with a specific antibody. Also called *antigenic determinant*.

Epstein-Barr virus (EBV) - agent that attaches to B lymphocytes by a specific receptor designated CD21 on the B lymphocyte membrane surface.

Error detection - laboratory's multirule quality control procedure to detect a true error in the testing system and reject the control run.

Erythroblastic island - composite of erythroid cells in the bone marrow that surrounds a central macrophage. These groups of cells are usually disrupted when bone marrow smears are made but may be found in erythroid hyperplasia. The central macrophage is thought to transfer iron to the developing cells. The least mature cells are closest to the center of the island and the more mature cells are on the periphery.

Erythroblastosis fetalis - hemolytic anemia occurring in newborns as a result of fetal-maternal blood group incompatibility involving the Rh factor of ABO blood groups. It is caused by an antigen–antibody reaction in the newborn when maternal antibodies traverse the placenta and attach to antigens on the fetal cells.

Erythrocyte - red blood cell (RBC) that has matured to the nonnucleated stage. The cell is about 7 μm in diameter. It contains the respiratory pigment hemoglobin, which readily combines with oxygen to form oxyhemoglobin. The cell develops from the pluripotential stem cell in the bone marrow under the influence of the hematopoietic growth factor erythropoietin and is released to the peripheral blood as a reticulocyte. The average life span is about 120 days, after which the cell is removed by cells in the mononuclear-phagocyte system. The average concentration is about 5×10^{12}/L for males and 4.5×10^{12}/L for females.

Erythrocytosis - abnormal increase in the number of circulating erythrocytes as measured by the erythrocyte count, hemoglobin, or hematocrit.

Erythron - summation of the stages of erythrocytes in the marrow, peripheral blood, and within vascular areas of specific organs such as the spleen.

Erythrophagocytosis - phagocytosis of an erythrocyte by a histiocyte; the erythrocyte can be seen within the cytoplasm of the histiocyte as a pink globule or, if digested, as a clear vacuole on stained bone marrow or peripheral blood smears.

Erythropoiesis - formation and maturation of erythrocytes in the bone marrow. It is under the influence of the hematopoietic growth factor erythropoietin.

Erythropoietin - hormone secreted by the kidney that regulates erythrocyte production by stimulating the stem cells of the bone marrow to mature into erythrocytes. Its primary effect is on the committed stem cell CFU-E.

Essential thrombocythemia - myeloproliferative disorder affecting primarily the megakaryocytic element in the bone marrow. There is extreme thrombocytosis in the blood (usually $>1{,}000 \times 10^9$/L). Also called *primary thrombocythemia, hemorrhagic thrombocythemia,* and *megakaryocytic leukemia*.

Euchromatin - region of the chromosome that contains genetically active DNA, is lighter staining, and replicates early in S phase of the cell cycle. *See* heterochromatin.

Evan's syndrome - condition characterized by a warm autoimmune hemolytic anemia and concurrent severe thrombocytopenia.

Exchange transfusion - simultaneous withdrawal of blood and infusion with compatible blood.

Exon - protein-coding DNA sequence of a gene.

Extracellular matrix - noncellular components of the hematopoietic microenvironment in the bone marrow.

Extramedullary erythropoiesis - red blood cell production occurring outside the bone marrow.

Extramedullary hematopoiesis - formation and development of blood cells at a site other than the bone marrow.

Extravascular - occurring outside of the blood vessels.

Extrinsic pathway - one of the three interacting pathways in the coagulation cascade. The extrinsic pathway is initiated when tissue factor comes into contact with blood and forms a complex with factor VII. The complex activates factor X. The term *extrinsic* is used because the pathway requires tissue factor, a factor extrinsic to blood.

Extrinsic Xase - complex of tissue factor and factor VIIa that forms when a vessel is injured.

Exudate - effusion that is formed by increased vascular permeability and/or decreased lymphatic resorption. This indicates a true pathologic state in the anatomic region, usually either infection or tumor.

▶ F

FAB classification - current internationally accepted scheme for the classification of the acute leukemias. Cell identification is based on cell identification by a combination of bright-light microscopy and cytochemical testing. (FAB = French-American-British)

Factor V_{Leiden} - mutant form of F-V in which Arg 506 is replaced with Gln. This makes the molecule resistant to inactivation by activated protein C.

Factor VIII:C assay - method that determines the amount of F-VIII.

Factor VIII concentrate - lyophilized preparation of concentrated F-VIII used for replacement therapy of F-VIII in patients with hemophilia A.

Factor VIII inhibitor - IgG immunoglobulin with antibody specificity to F-VIII. The inhibitor inactivates the factor. The antibodies are time and temperature dependent. F-VIII inhibitors are associated with hemophilia.

Factor VIII/vWF complex - plasma form of VWF associated with F-VIII.

Faggot cell - cell in which there is a large collection of Auer rods and/or phi bodies.

False rejection - rejection of a control run that is not truly out of control. The result falling outside the control limits or violating a Westgard rule is due to the inherent imprecision of the test method.

Fanconi anemia (FA) - autosomal recessive disorder characterized by chromosomal instability. Patients have a complex assortment of congenital anomalies in addition to a progressive bone marrow hypoplasia.

Favism - sensitivity to a species of bean, *Vicia faba*. The condition is commonly found in Sicily and Sardinia in individuals who have inherited glucose-6-phosphate dehydrogenase deficiency. It is characterized by fever, acute hemolytic anemia, vomiting, and diarrhea after ingestion of the bean or inhalation of the plant pollen.

Fee for service - payment method for health care in which consumers choose their own health care providers and the provider determines the fees for the services. The fees may be paid by the patient or a third-party payer.

Ferritin - iron-phosphorus-protein compound formed when iron complexes with the protein apoferritin. It is a storage form of iron found primarily in the bone marrow, spleen, and liver. Small amounts can be found in the peripheral blood proportional to that found in the bone marrow.

Ferroportin - basolateral tranporter protein of ferrous iron across the basolateral membrane (also known as *IREG1*). It is the only known cellular exporter of iron.

Fibrin degradation products (FDP) - breakdown products of fibrin or fibrinogen that are produced when plasmin's proteolytic action cleaves these molecules. The four main products are fragments X, Y, D, and E. The presence of fibrin degradation products indicates either fibrinolysis or fibrinogenolysis.

Fibrin monomer - structure resulting when thrombin cleaves the A and B fibrinopeptides from the α and β chains of fibrinogen.

Fibrinogen group - group of coagulation factors that are activated by thrombin and are consumed during the formation of fibrin and therefore absent from serum. It includes factors I, V, VIII, and XIII. Also called *consumable group*.

Fibrinolysis - breakdown of fibrin.

Fibrin polymer - complex of covalently bonded fibrin monomers. The bonds between glutamine and lysine residues are formed between terminal domains of γ chains and polar appendages of α chains of neighboring residues.

Fibronectin - extracellular-matrix glycoprotein capable of binding heparin.

Fibrosis - abnormal formation of fibrous tissue.

Flame cell - plasma cell with reddish-purple cytoplasm. The red tinge is caused by the presence of a glycoprotein and the purple by ribosomes.

Flow chamber - specimen handling area of a flow cytometer where cells are forced into single file and directed in front of the laser beam.

Fluorescence in situ hybridization (FISH) - technique in which whole chromosomes (metaphase or interphase) are hybridized to a complementary probe that is labeled with a fluorochrome and visualized by microscopy.

Fluorochrome - molecule excited by light of one wavelength and emits light of a different wavelength.

Forward light scatter - laser light scattered in a forward direction in a flow cytometer. Forward light scatter is related to particle size (e.g., large cells produce more forward scatter).

Free erythrocyte protoporphyrin (FEP) - protoporphyrin within the erythrocyte that is not complexed with iron. The concentration of FEP increases in iron-deficient states. It is now known that in the absence of iron, erythrocyte protoporphyrin combines with zinc to form zinc protoporphyrin (ZPP).

Fresh frozen plasma (FFP) - colorless fluid portion of blood that is frozen at –18° C or colder within 6 hours of collection. It is formed by removal of all cellular components.

F-test - statistical tool used to compare features of two or more sets of data.

Functional hyposplenism - reduced splenic function due not to the loss of splenic tissue but to the accumulation of cells sequestered in the spleen.

▶ G

Gammopathy - abnormal condition in which there is an increase in serum immunoglobulins.

Gating - in flow cytometry, isolating cells with the same light scattering or fluorescence properties by placing a gate around them electronically.

Gene - functional segment of DNA that serves as a template for RNA transcription and protein translation. Regulatory sequences control gene expression so that only a small fraction of the estimated 100,000 genes is ever transcribed by a given cell.

Gene cluster - group of closely linked genes that can be affected as a group.

Gene promoter - DNA sequence that RNA polymerase binds to in order to begin transcription of a gene.

Gene rearrangement - process in which segments of DNA are cut and spliced to produce new DNA sequences. During normal lymphocyte development, rearrangement of the immunoglobulin genes and the T cell receptor genes results in new gene sequences that encode the antibody and surface antigen receptor proteins necessary for immune function.

Gene therapy - introduction of a normally functioning gene into the appropriate target cell of an affected individual.

Genome - total aggregate of inherited genetic material. In humans, the genome consists of 3 billion base pairs of DNA divided among 46 chromosomes including 22 pairs of autosomes numbered 1–22 and the two sex chromosomes.

Genomics - study of all nucleotide sequences, including structural genes, regulatory sequences, and noncoding DNA segments, in the chromosomes of an organism.

Genotype - genetic constitution of an individual, often referring to a particular gene locus.

Germinal center - lightly staining center of a lymphoid follicle where B cell activation occurs.

Germline - cell lineage that consists of germ cells.

Glanzmann's thrombasthenia - rare hereditary platelet disorder characterized by a genetic mutation in one of the genes coding for

the glycoproteins IIb or IIIa and resulting in the inability of platelets to aggregate.

Global testing - specialized global instrumentation that provides analysis on the entire hemostatic process including coagulation, anticoagulant effects, fibrin formation and stabilization, clot retraction, and fibrinolysis on a whole blood sample.

Globin - protein portion of the hemoglobin molecule.

Glossitis - inflammation of the tongue.

Glucose-6-phosphate-dehydrogenase (G6PD) - enzyme within erythrocytes that is important in carbohydrate metabolism. It dehydrogenates glucose-6-phosphate to form 6-phosphogluconate in the hexose monophosphate shunt. This reaction produces NADPH from NADP and provides reducing power to the erythrocyte, protecting the cell from oxidant injury.

Glutathione - tripeptide that takes up and gives off hydrogen and prevents oxidant damage to the hemoglobin molecule. A deficiency of glutathione is associated with hemolytic anemia.

Glycocalin - portion of glycoprotein Ib of the platelet membrane that is external to the platelet surface and contains binding sites for von Willebrand factor and thrombin.

Glycocalyx - amorphous coat of glycoproteins and mucopolysaccharides covering the surface of cells, particularly the platelets and endothelial cells.

Glycolysis - anaerobic conversion of glucose to lactate and pyruvic acid resulting in the production of energy (ATP).

Glycoprotein Ib - glycoprotein of the platelet surface that contains the receptor for von Willebrand factor and is critical for initial adhesion of platelets to collagen after an injury.

Glycoprotein IIb/IIIa complex - complex of membrane proteins on the platelet surface that is functional only after activation by agonists and then becomes a receptor for fibrinogen and von Willebrand factor. It is essential for platelet aggregation.

Glycosylated hemoglobin - hemoglobin that has glucose irreversibly attached to the terminal amino acid of the beta chains. Also called HbA_{1c}.

Golgi apparatus - cytoplasmic organelle composed of flattened sacs or cisternae arranged in stacks. In secretory cells, it functions in concentrating and packaging secretory products. It does not stain with Romanowsky stains and appears as a clear area usually adjacent to the nucleus.

Gower hemoglobin - embryonic hemoglobin detectable in the yolk sac for up to 8 weeks gestation. It is composed of two zeta (ζ) chains and two epsilon (ε) chains.

Graft-versus-host disease (GVHD) - tissue injury secondary to HLA-mismatch grafts resulting from immunocompetent donor T lymphocytes that recognize HLA antigens on the host cells and initiate a secondary inflammatory response.

Graft versus leukemia - favorable effect seen when immunocompetent donor T cells present in the allograft destroy the recipient's leukemic cells.

Granulocytopenia - decrease in granulocytes below 1.8×10^9/L.

Granulocytosis - increase in granulocytes above 7.0×10^9/L. It is usually seen in bacterial infections, inflammation, metabolic intoxication, drug intoxication, and tissue necrosis.

Granulomatous - distinctive pattern of chronic reaction in which the predominant cell type is an activated macrophage with epithelial-like (epithelioid) appearance.

Gray platelet syndrome (alpha storage pool disease) - rare hereditary platelet disorder characterized by the lack of platelet alpha granules.

▶ H

Hairy cell - neoplastic cell of hairy cell leukemia characterized by circumferential, cytoplasmic, hairlike projections.

Ham test - specific laboratory test for paroxysmal nocturnal hemoglobinuria (PHN). When erythrocytes from a patient with PNH are incubated in acidified serum, the cells lyse due to complement activation. Also called *acid-serum lysis test*.

Haploid - number of chromosomes in a gamete that is n; consists of one of each of the autosomes and one of the sex chromosomes. For human cells, n = 23.

Haplotype - one of the two alleles at a genetic locus.

Haptoglobin - serum α_2-globulin glycoprotein that transports free plasma hemoglobin to the liver.

HDFN - *See* hemolytic disease of the fetus and newborn.

Health Insurance Portability and Accountability Act (HIPAA) - law that mandates health care entities to establish measures that ensure the confidentiality of patient information.

Heinz bodies - inclusions in the erythrocyte composed of denatured or precipitated hemoglobin. It appears as purple-staining body on supravitally stained (crystal violet) smears.

HELLP syndrome - obstetric complication characterized by hemolysis (H), elevated liver enzymes (EL), and a low platelet count (LP). The etiology and pathogenesis are not well understood.

Helmet cell - abnormally shaped erythrocyte with one or several notches and projections on either end that look like horns. The shape is caused by trauma to the erythrocyte. Also called *keratocyte* and *horn-shaped cells*.

Hematocrit - packed cell volume of erythrocytes in a given volume of blood following centrifugation of the blood. It is expressed as a percentage of total blood volume or as a liter of erythrocytes per liter of blood (L/L). Also referred to as *packed cell volume* (*PCV*).

Hematogones - precursor B lymphocytes present normally in the bone marrow.

Hematologic remission - absence of neoplastic cells in the peripheral blood and bone marrow and the return to normal levels of hematologic parameters.

Hematology - study of formed cellular blood elements.

Hematoma - localized collection of blood under the skin or in other organs caused by a break in the wall of a blood vessel.

Hematopoiesis - production and development of blood cells normally occurring in the bone marrow under the influence of hematopoietic growth factors.

Hematopoietic microenvironment - specialized, localized environment in hematopoietic organs that supports the development of hematopoietic cells.

Hematopoietic progenitor cell - hematopoietic precursor cell developmentally located between stem cells and the morphologically recognizable blood precursor cells; includes multilineage and unilineage cell types.

Hematopoietic stem cell - hematopoietic precursor cell capable of giving rise to all lineages of blood cells.

Heme - nonprotein portion of hemoglobin and myoglobin that contains iron nestled in a hydrophobic pocket of a porphyrin ring (ferroprotoporphyrin). It is responsible for the characteristic color of hemoglobin.

Hemochromatosis - clinical condition resulting from abnormal iron metabolism characterized by accumulation of iron deposits in body tissues.

Hemoconcentration - increased concentration of blood components due to loss of plasma from the blood.

Hemoglobin - intracellular erythrocyte protein that is responsible for the transport of oxygen and carbon dioxide between the lungs and body tissues.

Hemoglobin distribution width - measure of the distribution of hemoglobin within an erythrocyte population. It is derived from the hemoglobin histogram generated by the Bayer/Technicon instruments.

Hemoglobin electrophoresis - method of identifying hemoglobins based on differences in their electrical charges.

Hemoglobinemia - presence of excessive hemoglobin in the plasma.

Hemoglobinopathy - disease that results from an inherited abnormality of the structure or synthesis of the globin portion of the hemoglobin molecule.

Hemoglobinuria - presence of hemoglobin in the urine.

Hemojuvelin (HJV) - glycosylphosphatidylnositol-anchored protein that has been shown to regulate hepcidin expression.

Hemolysis - destruction of erythrocytes resulting in the release of hemoglobin. In hemolytic anemia, this term refers to the premature destruction of erythrocytes.

Hemolysis, elevated liver enzymes and low platelet (HELLP) syndrome - severe form of preeclampsia characterized by hemolysis, elevated liver enzymes, and low platelet count. It may be a cause of microangiopathic hemolytic anemia.

Hemolytic anemia - disorder characterized by a decreased erythrocyte concentration due to premature destruction of the erythrocyte.

Hemolytic disease of the fetus and newborn (HDFN) - alloimmunne disease characterized by fetal red blood cell destruction as a result of incompatibility between maternal and fetal blood groups.

Hemolytic transfusion reaction - interaction of foreign (nonself) erythrocyte antigens and plasma antibodies due to the transfusion of blood. There are two types of transfusion reactions: immediate (within 24 hours) and delayed (occurring 2 to 14 days after transfusion).

Hemolytic uremic syndrome (HUS) - disorder characterized by a combination of microangiopathic hemolytic anemia, acute renal failure, and thrombocytopenia.

Hemopexin - plasma glycoprotein (β-globulin) that binds the heme molecule in plasma in the absence of haptoglobin.

Hemophilia A - sex-linked (X-linked) hereditary hemorrhagic disorder caused by a genetic mutation of the gene coding for coagulation F-VIII.

Hemophilia B - sex-linked (X-linked) hereditary hemorrhagic disorder caused by a genetic mutation of the gene coding for coagulation F-IX.

Hemorrhage - loss of a large amount of blood either internally or externally.

Hemorrhagic disease of the newborn - severe bleeding disorder in the first week of life caused by deficiencies of the vitamin K-dependent clotting factors due to vitamin K deficiency.

Hemosiderin - water insoluble, heterogeneous iron–protein complex found primarily in the cytoplasm of cells (normoblasts and histocytes in the bone marrow, liver, and spleen); the major long-term storage form of iron. It is readily visible microscopically in unstained tissue specimens as irregular aggregates of golden yellow to brown granules. It may be visualized with Prussian-blue stain as blue granules. The granules are normally distributed randomly or diffuse.

Hemosiderinuria - presence of iron (hemosiderin) in the urine as a result of intravascular hemolysis and disintegration of renal tubular cells.

Hemostasis - localized, controlled process that results in arrest of bleeding after an injury.

Heparin - polysaccharide that inhibits coagulation of blood by preventing thrombin from cleaving fibrinogen to form fibrin. It is commercially available in the form of a sodium salt for therapeutic use as an anticoagulant.

Heparin associated thrombocytopenia (HAT) - thrombocytopenia associated with heparin therapy in some patients due to a nonimmune-mediated direct platelet activation effect.

Heparin-induced thrombocytopenia (HIT) - thrombocytopenia associated with heparin therapy in some patients due to an immune-mediated destruction of platelets due to heparin-dependent platelet-activating IgG antibodies produced against the platelet factor 4 (PF4)-heparin complex.

Hepcidin - master iron-regulating protein that regulates iron recycling/balance via interaction with ferroportin 1. It is a negative regulator of intestinal iron absorption.

Hephaestin - facilitates export of iron and oxidizes Fe^{++} iron to Fe^{+++} for binding to apotransferrin.

Hereditary elliptocytosis - autosomal-dominant condition characterized by the presence of increased numbers of elongated and oval erythrocytes. The abnormal shape is due to a horizontal interaction defect with abnormal spectrin, deficiency, or defect in band 4.1 or deficiency of glycophorin C and abnormal band 3.

Hereditary erythroblastic multinuclearity with positive acidified serum test (HEMPAS) - type II congenital dyserythropoietic anemia (CDA). CDA is characterized by both abnormal and ineffective erythropoiesis. Type II is distinguished by a positive acidified serum test but a negative sucrose hemolysis test.

Hereditary pyropoikilocytosis (HPP) - rare but severe hemolytic anemia inherited as an autosomal recessive disorder. It is characterized by marked erythrocyte fragmentation. The defect is most likely a spectrin abnormality in the erythrocyte cytoskeleton.

Hereditary spherocytosis - chronic hemolytic anemia caused by an inherited erythrocyte membrane disorder. The vertical interaction

defect is most commonly due to a combined spectrin and ankyrin deficiency. The defect causes membrane instability and progressive membrane loss. Secondary to membrane loss, the cells become spherocytes and are prematurely destroyed in the spleen. The condition is usually inherited as an autosomal dominant trait.

Hereditary stomatocytosis - rare hemolytic anemia inherited in an autosomal dominant fashion. The erythrocyte membrane is abnormally permeable to sodium and potassium. The cell becomes overhydrated, resulting in the appearance of stomatocytes. The specific membrane abnormality has not been identified.

Hereditary xerocytosis - hereditary disorder in which the erythrocyte is abnormally permeable to sodium and potassium with an increased potassium efflux. The erythrocyte becomes dehydrated and appears as either target or spiculated cells. The cells are rigid and become trapped in the spleen.

Heterochromatin - region of the chromosome that contains genetically inactive DNA, is dark staining, and replicates late in S phase of the cell cycle.

Heterologous - refers to morphologically nonidentical chromosomes that have different gene loci.

Heterophile antibodies - antibodies that can react against a heterologous antigen that did not stimulate the antibody's production. In infectious mononucleosis, heterophile antibodies are produced in response to infection with Epstein-Barr virus and react with sheep, horse, and beef erythrocytes.

Heterozygous - different genes at a gene locus.

Hexose-monophosphate shunt - metabolic pathway that converts glucose-6-phosphate to pentose phosphate. This pathway couples oxidative metabolism with the reduction of nicotinamide adenine dinucleotide-phosphate (NADPH) and glutathione. This provides the cell with reducing power and prevents injury by oxidants.

HFE - transmembrane protein that associates with beta2-microglobulin. It binds to the transferrin receptor (TfR) on cells and regulates the interaction of the receptor with transferrin. When bound to TfR, it reduces the affinity of the receptor for iron-bound transferrin (Tf-Fe) by 5- to 10-fold. Mutations are associated with hereditary hemochromatosis.

Histogram - graphical representation of the number of cells within a defined parameter such as size.

HIV-I (human immunodeficiency virus type-I) - virus that causes acquired immunodeficiency syndrome (AIDS).

Hodgkin lymphoma (disease) - malignancy that most often arises in lymph nodes and is characterized by the presence of Reed-Sternberg cells and variants with a background of varying numbers of benign lymphocytes, plasma cells, histiocytes, and eosinophils. The origin of the malignant cell is still controversial.

Homologous - having two morphologically identical chromosomes that have identical gene loci but may have different gene alleles because one member of a homologous pair is of maternal origin and the other is of paternal origin.

Homozygous - identical genes at a gene locus.

Horizontal interactions - side-by-side interactions involving the proteins of the erythrocyte membrane.

Howell-Jolly bodies - erythrocyte inclusions composed of nuclear remnants (DNA). On Romanowsky-stained blood smears, they appear as a dark purple spherical granule usually near the periphery of the cell. They are commonly associated with megoblastic anemia and splenectomy.

Humoral immunity - immunity imparted as a result of B lymphocyte activation. The B lymphocyte differentiates to a plasma cell that produces antibodies specific to the antigen that stimulated the response.

Hybridization - process in which one nucleotide strand binds to another strand by formation of hydrogen bonds between complementary nucleotides.

Hydrodynamic focusing - phenomenon that allows cells/particles to flow in a single column due to differences in the pressures of two columns of fluid in a flow chamber of a flow cytometer. The particles are contained in an inner column of sample fluid that is surrounded by a column of stream sheath fluid. The gradient between the sample and sheath fluid keeps the fluids separate (laminar flow) and is used to control the diameter of the column of sample fluid. The central column of sample fluid is narrowed to isolate single cells that pass through a laser beam like a string of beads.

Hydrops fetalis - genetically determined hemolytic disease (thalassemia) resulting in production of an abnormal hemoglobin (hemoglobin Bart's, γ_4) that is unable to carry oxygen. No alpha(α) globin chains are synthesized.

Hypercoagulable state - condition associated with an imbalance between clot-promoting and clot-inhibiting factors. This leads to an increased risk of developing thrombosis.

Hyperdiploid - number of chromosomes per cell that is more than 2n. For human cells, this would be >46.

Hypereosinophilic syndrome - persistent blood eosinophilia over 1.5×10^9/L with tissue infiltration, absence of clonal genetic aberrations, and no apparent cause of the increase in eosinophils.

Hyperhomocysteinemia - elevated levels of homocysteine in the blood as a result of impaired homocysteine metabolism. It can be due to acquired or congenital causes. It is associated with premature atherosclerosis and arterial thrombosis.

Hyperplasia - increase in the number of cells per unit volume of tissue. This can be brought about by an increase in the number of cells replicating, an increase in the rate of replication, or prolonged survival of cells. The cells usually maintain normal size, shape, and function. The stimulus for the proliferation may be acute injury, chronic irritation, or prolonged, increased hormonal stimulation. In hematology, a hyperplastic bone marrow is one in which the proportion of hematopoietic cells to fat cells is increased.

Hypersplenism - disorder characterized by enlargement of the spleen and pancytopenia in the presence of a hyperactive bone marrow.

Hypocellularity - decreased cellularity of hematopoietic precursors in the bone marrow.

Hypochromic - lack of color; used to describe erythrocytes with an enlarged area of pallor due to a decrease in the cell's hemoglobin content. The mean corpuscular hemoglobin concentration (MCHC) and mean corpuscular hemoglobin (MCH) are decreased.

Hypodiploid - number of chromosomes per cell that is less than 2n. For human cells, this would be <46.

Hypofibrinogenemia - condition in which there is an abnormally low fibrinogen level in the peripheral blood. It may be caused by a mutation in the gene controlling the production of fibrinogen or an acquired condition in which fibrinogen is pathologically converted to fibrin.

Hypogammaglobulinemia - condition associated with a decrease in resistance to infection as a result of decreased γ-globulins (immunoglobulins) in the blood.

Hypoplasia - condition of underdeveloped tissue or organ usually caused by a decrease in the number of cells. A hypoplastic bone marrow is one in which the proportion of hematopoietic cells to fat cells is decreased.

Hypoproliferative - decreased production of any cell type.

Hypoxia - deficiency of oxygen to the cells.

I

Idiopathic - pertaining to disorders or diseases in which the pathogenesis is unknown.

Idiopathic (or immune) thrombocytopenic purpura (ITP) - acquired condition in which the platelets are destroyed by immune mechanisms faster than the bone marrow is able to compensate. Platelets are decreased.

Immature reticulocyte fraction (IRF) - index of reticulocyte maturity provided by flow cytometry. The IRF may be helpful in evaluating bone marrow erythropoietic response to anemia, monitoring anemia, and evaluating response to therapy.

Immune hemolytic anemia - disorder caused by premature, immune-mediated destruction of erythrocytes. Diagnosis is confirmed by the demonstration of immunoglobulin (antibodies) and/or complement on the erythrocytes.

Immune thrombocytopenic purpura (ITP) - autoimmune disorder in which autoreactive antibodies bind to platelets, shortening the platelet life span.

Immune response - body's defense mechanism that includes producing antibodies to foreign antigens.

Immunoblast - T or B lymphocyte that is mitotically active as a result of stimulation by an antigen. The cell is morphologically characterized by a large nucleus with prominent nucleoli, a fine chromatin pattern, and an abundant, deeply basophilic cytoplasm.

Immunocompetent - having the ability to respond to stimulation by an antigen.

Immunoglobulin - molecule produced by B lymphocytes and plasma cells. It reacts with antigen. It consists of two pairs of polypeptide chains: two heavy and two light chains linked together by disulfide bonds. Also called *antibody.*

Immunohistochemical stains - stains applied using immunologic principles and techniques to study cells and tissues. Usually a labeled antibody is used to detect antigens (markers) on a cell.

Immunophenotyping - identifying antigens using detection antibodies.

Immunosuppressed - suppressed ability to produce antibodies to antigens.

Immunotherapy - form of therapy in which different immune cells are manipulated in vivo or in vitro and later infused to alter the immune function of other cells.

Indirect antiglobulin test (IAT) - laboratory test used to detect the presence of serum antibodies against specific erythrocyte antigens.

Induction therapy - initial phase of cancer chemotherapy. Its function is to rapidly drop the tumor burden and induce a remission back to a normal state.

Ineffective erythropoiesis - premature death of erythrocytes in the bone marrow preventing release into circulation.

Infectious lymphocytosis - A condition found in young children. The most striking hematologic finding is a leukocytosis of $40–50 \times 10^9$/L with 60–97% small, normal-appearing lymphocytes. It is thought to be a reactive immune response to a viral infection and is no longer considered a unique disease.

Infectious mononucleosis - self-limiting lymphoproliferative disease caused by infection with Epstein-Barr virus (EBV). The usually increased leukocyte count is related to an absolute lymphocytosis. Various forms of reactive lymphocytes are present. Serologic tests to detect the presence of heterophil antibodies are helpful in differentiating this disease from more serious diseases. Also known as the *kissing disease.*

Innate immune response - body's first response to common classes of invading pathogens. It is rapid but limited. The leukocyte receptors that participate in it are always available and do not require cell activation in order to be expressed. Once a pathogen is recognized, effector cells can attack, engulf, and kill it. Neutrophils, monocytes, and macrophages play a major role in the innate immune system.

In situ hybridization - detection of specific DNA or RNA sequences in tissue sections or cell preparations using a labeled complementary nucleic acid sequence or probe.

Integral proteins - proteins embedded between phospholipids within a cell membrane.

Internal quality control program - system designed to verify the validity of laboratory test results that is followed as part of the daily laboratory operations. Typically, it is monitored using Levey-Jennings plots and Westgard rules.

International normalized ratio (INR) - method of reporting prothrombin time results when monitoring long-term oral anticoagulant therapy. Results are independent of the reagents and methods used.

International Sensitivity Index (ISI) - value provided by the manufacturer of thromboplastin reagents. It indicates the responsiveness of the particular lot of reagent compared to the international reference thromboplastin.

Intrinsic coagulation pathway - one of the three interacting pathways in the coagulation cascade. The intrinsic pathway is initiated by exposure of the contact coagulation factors (F-XII, F-XI, prekallikrein, and high-molecular-weight kininogen) with vessel subendothelial tissue. The intrinsic pathway activates F-X. The term *intrinsic* is used because all intrinsic factors are contained within the blood.

Intrinsic factor - glycoprotein secreted by the parietal cells of the stomach that is necessary for binding and absorption of dietary vitamin B_{12}.

Intrinsic Xase - complex of F-IXa, F-VIIIa, phospholipid, and calcium that assembles on membrane surfaces.

Intron - DNA base sequence interrupting the protein coding sequence of a gene; this sequence is transcribed into RNA but is cut out of the message before it is translated into protein.

IRE - stem-loop-stem structure in either the 5′ or 3′ noncoding regions of mRNA recognized and bound by iron-binding proteins

(IRE-BP or IRP). The binding affinity of IRP for the IRE is determined by the amount of cellular iron. The IRP binds to the IRE region when iron is scarce and dissociates when iron is plentiful. When bound, the IRP modulates the translation of the mRNA. The translation of the proteins involved in iron metabolism including ferritin, ferroportin, ALA synthase2, transferrin, and DMT1 are regulated by this mechanism.

IRP - protein that binds to a stem-loop structure of ferritin and transferrin receptor mRNA. The stem-loop structure of mRNA is known as the iron-responsive element (IRE). It is also referred to as *IRE-BP* (*iron-responsive element-binding protein)*. The binding affinity of IRE-BP for the IRE is determined by the amount of cellular iron. The IRE-BP is involved in the regulation of transferrin receptors and ferritin.

Irreversibly sickled cells (ISC) - rigid cells that have been exposed to repeated sickling events and cannot revert to a normal discoid shape. They are ovoid or boat-shaped and have a high MCHC and low MCV.

Ischemia - deficiency of blood supply to a tissue caused by constriction of the vessel or blockage of the blood flow through the vessel.

Isoelectric focusing - technique of moving charged particles through a support medium with a continuous pH gradient. Individual proteins will move until they reach the pH that is equal to their isoelectric point.

Isopropanol precipitation - technique that identifies the presence of unstable hemoglobins due to their insolubility in isopropanol as compared to normal hemoglobins.

Isovolumetric sphering - method employed by the Bayer/Technicon instruments in which a specific buffered diluent is used to sphere and fix the blood cells without altering their volume.

▶ J

JAK2 gene - Janus kinase 2, codes for a tyrosine kinase closely associated with cytokine receptors. A gain in function mutation that gives the cell a proliferative advantage is common in the myeloproliferative disorders, especially polycythemia vera.

Jaundice - condition characterized by yellowing of the skin, mucous membranes, and the whites of the eye caused by accumulation of bilirubin.

Juvenile myelomonocytic leukemia - clonal hematopoietic neoplasm of childhood characterized by proliferation of the granulocytic and monocytic lineages. There is a peripheral blood monocytosis ($>1 \times 10^9$/L), with <20% blasts (including promonocytes).

▶ K

Karyolysis - destruction of the nucleus.

Karyorrhexis - disintegration of the nucleus resulting in the irregular distribution of chromatin fragments within the cytoplasm.

Karyotype - systematic display of a cell's chromosomes that determines the number of chromosomes present and their morphology.

Kernicterus - toxic buildup of bilirubin in brain tissue; associated with hyperbilirubinemia.

Keratocytes - abnormally shaped erythrocytes with one or several notches and projections on either end that look like horns. Also called *helmet cells* and *horn-shaped cells*. The shape is caused by trauma to the erythrocyte.

Killer cell - population of cytolytic lymphocytes identified by monoclonal antibodies. Involved in several activities such as resistance to viral infections, regulation of hematopoiesis, and activities against tumor cells.

Knizocytes - abnormally shaped erythrocyte that appears on stained smears as a cell with a dark stick-shaped portion of hemoglobin in the center and a pale area on either end. The cell has more than two concavities.

▶ L

L&H/popcorn cell - *See* Popcorn cell.

Lacunar cell - neoplastic cell variant found in NS Hodgkin lymphoma characterized by abundant pale-staining cytoplasm. It is also characterized by cytoplasmic clearing and delicate, multilobated nuclei.

Large granular lymphocyte - null cell with a low nuclear-to-cytoplasmic ratio, pale blue cytoplasm, and azurophilic granules. It does not adhere to surfaces or phagocytose.

Latex immunoassay (LIA) test - immuno-turbidimetric assay using microlatex particles coated with specific antibodies. In the presence of the antigen to be tested, the particles agglutinate producing an adsorption of light proportional to the antigen level present in the sample.

Laurell "rocket" technique (EIA-Electroimmunoassay) - agarose plates containing antibody are electrophoresed with an antigen (in PPP) until a "rocket" of precipitated antigen–antibody forms (measured following the staining of the gel). The height of the rocket is proportional to the quantity of antigen present in the PPP.

Lecithin:cholesterol acyl transferase (LCAT) deficiency - rare autosomal disorder that affects metabolism of high-density lipoproteins. It is characterized by a deficiency of an enzyme that catalyzes the formation of cholesterol esters from cholesterol. Its onset is usually during young adulthood.

Leptocyte - abnormally shaped erythrocyte that is thin and flat with hemoglobin at the periphery. It is usually cup shaped.

Leukemia - progressive, malignant disease of the hematopoietic system characterized by unregulated, clonal proliferation of the hematopoietic stem cells. The malignant cells eventually replace normal cells. It is generally classified as chronic or acute, and lymphoid or myelogenous.

Leukemic hiatus - gap in the normal maturation pyramid of cells with many blasts and some mature forms but very few intermediate maturational stages. Eventually, the immature neoplastic cells fill the bone marrow and spill over into the peripheral blood producing leukocytosis (e.g., acute leukemia).

Leukemic stem cell - rare cell with infinite proliferative potential that drives the formation and growth of tumors.

Leukemoid reaction - transient, reactive condition resulting from certain types of infections or tumors characterized by an increase in the total leukocyte count to more than 25×10^9/L and a shift to the left in leukocytes (usually granulocytes).

Leukocyte - white blood cell (WBC) of which there are five types: neutrophils, eosinophils, basophils, lymphocytes, and monocytes.

The function of these cells is to defend against infection and tissue damage. The normal reference range for total leukocytes in peripheral blood is $4.5–11.0 \times 10^9$/L.

Leukocyte alkaline phosphatase (LAP) - enzyme present within the specific (secondary) granules of granulocytes (from the myelocyte stage onward). It is useful in distinguishing leukemoid reaction/reactive neutrophilia (high LAP) from chronic myelogenous leukemia (low LAP).

Leukocytosis - increase in WBCs in the peripheral blood; WBC count over 11×10^9/L.

Leukoerythroblastic reaction - condition characterized by the presence of nucleated erythrocytes and a shift to the left in neutrophils in the peripheral blood; often associated with myelophthisis.

Leukopenia - decrease in leukocytes below 4×10^9/L.

Leukopoiesis - production of leukocytes.

Linearity - range of concentration over which the test method can be used without modifying the sample (i.e., diluting the sample).

Linearity check material - commercially available matter with known concentrations of the analytes and no interfering substances or conditions. Linearity check material is used to determine an instrument's or method's linearity.

Linear regression analysis - statistical tool used to determine a single line through a data set that describes the relationship between two methods, *X* and *Y*. General equation is $Y = a + bx$, where *a* denotes the *y*-intercept; *b* is the slope; and *Y* is the predicted mean value of *Y* for a given *x* value.

Linkage analysis - process of following the inheritance pattern of a particular gene in a family based on its tendency to be inherited with another locus on the same chromosome.

Locus - specific position on the chromosome.

Low-molecular-weight heparin (LMWH) - heparin molecules of M.W. 2,000–12,000 Daltons.

LRP receptor (LDL receptorlike protein) - receiver on hepatocytes that removes plasmin/antiplasmin, plasminogen activator/plasminogen activator inhibitor, and thrombin/antithrombin complexes from the circulation.

Lupuslike anticoagulant - circulating substance that arises spontaneously in patients with a variety of conditions (originally found in patients with lupus erythematosus) and directed against phospholipid components of the reagents used in laboratory tests for clotting factors. *See* Antiphospholipid antibody.

Lymphadenopathy - abnormal enlargement of lymph nodes.

Lymphoblast - lymphocytic precursor cell found in the bone marrow. The cell is 10–20 μm in diameter and has a high nuclear/cytoplasmic ratio. The nucleus has a fine (lacy) chromatin pattern with one or two nucleoli. The cytoplasm is agranular and scant. It stains deep blue with Romanowsky stain. The cell contains terminal deoxynucleotidyltransferase (TdT) but no peroxidase, lipid, or esterase.

Lymphocyte - mature leukoctye with variable size depending on the state of cellular activity and amount of cytoplasm. The nucleus is usually round with condensed chromatin and stains deep, dark purple with Romanowsky stains. The cytoplasm stains a light blue. Nucleoli are usually not visible. A few azurophilic granules may be present. These cells interact in a series of events that allow the body to attack and eliminate foreign antigen. They have a peripheral blood concentration in adults from 1.0 to 4.8×10^9/L (20–40% of leukocytes). The concentration in children less than 10 years old is higher.

Lymphocytic leukemoid reaction - response characterized by an increased lymphocyte count with the presence of reactive or immature appearing lymphocytes. It is associated with whooping cough, chicken pox, infectious mononucleosis, infectious lymphocytosis, and tuberculosis.

Lymphocytopenia - decrease in the concentration of lymphocytes in the peripheral blood ($<1.0 \times 10^9$/L). Also called *lymphopenia*.

Lymphocytosis - increase in peripheral blood lymphocyte concentration ($>4.8 \times 10^9$/L in adults or $>9 \times 10^9$/L in children).

Lympho-epithelial lesion - infiltration of epithelium by groups of lymphocytes. Infiltration of mucosal epithelium by neoplastic lymphocytes is characteristic of MALT lymphoma.

Lymphoid follicle - sphere of B cells within lymphatic tissue.

Lymphokines - substances released by sensitized lymphocytes and responsible for activation of macrophages and other lymphocytes.

Lymphoma - malignant proliferation of lymphocytes. Most cases arise in lymph nodes, but it can begin at many extranodal sites. The lymphomas are classified as to B or T cell and low, intermediate, or high grade.

Lymphoma classification - process of dividing (grading) lymphomas into groups, each with a similar clinical course and response to treatment. Current schemes use a combination of morphologic appearance, phenotype, and genotype.

Lyonization - process in which all but one X chromosome in a cell are randomly inactivated.

Lypholized - serum or plasma sample that has been freeze dried. The sample is reconstituted with a diluent, typically distilled or deionized water.

Lysosmal granules - granules containing lysosomal enzymes.

Lysosome - membrane-bound sacs in the cytoplasm that contain various hydrolytic enzymes.

▶ M

Macrocyte - abnormally large erythrocyte. The MCV is >100 fL. Oval macrocytes are characteristically seen in megaloblastic anemia.

Macro-ovalocyte - abnormally large erythrocyte with an oval shape. This cell is characteristically seen in megaloblastic anemia.

Macrophage - large tissue cell (10–20 μm) derived from monocytes. The cell secretes a variety of products that influence the function of other cells. It plays a major role in both nonspecific and specific immune responses.

Maintenance therapy - third and final phase of cancer chemotherapy whose function is to prevent the repair and/or return of the malignant clone, thus allowing the normal immune system to clear away all remaining disease.

Malignant neoplasm - clone of identical, anaplastic (dedifferentiated), proliferating cells. Malignant cells can metastasize.

Marginating pool - population of neutrophils that are attached to or marginated along the vessel walls and not actively circulating. This is about one-half of the total pool of neutrophils in the vessels.

Material safety data sheet (MSDS) - document that provides safety information for clinical laboratory professionals who use hazardous materials; includes pertinent safety information regarding the proper storage and disposal of a chemical, precautions that should be taken in handling the chemical, potential health hazards associated with exposure to it, and whether the chemical is a fire or explosive hazard.

Mastocytosis - heterogeneous group of mast cell diseases characterized by the abnormal proliferation of mast cells in one or more organ systems. It is suggested that mast cell disorders be classified as myeloproliferative disorders. Two major groups of mast cell disorders are cutaneous and systemic.

Maturation - process of attaining complete development of the cell.

Maturation index - mathematical expression that attempts to separate AML-M5 and AML-M1 with and without maturation.

Mean cell hemoglobin (MCH) - indicator of the average weight of hemoglobin in individual erythrocytes reported in picograms. The reference interval for MCH is 28–34 pg. This parameter is calculated from the hemoglobin and erythrocyte count: MCH (pg) = Hemoglobin (g/dL) ÷ Erythrocyte count ($\times 10^{12}$/L) × 10.

Mean cell hemoglobin concentration (MCHC) - measure of the average concentration of hemoglobin in grams per deciliter of erythrocytes. The reference interval is 32–36 g/dL. The MCHC is useful when evaluating erythrocyte hemoglobin content on a stained smear. This parameter correlates with the extent of chromasia exhibited by the stained cells and is calculated from the hemoglobin and hematocrit. MCHC (g/dL) = hemoglobin (g/dL) ÷ hematocrit (L/L).

Mean cell volume (MCV) - average volume of individual erythrocytes reported in femtoliters. The reference interval for MCV is 80–100 fL. This parameter is useful when evaluating erythrocyte morphology on a stained blood smear. The MCV usually correlates with the diameter of the erythrocytes observed microscopically. The MCV can be calculated from the hematocrit and erythrocyte count: MCV (fL) = Hematocrit (L/L) ÷ Erythrocyte Count ($\times 10^{12}$/L) × 1000.

Mean platelet volume - mean volume of a platelet population; analogous to the MCV of erythrocytes.

Medical decision level - concentration of an analyte indicating that medical intervention is required for proper patient care.

Medullary hematopoiesis - blood cell production and development in the bone marrow.

Megakaryocyte - large cell found within the bone marrow characterized by the presence of large or multiple nuclei and abundant cytoplasm. It gives rise to the blood platelets.

Megaloblastic - asynchronous maturation of any nucleated cell type characterized by delayed nuclear development in comparison to the cytoplasmic development. The abnormal cells are large and are characteristically found in pernicious anemia and other megaloblastic anemia.

Metacentric - chromosome that has the centromere near center so that the short arm and long arms are equal in length.

Meninges - three membranes covering the brain and spinal cord.

Metamyelocyte - granulocytic precursor cell normally found in the bone marrow. The cell is 10–15 μm in diameter. The cytoplasm stains pink and there is a predominance of specific granules. The nucleus is indented with a kidney bean shape. The nuclear chromatin is condensed and stains dark purple.

Methemoglobin - hemoglobin with iron that has been oxidized to the ferric state (Fe^{+++}); is incapable of combining with oxygen.

Methemoglobin reductase pathway - metabolic pathway that uses methemoglobin reductase and NADH to maintain heme iron in the reduced state (Fe^{++}).

Microangiopathic hemolytic anemia (MAHA) - any hemolytic process that is caused by prosthetic devices or lesions of the small blood vessels.

Microcyte - abnormally small erythrocyte. The MCV is typically less than 80 fL and its diameter is less than 7.0 μm on a stained smear.

Microenvironment - unique environment in the bone marrow where orderly proliferation and differentiation of precursor cells take place.

Micromegakaryocyte - small, abnormal megakaryocyte sometimes found in the peripheral blood in MDS and the myeloproliferative syndromes.

Microtubule - cylindric structure (20–27 μm in diameter) composed of protein subunits. It is a part of the cytoskeleton, helping some cells maintain shape. Microtubules increase during mitosis and form the mitotic spindle fibers. They also assist in transporting substances in different directions. In the platelet, a band of tubules located on the circumference is thought to be essential for maintaining the disc shape in the resting state.

Minimal (minimum) residual disease - condition with the presence of malignant cells detected by molecular tests when all other tests are negative.

Mitotic pool - population of cells within the bone marrow that is capable of DNA synthesis. Also called *proliferating pool*.

Mixed lineage acute leukemia - acute leukemia that has both myeloid and lymphoid populations present or blasts that possess myeloid and lymphoid markers on the same cell.

Molecular remission - absence of detectable molecular abnormalities using PCR or related molecular technologies in patients who had identifiable abnormalities before therapy. This is the most sensitive test for detecting minimal residual disease.

Monoblast - monocytic precursor cell found in bone marrow. It is about 14–18 μm in diameter with abundant agranular, blue-gray cytoplasm. The nucleus may be folded or indented. The chromatin is finely dispersed, and several nucleoli are visible. The monoblast has nonspecific esterase activity that is inhibited by sodium fluoride.

Monoclonal gammopathy - alteration in immunoglobulin production that is characterized by an increase in one specific class of immunoglobulin.

Monocyte - mature leukocyte found in bone marrow or peripheral blood. Its morphology depends on its activity. The cell ranges in size from 12–30 μm with an average of 18 μm. The blue-gray cytoplasm is evenly dispersed with fine dustlike granules. There are two types of granules. One contains peroxidase, acid phosphatase, and arylsulfatase. Less is known about the content of the other granule. The nuclear chromatin is loose and linear forming a lacy pattern. The nucleus is often irregular in shape.

Monocytopenia - decrease in the concentration of circulating monocytes ($<0.1 \times 10^9$/L).

Monocytosis - increase in the concentration of circulating monocytes ($>0.8 \times 10^9$/L).

Mononuclear phagocyte (MNP) system - collection of monocytes and macrophages found both intravascularly and extravascularly. It plays a major role in initiating and regulating the immune response.

Monosomy - one daughter cell with a missing chromosome (one copy instead of two).

Morulae - basophilic, irregularly shaped granular, cytoplasmic inclusions found in leukocytes in an infectious disease called *ehrlichiosis.*

Mosaic - process that occurs in the embryo shortly after fertilization, resulting in congenital aberrations in some cells and some normal cells.

Mott cell - pathologic plasma cell whose cytoplasm is filled with colorless globules. These globules most often contain immunoglobulin (Russell bodies) and form as a result of accumulation of material in the RER, SER, or Golgi complex due to an obstruction of secretion. The cell is associated with chronic plasmocyte hyperplasia, parasitic infection, and malignant tumors. Also called *grape cell.*

Multimer analysis - analysis that determines the structure of VWF multimers.

Multiple myeloma - plasma cell malignancy characterized by increased plasma proteins.

Mutation - any change in the nucleotide sequence of DNA. In instances in which large sequences of nucleotides are missing, the alteration is referred to as a *deletion.*

Myeloblast - first microscopically identifiable granulocyte precursor. It is normally found in the bone marrow. The cell is large (15–20 μm) with a high nuclear/cytoplasmic ratio. The nucleus has a fine chromatin pattern with a nucleoli. There is moderate amount of blue, agranular cytoplasm.

Myelocyte - granulocytic precursor cell normally found in the bone marrow. The cell is 12–18 μm in diameter with a pinkish granular cytoplasm. Both primary and secondary granules are present.

Myelodysplastic syndromes (MDS) - group of primary neoplastic pluripotential stem cell disorders characterized by one or more cytopenias in the peripheral blood with prominent maturation abnormalities (dysplasia) in the bone marrow.

Myelodysplastic/myeloproliferative diseases - category of neoplasms in the WHO classification but not found in the FAB classification system. It includes clonal hematopoietic neoplasms that have some clinical, laboratory, or morphologic findings of both a myelodysplastic syndrome (MDS) and a chronic myeloproliferative disease (MPD).

Myeloid-to-erythroid ratio (M:E ratio) - ratio of granulocytes and their precursors to nucleated erythroid precursors derived from performing a differential count on bone marrow nucleated hematopoietic cells. Monocytes and lymphocytes are not included. The normal ratio is usually between 1.5:1 and 3.5:1, reflecting a predominance of myeloid elements.

Myeloid/NK cell acute leukemia - acute leukemia in which the neoplastic cells coexpress myeloid antigens (CD33, CD13, and/or CD15) and NK cell-associated antigens (CD56, CD16, CD11b), while they lack HLA-DR and T lymphocyte associated antigens CD3 and CD8.

Myeloperoxidase - enzyme present in the primary granules of myeloid cells including neutrophils, eosinophils, and monocytes.

Myelophthisis - replacement of normal hematopoietic tissue in bone marrow by fibrosis, leukemia, or metastatic cancer cells.

Myeloproliferative disorders (MPD) - group of neoplastic clonal disorders characterized by excess proliferation of one or more cell types in the bone marrow.

▶ N

Natural killer cell - type of lymphoid cell that has the capacity for spontaneous cytotoxicity for various target cells. Its cytotoxicity is non-MHC restricted. It possesses CD16 (the FcγIII receptor for IgG) and CD56. NK cells constitute about 15% of the circulating lymphocytes in the peripheral blood.

Necrosis - pathologic cell death resulting from irreversible damage; "cell murder."

Neonatal alloimmune thrombocytopenia (NAIT) - thrombocytopenia due to immune destruction of platelets that occurs in newborns due to the transfer of maternal alloantibodies.

Neoplasm - abnormal formation of new tissue (such as a tumor) that serves no useful purpose; may be benign or malignant.

Neutropenia - decrease in neutrophils below 1.8×10^9/L.

Neutrophil - mature white blood cell with a segmented nucleus and granular cytoplasm. This cell constitutes the majority of circulating leukocytes. The absolute number varies between 1.8 and 7.0×10^9/L. Also called *granulocytes* or *segs*.

Neutrophilia - increase in neutrophils over 7.0×10^9/L. It is seen in bacterial infections, inflammation, metabolic intoxication, drug intoxication, and tissue necrosis.

Nondisjunction - error in segregation that occurs in mitosis or meiosis so that sister chromatids do not disjoin. A spindle fiber malfunction results in one daughter cell with an extra chromosome (trisomy) and one daughter cell with a missing chromosome (monosomy).

Nonspecific granules - large, blue-black granules found in promyelocytes. The granules have a phospholipid membrane and stain positive for peroxidase.

Nonthrombocytopenic purpura - condition in which platelets are normal in number but purpura are present; purpura is considered to be caused by damage to the blood vessels.

Normal pooled plasma - platelet-poor plasma collected from at least 20 individuals for coagulation testing. Plasmas should give PT and APTT results within the laboratory's reference interval. The plasma is pooled and used in mixing studies to differentiate a circulating inhibitor from a factor deficiency.

Normoblast - nucleated erythrocyte precursor in the bone marrow. Also known as *erythroblast.*

Normogram - chart that displays the relationship between numerical variables.

Nuclear-cytoplasmic asynchrony - condition in which the cellular nucleus matures more slowly than the cytoplasm, suggesting a disturbance in coordination. As a result, the nucleus takes on the appearance of a nucleus associated with a younger cell than its cytoplasmic development indicates. This is a characteristic of megaloblastic anemias.

Nuclear-to-cytoplasmic ratio (N:C ratio) - ratio of the volume of the cell nucleus to the volume of the cell's cytoplasm. This is usually estimated as the ratio of the diameter of the nucleus to the diameter of the cytoplasm. In immature hematopoietic cells, the N:C ratio is usually higher than in more mature cells. As the cell matures, the nucleus condenses and the cytoplasm expands.

Nucleolus (pl: nucleoli) - spherical body within the nucleus in which ribosomes are produced. It is not visible in cells that are not synthesizing proteins or that are not in mitosis or meiosis. It stains a lighter blue than the nucleus with Romanowsky stains.

Nucleotide - basic building block of DNA composed of nitrogen base (A = adenine, T = thymine, G = guanine, or C = cytosine) attached to a sugar (deoxyribose) and a phosphate molecule.

Nucleus (pl: nuclei) - characteristic structure in the eukaryocytic cell that contains chromosomes and nucleoli. It is separated from the cytoplasm by a nuclear envelope. The structure stains deep bluish-purple with Romanowsky stain. In young, immature hematopoietic cells, the nuclear material is open and dispersed in a lacy pattern. As the cell becomes mature, the nuclear material condenses and appears structureless.

Null cell - *See* Large granular lymphocytes.

▶ O

Oncogene - altered gene that contributes to the development of cancer. Most oncogenes are altered forms of normal genes that function to regulate cell growth and differentiation. The normal gene counterpart is known as a proto-oncogene.

Open canalicular system (OCS) - membrane system in the platelet forming twisted channels that lead from the platelet surface to the interior of the platelet. It is a remnant of the demarcation membrane system of the megakaryocyte. Also called *surface connected canalicular system* (*SCCS*).

Opportunistic organisms - organisms that are usually part of the normal flora but can cause disease if there is a significant change in host resistance or within the organism itself.

Opsonin - antibody or complement that coats microorganisms or other particulate matter found within the blood stream so that the foreign material may be more readily recognized and phagocytized by leukocytes.

Optimal counting area - area of the blood smear where erythrocytes are just touching but not overlapping; used for morphologic evaluation and identification of cells.

Oral anticoagulant - group of drugs (e.g., coumadin, warfarin) that prevent coagulation by inhibiting the activity of vitamin K, which is required for the synthesis of functional prothrombin group coagulation factors.

Orthochromatic normoblast - nucleated precursor of the erythrocyte that develops from the polychromatophilic normoblast. It is the last nucleated stage of erythrocyte development. The cell normally is found in the bone marrow.

Osmotic fragility - laboratory procedure employed to evaluate the ability of erythrocytes to withstand different salt concentrations; this depends on the erythrocyte's membrane, volume, surface area, and functional state.

Osteoblast - cell involved in formation of calcified bone.

Osteoclast - cell involved in resorption and remodeling of calcified bone.

Outlier - data point that falls outside the expected range for all data. An outlier is not considered to be part of the population that was sampled.

Oxygen affinity - ability of hemoglobin to bind and release oxygen. An increase in CO_2, acid, and heat decreases oxygen affinity, while an increase in pO_2 increases oxygen affinity.

Oxyhemoglobin - compound formed when hemoglobin combines with oxygen.

▶ P

P_{50} value - partial pressure of oxygen at which 50% of hemoglobin is saturated with oxygen.

P53 gene - normally functions as an antioncogene by preventing proliferation of DNA-damaged cells, promoting apoptosis of these damaged cells, and preventing unwanted DNA amplification. When mutated, this gene may lose its tumor suppressive effect.

Paired *t*-test - statistical tool used to compare the difference between two paired data sets. Paired *t*-test determines whether a statistically significant difference exists between the two paired data sets.

Pancytopenia - marked decrease of all blood cells in the peripheral blood.

Panhypercellular - increase in all blood cells in the peripheral blood.

Panmyelosis - panhypercellularity in the bone marrow.

Pappenheimer bodies - iron-containing particles in mature erythrocyte. On Romanowsky stain, they are visible near the periphery of the cell and often occur in clusters.

Paroxysmal cold hemoglobinuria (PCH) - autoimmune hemolytic anemia characterized by hemolysis and hematuria upon exposure to cold.

Paroxysmal nocturnal hemoglobinuria (PNH) - stem cell disease in which the erythrocyte membrane is abnormal, making the cell more susceptible to hemolysis by complement. There is a lack of decay accelerating factor (DAF) and C8 binding protein (C8bp) on the membrane, which are normally responsible for preventing amplification of complement activation. The deficiency of DAF and C8bp is due to the lack of glycosyl phosphatidyl inositol (GPI), a membrane glycolipid that serves to attach (anchor) proteins to the cell membrane. Intravascular hemolysis is intermittent.

Passenger lymphocyte syndrome - immune hemolytic following solid organ, bone marrow, or stem cell transplant . The donor B lymphocytes that are transplanted with the organ or the bone marrow produce antibodies against recipient's blood group antigens. Hemolysis is primarily due to ABO incompatibility between donor and recipient (Group O donor and Group A or B recipient). Although ABO is the most frequent antigen system involved, Rh, Kell, Kidd, or other blood group systems may be involved.

Pelger-Huët anomaly - inherited benign condition characterized by the presence of functionally normal neutrophils with a bilobed or round nucleus. Cells with the bilobed appearance are called *pince-nez cells*.

Percent saturation - portion of transferrin that is complexed with iron.

Pericardial cavity - body cavity that contains the heart.

Pericardium - membrane that lines the pericardial cavity.

Peripheral membrane protein - protein that is attached to the cell membrane by ionic or hydrogen bonds but is outside the lipid framework of the membrane.

Peritoneal cavity - space between the inside abdominal wall and outside of the stomach, small and large intestines, liver, superior aspect of the bladder, and uterus.

Peritoneum - lining of the peritoneal cavity.

Pernicious anemia - megaloblastic anemia resulting from a lack of intrinsic factor. The intrinsic factor is needed to absorb cobalamin (vitamin B_{12}) from the gut.

Petechiae - small, pinhead-size purple spots caused by blood escaping from capillaries into intact skin. These are associated with platelet and vascular disorders.

Phagocytosis - cellular process of cells engulfing and destroying a foreign particle through active cell membrane invagination.

Phagolysosome - digestive vacuole (secondary lysosome) formed by the fusion of lysosomes and a phagosome. The hydrolytic enzymes of the lysosome digest the phagocytosed material.

Phagosome - formation of an isolated vacuole within the process of opsonization.

Pharmacokinetics - quantitative study of a drug's disposition in the body over time.

Phase microscopy - type of light microscopy in which an annular diaphragm is placed below or in the substage condenser, and a phase-shifting element is placed in the rear focal plane of the objective. This causes alterations in the phases of light rays and increases the contrast between the cell and its surroundings. This methodology is used to count platelets.

Phenotype - physical manifestation of an individual's genotype, often referring to a particular genetic locus.

Phi body - smaller version of the Auer rod.

Photomultiplier tube - light detector used in flow cytometers and other analytical instruments.

Pia mater - thin membrane directly covering the central nervous system; middle layer of the meninges.

Pica - perversion of appetite that leads to bizarre eating practices; a clinical finding in some individuals with iron deficiency anemia.

Pitting - removal of abnormal inclusions from erythrocytes by the spleen.

PIVKA (protein-induced by vitamin-K absence or antagonist) - these factors are the nonfunctional forms of the prothrombin group coagulation factors. They are synthesized in the liver in the absence of vitamin K and lack the carboxyl (COOH) group necessary for binding the factor to a phospholipid surface.

Plasma cell - transformed, fully differentiated B lymphocyte normally found in the bone marrow and medullary cords of lymph nodes. It may be seen in the circulation in certain infections and disorders associated with increased serum γ-globulins. The cell is characterized by the presence of an eccentric nucleus containing condensed, deeply staining chromatin and deep basophilic cytoplasm. The large Golgi apparatus next to the nucleus does not stain, leaving an obvious clear paranuclear area. The cell has the PC-1 membrane antigen and cytoplasmic immunoglobulin.

Plasma cell neoplasm - monoclonal neoplasm of immunoglobulin secreting cells.

Plasma exchange - removal of patient plasma and replacement with donor plasma.

Plasmacytoid lymphocyte - an intermediate cell in immunoblast development between the B lymphocyte and the plasma cell. It has morphologic similarity to the lymphocyte but has marked cytoplasmic basophila similar to that of plasma cells. It is occasionally seen in the peripheral blood of patients with viral infection.

Plasmacytosis - presence of plasma cells in the peripheral blood or an excess of plasma cells in the bone marrow.

Plasmin - proteolytic enzyme with trypsinlike specificity that digests fibrin or fibrinogen as well as other coagulation factors. Plasmin is formed from plasminogen.

Plasminogen - β-globulin, single-chain glycoprotein that circulates in the blood as a zymogen. Large amounts of plasminogen are absorbed with the fibrin mass during clot formation. Plasminogen is activated by intrinsic and extrinsic activators to form plasmin.

Plasminogen activator inhibitor-1 (PAI-1) - primary inhibitor of tissue plasminogen activator (t-PA) and urokinaselike plasminogen activator (tcu-PA) released from platelet α granules during platelet activation.

Plasminogen activator inhibitor-2 (PAI-2) - inhibitor of tissue plasminogen activator and urokinaselike plasminogen activator. Secretion of PAI-2 is stimulated by endotoxin and phorbol esters. Increased levels impair fibrinolysis and are associated with thrombosis.

Platelet - round or oval disc-shaped structure in the peripheral blood formed from the cytoplasm of megakaryocytes in the bone marrow. Platelets play an important role in primary hemostasis by adhering to the ruptured blood vessel wall and aggregating to form a platelet plug over the injured area. Platelets are also important in secondary hemostasis by providing platelet phospholipids important for the activation of coagulation proteins. The normal reference range for platelets is $150–450 \times 10^9$/L.

Platelet activation - stimulation of a platelet that occurs when agonists bind to the platelet's surface and transmit signals to the cell's interior. Activated platelets form aggregates known as the *primary platelet plug*.

Platelet adhesion - platelet attachment to collagen fibers or other nonplatelet surfaces.

Platelet aggregation - platelet-to-platelet interaction that results in a clumped mass; may occur in vitro or in vivo.

Platelet clump - aggregation of platelets; may occur when blood is collected by capillary puncture (due to platelet activation) and when blood is collected in EDTA anticoagulant (due to unmasking of platelet antigens that can react with antibodies in the serum).

Platelet distribution width (PDW) - coefficient of variation of platelet volume distribution; analogous to RDW.

Platelet factor 4 - protein present in platelet's alpha granules that is capable of neutralizing heparin.

Plateletpheresis - procedure in which platelets are removed from the circulation.

Platelet-poor plasma (PPP) - citrated plasma containing less than 15×10^9/L platelets. It is prepared by centrifugation of citrated whole blood at a minimum RCF of $1000 \times g$ for 15 minutes. PPP is used for the majority of coagulation tests.

Platelet procoagulant activity - property of platelets that enables activated coagulation factors and cofactors to adhere to the platelet surface during the formation of fibrin.

Platelet-rich plasma (PRP) - citrated plasma containing approximately $200–300 \times 10^9$/L platelets. It is prepared by centrifugation of citrated whole blood at an RCF of $150 \times g$ for 10 minutes. PRP is used in platelet aggregation studies.

Platelet satellitism - adherence of platelets to neutrophil membranes in vitro; this can occur when blood is collected in EDTA anticoagulant.

Platelet secretion - release of the contents of the platelet alpha granules and dense bodies during platelet activation.

Platelet-type pseudo-VWD - platelet disorder characterized by an increased affinity of the platelet GPIb/IX receptor for VWF , resulting in spontaneous binding of the large VWF multimers to the platelet. It resembles VWD clinically and often presents with similar laboratory test results but is not associated with genetic mutations involving the *VWF* gene and thus is not considered "true" VWD.

Pleura - lining of the pleural cavities.

Pleural cavity - space between the chest wall and the lungs.

Plethora - excess of blood.

Plumbism - lead poisoning.

Pluripotential cell - cell that differentiates into many different cell lines. It has the potential to self-renew, proliferate, and differentiate into erythrocytic, myelocytic, monocytic, lymphocytic, and megakaryocytic blood cell lineages.

Poikilocytosis - term used to describe the presence of variations in the shape of erythrocytes.

Point of care (POC) instrument - instrument that allows for analytical testing of patient specimens outside the laboratory setting (e.g., home testing or physician's office testing).

Polychromatophilia - quality of being stainable with more than one portion of the stain; the term is commonly used to describe erythrocytes that stain with a grayish or bluish tinge with Romanowsky stains due to residual RNA, which takes up the blue portion of the dye.

Polychromatophilic erythrocyte - erythrocyte with a bluish tinge when stained with Romanowsky stain; contains residual RNA. If stained with new methylene blue, these cells show reticulum and are identified as reticulocytes.

Polyclonal - arising from different cell clones.

Polyclonal gammopathy - alteration in immunoglobulin production that is characterized by an increase in immunoglobulins of more than one class.

Polycythemia - condition associated with increased erythrocyte count.

Polycythemia vera - myeloproliferative disorder associated with an increased proliferation of erythroid cells.

Polymerase chain reaction - procedure for copying a specific DNA sequence many times.

Polymorphic variants - variant morphology of a portion of a chromosome that has no clinical consequence.

Polymorphonuclear neutrophil (PMN) - mature granulocyte found in bone marrow and peripheral blood. The nucleus is segmented into 2 or more lobes. The cytoplasm stains pinkish and there is abundant specific granules. This is the most numerous leukocyte in the peripheral blood ($1.8–7.0 \times 10^9$/L). Its primary function is defense against foreign antigens. It is active in phagocytosis and killing microorganisms. Also called *segmented neutrophil* or *seg*.

Polyploid/polyploidy - number of chromososmes per cell that is a multiple of *n* (23) other than 1 or 2 (e.g., 3n[69], 4n[92]).

Popcorn cell (L&H cell) - neoplastic cell variant found in LP Hodgkin lymphoma characterized by a delicate multilobated nucleus and multiple, small nucleoli. The L&H cell has a B cell phenotype: LCA+ (leukocyte common antigen), CD20+, CD 15.

Porphyrins - highly unsaturated tetrapyrrole ring bonded by four methane (−CH=) bridges. Substituents occupy each of the eight peripheral positions on the four pyrrole rings. The kind and order of these substituents determine the type of porphyrin. Porphyrins are metabolically active only when they are chelated.

Portland hemoglobin - embryonic hemoglobin found in the yolk sac and detectable up to 8 weeks gestation. It is composed of two zeta (ζ) and two gamma (γ) chains.

Postmitotic pool - neutrophils in the bone marrow that are not capable of mitosis. These cells include metamyelocytes, bands, and segmented neutrophils. Cells spend about 5–7 days in this compartment before being released to the peripheral blood. Also called *maturation-storage pool*.

Post translational modification - process occuring in eukaryotic cells that modify the protein product produced by ribosomal translation; it may involve the addition of sugar groups (glycosylation) and phosphate groups (phosphorylation) or other modifications to amino acids (e.g., gamma carboxylation of coagulation proteins).

Primary aggregation - earliest association of platelets in an aggregate that is reversible.

Primary fibrinogenolysis - clinical situation that occurs when there is a release of excessive quantities of plasminogen activators into the blood in the absence of fibrin clot formation. Excess plasmin degrades fibrinogen and the clotting factors, leading to a potentially dangerous hemorrhagic condition.

Primary hemostasis - initial arrest of bleeding that occurs with blood vessel/platelet interaction.

Primary hemostatic plug - aggregate of platelets that initially halts blood flow from an injured vessel.

Primary thrombocytosis - increase in platelets that is not secondary to another condition. It usually refers to the thrombocytosis that occurs in neoplastic disorders.

Probe - tool for identifying a particular nucleotide sequence of interest. A probe is composed of a nucleotide sequence that is complementary to the sequence of interest and is therefore capable of hybridizing to that sequence. Probes are labeled in a way that is detectable, such as by radioactivity.

Procoagulant - inert precursor of a natural substance that is necessary for blood clotting or a property of anything that favors formation of a blood clot.

Proficiency testing - utilizing unknown samples from an external source (e.g., College of American Pathologists) to monitor the quality of a given laboratory's test results.

Progenitor cell - parent or ancestor cells that differentiate into mature, functional cells.

Prolymphocyte - immediate precursor cell of the lymphocyte; normally found in bone marrow. It is slightly smaller than the lymphoblast and has a lower nuclear to cytoplasmic ratio. The nuclear chromatin is somewhat clumped, and nucleoli are usually present. The cytoplasm stains light blue and is agranular.

Promonocyte - monocytic precursor cell found in the bone marrow. The cell is 14–18 μm in diameter with abundant blue-gray cytoplasm. Fine azurophilic granules may be present. The nucleus is often irregular and deeply indented. The chromatin is finely dispersed and stains a light purple blue. Nucleoli may be present. Cytochemically, the cells stain positive for nonspecific esterase, peroxidase, acid phosphatase, and arylsulfatase. The cell matures to a monocyte.

Promyelocyte - granulocytic precursor cell normally found in the bone marrow. The cell is 15–21 μm in diameter. The cytoplasm is basophilic, and the nucleus is quite large. The nuclear chromatin is lacy, staining a light purple blue. Several nucleoli are visible. The distinguishing feature is the presence of large blue-black primary (azurophilic) granules. The granules have a phospholipid membrane that stains with Sudan black B. The granules contain acid phosphatase, myeloperoxidase, acid hydrolases, lysozyme, sulfated mucopolysaccharides, and other basic proteins. The promyelocyte matures to a myelocyte. Also called *progranulocyte*.

Pronormoblast - precursor cell of the erythrocyte. The cell is derived from the pluripotential stem cell and is found in the bone marrow. The cell is 12–20 μm in diameter and has a high nuclear-cytoplasmic ratio. The cytoplasm is deeply basophilic with Romanowsky stains. The nuclear chromatin is fine, and there is one or more nucleoli. The cell matures to a basophilic normoblast. Also called *rubriblast*.

Proteomics - study of the structure and function of proteins in a cell or tissue at a specific time under certain predefined conditions; includes information on the way the proteins function and interact with each other inside cells.

Proteosome - eukaryotic assembly of proteins that degrades other proteins.

Prothrombinase complex - complex formed by coagulation factors Xa and V, calcium, and phospholipid. This complex activates prothrombin to thrombin.

Prothrombin group - group of coagulation factors that are vitamin K dependent for synthesis of their functional forms and that require calcium for binding to a phospholipid surface. Includes factors II, VII, IX, and X. Also known as *vitamin K-dependent factors*.

Prothrombin time (PT) - screening test used to detect deficiencies in the extrinsic and common pathway of the coagulation cascade and to monitor the effectiveness of oral anticoagulant therapy.

Prothrombin time ratio - proportion calculation derived by dividing the patient's prothrombin time result by midpoint of the laboratory's normal range and used to calculate the International Normalized Ratio (INR).

Prourokinase - immature, single-chain form of urokinase that is prepared from urine and by recombinant DNA techniques and can be activated to a two-chain form by plasmin.

Pseudochylous - fluid that appears chylous due to the presence of many inflammatory cells; does not contain lymph fluid or chylomicrons.

Pseudodiploid - cell that has a chromosome count of 2*n* (46) but with a combination of numerical and/or structural aberrations (e.g., 46, XY, −5, −7, 2D8, 2D21).

Pseudoneutrophilia - increase in the concentration of neutrophils in the peripheral blood ($>7.0 \times 10^9$/L) occurring as a result of cells from the marginating pool entering the circulating pool. The response is immediate but transient. This redistribution of cells accompanies vigorous exercise, epinephrine administration, anesthesia, convulsion, and anxiety states. Also called *immediate* or *shift neutrophilia*.

Pseudo–Pelger-Huët cells - acquired condition in which neutrophils display a hyposegmented nucleus. Unlike the real Pelger-Huët anomaly, the nucleus of this cell contains a significant amount of euchromatin and stains more lightly. A critical differentiation point is that all neutrophils are equally affected in the genetic form of Pelger-Huët anomaly, but only a fraction of neutrophils are hyposegmented cells in the acquired state. It is associated with MDS and MPD and may also be found after treatment for leukemias.

Pulmonary embolism - obstruction of the pulmonary artery or one of its branches by a clot or foreign material that has been dislodged from another area by the blood current.

Pure red cell aplasia (PRCA) - anemia with selective decrease in erythrocyte precursors in the marrow.

Purging - technique by which undesirable cells that are present in the blood or bone marrow products are removed.

Purpura - (1) purple discoloration of the skin caused by petechiae and/or ecchymoses; (2) a diverse group of disorders that are characterized by the presence of petechiae and ecchymoses.

Pyknotic - pertaining to degeneration of the nucleus of the cell in which the chromatin condenses to a solid, structureless mass and shrinks.

▶ Q

Quality control limit - expected range of results. These limits are used to determine whether a test method is in control and to minimize the chance of inaccurate patient results. If the test method is out of control, an intervention is required to reconcile the problem.

Quebec platelet disorder - storage pool disorder of platelets due to abnormal proteolysis of alpha granule proteins due to increased levels of urinary-type plasminogen activator.

Quiescence (G_0) - phase in a cell that has exited the cell cycle and is in a nonproliferative state.

▶ R

R (relaxed) structure - conformational change in hemoglobin that occurs as the molecule takes up oxygen.

Radar chart - graphical representation of eight CBC parameters: WBC, RBC, Hb, Hct, MCV, MCH, MCHC, and PLT. Lines are drawn to connect the parameters; the chart resembles a radar oscilloscope. Changes in the shape of the radar chart indicate different hematologic disorders.

Radial immunodiffusion - diffusion technique in which antibody is incorporated into agarose gel and antigen is placed into wells in the gel. The antigen is quantitated by the size of a precipitin ring that forms as antigen diffuses from a sample well into the gel.

Random access - capability of an automated hematology instrument to process specimens independently of one another; may be programmed to run individual tests (e.g., Hb or platelet counts) or a panel of tests (e.g., CBC with reticulocyte count) without operator intervention.

Random variation - variation within an instrument or test method that is due to chance. This type of variation can be either positive or negative in direction and affects precision.

Rapoport-Leubering shunt - metabolic pathway in which 2,3-bisphosphoglycerate (2,3-BPG) is synthesized from 1,3-bisphosphoglycerate. 2,3-BPG facilitates the release of oxygen from hemoglobin in the erythrocyte. Also referred to as *2,3-DPG* (*diphosphoglycerate*).

Raynaud's phenomenon - secondary disorder resulting from vasoarterial spasms in the extremities of the body when exposed to the cold. It is characterized by blanching of the skin, followed by cyanosis, and finally redness when the affected area is warmed. Also referred to as *acrocyanosis*.

RBC indices - indices that help classify the erythrocytes as to their size and hemoglobin content. The values for hemoglobin, hematocrit, and erythrocyte are used to calculate the three indices: mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), and mean corpuscular hemoglobin (MCH). The indices give a clue as to what the erythrocytes should look like on a stained blood film.

Reactive lymphocyte - antigen-stimulated lymphocyte that exhibits a variety of morphologic features. The cell is usually larger than the resting lymphocyte and has an irregular shape. The cytoplasm is more basophilic. The nucleus is often elongated and irregular with a finer chromatin pattern than that of the resting lymphocyte. Often this cell is increased in viral infections. Also called *virocyte,* or *stimulated, transformed, atypical, activated,* or *leukocytoid lymphocyte*.

Reactive neutrophilia - increase in the concentration of peripheral blood neutrophils ($>7.0 \times 10^9$/L) as a result of reaction to a physiologic or pathologic process.

Reagent blank - measurement of absorbance due to reagent alone; eliminates false increase in sample absorbance due to reagent color.

Red thrombus - thrombus composed mostly of red blood cells; so named because of its red coloration.

Reed-Sternberg cell - cell found in the classic form of Hodgkin lymphoma. It is characterized by a multilobated nucleus and large inclusion-like nucleoli.

Reference interval - test value range that is considered normal. Generally the range is determined to include 95% of the normal population.

Reflex testing - follow-up testing that is performed based on results of screening tests.

Refractive Index - degree to which a transparent object will deflect a light ray from a straight path.

Refractory - pertains to disorders or diseases that do not respond readily to therapy.

Refractory anemia - subgroup of the myelodysplastic syndromes. Anemia refractory to all conventional therapy is the primary clinical finding. Blasts constitute <1% of nucleated peripheral blood cells. The bone marrow shows signs of dyserythropoiesis.

Refractory anemia with excess blasts (RAEB) - subgroup of the myelodysplastic syndromes. There are usually cytopenias and signs of dyspoiesis in the peripheral blood with <5% blasts. The bone marrow is usually hypercellular with dyspoiesis in all hematopoietic cell lineages. Bone marrow blasts vary from 5% to 20%.

Refractory anemia with excess blasts in transformation (RAEB-T) - subgroup of the myelodysplastic syndromes. There is(are) cytopenia(s) in the peripheral blood with more than 5% blasts. The bone marrow is usually hyperceullular with dyspoiesis and 20–30% blasts. In the WHO classification, this would be considered acute leukemia (>20% blasts).

Refractory anemia with ringed sideroblasts (RARS) - subgroup of the myelodysplastic syndromes characterized by <1% blasts in the peripheral blood, anemia, and/or thrombocytopenia and/or leukopenia. There are more than 15% ringed sideroblasts and <5% blasts in the bone marrow.

Refractory cytopenia with multilineage dysplasia (RCMD) - category in the WHO classification system for patients with dysplastic features in at least 10% of the cells in two or more cell lines, less than 5% blasts in the bone marrow, and less than 1% blasts in the peripheral blood.

Remission - diminution of the symptoms of a disease.

Replication - process by which DNA is copied during cell division. Replication is carried out by the enzyme DNA polymerase, which recognizes single-stranded DNA and fills in the appropriate complementary nucleotides to produce double-stranded DNA. Synthesis is initated at a free 5′ end where double-stranded DNA lies adjacent to single-stranded DNA, and replication proceeds in the 5′ direction. In the laboratory, DNA replication can be induced as a means of copying DNA sequences as exploited in the polymerase chain reaction.

Reportable range - range that is defined by a minimum value and a maximum value of calibration material.

Reticulated platelet - platelet newly released from the bone marrow and that possesses residual RNA.

Restriction endonuclease - enzyme that cleaves double-stranded DNA at specific nucleotide sequences. For example, HindIII cleaves DNA only where the sequence 5′-AAGCTT-3′ is present. Various other enzymes are known to cut various specific target sequences. Examples of common restriction endonucleases are BamH1, EcoR1, Mnl1, MstII, Pst1, and Xba1.

Restriction point - point that occurs in late G1; point when cell cycle progression becomes autonomous.

Reticular cell - one of the three major types of cell in the bone marrow stroma. It is also found in the spleen and lymph nodes. These cells branch to form reticular fibers. Also called *fibroblasts*.

Reticulocyte - first nonnucleated stage of erythrocyte development in the bone marrow. It contains RNA that is visualized as granules or filaments within the cell when stained supravitally with new methylene blue. Normally, reticulocytes constitute approximately 1% of the circulating erythrocyte population.

Reticulocyte production index (RPI) - indicator of the bone marrow response in anemia. The calculation corrects the reticulocyte

count for the presence of marrow reticulocytes in the peripheral blood. It is calculated as follows:

(Patient hematocrit [L/L] ÷ 0.45 [L/L]) × reticulocyte count (%) × (1 ÷ maturation time of shift reticulocytes) = RPI

Reticulocytosis - presence of excess reticulocytes in the peripheral blood.

Rh null disease - disorder associated with the lack of the Rh antigen on erythrocytes.

Rhopheocytosis - energy- and temperature-dependent process by which iron enters cells.

Ribosomes - cellular particle composed of ribonucleic acid (RNA) and protein whose function is to synthesize polypeptide chains from amino acids. The sequence of amino acids in the chains is specified by the genetic code of messenger RNA. Ribosomes appear singly or in reversibly dissociable units and may be free in the cytoplasm or attached to endoplasmic reticulum. The cytoplasm of blood cells that contain a high concentration of ribosomes stains bluish purple with Romanowsky stains.

Richter's transformation - transformation from CLL to another disease, usually large B cell lymphoma.

Ringed sideroblasts - erythroblasts with abnormal deposition of excess iron within mitochondria resulting in a ring formation around the nucleus.

Ristocetin - aggregating reagent that specifically evaluates VWF interaction with glycoprotein Ib on platelets.

Ristocetin induced platelet aggregation (RIPA) - measures ability of patient's VWF to bind to normal platelets, inducing platelet aggregation in a platelet aggregation assay.

RNA (ribonucleic acid) - single-stranded molecule composed of ribonucleotides (A, C, G, and U). RNA is produced by transcription of genes from a DNA template; RNA in turn serves as a template for protein translation.

Romanowsky-type stain - any stain consisting of methylene blue and its oxidation products and eosin Y or eosin B.

Rouleaux - erythrocyte distribution characterized by erythrocytes stacked like a roll of coins. This is due to abnormal coating of the cell's surface with increased plasma proteins, which decreases the zeta potential between cells.

Russell bodies - globule filled with immunoglobulin found in pathologic plasma cells called Mott cells. *See* Mott cell.

Russell's viper venom - venom that possesses thromboplastin-like activity and activates factor X.

► S

Satellite DNA - DNA containing many tandem repeats. Morphologically, it appears as a small ball-like structure making up the short arm of acrocentric chromosomes. This is the locus of the nucleolar organizing region.

Scatterplot - dot-plot histogram of two cellular characteristics. Together, the two characteristics allow definition of the leukocyte subpopulations.

Schilling test - definitive test useful in distinguishing vitamin B_{12} deficiency due to malabsorption, dietary deficiency, or absence of IF. It measures the amount of an oral dose of radioactively labeled crystalline B_{12} that is absorbed in the gut and excreted in the urine.

Schistocyte - fragment of an erythrocyte. A schistocyte may have a variety of shapes including triangle, helmet, and comma.

Scott syndrome - rare platelet disorder characterized by abnormal Ca++ induced phospholipids scrambling in which platelet membranes fail to support plasma procoagulant protein activation.

Secondary aggregation - irreversible aggregation of platelets that occurs over time.

Secondary fibrinolysis - clinical condition characterized by excessive fibrinolytic activity in response to disseminated intravascular clotting.

Secondary hemostasis - formation of fibrin that stabilizes a primary platelet plug.

Secondary hemostatic plug - primary platelet aggregate that has been stabilized by fibrin formation during secondary hemostasis.

Secondary thrombocytosis - increase in platelet concentration in the blood. The increase is in response to stimulation by another condition.

Secretion - energy-dependent discharge or release of products usually from glands in the body but also pertaining to the contents of platelet granules that are released after stimulation of the platelets by agonists; also product that is discharged or released.

Self-renewal - property of regenerating the same cells.

Sequestration crisis - sudden splenic pooling of sickled erythrocytes that may cause a massive decrease in erythrocyte mass within a few hours

Serine protease - family of serine proteases includes thrombin, factors VIIa, IXa, Xa, XIa, XIIa, and the digestive enzymes chymotrypsin and trypsin. They selectively hydrolyze arginine- or lysine-containing peptide bonds of other zymogens converting them to serine proteases. Each serine protease involved in the coagulation cascade is highly specific for its substrate.

Serpin - family of serine protease inhibitors that inhibit target molecules by formation of a 1:1 stoichiometric complex.

Severe combined immunodeficiency syndrome (SCIDS) - heterogeneous group of disorders based on diverse genetic origins, different inheritance patterns, and severity of clinical manifestations. The disease may be inherited either as a sex-linked trait or as an autosomal-recessive trait. This is the most severe immune deficiency disease.

Sézary's cell - circulating neoplastic cell found in Sézary's syndrome characterized by a very convoluted (cerebriform) nuclear outline.

Shelf life - time period for which a reagent or control is stable given appropriate storage conditions. Shelf life changes once the reagent or control is reconstituted if lypholyzed or opened if liquid.

Shift neutrophilia - *See* Pseudoneutrophilia.

Shift to the left - appearance of increased numbers of immature leukocytes in the peripheral blood.

Sickle cell (drepanocyte) - elongated crescent shaped erythrocyte with pointed ends. Sickle cell formation may be observed in wet preparations or in stained blood smears from patients with sickle cell anemia.

Sickle-cell anemia - genetically determined disorder in which hemoglobin S is inherited in the homozygous state. No hemoglobin A is present. Hemoglobins S, F, A_2 are present.

Sickle cell trait - genetically determined disorder in which hemoglobin S is inherited in the heterozygous state. The patient has one normal β-globin gene and one β^S-globin gene. Both hemoglobin A and hemoglobin S are present.

Side light scatter - laser light scattered at a 90° angle due to internal complexity and granularity of the particle (e.g., neutrophils produce much side scatter because of their numerous cytoplasmic granules).

Sideroacrestic - defect in iron utilization.

Siderocyte - erythrocyte that contains stainable iron granules.

Sideropenic - lack of iron.

Single nucleotide polymorphism (SNP) - change in which a single base in the DNA differs from the usual base at that position

Slope - angle or direction of the regression line with respect to the x and y axes. The slope is used to identify the presence of proportional systematic error.

Small lymphocytic lymphoma (SLL) - condition identical to CLL but primarily involves the lymph nodes. The two disorders appear to belong to one disease entity with differing clinical manifestations.

Smooth endoplasmic reticulum (SER) - *See* Endoplasmic reticulum.

Smudge cell - cell whose cytoplasmic membrane has ruptured, leaving a bare nucleus. Increased numbers of smudge cells are observed in lymphoproliferative disorders such as chronic lymphocytic leukemia. It can also be seen in reactive lymphocytosis and in other neoplasms.

Southern blot - procedure first described by Ed Southern for determining DNA structure. In this procedure, DNA is cleaved with restriction endonucleases that cut DNA at specific nucleotide sequences. The resulting DNA fragments are electrophoresed in an agarose gel to separate them by size and then treated with a solution of high pH that separates double-stranded DNA into two single-stranded parts. The single-stranded fragments are then transferred to a membrane where they can be hybridized to a complementary labeled probe. Probe hybridization permits identification of the DNA fragments containing the sequence of interest. The size and number of those fragments reflects the structure of the DNA.

Specificity - ability of a test method to determine only the analyte meant to be detected or measured.

Specimen run - interval, period of time, or number of specimens for which the accuracy and precision of the laboratory procedure is expected to remain stable.

Spectrin - predominant peripheral membrane protein found in the erythrocyte membrane. It is composed of dimeric chains, α and β, that associate to form tetramers.

Spent phase - stage in polycythemia vera in which after a period of 2–10 years, the patient may develop bone marrow failure accompanied by an increase in splenomegaly. Anemia and bleeding may be the primary clinical findings, secondary to a decreased platelet count and decreasing hematocrit. This phase is often a transition to AML.

Spherocyte - abnormally round erythrocyte with dense hemoglobin content (increased MCHC). The cell has no central area of pallor because it has lost its biconcave shape.

Splenectomy - removal of the spleen.

Splenomegaly - abnormal enlargement of the spleen.

Split sample - division of a single sample into two or more aliquots for the purpose of testing on two or more instruments within the same time period or retesting the sample at another time.

Spur cell anemia - acquired hemolytic condition associated with severe hepatocellular disease such as cirrhosis, in which there is an increase in serum lipoproteins, leading to excess of erythrocyte membrane cholesterol. The total phospholipid content of the membrane, however, is normal. The predominant poikilocyte is an erythrocyte with irregular points and no area of central pallor (acanthocytes).

Stab - *See* Band.

Stage - stage of a neoplasm indicates the extent and distribution of disease. Determining the stage of disease usually involves radiologic studies, peripheral blood examination, bone marrow aspiration, and biopsy.

Standard deviation - distribution of a set of data about the mean.

Standard error of the estimate ($S_{y/x}$) - measure of the variation in the regression line. The $S_{y/x}$ is used to identify random error.

Starry sky - morphologic appearance characteristic of high-grade lymphoma produced by numerous tingible body macrophages (stars) and a diffuse sheet of neoplastic cells (sky).

Stomatocyte - abnormal erythrocyte shape characterized by a slit-like area of central pallor. This cell has a uniconcave, cup shape.

Streptokinase - bacterial enzyme derived from group C-beta hemolytic steptococci that activates plasminogen to plasmin and is used as a thrombolytic agent in the treatment of thrombosis.

Stroma - extracellular matrix or microenvironment that supports hematopoietic cell proliferation in the bone marrow.

Stromal cells - cellular elements of the hematopoietic microenvironment in the red portion of bone marrow.

Submetacentric - chromosome that has the centromere positioned off center so that the short arm is shorter than the long arm.

Sucrose hemolysis test - screening test to identify erythrocytes that are abnormally sensitive to complement lysis. In this test, erythrocytes, serum, and sucrose are incubated together. Cells abnormally sensitive to complement will lyse. The test is used to screen for paroxysmal nocturnal hemoglobinuria. Also called *sugar-water test*.

Sulfhemoglobin - stable compound formed when a sulfur atom combines with each of the four heme groups of hemoglobin; it is incapable of carrying oxygen.

Supernatant - clear liquid remaining on top of a solution after centrifugation of the particulate matter.

Supravital stain - stain used to stain cells or tissues while they are still living.

Syngeneic stem cell transplantation - transplantation of stem cells between genetically identical twins.

Synovium - continuous membrane that lines the bony, cartilaginous, and connective tissue surfaces of a joint.

Systematic variation - variation within an instrument or test method that occurs in one direction and can be predicted. This type of variation affects accuracy.

▶ T

Target cell - abnormally shaped erythrocyte. The cell appears as a target with a bull's-eye center mass of hemoglobin surrounded by an achromic ring and an outer ring of hemoglobin. The osmotic fragility of this cell is decreased. Also called *Mexican hat cell* and *codocyte*.

Tartrate resistant acid phosphatase (TRAP) - acid phosphatase staining following tartrate incubation.

T cell ALL - immunologic subgroup of ALL. There are two types: early precursor T-ALL and T-ALL. T-ALL is differentiated using two CD markers, CD7 (gp40 protein) and CD2 (E-receptor), and TdT.

T cell receptor (TCR) - antigen receptor on immunocompetent T lymphocytes

Teardrop (dacryocytes) - erythrocyte that is elongated at one end to form a teardrop or pear-shaped cell. Teardrop may form after erythrocytes with cellular inclusions have transversed the spleen. A teardrop cell cannot return to its original shape because it has either been stretched beyond the limits of deformability of the membrane or has been in the abnormal shape for too long a time.

Telangiectasia - persistent dilation of superficially located veins.

Thalassemia - group of genetically determined microcytic, hypochromic anemias resulting from a decrease in synthesis of one or more globin chains in the hemoglobin molecule. The disorder may occur in the homozygous or heterozygous state. Heterozygotes may be asymptomatic but homozygotes typically have a severe, often fatal, disease. Thalassemia occurs most frequently in populations from the Mediterranean area and Southeast Asia.

Therapeutic range - level of a drug that is beneficial but not toxic to the individual.

Transcription error - error made in reporting test results when copying results manually from the instrument to a paper or typing them into a computer.

Threshold limit - level above which voltage pulses of particles are counted. Adjusting the threshold limit allows different types of cells to be counted.

Thrombin activatable fibrinolysis inhibitor (TAFI) - inhibitor of fibrinolysis activated by the thrombin-thrombomodulin complex, which inhibits fibrinolysis by cleaving free lysine groups on fibrin

Thrombocyte - *See* Platelet.

Thrombocytopenia - decrease in the number of platelets in the peripheral blood below the reference range for an individual laboratory (usually below 150×10^9/L).

Thrombocytopenia with absent radii (TAR) - inherited condition characterized by isolated hypoplasia of the megakaryocytic lineage, thrombocytopenia, and bilateral radial aplasial.

Thrombocytosis - increase in the number of platelets in the peripheral blood above the reference range for an individual laboratory (usually over 450×10^9/L).

Thromboembolism - blockage of a small blood vessel by a blood clot that was formed in the heart, arteries, or veins, dislodged and moved through blood vessels until reaching a smaller vessel and blocking further blood flow.

Thrombogenic - tendency to thrombose.

Thrombolytic therapy - therapy designed to dissolve or break down a thrombus.

Thrombomodulin - intrinsic membrane glycoprotein present on endothelial cells that serves as a cofactor with thrombin to activate protein C. It forms a 1:1 complex with thrombin inhibiting thrombin's ability to cleave fibrinogen to fibrin but enhances thrombin's ability to activate protein C.

Thrombophilia - tendency to form blood clots abnormally. Also referred to as *hypercoagulability*.

Thrombophlebitis - thrombosis within a vein that is accompanied by an inflammatory response, pain, and redness of the area.

Thrombopoietin - cytokine that regulates the maturation of megakaryocytes and the production of platelets.

Thrombosis - formation of a blood clot or thrombus, usually considered to be under abnormal conditions within a blood vessel.

Thrombotic thrombocytopenia purpura (TTP) - acute disorder characterized by microangiopathic anemia, decreased number of platelets, and renal failure as well as neurological symptoms. TTP is due to decreased activity of ADAMTS-13, resulting in the presence of ultralarge molecules of VWF in the circulation and platelet agglutination.

Thrombus - blood clot within the vascular system.

TIBC - total iron binding capacity; refers to the total amount of iron that transferrin can carry, about 250–450 μg/dL.

Tingible body macrophage - macrophage phagocytosing fragments of dying cells. It is found in areas of extensive apoptosis (reactive germinal centers and high-grade lymphoma).

Tissue factor - coagulation factor present on subvascular cells that forms a complex with factor VII when the vessel is ruptured. This complex activates factor X. Tissue factor is an integral protein of the cell membrane.

Tissue factor pathway inhibitor (TFPI) - intrinsic pathway inhibitor that inhibits both F-VIIa and F-Xa by forming a quarternary complex of TFPI-FXa-TF-FVIIa.

Tissue homeostasis - maintenance of an adequate number of cells to carry out the functions of the organism. Homeostasis is controlled by cell proliferation, cell differentiation, and cell death (apotosis).

Tissue plasminogen activator (t-PA) - serine protease that activates plasminogen to plasmin. It forms a bimolecular complex with fibrin increasing the catalytic efficiency of t-PA for plasminogen activation.

Toxic granules - large, dark blue-black primary granules in the cytoplasm of neutrophils that are present in certain infectious states. They are usually seen in conjunction with Döhle bodies.

Toxoplasmosis - condition that results from infection with *Toxoplasma gondii*. Acquired infection may be asymptomatic, or symptoms may resemble infectious mononucleosis. There is a leukocytosis with relative lymphocytosis or rarely an absolute lymphocytosis and the presence of reactive lymphocytes.

Trabecula - projection of calcified bone extending from cortical bone into the marrow space; provides support for marrow cells.

Transcription - synthesis of RNA from a DNA template.

Transcription factor - protein that controls when genes are switched on or off (i.e., whether genes are transcribed or not).