Waldenstrom’s Macroglobulinemia
Glossary and Abbreviations

The IWMF Vision Statement
Support everyone affected by Waldenstrom’s macroglobulinemia while advancing the search for a cure.

The IWMF Mission Statement
To offer mutual support and encouragement to the Waldenstrom’s macroglobulinemia community and others with an interest in the disease.
To provide information and educational programs that address patients’ concerns.
To promote and support research leading to better treatments and ultimately, a cure.

Published by the International Waldenstrom’s Macroglobulinemia Foundation (IWMF)

This information has been provided by the IWMF at no cost to you. Please consider joining and/or contributing to the IWMF to enable us to continue to provide materials like this to support research toward better treatments and a cure for Waldenstrom’s macroglobulinemia. You may join and/or contribute at our website, www.iwmf.com, or you may mail your contribution to: 6144 Clark Center Avenue, Sarasota, FL 34238.

IWMF is a 501(c)(3) Tax Exempt Non-Profit Organization, Fed ID #54-1784426.

Revised 2015
Preface

This glossary is designed to help patients with Waldenstrom’s macroglobulinemia to learn and understand pertinent medical terms that relate to our disease. These terms are no doubt unfamiliar to the majority of patients. However, for those who wish to build their medical vocabulary to better understand medical publications, we hope this will be a helpful guide.

Medical terminology is expanding rapidly in today’s world, and from time to time this Glossary will be updated and re-published.

The IWMF Board and Members are very fortunate to have as Trustees Guy Sherwood, MD, CCFP, ABHM, Sue Herms, and Pete DeNardis, along with a patient volunteer, Bret Blakeslee, who have diligently researched medical terms related to Waldenstrom’s macroglobulinemia and patiently developed this marvelous aid for us.

With many thanks and deep appreciation to each of them,

Judith May
Fall 2012

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Glossary for Waldenstrom’s Macroglobulinemia
Patients and Caregivers

Terms that are noted by linked underlines in a particular definition mean that a separate definition is available in the glossary.

The U.S. National Institutes of Health’s National Cancer Institute maintains an expansive on-line dictionary of cancer terms at www.cancer.gov/dictionary.

**ABO incompatibility:** Cause of transfusion reactions, in which the recipient’s isohemagglutinins (antibodies) react with the donor’s red blood cells. Patients with type O blood groups have isohemagglutinins to the A and B antigens; those with the type A blood group have isohemagglutinins to the B antigens; those with type B blood group have isohemagglutinins to the A antigen. An individual of the AB group has neither anti-A nor anti-B isohemagglutinins.

**ABT-199:** An oral drug that inhibits the anti-apoptotic protein BCL-2. It is being tested in patients with Waldenstrom’s macroglobulinemia.

**Acquired immunity:** Immunity resulting from infection or vaccination (active immunity) or by the transfer of antibodies or lymphocytes from a donor (passive immunity). It involves not only the body’s natural barriers to infection, but also the activation of white blood cells and generation of antibodies.

**Acute phase reactants:** Acute phase reactants are proteins that rise and fall with acute inflammation. Examples of acute phase reactants include C-reactive protein, C3 complement protein, fibrinogen, haptoglobin, and transferrin. Screening tests for acute phase reaction are non-specific and include the erythrocyte sedimentation rate (ESR).

**Adjuvant:** Any substance that enhances the immune response to an antigen; adjuvants may be included in vaccines to boost their efficacy.

**Afamin:** Afamin is a member of the albumin gene family, which comprises four genes that localize to chromosome 4 in a tandem arrangement. These four genes encode structurally-related serum transport proteins that are known to be evolutionarily related. The protein encoded by this gene is regulated developmentally, expressed in the liver, and secreted into the bloodstream.

**Affinity:** A measure of the binding force, or strength, of a single antigen-combining site with an antibody-combining site.

**Agglutination:** The aggregation (clumping) of antigen by antibodies. Agglutination applies to red blood cells as well as to bacteria and inert particles covered with antibodies.

**Albumin:** Albumin refers generally to any protein that is water soluble, is moderately soluble in concentrated salt solutions, and experiences heat denaturation. Albumins are commonly found in blood plasma. A number of blood transport proteins are known to be evolutionarily related, including serum albumin, alpha-fetal protein, vitamin D-binding protein and afamin. Albumin is the main protein of plasma; it binds water, cations, fatty acids, hormones, bilirubin, thyroxine, and drugs. Its main
function is to regulate the colloidal osmotic pressure of blood (the pressure which needs to be applied to a solution to prevent the inward flow of water across a semipermeable membrane).

**Alpha-fetal protein**: Alpha-fetal protein (also sometimes called alpha-1-fetoprotein or alpha-fetoglobulin) is a protein that in humans is encoded by the alpha-fetal protein gene. Alpha-fetal protein is a major plasma protein produced by the yolk sac and the liver during fetal development that is thought to be the fetal form of **serum albumin**. Alpha-fetal protein binds to copper, nickel, fatty acids, and bilirubin and is found in monomeric, dimeric and trimeric forms.

**Alkylating agent**: A chemotherapeutic agent, such as chlorambucil (Leukeran) or cyclophosphamide (Cytoxan), which blocks cell division.

**Allergen**: An antigen responsible for producing allergic reactions by inducing IgE formation.

**Allogeneic**: Having a genetic dissimilarity within the same species.

**Allogeneic transplantation**: A procedure in which a patient receives bone marrow or blood-forming stem cells from a genetically similar, but not identical, donor (a person other than an identical twin, for example).

**Allograft**: A tissue transplant (graft) between two genetically non-identical members of a species.

**Alopecia**: Hair loss, often a result of chemotherapy.

**Amino acids**: The building blocks of proteins, they are composed of amine and carboxylic acid functional groups, along with a side chain specific to each amino acid. The key elements of an amino acid are carbon, hydrogen, oxygen, and nitrogen.

**Amyloidosis**: A group of conditions of diverse etiologies characterized by the accumulation of insoluble fine protein fibers (amyloid) in various organs and tissues of the body such that vital function is compromised. The associated disease states may be inflammatory, hereditary, or neoplastic, and the deposition can be local, generalized, or systemic. Amyloidosis in Waldenström’s macroglobulinemia is usually caused by fragments of light chains and affects predominantly the kidneys and heart.

**Anaplastic**: Characteristic of a cell that has lost normal differentiation and orientation to other cells and to its axial framework and blood vessels, typical of tumor tissue.

**Anemia**: A condition in which the number of red cells or the amount of hemoglobin in the blood is abnormally low.

**Aneuploidy**: An abnormal number of chromosomes in a cell; an increase is called hyperploidy and a decrease is hypoploidy.

**Angiogenesis**: The formation of new blood vessels. Tumor angiogenesis, whereby the induction of the growth of new blood vessels to supply the tumor cells is generated by a soluble chemical mediator released by the tumor cells themselves, is increasingly becoming an important target for biological targeted cancer therapy.

**Antiangiogenesis**: The destruction of blood vessels; the prevention of angiogenesis.
Antibodies (Immunoglobulins): Proteins produced by certain white blood cells in response to a foreign substance (antigen). Each antibody can bind only to one specific antigen. Its purpose is to destroy that antigen. These structurally related proteins are formed by B-cells and plasma cells and are divided into five basic classes or isotypes (IgA, IgD, IgE, IgG, IgM) on the basis of structure and biologic activity.

Antibody-antigen complexes: Compounds formed by the attachment of an antibody to an antigen; most antibody-antigen complexes are harmless, but some may go on to form cryoprecipitable immunocomplexes, or other immunocomplexes that can cause tissue damage by activation of the immune system or by inciting an inflammatory reaction.

Antibody-dependent cell-mediated cytotoxicity (ADCC): A phenomenon in which targeted cells, coated with antibody, are destroyed by specialized killer cells (and other select cells) which bear receptors to the Fc portion of the coating antibody (Fc receptors). These receptors allow the killer cells, or select effector cells, to bind to the antibody coated target and destroy it.

Antigen: Short for antibody generator. An antigen is any foreign molecule which reacts with preformed antibody and the specific receptors on T- and B-cells; also used loosely to describe materials used for immunization. (Compare to Immunogen.)

Antigen-presenting cells: A specialized type of cell, bearing cell surface class II major histocompatibility complex antigens, involved in processing and presentation of antigen to helper T-cells.

Antimetabolite: A substance that replaces or inhibits the utilization of a metabolite. (A metabolite is usually a toxic product of metabolism.) A drug that is very similar to natural chemicals in a normal biochemical reaction in cells but different enough to interfere with the normal division and functions of cells.

Apheresis: A procedure in which whole blood is removed, a portion separated out, and the remainder returned, often with replacement fluid. (See Plasmapheresis.)

Apoptosis: Programmed cell death; a form of cell death in which the cell activates an internal death program.

Arteriosclerosis: Hardening and thickening of the walls of the smaller arteries (arterioles).

Arthralgia: Joint pain.

Asymptomatic: Without symptoms.

Ataxia: Loss of muscle coordination.

Atherosclerosis: An extremely common form of arteriosclerosis in which deposits of yellowish plaques (atheromas) containing cholesterol, lipid material, and lipophages are formed within the intima and media (inner and inner middle walls) of large and medium sized arteries.

Autoantibody: An antibody directed against a self-antigen, i.e. against a normal tissue constituent. The IgM antibody which causes peripheral neuropathy is considered an autoantibody.
**Autocrine action:** The ability of a **cytokine** to act on the cell that produced it.

**Autograft:** A tissue transplant from one site to another in a single individual.

**Autoimmune hemolytic anemia:** Hemolysis (destruction of **red blood cells**) by **autoantibodies**, as seen in certain diseases including **lymphomas**, after use of certain drugs, and for often unexplained reasons. **Cold agglutinin disease** is an autoimmune hemolytic anemia seen in some **Waldenstrom’s macroglobulinemia** patients.

**Autologous:** Derived from the same individual; “self”.

**Autologous transplantation:** A procedure in which **bone marrow** or blood-forming **stem cells** (cells from which all blood cells develop) are removed, stored, and later given back to the same person.

**Avidity:** The summation of multiple affinities, for example when an **antibody** binds to an **antigen** at multiple areas on both antibody and antigen.

**Axilla:** The underarm or armpit.

**B-cells / B-lymphocytes:** **White blood cells** formed in the **bone-marrow** by **hematopoietic stem cells**; precursors of **antibody**-forming **terminally differentiated plasma cells**. B-cells carry **immunoglobulin** and **class II MHC antigens** on their cell surfaces. **Waldenstrom’s macroglobulinemia** is a disorder of the B-cells.

**B-cell receptor:** A **protein** located on the outer surface of **B-cells**. When a B-cell is activated by its first encounter with an **antigen** that binds to the **variable** portion of this receptor, the cell proliferates and differentiates to generate a population of **antibody**-secreting **plasma cells** and **memory B-cells**. This receptor also helps with processing of antigen and presentation of antigen proteins to **helper T-cells**.

**B-R:** An abbreviation for a **chemoimmunotherapy treatment** combination consisting of **bendamustine** (Treanda) and **rituximab** (Rituxan).

**Basophils:** **White blood cells** that stain blue with specific basic dyes and are involved in the release of histamine and serotonin when stimulated, usually in an allergic reaction.

**BDR:** An abbreviation for a **treatment** combination consisting of **bortezomib** (Velcade), **dexamethasone**, and **rituximab** (Rituxan).

**Bence-Jones proteins:** Abnormal two-unit (dimers) complexes of **immunoglobulin light chains** found in the urine of some patients, particularly those with **multiple myeloma** and **Waldenstrom’s macroglobulinemia**.

**Bendamustine (Treanda):** A drug that is used to treat **chronic lymphocytic leukemia (CLL)** and slow-growing **B-cell non-Hodgkin’s lymphomas (NHL)** such as **Waldenstrom’s macroglobulinemia**. Bendamustine damages the **DNA** in cancer cells and cause them to die. It is a type of **alkylating agent** and a type of **antimetabolite**.

**Benign:** Not cancerous. Benign **tumors** may grow larger but do not spread to other parts of the body.
**Beta-2-microglobulin:** Cell membrane associated [protein](#) (part of the [class I major histocompatibility complex molecule](#)) that is specifically elevated in [inflammation](#), renal disease, AIDS, and in some cancers, including [Waldenstrom’s macroglobulinemia](#), [chronic lymphocytic leukemia](#), and [multiple myeloma](#). Urine levels of beta-2-microglobulin can be affected by kidney disease.

**Bifunctional:** In the case of [antibodies](#), his means having two functions (e.g. binding to [antigen](#) at the [Fab](#) ends of the antibody, and activating [immune system](#) cells or complement at the [Fc](#) end of the antibody).

**Biliary:** Having to do with the liver, bile ducts, and/or gallbladder.

**Bilirubin:** Bilirubin (formerly referred to as hematoidin) is the yellow breakdown product of normal heme catabolism. Heme is found in [hemoglobin](#), a principal component of [red blood cells](#). Bilirubin is excreted in bile and urine, and elevated levels may indicate certain diseases. It is responsible for the yellow color of bruises, the yellow color of urine (via its reduced breakdown product, urobilin), the brown color of feces (via its conversion to stercobilin), and the yellow discoloration in jaundice.

**Bing-Neel syndrome:** A condition that involves infiltration of the central nervous system (brain and spinal cord) by [Waldenstrom’s macroglobulinemia cells](#) and/or [IgM](#) deposition, or as a result of [hyperviscosity syndrome](#).

**Bioavailability:** The degree and rate at which a substance is absorbed into the body.

**Biomarker:** A biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment.

**Biopsy:** Surgical removal of a small piece of tissue or bone for microscopic evaluation.

**Blood cells or whole blood cells:** Blood is a specialized bodily fluid in animals that delivers necessary substances such as nutrients and oxygen to the cells and transports metabolic waste products away from those same cells. In [vertebrates](#), it is composed of blood cells suspended in a liquid called [blood plasma](#).

**Blood plasma:** The fluid part of [blood](#) and [lymph](#). Plasma, which constitutes 55% of blood fluid, is mostly water (92% by volume), and contains dissipated [proteins](#), glucose, mineral ions, hormones, carbon dioxide (plasma being the main medium for excretory product transportation), platelets, and [blood cells](#) themselves. [Albumin](#) is the main protein in plasma, and it functions to regulate the colloidal osmotic pressure of blood.

**Blood serum:** Blood serum is [blood plasma](#) with the [fibrinogens](#) removed. Serum includes all [proteins](#) not used in blood clotting (coagulation) and all the electrolytes, [antibodies](#), [antigens](#), hormones, and any exogenous substances (e.g., drugs and microorganisms).

**Blood type:** A blood type (also called a blood group) is a classification of [blood](#) based on the presence or absence of inherited [antigenic](#) substances on the surface of [red blood cells](#). These antigens may be [proteins](#), carbohydrates, glycoproteins, or glycolipids, depending on the blood group system. Some of these antigens are also present on the surface of other types of cells of various tissues. Several of these surface antigens can collectively form a blood group system. Blood types are inherited and represent contributions from both parents. There are 8 blood types in the standard ABO blood group; (type and mean average in the general population) O+...
(36.44%), O- (4.33% - universal donor), A+ (28.27%), A- (3.52%), B+ (20.59%), B- (1.39%), AB+ (5.06% - universal recipient), and AB- (0.45%)

**ABO blood group system:** The ABO system is the most important blood-group system in human blood transfusion. The associated anti-A and anti-B antibodies are usually immunoglobulin M antibodies. ABO immunoglobulin M antibodies are produced in the first years of life by sensitization to environmental substances such as food, bacteria, and viruses. The O in ABO is often called 0 (zero, or null) in other languages.

**Blood group AB:** These individuals have both A and B antigens on the surface of their RBCs, and their blood serum does not contain any antibodies against either A or B antigen. Therefore, an individual with type AB blood can receive blood from any group (with AB being preferable), but can donate blood only to another type AB individual.

**Blood group A:** These individuals have the A antigen on the surface of their RBCs and blood serum containing IgM antibodies against the B antigen. Therefore, a group A individual can receive blood only from individuals of groups A or O (with A being preferable) and can donate blood to individuals with type A or AB.

**Blood group B:** These individuals have the B antigen on the surface of their RBCs and blood serum containing IgM antibodies against the A antigen. Therefore, a group B individual can receive blood only from individuals of groups B or O (with B being preferable) and can donate blood to individuals with type B or AB.

**Blood group O:** (or blood group zero in some countries) These individuals do not have either A or B antigens on the surface of their RBCs, but their blood serum contains IgM anti-A and anti-B antibodies against the A and B blood group antigens. Therefore, a group O individual can receive blood only from a group O individual but can donate blood to individuals of any ABO blood group (i.e., A, B, O or AB). If a patient in a hospital situation were to need a blood transfusion in an emergency, and if the time taken to process the recipient’s blood would cause a detrimental delay, O Rh negative blood can be issued.

**Rh blood group system:** The Rh system is the second most significant blood-group system in human blood transfusion with currently 50 antigens. The most significant Rh antigen is the D antigen, because it is the most likely to provoke an immune response. It is common for D-negative individuals not to have any anti-D IgG or IgM antibodies, because anti-D antibodies are not usually produced by sensitization against environmental substances. However, D-negative individuals can produce IgG anti-D antibodies following a sensitizing event: possibly a fetomaternal transfusion of blood from a fetus in pregnancy or occasionally a blood transfusion with D positive RBCs. Rh disease can develop in these cases. Rh negative blood types occur less frequently in Asian populations (0.3%) than in Caucasians (15%).

**Blood vessel:** Blood vessels are the part of the circulatory system and transport blood throughout the body. There are three types of blood vessels.
**Artery:** A [blood vessel](#) that carries oxygen-rich [blood](#) from the heart to the body. An arteriole is a small diameter [blood vessel](#) in the microcirculation that extends and branches out from an artery and leads to [capillaries](#).

**Capillary:** A capillary enables the actual exchange of water, chemicals, and oxygen between the [blood](#) and the tissues.

**Intima:** Intima (or tunica intima) is the innermost layer of an [artery](#) or [vein](#) and is in direct contact with the [blood](#) flow.

**Media:** The media (or tunica media - middle coat) is the middle layer of an [artery](#) or [vein](#).

**Vein:** A [blood vessel](#) of varying size that carries [blood](#) to the heart after the cells have extracted the oxygen from the blood. A [venule](#) is a very small [blood vessel](#) in the microcirculation that allows deoxygenated blood to return from the [capillary](#) beds to the larger veins.

**Bone marrow:** Spongy tissue occupying the hollow central cavity of bones that is the site of [hematopoiesis](#). Following puberty, the marrow located in the spine, ribs, breastbone, hip, shoulders, and skull is most active in [blood cell](#) formation. In the adult, the bones of the hands, feet, legs and arms do not contain marrow in which blood cells are made. In these sites, the marrow is filled with fat cells.

**Bone marrow ablation:** A procedure to destroy [bone marrow](#) using radiation or high doses of anticancer drugs. It is done before a bone marrow or blood [stem cell transplant](#) to kill cancer cells and bone marrow cells. This makes room for healthy stem cells.

**Bone marrow aspiration:** A bone marrow aspiration is the removal by needle of fluid and [cells](#) from the [bone marrow](#).

**Bone marrow biopsy (BMB):** A bone marrow biopsy is the removal of soft tissue, called [bone marrow](#), from inside bone. Bone marrow is found in the hollow part of most bones. The sample is usually taken from the hip bone.

**Bone marrow microenvironment:** The immediate neighborhood of the cells in the [bone marrow](#); comprises cells that facilitate the survival, differentiation, and proliferation of hematopoietic cells.

**Bone marrow transplant:** A bone marrow transplant is a procedure to replace damaged or destroyed [bone marrow](#) with healthy bone marrow [stem cells](#). There are three kinds of bone marrow transplants. The first is the [autologous](#) bone marrow transplant ("auto" means "self") where stem cells are removed before the patient receives high-dose [chemotherapy](#) or radiation [treatment](#). After these treatments are done, stems cells are given back to the patient. The second is the [allogeneic](#) bone marrow transplant ("allo" means "other") where stem cells are removed from another person, called a donor. Most times, the donor must have the same or similar genetic makeup as the patient, so that he or she is a "match" to the recipient. Special blood tests are done to determine if a donor is a good match, and a brother or sister is most likely to be a good match. However, sometimes parents, children, and other relatives may be good matches. Donors who are not related to the patient may be found through national bone marrow registries. The third kind of bone marrow transplant is the [umbilical cord blood](#).
transplant where stem cells are removed from a newborn baby’s umbilical cord immediately after being born. The stem cells are stored until they are needed for a transplant. Umbilical cord blood cells are so immature that there is less of a concern that they will not match.

Bortezomib (Velcade): A drug used for the treatment of multiple myeloma and certain types of lymphoma, including Waldenstrom’s macroglobulinemia. It is in the drug class called proteasome inhibitors.

Bruton’s tyrosine kinase (BTK): An enzyme important in the development and activation of B-cells; it is over-expressed in Waldenstrom’s macroglobulinemia and is targeted by a drug called ibrutinib (Imbruvica).

Bruton’s tyrosine kinase (BTK) inhibitor: Any drug that suppresses the expression of Bruton’s tyrosine kinase; ibrutinib (Imbruvica) is one example.

CAR T-cell therapy: This is based on the principle that the T-cells in one’s own body can be used to seek out and kill cancer cells. In this type of therapy, receptors on the surface of one’s T-cytotoxic cells can be modified in the laboratory to recognize certain specific antigens on one’s tumor cells—these engineered T-cells are called chimeric antigen receptor (CAR) T-cells. They are grown in large quantities in the laboratory and then infused into the patient, where they seek out and destroy the tumor. This type of therapy is still being tested in clinical trials and is not yet available clinically.

CaRD: An abbreviation for a treatment combination consisting of carfilzomib (Kyprolis), rituximab (Rituxan), and dexamethasone.

Carfilzomib (Kyprolis): A newer member in the family of drugs called proteasome inhibitors that are used for the treatment of multiple myeloma and certain types of lymphoma, including Waldenstrom’s macroglobulinemia.

Catheter: A thin, flexible tube through which fluids enter or leave the body.

Cation: A cation is an ion with a net positive charge. An ion is an atom or molecule in which the total number of electrons is not equal to the total number of protons, giving it a net positive or negative electrical charge. A hydrogen atom contains a single proton and a single electron. Removal of the electron (with its negative charge) gives a cation, whereas addition of an electron (with its negative charge) gives an anion.

CD Markers (CD4, CD20, etc): See Cluster of differentiation.

Cell line: A family of constantly dividing cells, the product of a single cell. They are obtained from human or animal tissues and can replicate for long periods of time in vitro (in the lab). They are frequently used for research relating to embryonic stem cells, cloning of entire organisms, or the study of cancers and other diseases.

Cell surface receptors: Cell surface receptors (also known as surface receptors, membrane receptors, or transmembrane receptors) are specialized integral membrane proteins that take part in communication between the cell and the outside world. Extracellular signaling molecules (usually hormones, neurotransmitters, cytokines, growth factors, or cell recognition molecules) attach to the receptor, triggering changes in the function of the cell. This process is called signal transduction.
where the binding initiates a chemical change on the intracellular side of the membrane. In this way the receptors play a unique and important role in cellular communications and signal transduction.

**Chemoimmunotherapy:** The use of chemotherapy combined with immunotherapy. Chemotherapy uses drugs to kill or slow the growth of cancer cells; immunotherapy uses treatments such as monoclonal antibodies, growth factors, and vaccines to stimulate or restore the ability of the immune system to fight cancer. A common chemoimmunotherapy regimen is CHOP combined with rituximab, so-called R-CHOP.

**Chemokines:** These are cytokines produced by specialized immune cells that have cell-activating properties, and encourage migration, or attraction, of a target cell toward the concentration gradient (a change in the concentration of the subject item) of the chemokine in question.

**Chemotherapy:** Often just called chemo, this is a treatment with one or more of a specific group of anti-cancer drugs such as fludarabine, cyclophosphamide, CHOP, or CVP. Traditional chemotherapy agents are cytotoxic and act on cells that divide rapidly, one of the main properties of most cancer cells. They can also harm normal cells that divide rapidly, including cells of the bone marrow, digestive tract, and hair follicles. Even if a single chemo drug is given, it is often combined with pre-medicating drugs to reduce the side-effects of the main drug.

**Chlorambucil (Leukeran):** A drug used to treat several types of leukemias and lymphomas. It blocks cell growth by damaging the cell’s DNA and kills cancer cells. It is a type of alkylating agent.

**CHOP:** An abbreviation for a chemotherapy combination that is used to treat non-Hodgkin’s lymphoma and other types of cancer. It includes the drugs Cytoxan, hydroxydoxorubicin (also known as Doxorubicin or Adriamycin), Oncovin (also known as vincristine), and prednisone.

**Chromosomes:** Thread-like structures inside the nucleus of each cell that package the DNA. There are 23 pairs of chromosomes in most human body cells (except eggs and sperm), for a total of 46 chromosomes.

**Chronic lymphocytic leukemia (CLL):** Chronic lymphocytic leukemia is a type of cancer of the blood and bone marrow, the spongy tissue inside bones where blood cells are made. The term "chronic" in chronic lymphocytic leukemia comes from the fact that it typically progresses more slowly than other types of leukemia. The term "lymphocytic" refers to the cells affected by the disease - a group of white blood cells called lymphocytes which help the body fight infection. Chronic lymphocytic leukemia most commonly affects older adults.

**Cladribine (2CdA / Leustatin):** An anticancer drug that belongs to the family of drugs called nucleoside analogs.

**Class I major histocompatibility complex molecules (class I MHC):** Proteins expressed on the cell surface of virtually all cells that are used to present antigenic material to CD8 T-cytotoxic cells. The class I MHCs are therefore important in the recognition of self by the immune system, and for the identification of a virally infected cell or a cell that has become malignant.

**Class II major histocompatibility complex molecules (class II MHC):** Proteins expressed on the cell surface of macrophages and other antigen-presenting cells of the immune system that identify the target antigen to the T-helper cells. Class II MHCs play a pivotal role in the activation of CD4 T-helper cells.
**Class switch recombination:** The process by which an individual B-cell or its progeny can link immuneoglobulin heavy chain constant (C) genes to its recombined variable (V) gene to produce a different class (or isotype) of antibody with the same specificity. This process is irreversible (change from IgM production to IgG production, but not the reverse).

**Clinical trial:** A type of research study that tests how well new medical approaches work in people. These studies test new methods of screening, prevention, diagnosis, or treatment of a disease.

**Clonal:** Pertaining to a clone (i.e. from a single parent). Monoclonal IgM, as found in Waldenstrom’s macroglobulinemia, is the product of cells having a single direct parent (the malignant clone). The cancer cells of Waldenstrom’s macroglobulinemia are thus identical or monoclonal.

**Clonal selection:** The fundamental basis of lymphocyte activation in which antigen selectively causes activation, division, and differentiation only in those cells which express receptors with which it can combine. (See Clone.)

**Clone:** One of more of a group of genetically identical cells derived by reproduction from a single parent.

**Cluster of differentiation (CD):** Cluster of differentiation is a system used for the identification and investigation of cell surface molecules present on leukocytes and platelets initially but found in almost any kind of cell of the body, providing targets for immunophenotyping and for treatment with monoclonal antibodies. Also, these markers are often used to associate cells with certain immune functions. While using one CD molecule to define populations is uncommon (though a few examples exist), combining markers has allowed for cell types with very specific definitions within the immune system (i.e., the “cluster” of differentiation).

- **CD4:** Cluster of differentiation molecule 4 is a cell surface receptor protein of helper T-cells and other white blood cells. CD4 causes T-cells to proliferate in response to antigens, and it causes B-cells to produce immunoglobulins. CD4 also serves as the receptor for the human immunodeficiency virus (AIDS virus).

- **CD4 T-cells:** CD4 T-cells are a cluster of differentiation molecule for a functional subclass of T-cells, expressing the CD4 marker on their cell surfaces that help trigger B-cells to make antibodies. Helper T-cells also help generate cytotoxic T-cells. Helper T-cells recognize antigen in association with class II major histocompatibility complex molecules.

- **CD4/CD8 ratio:** The ratio of CD4 T-helper cells to CD8 T-suppressor/cytotoxic cells is normally 1.5-2.0. In AIDS this ratio is the single best monitor of the patient’s clinical status, where less than 0.5 is commonly seen, and values of 0.1 or less predict clinical deterioration. The ratio is most commonly determined by flow cytometry.

- **CD8:** CD8 is a cluster of differentiation cell surface receptor protein that is a marker for T-cells with suppressor and cytotoxic activity (Tc); binds to class I major histocompatibility complex antigens on antigen presenting cells.

- **CD8 Tc-cells:** CD8 Tc-cells are a functional subclass of cytotoxic T-cells that express the CD8 marker on their cell surface. CD8 Tc-cells can kill malignant or virally infected target cells that have antigenic fragments presented by class I major histocompatibility complex molecules on their cell membrane.
CD20: **Cluster of differentiation** molecule **B-lymphocyte antigen** CD20 or just CD20 is expressed on the surface of all **B-cells** beginning at the pro-B phase and progressively increasing in concentration until maturity. The **protein** has no known natural **ligand**, and its function is to enable optimal B-cell **immune response**, specifically against T-independent **antigens**. It is suspected that it acts as a calcium channel in the cell membrane. CD20 is the target of the **monoclonal antibodies** rituximab, liritumomab tiuxetan, and tositumomab, which are all active agents in the **treatment** of all B-cell **lymphomas** and **leukemias** (like Waldenström’s macroglobulinemia).

CD34: CD34 is a **cluster of differentiation** molecule for **hematopoietic stem cells** and is useful for their identification and isolation. It may also mediate the attachment of stem cells to bone marrow extracellular matrix or directly to stromal cells. CD34 is an important adhesion molecule and is required for **T-cells** to enter lymph nodes. Conversely, under other circumstances CD34 has been shown to act as molecular "Teflon" and block mast cell adhesion or to facilitate opening of vascular lumens. Regardless of its mode of action, under all circumstances CD34 has been shown to facilitate cell migration. CD34 is also the name for the human **gene** that encodes the **protein**.

Cofactor: A cofactor is a non-**protein** chemical compound that is bound to a protein and is required for the protein’s biological activity. These proteins are commonly **enzymes**, and cofactors can be considered "helper molecules" that assist in biochemical transformations. Cofactors work by changing the shape of an enzyme or by actually participating in the enzymatic reaction.

Cold agglutinin disease (CAD): An **autoimmune hemolytic anemia** caused by **autoantibodies** that bind to red blood cells at temperatures reached in the capillaries of the skin and subcutaneous tissues, causing red blood cell destruction (hemolysis). The **antibodies** are monoclonal in origin, having either kappa or lambda light chains but not both, and are seen in certain patients with Waldenström’s macroglobulinemia.

Colony-stimulating factors: Colony-stimulating factors (also called growth factors) are a group of **cytokines** which control the differentiation of **hematopoietic stem cells** and which stimulate the development of those cells in the **bone marrow**.

Combination therapy: **Treatment** that uses more than one drug or modality.

Comorbidity: The condition of having two or more diseases at the same time.

Complement-dependent cytotoxicity (CDC): The mechanism of cell destruction by activation of the complement **protein** cascade initiated by the formation of **antigen-antibody complexes**.

Complement proteins: A group of **serum proteins** involved in the control of inflammation, the activation of phagocytes, and the attack on cell membranes causing cell lysis. The system can be activated by interaction with the **antibodies** of the **immune system** (classical pathway).

Complete blood count (CBC): A complete blood count is a test panel requested by a doctor or other medical professional that gives information about the cells in a patient's blood. The cells that circulate in the bloodstream are generally divided into three types; white blood cells (leukocytes), red blood cells (erythrocytes), and platelets (thrombocytes). Abnormally high or low counts may indicate the presence of many forms of disease, and hence blood counts are amongst the most commonly
performed blood tests in medicine, as they can provide an overview of a patient’s general health status.

**Red blood cell count:** A red blood cell count is a useful blood test that can provide information about how many red blood cells are in a person's blood as one component of a complete blood count.

**White blood cell count:** The white blood cell count is used as part of a full complete blood count to screen for a wide range of diseases and conditions; to help diagnose an infection or inflammatory process; to determine the presence of other diseases that affect white blood counts such as allergies, leukemia or immune disorders, to name a few; to monitor the progression of conditions such as those named above; to monitor the body's response to various treatments, and/or to monitor bone marrow function. Some treatments, such as radiation and chemotherapy, are known to affect white blood cells and may be monitored using white blood cell counts.

**Complete response (CR):** In Waldenstrom's macroglobulinemia, a complete response following treatment is defined as the absence of serum monoclonal IgM by immunofixation, normal serum IgM level, complete resolution of enlarged lymph nodes and enlarged spleen if present at baseline, and normal bone marrow aspirate and biopsy.

**Comprehensive metabolic panel (CMP):** A panel of 14 blood tests which serves as an initial broad screening tool for physicians, nurse practitioners, and physician assistants. Because it is often ordered as a routine part of an annual physical examination or check-up, over time the CMP provides an important baseline of a patient's basic physiology. Any changes or abnormal results, and in particular combinations of abnormal results, thus provide important initial data for differential diagnosis, in which case more specialized tests may be indicated. In and of itself, however, the CMP provides an important gross check on the status of kidney function, liver function, and electrolyte and fluid balance. In addition to being used at routine physicals of healthy patients, the CMP is routinely administered to monitor the status of a patient with a chronic disease.

**Constitutional symptoms:** Constitutional symptoms refer to a group of symptoms that can affect many different parts of the body. Examples include weight loss, fevers, fatigue, and malaise. Other examples include chills, night sweats, and decreased appetite. Generally, they are very nonspecific, with a vast number of diseases and conditions as potential causes, thereby requiring further evaluation for any diagnosis.

**Computerized axial tomography (CT or CAT) scan:** Commonly called a CAT scan, this is an X-ray procedure that uses a computer to produce a detailed picture of a cross section of the body. Adding intravenous contrast material helps outline blood vessels and kidney function, whereas oral contrast helps better define organs such as the stomach and intestines.

**Constant region:** The terminal portion of an antibody's heavy and light chains, which does not vary within distinct immunoglobulin classes.

**C-reactive protein (CRP):** A protein found in the blood, the level of which rises with inflammation.

**Cryoglobulin(s):** Abnormal proteins detected in the laboratory by chilling serum to below 32 degrees Celsius where the proteins become insoluble. At a normal body temperature of 37 degrees Celsius,
Cryoglobulins are soluble. Serum specimens from patients with cryoglobulins must be kept warm until testing.

**Cryoglobulinemia:** Clinical disease characterized by cryoglobulins in the serum; often associated with immune complex antigen-antibody (cryoprecipitable immunocomplex) deposits in the kidneys and other tissues. Three types of cryoglobulinemia have been described: Type I (monoclonal cryoglobulinemia); Type II (mixed cryoglobulinemia) was first noted in Waldenström's macroglobulinemia, and can be seen as well is seen in auto-immune disorders; Type III (mixed polyclonal-polyonal cryoglobulinemia) can be seen with auto-immune diseases, infections, and other medical diseases.

**Cryoprecipitable immunocomplex:** Precipitate formed when an antibody-cryoglobulin immune complex is exposed to temperatures below normal body temperature of 37 degrees Celsius. Clinical findings include joint pain, red non-blanching rashes, cold intolerance (particularly of the extremities such as the fingers, toes and nose), and other symptoms.

**CT or CAT (computerized axial tomography) scan:** See Computerized axial tomography scan.

**CVP:** An abbreviation for a chemotherapy combination used to treat slow-growing forms of non-Hodgkin's lymphoma (NHL) and chronic lymphocytic leukemia (CLL). It includes the drugs Cytoxan, Oncovin (also called vincristine), and prednisone.

**CXCR4:** A chemokine that is important in the homing of stem cells to the bone marrow. Mutations in CXCR4 have recently been identified in approximately 25-30% of patients with Waldenström's macroglobulinemia and may impact the clinical presentation and overall survival in patients with the disease.

**Cyclophosphamide (Cytoxan):** A drug used to treat many types of cancer; it attaches to DNA in cells and kills cancer cells. It is a type of alkylating agent.

**Cytokines (lymphokines):** A generic term for non-antibody proteins released by one cell population which act as intercellular mediators, as in the generation of an immune response.

**Cytomegalovirus (CMV):** A type of herpes virus that may be carried in an inactive state for life by healthy individuals but may be dangerous in people with suppressed immune systems.

**Cytopenias:** Lower-than-normal numbers of blood cells. See leukopenia, lymphopenia, neutropenia, and thrombocytopenia.

**Cytoplasm:** The cytoplasm is the gel-like substance residing between the cell membrane holding all the cell's internal sub-structures (called organelles), except for the nucleus.

**Cytotoxicity:** Cytotoxicity is the quality of being toxic to cells.

**Denaturation:** Denaturation is a process in which proteins or nucleic acids lose the tertiary structure and secondary structure which is present in their native state, by application of some external stress or compound such as a strong acid or base, a concentrated inorganic salt, an organic solvent (e.g., alcohol or chloroform), or heat. If proteins in a living cell are denatured, this results in disruption of cell activity and possibly cell death. Denatured proteins can exhibit a wide range of characteristics, from loss of solubility to communal aggregation.
Dendritic cells: A set of immune cells present in tissues, which capture antigens and migrate to the lymph nodes and spleen, where they are particularly active in presenting the processed antigen to T-cells.

Deoxyribonucleic acid (DNA): Deoxyribonucleic acid is a nucleic acid containing the genetic instructions used in the development and functioning of all known living organisms (with the exception of ribonucleic acid viruses). The deoxyribonucleic acid segments carrying this genetic information are called genes. Likewise, other deoxyribonucleic acid sequences have structural purposes, or are involved in regulating the use of this genetic information. Along with ribonucleic acid and proteins, deoxyribonucleic acid is one of the three major macromolecules that are essential for all known forms of life.

Dexamethasone: A synthetic steroid (similar to steroid hormones produced naturally in the adrenal gland). Dexamethasone is used to treat leukemia and Lymphoma and may be used to treat some of the problems caused by other cancers and their treatment.

Diagnosis: A diagnosis is the identification of the nature and cause of anything. Diagnosis is used in many different disciplines with variations in the use of medicine, logics, analytics, and experience to determine the cause and effect relationships.

Diffuse large B-cell lymphoma (DLBCL): A cancer of B-cells, it is the most common type of non-Hodgkin’s lymphoma in adults. It is an aggressive cancer that usually arises from normal B-cells, but it can also represent a malignant transformation from another type of leukemia or lymphoma. It is most commonly characterized by rapidly enlarging lymph nodes, fever, weight loss, and night sweats.

Dilation: Enlargement.

Diploid: Diploid is the term used when human cells, excluding sperm or egg, exhibit the normal number of chromosomes. Diploid cells have two copies of each chromosome, usually one from the mother and one from the father. Nearly all mammals are diploid organisms. Human diploid cells have 46 chromosomes and human haploid gametes (eggs and sperm) have 23 chromosomes.

Domain: A compact segment of an immunoglobulin molecule, made up of about 110 amino acids around a disulfide bond, encoded by a unique segment of DNA and surrounded by non-translated sequences.

DRC: An abbreviation for a chemoimmunotherapy treatment combination consisting of dexamethasone, rituximab (Rituxan), and cyclophosphamide (Cytoxan).

Ear, nose, and throat: Otolaryngology or ENT (ear, nose, and throat) is the branch of medicine and surgery that specializes in the diagnosis and treatment of disorders of the head and neck.

Effector cells: Cells that perform a specific function in response to a stimulus; usually used to describe cells in the immune system such as natural killer cells, neutrophils, macrophages, etc.

Effector functions: The end effect(s) of effector cells, which are cells of the immune system. These end effects primarily involve the inflammatory response to a stimulus and vary according to the special type of cell involved.

Efficacy: Effectiveness; the ability of a treatment to produce the desired result.
**Endothelial**: Pertaining to the layer of cells that line the cavities of the heart and of the blood and lymph vessels. (See Vascular endothelium.)

**Engorgement**: Filling with blood to the point of congestion, i.e. engorgement of retinal veins.

**Enzymes**: Enzymes are proteins that catalyze (i.e., increase the rates of) chemical reactions. In enzymatic reactions, the molecules at the beginning of the process, called substrates, are converted into different molecules, called products. Almost all chemical reactions in a biological cell need enzymes in order to occur at rates sufficient for life. Since enzymes are selective for their substrates and speed up only a few reactions from among many possibilities, the set of enzymes made in a cell determines which metabolic pathways occur in that cell.

**Eosinophils**: A population of leukocytes (white blood cells) which stain with acidic dyes (red) and which are particularly involved in reactions against parasitic worms and in some hypersensitivity reactions involving IgE.

**Epigenetics**: The study of inherited changes in phenotype (appearance) or gene expression caused by mechanisms other than changes in the DNA. These changes may remain through cell divisions for the remainder of the cell’s life and may also last for multiple generations. However, there is no change in the underlying DNA sequence of the organism; instead, non-genetic factors (stress, environment, diet) cause the organism’s genes to behave differently.

**Epithelial tissues**: Epithelium is one of the four basic types of animal tissue, along with connective tissue, muscle tissue and nervous tissue. Epithelial tissues line the cavities and surfaces of structures throughout the body and also form many glands. Functions of epithelial cells include secretion, selective absorption, protection, transcellular transport, and detection of sensation.

**Epitope**: The part of an antigen that an antibody will recognize and bind to.

**Epstein-Barr virus (EBV)**: A herpes virus that causes infectious mononucleosis and is associated with the development of Burkitt’s lymphoma, nasopharyngeal carcinoma, and lymphoma in immunocompromised patients.

**Erythrocyte sedimentation rate (ESR)**: The erythrocyte sedimentation rate, also called a sedimentation rate or Westergren erythrocyte sedimentation rate, is the rate at which red blood cells settle to the bottom of a test tube in a period of 1 hour. It is a common hematology test and is a non-specific measure of inflammation.

**Erythrocytes (red blood cells / RBCs)**: The blood cells that contain hemoglobin. Hemoglobin binds oxygen when red blood cells pass through the lung and releases it to the tissues of the body. The red blood cells make up a little less than half the volume of blood in healthy individuals.

**Erythropoietin**: A hormone produced mainly by the kidneys that is required for the normal production of red blood cells. Released into the bloodstream in response to decreased levels of oxygen in the blood (as in anemia), erythropoietin (EPO) interacts with the EPO receptor on red blood cell progenitors to increase production of red blood cells. Epoetin alfa (Epogen, Procrit) and darbepoetin alfa (Aranesp) are laboratory-made forms of the human hormone EPO that can be used to treat anemia.
**Etiology:** In medicine, the term refers to the causes of diseases or pathologies. Where no etiology can be ascertained, then the disorder is said to be idiopathic.

**Everolimus (RAD001 or Afinitor):** A drug that inhibits mammalian target of rapamycin (mTOR) and is used for the treatment of relapsed Waldenstrom’s macroglobulinemia.

**Extramedullary disease:** manifestation of a lymphoid mass outside of the bone marrow. In some Waldenstrom’s macroglobulinemia patients, tissue masses do occur in such regions.

**Fab:** The fragment of antibody containing the antibody-binding site, consisting of a light chain and part of the heavy chain; generated by cleavage of the antibody with the enzyme papain, which cuts at the hinge region.

**Fc:** The fragment of antibody without antigen-binding sites, responsible for binding to antibody receptors on cells and complement; generated by cleavage of the antibody with papain. The Fc fragment contains the constant (C) terminal domains of the immunoglobulin heavy chains.

**Fc receptors:** Surface molecules on a variety of cells that bind to the Fc regions of immunoglobulins. They are antibody class specific and isotype selective.

**Fibrin:** Fibrin (also called Factor Ia) is a fibrous, non-globular protein involved in the clotting of blood. It is formed from fibrinogen and is then polymerized to form a "mesh," with the end result of a hemostatic plug or clot (in conjunction with platelets) over a wound site.

**Fibrinogen:** A protein present in the blood plasma that, through the action of thrombin in the presence of calcium ions, is converted into fibrin. This is essential for clotting of the blood.

**Fibroblast:** Any cell from which connective tissue is developed. Fibroblasts can differentiate into osteoblasts (amongst others) which are found in bone.

**FISH (fluorescence in situ hybridization) analysis:** A laboratory technique used to look at genes and chromosomes in cells and tissues. Pieces of DNA that contain a fluorescent dye are made in the laboratory and added to cells or tissues on a glass slide. When these pieces of DNA bind to specific genes or areas of chromosomes on the slide, they light up when viewed under a microscope with a special light.

**Flow cytometry:** Flow cytometry is a technique for counting and examining microscopic particles, such as cells. These cells are suspended in a stream of fluid, and a beam of light (usually a laser) is passed through the stream. An electronic detection apparatus measures the way in which the cells scatter (bounce) the light, and analysis of the scatter can determine the physical structure of the cells. Flow cytometers can also use antibodies tagged with fluorescent stains that bind to specific antigens on the cell surfaces. When a stain is added to the cell sample, a laser beam excites the cells so that they fluoresce and emit a specific color of light, depending of the type of stain used.

**Fludarabine (Fludara):** The active ingredient in a drug used to treat chronic lymphocytic leukemia (CLL) and non-Hodgkin’s lymphomas, including Waldenstrom’s macroglobulinemia. Fludarabine blocks cells from making DNA and kills cancer cells. It is a type of nucleoside analog.

**Follicles:** Large areas of B-cells, organized around dendritic cells and found in peripheral lymphoid tissues, such as lymph nodes, spleen, and Peyer’s patches.
**Follicular lymphoma (FL):** Follicular lymphoma is the most common of the indolent non-Hodgkin’s lymphomas and the second-most-common form of non-Hodgkin’s lymphoma overall. It is defined as a lymphoma of follicle center B-cells (centrocytes and centroblasts), which has at least a partially follicular pattern. It is positive for the B-cell markers CD10, CD19, CD20, and CD22 but almost always negative for CD5.

**Funduscopic exam:** The examination of the back of the eye (fundus) with an ophthalmoscope; it allows a magnified evaluation of the blood vessels, nerves, and retina.

**Gamma glutamyl transferase:** An enzyme that is very sensitive to biliary (bile duct) obstruction. Gamma glutamyl transferase is located on the cell membrane and is involved in amino acid transport across cell membranes. It is most abundant in the liver but is also present in the kidney and pancreas. It is used in the diagnosis of liver disease, gallbladder disease, and is especially sensitive to alcohol intake.

**Gastroesophageal reflux disease (GERD):** Gastroesophageal reflux disease is a condition in which the stomach contents (food or liquid) leak backwards from the stomach into the esophagus (the tube from the mouth to the stomach). This action can irritate the esophagus, causing heartburn and other symptoms.

**Gastrointestinal (GI):** Adjective referring collectively to the esophagus, stomach, small intestine, large intestine, and anus.

**Gene:** A region of DNA that controls a hereditary trait in an individual.

**General practitioner (GP):** A general practitioner is a medical practitioner who treats acute and chronic illnesses and provides preventive care and health education for all ages and all sexes.

**Genome:** See Genotype.

**Genome sequencing:** Any method or technology for determining the order of DNA found in the genes of an individual.

**Exome sequencing:** A technique for sequencing only the protein-coding genes in a genome. It consists of first selecting only the subset of DNA that encodes proteins (known as exons) and then sequencing that DNA. There are 180,000 exons in a human genome, or approximately 1% of the total DNA; mutations that affect the exons are much more likely to have severe consequences than those in the remaining 99% of the human genome.

**Whole genome sequencing:** A technique that determines the complete DNA sequence of a genome.

**Genotype:** The entire genetic constitution of an individual; also called genome.

**Germinal centers:** Sites of intense B-cell proliferation, differentiation, somatic hypermutation, and class switching during antibody responses; these are found in lymphoid follicles in peripheral lymphoid tissues.

**Globulin:** Globulin, in human biochemistry, is one of the three types of serum proteins, the others being albumin and fibrinogen. Some globulins are produced in the liver, while others are made by the
**immune system.** The term globulin encompasses a heterogeneous group of proteins with typical high molecular weight and both solubility and electrophoretic migration rates lower than for albumin.

**Graft vs. host disease (GVHD):** A reaction of white blood cells in transplanted tissue (the graft) against the tissues of the recipient (the host).

**Granulocytes:** White blood cells that attack and destroy bacteria. (See neutrophils.)

**Granulocyte-colony stimulating factor (G-CSF):** A class of cytokines which controls the differentiation of hematopoietic stem cells to granulocytes such as neutrophils and natural killer cells (e.g. Neupogen, Neulasta).

**Half-life / (antibody half-life):** A measure of the mean survival time of antibody molecules following their formation, usually expressed as the time required to eliminate 50% of a known quantity of immunoglobulin from the body – varies from one immunoglobulin class to another.

**Haploid:** Having a single set of chromosomes, as normally carried by a gamete (sperm or egg). In man, the haploid number is 23.

**Haptens:** Small molecules that can bind antibody but cannot by themselves elicit an adaptive immune response. Haptens must be chemically linked to protein carriers to elicit an immune response.

**Haptoglobin:** A protein in the circulation that is an acute phase reactant; its level in the serum increases in response to acute inflammation or infection, stress, or necrosis (death of tissue). Its major role is to bind hemoglobin released from red blood cells that undergo natural cell death, preventing the accumulation of hemoglobin in the plasma. After the iron has been removed and "recycled" in the body, the haptoglobin-bound hemoglobin is eliminated by the reticuloendothelial monocyte-phagocytic system.

**HDAC (histone deacetylase) inhibitor:** See Histone deacetylase inhibitor.

**Heavy chains:** Heavy chains are the large polypeptide subunits of a protein complex. These are the larger of the two types of chains that comprise a normal immunoglobulin or antibody molecule.

**Hematocrit (Hct):** A measure of red blood cells as a percentage of whole blood.

**Hematologic cancer:** A cancer of the blood or bone marrow, such as leukemia or lymphoma.

**Hematologist:** A hematologist is a doctor who specializes in hematology. A hematologist’s routine work mainly includes the care and treatment of patients with hematological diseases, although some may also work in the hematology laboratory.

**Hematologist / oncologist:** A hematologist-oncologist is a doctor with special training in the diagnosis and treatment of blood diseases, especially blood cell cancers. This type of doctor is trained in hematology (the study of blood) and oncology (the study of cancer).

**Hematology:** Hematology, also spelled haematology, is the branch of biology, physiology, internal medicine, pathology, clinical laboratory work, and pediatrics that is concerned with the study of blood, the blood-forming organs, and blood diseases.
Hematopoiesis: The process of blood formation.

Hematopoietic stem cells (HSCs): Residing in the bone marrow, these are the single common ancestor to all the functional cells found in the blood and immune cells. The stem cells represent less than 0.01% of bone marrow cells in adults, and give rise to a larger, intermediately differentiated population of progenitor cells. These progenitor cells in turn divide and differentiate further through several stages into mature cells responsible for specific tasks. These stem cells are also able to re-create themselves through self-renewal. This potential for unlimited life span and future proliferation is their most important defining property.

Hemoglobin (Hb): Hemoglobin is the iron-containing oxygen-transport protein in the red blood cells of almost all vertebrates as well as the tissues of some invertebrates. Hemoglobin in the blood carries oxygen from the respiratory organs (lungs or gills) to the rest of the body (i.e. the tissues) where it releases oxygen to metabolize nutrients and provide energy to power the functions of the organism; hemoglobin also collects the resultant carbon dioxide to bring it back to the respiratory organs to be released from the organism.

Hemolysis: Hemolysis is the rupturing of erythrocytes (red blood cells) and the release of their contents (hemoglobin) into surrounding blood plasma.

Hemolytic: Relating to or involving or causing hemolysis.

Hemolytic anemia: A form of anemia due to hemolysis of erythrocytes (red blood cells), either in the blood vessels (intravascular) or elsewhere in the human body (extravascular). It has numerous possible causes, ranging from relatively harmless to life-threatening. Hemolytic anemia is either inherited or acquired. Treatment depends on the cause and nature of the hemolysis.

Hepatic: Refers to the liver.

Hepatitis: Hepatitis is a medical condition defined by the inflammation of the liver and characterized by the presence of inflammatory cells in the organ. The condition can be self-limiting (healing on its own) or can progress to fibrosis (scarring) and cirrhosis. Hepatitis may occur with limited or no symptoms but often leads to jaundice, anorexia (poor appetite), and malaise. Hepatitis is acute when it lasts less than six months and chronic when it persists longer. A group of viruses known as the hepatitis viruses cause most cases of hepatitis worldwide, but it can also be due to toxins (notably alcohol, certain medications, some industrial organic solvents, and plants), other infections, and autoimmune diseases.

Hepatitis A virus: An acute, rarely fatal disease of global distribution caused by a picornavirus, hepatitis A is a common cause of morbidity (poor health) in many countries. Approximately 30% of the U.S. population has evidence of previous infection. Hepatitis A virus is most often transmitted by the oral-fecal route and is often caused by the consumption of contaminated food. The clinical findings include fever, nonspecific gastrointestinal malaise, hepatosplenomegaly, jaundice, and itching. The disease duration is four to six weeks and is followed by full recovery. Antibody formation provides protection against repeated infection. The laboratory findings include increased transaminases (catalyzation between an amino acid and an α-keto acid) and darkened urine due to increased bilirubin. A hepatitis A vaccine that is safe and effective is available.
**Hepatitis B virus:** Hepatitis B virus is a small, highly contagious DNA virus that is transmitted from person to person by the exchange of body fluids (e.g. blood, semen). Hepatitis B virus was a major health hazard of blood transfusions prior to the availability of specific serologic tests, which are highly sensitive and now performed on all donated blood. Hepatitis B virus remains a public health hazard because it is also a sexually transmitted disease. The symptoms of hepatitis B virus infection are quite varied and range from minor aches and pains to death. There are several stages of the disease; acute, convalescent, and chronic. The stages are determined by the presence of various viral antigens and antibodies to viral antigens in the blood. A hepatitis B virus vaccine that is safe and effective is available. Rituximab therapy has been associated with reactivation of quiescent hepatitis B virus infection.

**Hepatitis C virus:** Hepatitis C virus is another virus that primarily infects the liver and is believed to play a role in causing liver cancer. As with hepatitis B, hepatitis C virus is transmitted through body fluids such as blood and semen and can be transmitted from mother to infant. Polymerase chain reaction tests have been developed to detect and follow the course of hepatitis C virus disease.

**Hepatitis D virus:** Hepatitis D virus is an incomplete RNA virus that may require co-infection with hepatitis B virus to cause hepatic disease. Patients with hepatitis D virus are also usually positive for certain hepatitis B virus antibodies. Hepatitis D virus is often associated with an intense, severe hepatitis and cirrhosis (cirrhosis develops in 60-70% of hepatitis D virus-infected patients) and is endemic in many parts of the world.

**Hepatosplenomegaly:** Hepatosplenomegaly is the simultaneous enlargement of both the liver (hepatomegaly) and the spleen (splenomegaly). Hepatosplenomegaly can occur as the result of blood disorders, lymphoma, acute viral hepatitis, infectious mononucleosis, and histoplasmosis (also known as "Spelunker's Lung") or it can be the sign of a serious and life threatening lysosomal storage disease. Systemic venous hypertension can also increase the risk for developing hepatosplenomegaly, which may be seen in those patients with right-sided heart failure.

**Herpes virus:** Any of a family of DNA viruses with prolonged dormancy (latency) lasting up to years; seven (and possibly eight) human herpes viruses have been identified. Herpes viruses can be detected by culture or by serologic blood tests.

**Hinge region:** The portion of an immunoglobulin heavy chain between the Fc and Fab regions which permits flexibility within the molecule and allows the two combining sites to operate independently.

**Histamine:** A substance stored in mast cells and released by antigen binding to IgE antibodies, it produces some of the symptoms of immediate allergic reactions.

**Histology:** That department of anatomy which deals with the minute structure, composition, and function of the tissues.

**Histone deacetylase (HDAC) inhibitor:** A class of anti-cancer drugs that act by interfering with the action of the enzyme histone deacetylase, which is responsible for the coiling and uncoiling of DNA in the cell during cell division.

**Hyperploidy / Hypoploidy:** See Aneuploidy.
**Hypervariable regions**: Portions of the immunoglobulin light chains and heavy chains that are highly variable in amino acid sequence from one immunoglobulin molecule to another, and that, together, constitute the antigen-binding site of an antibody molecule.

**Hyperviscosity**: Excessive blood thickness.

**Hyperviscosity syndrome**: A group of symptoms triggered by increase in the viscosity of the blood. Symptoms include spontaneous bleeding from mucous membranes, visual disturbances, and neurologic symptoms ranging from headache, dizziness, and vertigo to seizures and coma.

**Hypogammaglobulinemia**: A type of immune deficiency characterized by a reduction in immunoglobulins (A, G, M, etc.)

**Ibrutinib (Imbruvica)**: An oral drug that targets Bruton’s tyrosine kinase (BTK), an enzyme which is important in the development and activation of B-cells and which is over-expressed in Waldenstrom’s macroglobulinemia (WM). It is the first, and so far only, drug FDA-approved for the treatment of WM.

**Idelalisib (Zydelig)**: An oral drug that acts as an inhibitor of phosphoinositide 3-kinase. It is used in chronic lymphocytic leukemia and is being tested in patients with Waldenstrom’s macroglobulinemia.

**Idiopathic**: A disease or condition of unknown cause (See Etiology.)

**Idiotype**: The unique set of antigenic determinants on the surface of a cell that can be used to specifically identify it.

**Iliac**: Pertaining to the anatomical structure of the ileum which is the distal portion of the small intestine, extending from the jejunum (the section of the small intestine between the duodenum and the ileum) to the cecum (the large blind pouch forming the beginning of the large intestine.). The term iliac is often used in reference to the iliac arteries or the iliac lymph nodes.

**Immune system**: An immune system is a system of biological structures and processes within an organism that protects against pathogens. To function properly, an immune system must detect a wide variety of injuries or infectious agents, including viruses, bacteria, and parasites, and distinguish them from the organism’s own healthy tissue and processes. Also, pathogens can rapidly evolve and adapt to avoid detection and destruction by the immune system. As a result, multiple layer defense mechanisms have also evolved to recognize and neutralize pathogens. These layers start with the surface of the organism. If a pathogen breaches these barriers, the innate immune system provides an immediate, but non-specific response. If pathogens successfully evade the innate response, the adaptive immune system engages. Both innate and adaptive immunity depend on the ability of the immune system to distinguish between self and non-self molecules. In immunology, self-molecules are those components of an organism’s body that can be distinguished from foreign substances by the immune system. One class of non-self molecules, called antigens (short for antibody generators), are defined as substances that bind to specific immune receptors and elicit an immune response.

**Immune response**: The activation of any aspect of the immune system either by self or foreign material.

**Immunity**: The condition of being immune; the protection against infectious disease conferred either by the immune response generated by immunization or previous infection or by other non-immunologic factors.
**Immunization:** The induction of immunity by either (1) the stimulation of the immune system and subsequent production of antibody by exposure to an antigen in order to confer protection against disease (e.g. active immunity by administration of a vaccine) or (2) the conferring of specific immune reactivity on previously non-immune individuals by the administration of sensitized lymphoid cells or serum from immune individuals (e.g. passive immunity by intravenous IgG administration).

**Immunogen:** A substance capable of inducing an immune response, in most contexts synonymous with antigen (but not always).

**Surface barriers:** The immune system protects organisms from infection with layered defenses of increasing specificity. In simple terms, physical barriers prevent pathogens such as bacteria and viruses from entering the organism. For instance, the skin is the organism's primary barrier to pathogens. But the skin doesn't cover the organism's entire surface so coughing and sneezing mechanically eject pathogens and other irritants from the respiratory tract. The flushing action of tears and urine also mechanically expels pathogens, while mucus secreted by the respiratory and gastrointestinal tract serves to trap and entangle microorganisms.

**Innate immune system / natural immune system:** In general this is immunity based on the genetic constitution of the individual. Differences in innate immunity between various people may, in addition, be attributable to age, race, and to the hormonal and metabolic conditions of the individual. More specifically, microorganisms or toxins that successfully enter an organism encounter the cells and mechanisms of the innate immune system. The innate response is usually triggered when microbes are identified by pattern recognition receptors, which recognize components that are conserved among broad groups of microorganisms, or when damaged, injured or stressed cells send out alarm signals, many of which (but not all) are recognized by the same receptors as those that recognize pathogens. Innate immune defenses are non-specific, meaning these systems respond to pathogens in a generic way. This system does not confer long-lasting immunity against a pathogen. The innate immune system is the dominant system of host defense in most organisms.

**Inflammation:** A localized protective response elicited by injury or destruction of tissues, which serves to destroy, dilute, or wall off (sequester) both the injurious agent and the injured tissue. It is characterized in the acute form by the classical signs of pain (dolor), heat (calor), redness (rubor), swelling (tumor), and loss of function. In cell anatomy, it involves a complex series of events, including dilatation of arterioles, capillaries, and venules, with increased permeability and blood flow; exudation (oozing forth) of fluids, including plasma proteins; and leukocytic migration into the inflammatory focus. Inflammation is often categorized by its time course, resulting in acute vs. chronic inflammation. Acute inflammation consists of the initial response of the body to tissue injury, while chronic inflammation is the prolonged tissue reaction following the initial response.

**Complement system:** The complement system consists of a number of small proteins found in the blood, generally synthesized by the liver, that cause a biochemical cascade which attacks the surface of foreign cells. It contains over 20 different proteins and is named for its ability to "complement" the killing of pathogens by antibodies. In humans, this response is activated by complement binding to antibodies that have attached to these microbes or the binding of complement proteins to carbohydrates on the surfaces.
of microbes. This recognition signal triggers a rapid killing response by immune cells or can also kill cells directly by disrupting their plasma membrane.

**Leukocytes:** Leukocytes act like independent, single-celled organisms and are the second arm of the **innate immune system**. The innate leukocytes include the phagocytes (macrophages, neutrophils, and dendritic cells), mast cells, eosinophils, basophils, and natural killer cells. These cells identify and eliminate pathogens, either by attacking larger pathogens through contact or by engulfing and then killing microorganisms. Neutrophils and macrophages are phagocytes that travel throughout the body in pursuit of invading pathogens. During the acute phase of inflammation, particularly as a result of bacterial infection, neutrophils migrate toward the site of inflammation in a process called chemotaxis, and are usually the first cells to arrive at the scene of infection. Macrophages are versatile cells that reside within tissues and produce a wide array of chemicals including enzymes, complement proteins, and regulatory factors such as interleukin 1. Macrophages also act as scavengers, ridding the body of worn-out cells and other debris, and as antigen-presenting cells that activate the **adaptive immune system**. Dendritic cells are phagocytes in tissues that are in contact with the external environment; therefore, they are located mainly in the skin, nose, lungs, stomach, and intestines. They are named for their resemblance to neuronal dendrites, as both have many spine-like projections, but dendritic cells not connected to the nervous system. Dendritic cells serve as a link between the bodily tissues and the **innate** and **adaptive immune systems**, as they present antigen to T-cells, one of the key cell types of the adaptive immune system.

**Adaptive immune system:** The adaptive immune system is activated by the **innate response**. This aspect of the **immune system** adapts its response during an infection to improve its recognition of the pathogen. This improved response is then retained after the pathogen has been eliminated, in the form of an immunological memory, and allows the adaptive immune system to mount faster and stronger attacks each time this pathogen is encountered. The adaptive immune system allows for a stronger **immune response** as well as immunological memory, where each pathogen is "remembered" by a signature **antigen**. The adaptive immune response is antigen-specific and requires the recognition of specific "non-self" antigens during a process called antigen presentation. Antigen specificity allows for the generation of responses that are tailored to specific pathogens or pathogen-infected cells. The ability to mount these tailored responses is maintained in the body by "memory cells". Should a pathogen infect the body more than once, these specific memory cells are used to quickly eliminate it.

The cells of the adaptive immune system are special types of **leukocytes**, called **lymphocytes**. B-cells and T-cells are the major types of lymphocytes and are derived from the **bone marrow**. B-cells are involved in the humoral immune response, whereas T-cells are involved in cell-mediated immune response. Both B-cells and T-cells carry receptor molecules that recognize specific targets. T-cells recognize a "non-self" target, such as a pathogen, only after antigens (small fragments of the pathogen) have been processed and presented in combination with a "self" receptor called a **major histocompatibility complex (MHC) molecule**. There are two major subtypes of T-cells: the killer T-cell and the helper-T cell. Killer T-cells only recognize antigens coupled to Class I MHC molecules, while helper T-cells only recognize antigens coupled to Class II MHC molecules. These two mechanisms of antigen presentation reflect the different roles of the two types of T-cells. A third, minor subtype recognizes intact antigens that are not bound to MHC receptors. In contrast, the B-cell antigen-specific receptor is an **antibody**.
molecule on the B-cell surface and recognizes whole pathogens without any need for antigen processing. Each lineage of B-cell expresses a different antibody, so the complete set of B-cell antigen receptors represent all the antibodies that the body can manufacture. When B-cells and T-cells are activated and begin to replicate, some of their offspring become long-lived memory cells. Throughout the lifetime of an animal, these memory cells remember each specific pathogen encountered and can mount a strong response if the pathogen is detected again. This is "adaptive" because it occurs during the lifetime of an individual as an adaptation to infection with that pathogen and prepares the immune system for future challenges. Immunological memory can be in the form of either passive short-term memory or active long-term memory. Several layers of passive protection are provided by the mother. This is passive immunity because the fetus does not actually make any memory cells or antibodies, only receives them from the mother through the placenta. This passive immunity is usually short-term, lasting from a few days up to several months. In medicine, protective passive immunity can also be transferred artificially from one individual to another via antibody-rich serum. Long-term active memory is acquired following infection by activation of B- and T-cells. Active immunity can also be generated artificially, through vaccination.

**Immunofixation**: A laboratory test used to determine the presence and type of monoclonal immunoglobulins found in the serum or urine.

**Immunoglobulins (Igs)**: Any of the structurally related molecules formed by B-cells as antibodies; immunoglobulins are divided into five basic classes or isotypes (immunoglobulin M, immunoglobulin G, immunoglobulin A, immunoglobulin E, and immunoglobulin D with their related subclasses) on the basis of structure and biologic activity. These are each discussed below:

**Immunoglobulin A (IgA)**: Immunoglobulin A is an antibody that plays a critical role in mucosal immunity. More immunoglobulin A is produced in mucosal linings than all other types of antibody combined; between three and five grams are secreted into the intestinal lumen each day. This accumulates to 75% of the total immunoglobulin produced in the entire body. Immunoglobulin A has two subclasses (IgA1 and IgA2) and can exist in a dimeric form called secretory immunoglobulin A (sIgA). In its secretory form, immunoglobulin A is the main immunoglobulin found in mucous secretions, including tears, saliva, colostrum, and secretions from the genitourinary tract, gastrointestinal tract, prostate and respiratory epithelium.

**Immunoglobulin D (IgD)**: Immunoglobulin D is an antibody isotype that makes up about 1% of proteins in the plasma membranes of immature B-lymphocytes where it is usually co-expressed with another cell surface antibody called immunoglobulin M. Immunoglobulin D is also produced in a secreted form that is found in very small amounts in blood serum. Immunoglobulin D’s function has always been a puzzle in immunology since its discovery in 1964. Immunoglobulin D was recently found to be present in species from cartilaginous fish to humans (probably with the exception of birds). This nearly ubiquitous appearance in species with an adaptive immune system demonstrates that immunoglobulin D is as ancient as immunoglobulin M and suggests the notion that immunoglobulin D has important immunological functions. In B-cells, immunoglobulin D’s function is to signal the B-cells to be activated. By being activated, they are ready to take part in the defense of the body in the immune system.

**Immunoglobulin E (IgE)**: Immunoglobulin E is a class of antibody that has been found only in mammals. Its main function is immunity to parasites, including parasitic worms such as Schistosoma mansoni (schistosomiasis), Trichinella spiralis (trichinosis), and Fasciola hepatica
(fascioliasis), and may be important during immune defense against certain protozoan parasites such as *Plasmodium falciparum* (malaria). It also plays an essential role in type I hypersensitivity (allergy disorder). Although immunoglobulin E is typically the least abundant isotype (blood serum immunoglobulin E levels in a normal individual are only 0.05% of the immunoglobulin concentration, compared to 10 mg/ml for the immunoglobulin Gs, the isotypes responsible for most of the classical adaptive immune response).

**Immunoglobulin G (IgG):** Immunoglobulin G is an antibody molecule composed of four peptide chains - two heavy chains and two light chains. Each immunoglobulin G has two antigen binding sites. Other immunoglobulins may be described in terms of polymers with the immunoglobulin G structure considered a monomer. Immunoglobulin G constitutes 75% of serum immunoglobulins in humans. Immunoglobulin G antibodies are involved in predominantly the secondary immune response (responses of the lymph nodes). The presence of specific immunoglobulin G, in general, corresponds to maturation of the antibody response.

**Immunoglobulin M (IgM):** A specific immunoglobulin, an excess of which characterizes Waldenström's macroglobulinemia. Immunoglobulin M is a basic antibody that is produced by B-cells. Immunoglobulin M is, by far, physically the largest antibody in the human circulatory system. It is the first antibody to appear in response to initial exposure to antigen. Immunoglobulin M antibodies appear early in the course of an infection and usually reappear, to a lesser extent, after further exposure. This biological property of immunoglobulin M makes it useful in the diagnosis of infectious diseases. Demonstrating immunoglobulin M antibodies in a patient’s serum indicates recent infection.

**Immunomodulatory drugs (IMIDs):** A class of drugs that constitute thalidomide, lenalidomide and pomalidomide, used in the treatment of multiple myeloma and, less commonly, Waldenstrom’s macroglobulinemia. Immunomodulatory drugs are not traditional chemotherapy drugs; their mechanism of action is not completely understood, but they are antiangiogenic and help stimulate T-cell and natural killer cell production.

**Immunophenotyping:** Immunophenotyping allows cells to be defined or targeted based on what molecules are present on their surface. This process is used to diagnose specific types of leukemia and lymphoma by comparing the cancer cells to normal cells of the immune system.

**Immunosuppression:** An extreme weakening of the immune response caused by drugs or other means. Immunosuppression involves an act that reduces the activation or efficacy of the immune system. Some portions of the immune system itself have immunosuppressive effects on other parts of the immune system, and immunosuppression may occur as an adverse reaction to treatment for other conditions.

**Immunotherapy:** Treatment to boost or restore the ability of the immune system to fight cancer, infections, and other diseases; also used to lessen certain side effects that may be caused by some cancer treatments. Agents used in immunotherapy include monoclonal antibodies, growth factors, and vaccines. These agents may also have a direct antitumor effect.

**IMO-8400:** An oral drug that targets the Toll-like receptors 7, 8, and 9. It is being tested in patients with Waldenstrom’s macroglobulinemia.

**In vitro:** In the laboratory; outside the body.
In vivo: In the body.

Incurable: Not curable. Although it is not always possible to be certain, doctors are often able to tell whether or not a particular cancer might be cured. Even if cancer is incurable, treatment can be offered to prolong life and control symptoms.

Indolent: Slow growing.

Infarct: An area of coagulation necrosis in a tissue due to local ischemia resulting from obstruction of circulation to the area, most commonly by a thrombus (blood clot) or embolus (clot that has traveled to an area and compromised the circulation – may be blood clot, air, fat, or amniotic fluid embolus).

Inflammation: A localized protective response elicited by injury or destruction of tissues, which serves to destroy, dilute, or wall off (sequester) both the injurious agent and the injured tissue. It is characterized in the acute form by the classical signs of pain (dolor), heat (calor), redness (rubor), swelling (tumor), and loss of function. Histologically, it involves a complex series of events, including dilatation of arterioles, capillaries, and venules, with increased permeability and blood flow; exudation of fluids, including plasma proteins; and leukocytic migration into the inflammatory focus.

Infusion: The introduction of a fluid into a vein.

Ingestion: Taking into the body by mouth.

Inguinal: Pertaining to the anatomical area of the inguen (groin).

Injection: Use of a syringe and needle to push fluids or drugs into the body; often called a "shot."

Innate immunity (natural immunity): Immunity based on the genetic constitution of the individual. Differences in innate immunity between various people may, in addition, be attributable to age, race, and to the hormonal and metabolic conditions of the individual.

Interferons: Any of a family of immune regulatory proteins (immunomodulators) produced by T-cells and other cells in response to DNA, viruses, antigens, and other substances usually associated with infected or malignant cells. Interferons increase the bacteriocidal, viricidal, and tumoricidal activities of macrophages. (See Lymphokines.)

Interleukins: A family of factors produced by lymphocytes, monocytes, and other cells that induce growth and differentiation of lymphoid cells and hematopoietic stem cells. (See Lymphokines.)

Intravenous (IV): Into the vein.

Intravenous catheter: A thin plastic tube that is inserted into a vein to allow the addition of substances to the blood.

Intravenous immunoglobulin G (IVIg): Intravenous immunoglobulin is a blood product administered into the vein. It contains the pooled, polyvalent immunoglobulin G extracted from the plasma of over one thousand blood donors. Intravenous immunoglobulin G’s effects last between 2 weeks and 3 months.
**Irradiation**: The use of high-energy radiation from X-rays, gamma rays, neutrons, protons, and other sources to kill cancer cells and shrink tumors.

**Ischemia**: Deficiency of blood in a part, due to functional constriction or actual obstruction of a blood vessel (e.g. myocardial ischemia is the deficiency of blood supply to the heart muscle due to obstruction or constriction of the coronary arteries).

**Isoenzyme (isozyme)**: One of the various structural forms of an enzyme, each having the same mechanism but with differing chemical, physical, or immunological characteristics.

**Isohemagglutinins**: The naturally occurring immunoglobulin M and immunoglobulin G antibodies against the red blood cell antigens of the ABO blood groups. These antibodies to the A and B antigens have the ability to agglutinate human red blood cells. (See ABO incompatibility.)

**Isotypes**: Subtypes / classes of immunoglobulins present in all normal individuals (e.g. immunoglobulin M, immunoglobulin G, immunoglobulin A, immunoglobulin E, and immunoglobulin D).

“J” chain: Polypeptide chain found in the immunoglobulin M pentamer that “joins” five immunoglobulin M molecules together by disulfide bonds to form the typical five-unit immunoglobulin M structure.

**Joining (J) segment**: Short segment of amino acids, coded on the DNA in a J gene, that joins the V (variable) and C (constant) genes of an antibody molecule. The existence of several genes for J regions provides another degree of variability in the generation of the enormous diversity of antibodies that is required by the immune system.

**Kappa light chains**: One of the two types of light chains found in the immunoglobulin molecule. Both types of light chains are present in all individuals, and either the kappa or lambda light chain types may combine with any of the heavy chain types, but in any one type of immunoglobulin molecule both light chains and heavy chains are of the same type. Light chains are also found as two-unit structures (dimers) in the urine in certain abnormal conditions, particularly in multiple myeloma, and are called Bence-Jones proteins.

**Karyotype**: The characterization of the chromosomal composition of an individual or a species, including number, form, and size of the chromosomes.

**Lactate dehydrogenase (LDH)**: Lactate dehydrogenase is an enzyme present in the cytoplasm of all cells. Measurement of total lactate dehydrogenase activity is used to screen liver, muscle, and myocardial disease. Lactate dehydrogenase is often used as well as a marker for certain leukemias, lymphomas, anemia, and multiple myeloma. Lactate dehydrogenase isoenzymes can be fractionated to determine the predominant source of lactate dehydrogenase. Isoenzymes are noted in the heart muscle and red blood cells (LD1); concentrated in white blood cells (LD2); highest in the lungs and platelets (LD3); highest in the kidney, placenta, and pancreas (LD4); highest in the liver and skeletal muscle (LD5).

**Lambda light chains**: See Kappa light chains.

**Lenalidomide (Revlimid)**: A drug that is similar to thalidomide and is used to treat multiple myeloma and other types of cancer.
**Leukemia:** A progressive, malignant disease of the blood-forming organs, characterized by distorted proliferation and development of leukocytes and their precursors in the blood and bone marrow and crowding out normally developing blood cells.

**Leukocytes:** White blood cells formed in the bone marrow, including lymphocytes, neutrophils, eosinophils, monocytes/macrophages, basophils, and natural killer cells.

**Leukopenia:** An abnormally low number of white blood cells.

**Ligand:** In biochemistry and pharmacology, a ligand is a substance (usually a small molecule) that forms a complex with a biomolecule to serve a biological purpose. In a narrower sense, it is a signal triggering molecule, binding to a site on a target protein. A ligand may function as agonist or antagonist. Many ligands are found in biological systems, such as cofactors and porphyrin in hemoglobin.

- **Agonist:** An agonist is a chemical that binds to a receptor of a cell and triggers a response by that cell. Agonists often mimic the action of a naturally occurring substance.

- **Antagonist:** An antagonist blocks the action of the agonist.

- **Inverse agonist:** An inverse agonist causes an action opposite to that of the agonist.

**Light chain:** A light chain is the small polypeptide subunit of a protein complex. More specifically, it can refer to any of the following light chains:

  · **Immunoglobulin** light chains (See Kappa and lambda light chains below.)

  · Ferritin light chains. Ferritin is the major intracellular iron storage protein. It is composed of 24 subunits of the heavy and light ferritin chains.

  · Myosin light chains. Myosin is the most common protein in muscle cells, responsible for the elastic and contractile properties of muscle. Each molecule of smooth muscle cell myosin contains two pairs of light molecular weight chains.

  · Kinesin light chains. Kinesins are motor proteins that move along microtubule filaments and are powered by ATP. The active movement of kinesins supports several cellular functions including mitosis, meiosis and transport of cellular cargo, such as in axonal transport. Kinesin motor proteins move toward the microtubules' plus end, which is usually oriented towards the cell membrane, and are called “plus-end directed motors”.

  · Dynein light chains. Dyneins are motor proteins that move along microtubule filaments and are powered by ATP. Dynein motor proteins transport various types of cellular cargo by moving along microtubules towards their minus-ends, which are usually oriented towards the cell center, and are called "minus-end directed motors”.

  · Kappa and lambda light chains. There are only two types of light chains found in the basic four-chain immunoglobulin molecule. Kappa light chains, encoded by the immunoglobulin kappa locus on chromosome 2, and lambda light chains, encoded by the immunoglobulin lambda locus on chromosome 22. Both types of light chains are present in all individuals, and either of the kappa or lambda light chain types may combine with any of the heavy chain types,
but in any one type of \textit{B-cell} immunoglobulin molecule both light chains and heavy chains are of the same type.

In a healthy individual, the total kappa to lambda ratio is roughly 2:1 in \textit{serum} (measuring intact whole \textit{antibodies}) or 1:1.5 if measuring free light chains, with a highly divergent ratio indicative of neoplasm. Both the kappa and the lambda chains can increase proportionately, maintaining a normal ratio. This is usually indicative of something other than a blood cell dyscrasia (abnormality), such as kidney disease.

If the \textit{lymph node} or similar tissue is reactive, or otherwise benign, it should possess a mixture of kappa positive and lambda positive cells. If, however, one type of light chain is significantly more common than the other, the cells are likely all derived from a small \textit{clonal} population, which may indicate a malignant condition, such as \textit{B-cell lymphoma}. Light chains are also found as two-unit structures (dimers) in the urine in certain abnormal conditions, particularly in \textit{multiple myeloma}. (See \textit{Bence-Jones proteins}.)

Increased levels of free immunoglobulin light chains have also been detected in various \textit{inflammatory} diseases. It is important to note that, in contrast to increased levels in \textit{lymphoma} patients, these immunoglobulin light chains are \textit{polyclonal}. Recent studies have shown that these immunoglobulin light chains can bind to \textit{mast cells} and, using their ability to bind \textit{antigen}, facilitate activation of these mast cells.

\textbf{Light chain deposition disease:} Antibodies are made up of small \textit{protein} segments called \textit{light chains} and \textit{heavy chains}. Certain cells in the body called \textit{B-cells} often make "extra" light chains that are broken down into small pieces by the kidney, which are then reabsorbed and used again in the body. Patients with light chain deposition disease make far too many light chains, which get deposited in many different tissues in the body, including the kidney. Some patients with light chain deposition disease will make so many that they overwhelm the kidneys’ ability to recycle or get rid of them.

\textbf{Lipophages:} These cells are \textit{macrophages} that have taken up lipoproteins (fat). The presence of fat in macrophages can indicate a metabolic disorder such as hypercholesterolemia (the presence of high levels of cholesterol in the blood). Such cells can be seen at wound sites during wound healing and appear at skin wound sites together with iron-laden macrophages (siderophages) at a wound healing age of 2-3 days. Such macrophages are the hallmark of mesenteric panniculitis, an extremely rare disease in which the normal fatty architecture of the \textit{mesentery} is replaced by fibrosis (scarring), \textit{necrosis}, and calcification (hardening of the soft tissue due to a buildup of calcium salts). These cells are seen also in radiation-induced atheromatosis (deposit or degenerative accumulation of lipid-containing plaques on the innermost layer of the wall of an \textit{artery}).

\textbf{Lipoprotein:} Any of the lipid-protein complexes in which the lipids are transported in the \textit{blood}.

\textbf{Lumen:} A lumen in biology is the inside space of a tubular structure, such as an \textit{artery} or the intestine.

\textbf{Lymph:} Thin clear fluid that circulates through the \textit{lymphatic vessels} and carries \textit{lymphocytes} that fight infection and disease.

\textbf{Lymph nodes:} Part of the \textit{immune system’s lymphatic system}, these are bean-shaped organs found in the underarms, groin, neck, and abdomen that act as filters for the lymph fluid as it
passes through them. The lymph nodes are major sites of antigen trapping by lymphocytes, which in turn activate an immune response.

**Lymph vessels**: In anatomy, lymph vessels (or lymphatic vessels) are thin walled, valved structures that carry lymph. As part of the lymphatic system, lymph vessels are complementary to the cardiovascular system.

**Lymphadenopathy**: Enlargement of the lymph nodes.

**Lymphatic system**: Part of the immune system, considered a secondary lymphoid tissue/organ; includes lymph, ducts, organs, lymph vessels, lymphocytes, and lymph nodes, whose function is to carry lymphatic fluid and white blood cells to fight disease and infection.

**Lymphocytes**: Any of the mononuclear, non-phagocytic white blood cells (including T-cells and B-cells), found in the blood that are the body’s immunologically competent cells and their precursors.

**Lymphoid stem cell**: Progenitor stem cell for lymphocytes.

**Primary lymphoid organs (or central lymphoid organs)**: Lymphoid organs which generate lymphocytes from immature progenitor cells. These organs include the fetal liver, adult bone marrow, and thymus. (See Secondary lymphoid organs.)

**Lymphokines (cytokines)**: A general term for soluble hormone-like mediators of immune responses that are released by sensitized lymphocytes on contact with an antigen. Produced by activated T-cells, natural killer cells, and other select cells of the immune system, they can either enhance or suppress the immune system by promoting cell proliferation, growth and/or differentiation, and regulate cell function by acting on gene transcription and the inflammatory response. Interferon, interleukins, and colony-stimulating factors such as granulocyte-colony stimulating factor are lymphokines.

**Lymphoma**: Cancer of the lymphatic system, which includes the bone marrow, spleen, thymus, lymph nodes, and vessels that carry fluid and infection-fighting cells, or any neoplastic disorder of the lymphoid tissue. The lymphomas are classified generally in two subsets. These are Hodgkin’s lymphoma and the non-Hodgkin’s lymphomas, which are then subsequently classified as low grade (includes Waldenstrom’s macroglobulinemia), intermediate grade, and high grade (includes diffuse large B-cell lymphoma).

**Lymphopenia**: A condition in which there is a lower-than-normal number of lymphocytes in the blood.

**Lymphoplasmacytic lymphoma (LPL)**: A modern term for Waldenstrom’s macroglobulinemia under the REAL classification system (Revised European-American Classification of Lymphoid Neoplasms). It refers to the morphology of the cells which are intermediate in appearance between lymphocytes and plasma cells. Other classification systems refer to Waldenstrom’s macroglobulinemia as a subset of lymphoplasmacytic lymphoma which specifically secretes monoclonal IgM immunoglobulin.

**Lysis**: Lysis refers to the breaking down of a cell, often by viral, enzymatic, or osmotic mechanisms that compromise its integrity.
Lysosomal storage disease: A group of approximately 50 rare inherited metabolic disorders that result from defects in lysosomal function. Lysosomal storage diseases result when the lysosome, a specific organelle in the body's cells, malfunctions. Lysosomal storage disorders are caused by lysosomal dysfunction usually as a consequence of deficiency of a single enzyme required for the metabolism of lipids (fats), glycoproteins (sugar containing proteins) or so-called mucopolysaccharides (a family of carbohydrates important for life).

Lysosomes: Intracellular vesicles that contain various enzymes normally involved in the process of localized intracellular digestion.

Lysozymes: Naturally occurring enzymes found in saliva, tears, and lysosomes that aid in digestion of intracellular material and / or in the breakdown of some bacterial cell walls.

M-spike: Also called monoclonal spike, monoclonal protein, or monoclonal immunoglobulin. An IgM M-spike is so characteristic of Waldenstrom's macroglobulinemia that it can be used for both diagnosis of disease and follow-up of patients. This monoclonal immunoglobulin can be detected using serum protein electrophoresis which separates the blood proteins into groups based on charge and size. There's a predictable pattern of proteins in normal serum with each protein migrating to a certain point on an electrophoretic gel plate. Immunoglobulins migrate to a unique place called the gamma region, and because they are all different (in normal patients), they migrate to slightly different places within that region, giving a gentle bell-shaped curve or smear (depending on whether you're looking at a tracing or the actual bands on the gel). In Waldenstrom's macroglobulinemia, the immunoglobulin is monoclonal, so that all of it migrates to exactly the same spot on the gel. This results in a big spike (if you're looking at a tracing) or a very distinct, crisp, strong band (if you’re looking at the gel itself).

Macrophage: A type of white blood cell that interacts with antigens and presents these antigens to T-cells, thus activating the T-cells. Macrophages that circulate in the blood are called monocytes, whereas those that reside in certain tissues are called tissue macrophages, or macrophages proper. Macrophages are capable of phagocytosis, and they secrete various substances that enhance the immune response to infectious agents and malignant cells. (See Antigen-presenting cells.)

Magnetic resonance imaging (MRI): Magnetic resonance imaging, also known as nuclear magnetic resonance imaging or magnetic resonance tomography, is a medical imaging technique used in radiology to visualize detailed internal structures. Images are produced by passing the patient through a tubular structure that generates a powerful electromagnetic field. The hydrogen ions in the body are subjected to a high-intensity radiofrequency magnetic field and respond by emitting a radiofrequency signal that is then processed by computer to produce an image on film or computer.

Maintenance rituximab (Rituxan): A series of regular infusions of rituximab given over a period of time (usually two years) in an effort to prolong the response a patient has had to a previous therapy containing rituximab.

Maintenance therapy: A treatment given at regular intervals after a disease has responded to previous therapy; maintenance therapy is given in order to help prevent spread or recurrence of the disease.

Major histocompatibility complex (MHC): A genetic region, found in all mammals, that is primarily responsible for the rapid rejection of grafts between individuals and functions in signaling between lymphocytes and antigen-presenting cells. Major histocompatibility complex class I antigens are
associated with a small polypeptide called **B2-microglobulin**, interact with **T-cytotoxic** and **natural killer cells**, and are involved in identification of cells infected with viruses. **Major histocompatibility complex class II antigens** are characterized by their ability to stimulate **lymphocytes** and are found on **B-cells, macrophages, dendritic cells**, and other accessory **immune system** cells.

**Class I major histocompatibility complex molecules:** Proteins expressed on the cell surface of virtually all cells that are used to present **antigenic** material to **cytotoxic CD8 T-cells**. The class I major histocompatibility complex molecules are therefore important in the recognition of self by the **immune system**, and for the identification of a virally infected cell or a cell that has become malignant.

**Class II major histocompatibility complex molecules:** Proteins expressed on the cell surface of **macrophages** and other **antigen-presenting cells** of the **immune system** that identify to the **T-helper cells** the target antigen. Class II major histocompatibility complex molecules play a pivotal role in the activation of **CD4 helper T-cells**.

**Mast cells:** Non-mobile cells distributed near **blood vessels** in most tissues. These cells are full of granules containing **inflammatory** mediators and are often associated with allergic reactions.

**Median:** Situated in the middle; fifty percent of a population on either side.

**Mediastinum:** The mass of tissues and organs separating the two lung pleural sacs, between the sternum in front and the vertebral column behind, and from the thoracic inlet above and the diaphragm below. It contains the heart and its pericardium, the bases of the great **vessels**, the trachea and bronchi, esophagus, **thymus, lymph nodes**, thoracic duct, phrenic and vagus nerves and other structures and tissues.

**Meiosis:** Meiosis is a special type of cell division necessary for sexual reproduction in eukaryotes. Eukaryotes are every living thing whose cells exhibit a membrane around a nucleus - this includes everything known living thing except bacteria and Archaea. The cells produced by meiosis are **haploid**, otherwise known as gametes or spores. In many organisms, including all animals and land plants (but not some other groups such as fungi), gametes are called sperm and egg cells.

**Memory cells:** Long lived **B-cells** which have already been primed with their **antigen**, but have not undergone **terminal differentiation** into **plasma cells**. They react more readily than naive **lymphocytes** when re-stimulated with the same antigen.

**Mesentery:** The mesentery is the double layer of **peritoneum** that suspends the jejunum and ileum from the posterior wall of the abdomen. Its meaning, however, is frequently extended to include double layers of peritoneum connecting various components of the abdominal cavity.

**Metabolism:** The sum of all the physical and chemical processes by which living organized substance is produced and maintained (anabolism), and also the transformation by which energy is made available for the uses of the organism (catabolism).

**MicroRNA (miRNA):** A type of **RNA** found in cells and in blood. MicroRNAs are smaller than many other types of RNA and can bind to messenger RNAs (mRNAs) to block them from making proteins. MicroRNAs are being studied in the diagnosis and treatment of cancer.
Mini-allogeneic transplant (reduced intensity or non-myeloablative transplant): A type of allogeneic transplant in which lower doses of chemotherapy or radiation are used to prepare the patient for transplant. This type of transplant aims just to suppress the patient’s immune system sufficiently to allow engraftment of donor cells rather than completely kill the recipient’s bone marrow.

Minor response: In Waldenstrom’s macroglobulinemia, a minor response following treatment is characterized by a detectable monoclonal IgM protein, a reduction in serum IgM level of equal to or greater than 25% but less than 50% from baseline, and no new signs or symptoms of active disease.

Mitosis: The process of cell division which results in two cells with the same chromosome and DNA content as the original cell.

Mixed cryoglobulinemia: Type II cryoglobulinemia characterized by monoclonal IgM autoantibody with anti-immunoglobulin G activity that forms cryoprecipitable immunocomplexes with or without clinical symptoms. (See cryoglobulinemia, cryoglobulins.)

Monoclonal: A group of cells produced from a single ancestral cell by repeated cellular replication. See Clone.

Monoclonal antibodies (MABs): Laboratory-produced identical antibodies that can target a specific antigen.

Monoclonal antibody therapy: The use of laboratory-developed antibodies that can locate and bind to antigens in the body, including tumor cells. Each monoclonal antibody is made to bind one specific antigen. They can be used alone or to carry drugs, toxins, or radioactive materials directly to a tumor.

Monoclonal gammopathy: A disorder characterized by a disturbance in the body’s synthesis of a single antibody.

Monoclonal gammopathy of undetermined significance (MGUS): Formerly known as benign monoclonal gammopathy. A benign condition in which a paraprotein (immunoglobulin or immunoglobulin light chain that is produced in excess) is found in the blood during standard laboratory tests. It resembles multiple myeloma and similar diseases, but the levels of antibody are lower. It produces no symptoms or problems, and no treatment is indicated. Patients with MGUS are at increased risk of developing certain cancers, including multiple myeloma and Waldenstrom’s macroglobulinemia.

Monocytes: A type of white blood cell that is mobile and present in the circulation, comprises 2-5% of the circulating white blood cells, and breaks down old blood cells and microorganisms.

Monokines: A group of molecules released by monocytes and macrophages that act as soluble mediators of immune responses but that are not antibodies or complement components.

Monospot test: The monospot test, a form of heterophile (antibodies induced by external antigens that cross-react with self-antigens) antibody test, is a rapid test for infectious mononucleosis due to Epstein-Barr virus. The test is sensitive for heterophile antibodies produced by the human immune system in response to Epstein-Barr virus infection. The specificity of the test is high, virtually 100%, so a positive test is useful in confirming Epstein-Barr virus. Rarely, however, a false positive heterophile antibody test may result from toxoplasmosis (a parasitic disease), rubella, lymphoma, and leukemia. However, the sensitivity is only moderate, so a negative test does not exclude Epstein-Barr
virus. This lack of sensitivity is especially the case in young children, many of whom will not produce the heterophile antibody at any stage and thus have a false negative test result.

**Monotherapy:** Treatment of a condition by means of a single drug or modality.

**MRI (magnetic resonance imaging):** See Magnetic resonance imaging.

**mTOR:** A protein that helps control several cell functions, including cell division and survival, and binds to rapamycin and other drugs. mTOR may be more active in some types of cancer cells than it is in normal cells. Blocking mTOR may cause the cancer cells to die. It is a type of serine/threonine protein kinase. Also called mammalian target of rapamycin.

**Mucosa-associated lymphoid tissue (MALT):** Generic term for lymphoid tissue associated with the gastrointestinal tract, bronchial tree, and other mucosal tissue.

**Mucous membranes:** The mucous membranes (also known as mucosae; singular mucosa) are linings involved in absorption and secretion. They line cavities that are exposed to the external environment and internal organs. They are at several places contiguous with skin; the nostrils, the mouth, the lips, the eyelids, the ears, the genital area, and the anus. The sticky, thick fluid secreted by the mucous membranes and glands is termed mucus, although not every mucous membrane secretes mucus.

**Mucositis:** A complication of some cancer therapies in which the lining of the digestive system becomes inflamed; often seen as sores in the mouth.

**Multi-focal motor neuropathy:** Multi-focal motor neuropathy is a progressively worsening condition where muscles in the extremities gradually weaken. The disorder, a pure motor neuropathy syndrome, is usually asymmetric. While multi-focal motor neuropathy usually involves no pain (except for muscle cramps) and is rarely fatal, it can lead to significant disability, with loss of function in the hands affecting ability to work and perform everyday tasks, and with loss of function in the feet leading to foot drop or the inability to stand and walk. Many untreated patients end up using aids like canes and walkers. Treatment for multifocal motor neuropathy varies. Some individuals experience only mild, modest symptoms and require no treatment. For others, treatment generally consists of intravenous immunoglobulin or immunosuppressive therapy with cyclophosphamide. Improvement in muscle strength usually begins within 3 to 6 weeks after treatment is started. Most patients who receive treatment early experience little, if any, disability. However, there is evidence of slow progression over many years.

**Multiple myeloma (MM):** Multiple myeloma, also known as plasma cell myeloma or Kahler’s disease (after Otto Kahler), is a cancer of plasma cells, a type of white blood cell normally responsible for producing antibodies. In multiple myeloma, collections of abnormal plasma cells accumulate in the bone marrow, where they interfere with the production of normal blood cells. Most cases of myeloma also feature the production of a paraprotein, an abnormal antibody which can cause kidney problems. Bone lesions and hypercalcemia (high calcium levels) are also often encountered.

**Mutation:** Any change in the DNA of a cell.

**Mycoplasma:** A genus of tiny bacteria without cell walls that infect epithelial cells and cause "walking pneumonia" (which resolves in four to six weeks). Without a cell wall, they are unaffected by many common antibiotics such as penicillin or other beta-lactam antibiotics that target cell wall synthesis.
Mycoplasmas can take on many different shapes which make them difficult to identify, even under a high powered electron microscope. Mycoplasmas can also be very hard to culture in the laboratory and are often missed as pathogenic causes of diseases for this reason. Over 100 documented species of mycoplasmas have been recorded to cause various diseases in humans, animals, and plants. *Mycoplasma pneumoniae* and at least 7 other *Mycoplasma* species have now been linked as a direct cause or significant co-factor to many chronic diseases including rheumatoid arthritis, Alzheimer's, multiple sclerosis, fibromyalgia, chronic fatigue, diabetes, Crohn's Disease, ALS, nongonococcal urethritis, asthma, lupus, infertility, AIDS, and certain cancers and leukemia, just to name a few. *Mycoplasma* is the smallest known cell on the planet and is about 0.1 micron (µm) in diameter. Commonly, serum is required for antibody detection and throat, nasal, or genitourinary swabs are used for culture.

**MYD88**: A gene called myeloid differentiation primary response gene 88 that codes for the MYD88 protein, which plays a central role in the innate and adaptive immune response. This protein is an essential one in the interleukin-1 and Toll-like receptor signaling pathways.

**MYD88 L265P**: A mutation in the MYD88 gene that changes the amino acid leucine to proline at amino acid position 265. This mutation is found in at least 90% of Waldenstrom's macroglobulinemia patients and is important to the continued growth and proliferation of WM cells because of its action on the NF kappa B pathway.

**Myelin**: The fatty substance that covers and protects nerves.

**Myelodysplasia**: Production of abnormal blood cells in the bone marrow that can lead to leukemia.

**Myelodysplastic syndrome (MDS)**: (formerly known as pre-leukemia) A diverse collection of hematological medical conditions that involve ineffective production or abnormality (dysplasia) of the myeloid class of blood cells. Patients with MDS often develop severe anemia and require frequent blood transfusions. MDS can occur as the result of mutations induced by previous therapies, such as chemotherapy or radiation, given for a pre-existing condition.

**Myelosuppression**: A condition in which bone marrow activity is decreased, resulting in decreased platelets and red and white blood cells. Myelosuppression can be a side effect of some cancer treatments.

**Myoglobin**: A protein in muscle that binds reversibly with oxygen. It makes oxygen available to tissues as needed during exercise or other muscle activity. Myoglobin is increased in muscular dystrophy, inflammation, ischemia, or trauma to the muscle, as well as in myocardial infarction (heart attack).

**Natural immunity**: See *Innate immunity*.

**Natural isohemagglutinins**: It has been well established that blood group antigens, substances A and B, are genetically determined and develop during intrauterine life. In contrast, the blood group antibodies, the so-called "natural" isohemagglutinins, are believed by most authors to appear three to six months after birth. Whether these isohemagglutinins are inborn or the result of an antigenic stimulus has been a subject of experimentation and long debate. The theory that isohemagglutinin production takes place after birth from exposure to group A and B antigens found normally in ingested food and in the developing intestinal flora has many proponents. However, the presence of
isoheamagglutinins in neonatal sera has been demonstrated, and it is thought that these are maternal in origin and transferred through the placenta. (See Isohemagglutinins, ABO incompatibility.)

Natural killer (NK) cell: A type of white blood cell, comprising 3-5% of peripheral leukocytes, which has an intrinsic ability to kill various targeted cells.

Necrosis: The sum of the morphological changes indicative of cell death and caused by the progressive degradative action of enzymes; it may also affect groups of cells or part of a structure or an organ.

Neoplasia: Abnormal and uncontrolled cell growth.

Neoplastic: Refers to a neoplasm, which is a mass of tissue caused by the abnormal proliferation of cells. The growth of neoplastic cells exceeds and is not coordinated with that of the normal tissues around it.

Nephelometry: A technique used to determine levels of IgM, IgG, and IgA and based on the principle that a suspension of small particles will scatter light passed through it rather than simply absorbing it. For instance, IgM (or another immunoglobulin) and an antibody to it are mixed in concentrations such that only small aggregates are formed that do not quickly settle to the bottom. As light passes through the sample, the amount of scatter is measured and compared to the amount of scatter from known mixtures.

Nerve conduction studies: A noninvasive method for assessing a nerve’s ability to carry an impulse and measure its speed of transmission. Typically, two metal plates are placed on the skin at a distance from each other; an electrical stimulus passes through one plate and causes the nerve to fire, resulting in a muscle action potential that can be measured.

Neurological: Relating to the nervous system.

Neutropenia: A lower-than-normal level of neutrophils, a type of white blood cells.

Neutrophils: Also known as polymnuclear neutrophils or polymorphonuclear neutrophils, these are multinucleate types of white blood cells that have more than one nucleus per cell with one common cytoplasm. Normally, neutrophils contain a nucleus divided into 3 - 5 lobes connected by slender threads of DNA material. Neutrophil granulocytes are the most abundant type of white blood cells in mammals and form an essential part of the innate immune system. In general, they are subdivided into segmented neutrophils (or segs) and banded neutrophils (or bands). They form part of the polymorphonuclear cell family together with basophils and eosinophils.

Neutrophils are normally found in the blood stream. During the beginning (acute) phase of inflammation, particularly as a result of bacterial infection, environmental exposure, and some cancers, neutrophils are one of the first-responders of inflammatory cells to migrate towards the site of inflammation. They are the predominant cells in pus, accounting for its whitish/yellowish appearance. Neutrophils have the property of responding to chemokines and cytokines, adherence to immune antibody-antigen complexes, and phagocytosis.
**NF kappa B:** A protein complex that controls transcription of DNA and plays a key role in regulating the immune response to infection. Incorrect regulation of NF kappa B has been linked to cancer, inflammatory, and autoimmune diseases. It plays an important role in the growth and proliferation of Waldenstrom’s macroglobulinemia cells.

**Niacin (nicotinic acid):** A water-soluble “B-complex” vitamin that is integrated in the coenzyme nicotinamide adenine dinucleotide, one of the hydrogen ion acceptors for enzymes known as dehydrogenases. Niacin is formed in the body from tryptophan and is present in high-protein foods (e.g. poultry, meats, yeast). Niacin deficiency (pellagra) is characterized by anorexia (loss of appetite), glossitis (swollen red tongue), headaches, insomnia, rashes, depression, and pseudodementia. Niacin is decreased in chronic illness such as cancer, malnutrition, and diabetes.

**Night sweats:** Sleep hyperhidrosis, more commonly known as the night sweats, is the occurrence of excessive sweating during sleep. The sufferer may or may not also suffer from excessive perspiration while awake.

**Non-Hodgkin’s lymphoma (NHL):** The non-Hodgkin lymphomas are a diverse group of blood cancers that include any kind of lymphoma except Hodgkin’s lymphomas. Non-Hodgkin lymphomas can occur at any age and are often marked by lymph nodes that are larger than normal, fever, and weight loss. These various types can be divided into aggressive (fast-growing), intermediate, and indolent (slow-growing) and can originate from either B-cells or T-cells.

**Nucleoside analog:** Part of a larger class of anti-cancer drugs termed antimetabolites, which act specifically on proliferating cells. Fludarabine (Fludara) and cladribine (2CdA or Leustatin) are two purine analogs commonly used in treating WM.

**Obinutuzumab (Gazyva):** A humanized monoclonal antibody that has been approved for the treatment of chronic lymphocytic leukemia and is being tested in patients with Waldenstrom’s macroglobulinemia. It targets the same CD20 protein on B-cells as rituximab.

**Ofatumumab (Arzerra / HuMax-CD20):** A drug used to treat chronic lymphocytic leukemia (CLL) that has not gotten better with other chemotherapy. It is also being studied in the treatment of other types of cancer, including non-Hodgkin’s lymphoma and Waldenstrom’s macroglobulinemia. Ofatumumab binds to CD20, a protein on the surface of normal B-cells and most B-cell tumors. It is a type of monoclonal antibody.

**Oncogenes:** Genes involved in regulating cell growth. When these genes are defective in structure or expression, they can cause cells to grow continuously to form a tumor.

**Oncologist:** Oncology is a branch of medicine that deals with cancer. A medical professional whose practice specializes in cancer is an oncologist.

**Opportunistic infection:** An infection caused by an organism that does not normally cause disease. Opportunistic infections occur in people with weakened or compromised immune systems.

**Organomegaly:** Abnormal enlargement of an organ.

**Overall survival:** The percentage of people in a study or treatment group who are still alive for a certain period of time after they were diagnosed with or started treatment for a disease, such as cancer.
Palliation: Treatment given to remove or relieve symptoms rather than to cure the disease.

Panobinostat (Farydak): One in a class of cancer drugs called histone deacetylase (HDAC) inhibitors, it is used in the treatment of multiple myeloma and is being tested in Waldenstrom’s macroglobulinemia.

Paracrine action: Denotes a type of function in which substances such as hormones or cytokines are synthesized by a cell, released, and affect the function of other nearby cells.

Paraprotein: An abnormal plasma protein, such as the monoclonal IgM of Waldenstrom’s macroglobulinemia.

Parathyroid hormone: Parathyroid hormone is a hormone that maintains the balance of calcium in the body. It is produced by the parathyroid gland and secreted in response to decreased serum calcium. Parathyroid hormone increases intestinal calcium absorption and mobilizes calcium from bone. It increases phosphorous excretion by the kidney. Parathyroid hormone is part of the evaluation of hypercalcemia and in the differential diagnosis of hyperparathyroidism (overactivity of the parathyroid glands resulting in excess production of parathyroid hormone).

Partial response (PR): (Also see Response). In Waldenstrom’s macroglobulinemia, a partial response to treatment is characterized by a detectable monoclonal IgM, a reduction in serum IgM equal to or greater than 50% but less than 90% from baseline, a reduction in the size of enlarged lymph nodes and enlarged spleen if present at baseline, and no new symptoms or signs of active disease.

Pathology: The scientific study of disease; the term is also used to describe detectable damage to tissues.

Perifosine: A substance that is being studied in the treatment of cancer, including Waldenstrom’s macroglobulinemia. It belongs to the family of drugs called alkylphospholipids.

Peripheral blood stem cells (PBSCs): Stem cells that circulate in the blood.

Peripheral neuropathy (PN): A clinical symptom where there is a permanent or transient problem with the functioning of the nerves outside the spinal cord. The symptoms of a neuropathy may include numbness, weakness, tingling, burning pain, and loss of reflexes (usually in hands and / or feet). The pain may be mild or severe and disabling.

Peritoneum: The thin serous membrane (a smooth membrane consisting of a thin layer of cells, which secrete serous fluid, and a thin connective tissue layer) lining the abdominopelvic walls and enclosing the visceral organs. A strong, colorless membrane with a smooth surface, it forms a double-layered sac that is closed in the male and is continuous with the mucous membrane of the uterine tubes in the female.

PET (positron emission tomography): See Positron emission tomography.

Petechiae: Pinpoint, unraised, round red spots under the skin caused by bleeding.

Peyer’s patches: Collections of lymphoid cells in the wall of the gut which form a secondary lymphoid tissue.
Phagocytes: Term referring to cells of the immune system (monocytes and macrophages) that are able to ingest microorganisms and other particulate antigens that are coated with antibody or complement. This process is mediated by specific cell surface receptors (Fc receptors).

Phagocytic: Refers to a specific cell having the capability of ingesting and destroying invading foreign particles, such as bacteria.

Phagocytosis: The process by which cells engulf material and enclose it within a special area (vacuole / phagosome) within the cell.

Phenotype: The entire physical, biochemical, and physiological makeup of an individual as determined both genetically and environmentally, as opposed to genotype.

PI3K/AKT/mTOR pathway: An intracellular signaling pathway important in apoptosis and cancer.

Pituitary function test: A general term for any laboratory test used to evaluate the function of the anterior pituitary. Pituitary function tests can be static, that is, the level of a pituitary hormone (e.g. adrenocorticotropic hormone) and linked feedback hormone (cortisol, which is secreted by the adrenal gland in response to adrenocorticotropic hormone) are measured in the serum; or dynamic, where hormones are administered to evaluate the response of the feedback organs to stimulation by hormones of the anterior pituitary (adenohypophysis).

Plasma: The fluid component of blood containing water, electrolytes, and various proteins.

Plasma cells: Terminally differentiated white blood cells of the B-cell lineage that produce antibodies. In multiple myeloma, the plasma cell becomes malignant and produces in most cases large amounts of IgG antibodies.

Plasmacytoid: Resembling or derived from a plasma cell.

Plasmacytoma: A collection of plasma cells found in a single location of soft tissue or bone rather than throughout the bone marrow.

Plasmacytosis: Possessing abnormal numbers of plasma cells in the blood.

Plasmapheresis (PP): The process of removing a donor's plasma to extract a specific component (monoclonal immunoglobulin M in the case of Waldenstrom’s macroglobulinemia patients) and returning the remaining plasma to the donor. The process uses continuous circulation of blood from a donor through an apparatus and back to the donor. This process makes it possible to remove specific substances from large volumes of plasma. Hemapheresis or apheresis is a similar procedure whereby platelets, red cells, white cells, stem cells or plasma constituents can be removed separately.

Platelets (thrombocytes): Cells formed in the bone marrow from hematopoietic stem cells; they circulate in the blood and are necessary to help the blood clot and control bleeding.

Polyclonal: Derived from different cells. Normal immunoglobulin M is polyclonal since it is derived from many different B-cells each producing a distinct unique immunoglobulin M as opposed to monoclonal immunoglobulin M produced by the Waldenstrom's macroglobulinemia malignant clone.
Polymerase chain reaction (PCR): A laboratory method using the enzyme polymerase (which catalyzes polymerization forming compounds of high molecular weight) to make many copies of a specific DNA sequence.

Polymorphism: In genetics, polymorphism refers to the occurrence together in the same population of two or more genetically determined phenotypes in such proportions that the rarest of them cannot be maintained merely by recurrent mutation.

Polymorphonuclear leukocytes (granulocytes): White blood cells with multilobed nuclei and cytoplasmic granules. They include neutrophils, eosinophils, and basophils.

Polymorphonuclear neutrophils: See Neutrophils.

Pomalidomide: A substance being studied in the treatment of prostate cancer, multiple myeloma, and other types of cancer. Pomalidomide is a newer drug in the same class as thalidomide. It stops the growth of blood vessels, stimulates the immune system, and kills cancer cells. Pomalidomide is a type of angiogenesis inhibitor and a type of immunomodulatory agent.

Porphyrins: Any of various organic pigments containing four pyrrole rings bonded to one another. The rings form the corners of a large flat square, in the middle of which is a cavity that often contains a metal atom. Porphyrins occur universally in protoplasm and function with bound metals such as iron in hemoglobin and magnesium in chlorophyll.

Positron emission tomography (PET): Commonly called a PET scan, this is a unique type of imaging test that produces a three-dimensional image or picture of functional processes in the body, helping doctors see how the organs and tissues inside your body are actually functioning.

Prednisolone: A drug that lessens inflammation and suppresses the body’s immune response; it is used to treat disorders in many organ systems and to treat the symptoms of several types of leukemia and lymphoma. It is also being studied in the treatment of other types of cancer. Prednisolone is a type of therapeutic glucocorticoid.

Prescription: A prescription is a health-care program implemented by a physician or other medical doctors in the form of instructions that govern the plan of care for an individual patient. Prescriptions may include orders to be performed by a patient, caretaker, nurse, pharmacist or other therapist. Commonly, the term prescription is used to mean an order to take certain medications.

Primary care provider (PCP): A primary care physician or family doctor is a physician / medical doctor who provides both the first contact for a person with an undiagnosed health concern as well as continuing care of varied medical conditions, not limited by cause, organ system, or diagnosis.

Primary lymphoid organs (central lymphoid organs): Lymphoid organs in which lymphocytes complete their initial maturation steps; they include the fetal liver, adult bone marrow, and thymus.

Progenitor cells: Cells derived from hematopoietic stem cells that in turn serve as interim stem cells for the other cell types during the process of cell maturation and differentiation.

Prognosis: A prediction of the course of the disease and its outcome.
**Progression-free survival:** The length of time during and after the treatment of a disease, such as cancer, that a patient lives with the disease but it does not get worse. In a clinical trial, measuring the progression-free survival is one way to see how well a new treatment works.

**Proteasome inhibitor:** A drug that blocks the action of proteasomes. A proteasome is a large protein complex that helps destroy other cellular proteins when they are no longer needed. When the action of the proteasome is blocked, this cellular protein “garbage” backs up in the cell and eventually kills it. Proteasome inhibitors are used in the treatment of multiple myeloma and Waldenstrom’s macroglobulinemia.

**Protein kinase C:** An enzyme found throughout the body’s tissues and organs. Several forms of the enzyme are involved in many cellular functions. It is being studied in the treatment of cancer.

**Proteins:** Proteins are biochemical compounds consisting of one or more polypeptides typically folded into a globular or fibrous form, facilitating a biological function. A polypeptide is a single linear polymer chain of amino acids bonded together by peptide bonds between the carboxyl and amino groups of adjacent amino acid residues. The sequence of amino acids in a protein is defined by the sequence of a gene, which is encoded by our DNA. In general, the genetic code specifies 20 standard amino acids; however, in certain organisms the genetic code can include selenocysteine and pyrrolysine.

**Proteomics:** The study of the structure and function of proteins, including the way they work and interact with each other inside cells.

**Protocol:** A detailed plan of a medical experiment, treatment, or procedure. In clinical trials, it states what the study will do, how it will be done, and why it is being done. It explains how many people will be in the study, who is eligible to take part in it, what study drugs or other interventions will be given, what tests will be done and how often, and what information will be collected.

**Purine analog:** See Nucleoside analog.

**Pyrexia:** A fever.

**R-CHOP:** An abbreviation for a chemoimmunotherapy combination that is used to treat non-Hodgkin’s lymphoma and mantle cell lymphoma and is being studied in the treatment of other types of cancer. It includes the drugs rituximab, Cytoxan, hydroxydoxorubicin (also known as Doxorubicin or Adriamycin), Oncovin (vincristine), and prednisone.

**RAD001 (Afinitor / everolimus):** See Everolimus.

**Radioimmunotherapy:** A type of systemic radiation therapy in which a radioactive substance is linked to an antibody that locates and kills tumor cells when injected into the body.

**Red blood cells (RBCs):** See Erythrocytes.

**Reference ranges:** In medicine, a set of values that a doctor uses to interpret a patient’s test results. The reference range for a given test is based on test results for 95% of the healthy population. Sometimes patients whose test results are outside of the reference values may be healthy, and some patients whose test results are within the reference values may have a health problem. The reference range for a test may be different for different groups of people (for example, men and women).

Regimen: A treatment plan that specifies the dosage, the schedule, and the duration of treatment.

Relapse: The return of disease after it has been treated and the patient has been in remission.

Remission: Disappearance of signs and symptoms of disease. A remission is a temporary end to the medical signs and symptoms of an incurable disease.

Resistance: In the context of cancer, resistance is the ability of cancer cells to circumvent the effects of drug therapy so that the drug does not work well and the cancer cells grow.

Response: A description of how cancer has responded to treatment.

Restriction fragment length polymorphism: In molecular genetics, a polymorphism in the DNA sequence that can be detected on the basis of differences in fragment length of DNA produced by digestion with a specific restriction enzyme.

Reticular: Pertaining to or resembling a net – most often used in context of the immune system.

Reticulocytes: Immature red blood cells that are normally present in extremely low numbers in the circulation; increased numbers may be an indication of the bone marrow’s response to anemia.

Reticuloendothelial monocyte-phagocytic system: A group of cells having the ability to take up and sequester inert particles, including macrophages or macrophage precursors, specialized endothelial cells lining the sinusoids of the liver, spleen and bone marrow, and reticular cells of lymphatic tissue (macrophages) and of bone marrow (fibroblasts).

Retinal: Pertaining to the retina, a sensory membrane of the eye.

Retroperitoneum: Pertaining to the anatomical area found behind the peritoneum. This area contains the kidneys, retroperitoneal lymph nodes, and other structures.

Rheumatoid factor (RF): A group of antibodies directed against a portion of immunoglobulin G and produced by inflammatory cells (neutrophils) in the joints of 80% of patients with rheumatoid arthritis. Rheumatoid factors may evoke immune complexes that activate the complement cascade and release enzymes from neutrophils, causing tissue injury. There are various ways of detecting rheumatoid factors in the serum – agglutination studies, nephelometry (measures suspended particulates in a liquid or gas colloid), fluorescence immunoassay (assays very small amounts of material using a fluorescent label for the antigen), and enzyme immunoassay (detects the presence of a substance in a liquid or wet sample).

Ribonucleic acid (RNA): One of the two major nucleic acids in the body, the other being DNA. The basic function of RNA is to convert the genetic information contained in DNA into proteins that carry out all cell activity.

Ribosome: A large intracellular molecular structure composed of two dissociable subunits that is the site of protein synthesis.
Rituximab (Rituxan): A drug used to treat certain types of B-cell non-Hodgkin’s lymphoma. It is also used with other drugs to treat chronic lymphocytic leukemia and rheumatoid arthritis. It is being studied in the treatment of other types of cancer and other conditions. Rituximab binds to a protein called CD20, which is found on B-cells, and it kills cancer cells by utilizing the patient’s own immune system. It is a type of monoclonal antibody.

Salvage therapy: Any therapy administered after first-line treatment has failed.

Secondary lymphoid organs and tissues: The secondary lymphoid tissues comprise well-organized encapsulated organs, the spleen and lymph nodes, and non-encapsulated accumulation of lymph tissue. These tissues and organs are usually the site of first encounter of immune cells with antigen. In general, lymphocytes are generated in primary lymphoid tissues and function in secondary lymphoid tissues. Secondary or peripheral lymphoid organs maintain mature naive lymphocytes and initiate an adaptive immune response. The peripheral lymphoid organs are the sites of lymphocyte activation by antigen. Activation leads to clonal expansion and affinity maturation. Mature lymphocytes re-circulate between the blood and the peripheral lymphoid organs until they encounter their specific antigen. Secondary lymphoid tissue provides the environment for the foreign or altered native molecules (antigens) to interact with the lymphocytes. It is exemplified by the lymph nodes, and the lymphoid follicles in tonsils, Peyer's patches, spleen, adenoids, skin, etc. that are associated with the mucosa-associated lymphoid tissue. (See Primary lymphoid organs.)

Sensitivity: As it pertains to diagnostic testing, this is the conditional probability that a person having a disease will be correctly identified by a clinical test, i.e., the number of true positive results divided by the number of true positives and false negative results. In other words, this is percentage of patients with disease who have a positive test for the disease in question.

Sepsis: Infection of the bloodstream, a very serious and frequently fatal condition.

Serum: The fluid component of clotted blood.

Serum protein electrophoresis (SPEP): A laboratory test that examines specific proteins in the blood called globulins by exposing the collected serum to an electric current to separate the serum protein components into five classifications by size and electrical charge (serum albumin, alpha-1 globulins, alpha-2 globulins, beta globulins, and gamma globulins). In Waldenstrom’s macroglobulinemia and related disorders, this technique is used to measure immunoglobulin proteins such as IgM, IgG, and IgA.

Serum viscosity (SV): The physical property of serum as it relates to its “thickness”. The serum viscosity is affected by the concentration of constituents in the serum. The greater the number of soluble molecules in the serum, the higher will be the viscosity.

Shingles: The disease caused when varicella zoster virus is reactivated later in life in a person who has had chickenpox.

Sign(s): Objective evidence of disease, usually observed by the physician. (See Symptom(s).)

Small fiber neuropathy: Small fiber neuropathy is caused by damage to the small, unmyelinated fibers in the peripheral nerves that innervate the skin and internal organs, including the cardiovascular system, gastrointestinal tract, and bladder, among others. These fibers convey pain and temperature sensations from the skin and mediate autonomic functions
Smoldering Waldenstrom's macroglobulinemia: Not yet full-blown Waldenstrom's macroglobulinemia. Smoldering Waldenstrom's macroglobulinemia is defined clinically as having a serum monoclonal immunoglobulin M protein equal to or greater than 3 g/dL and/or bone marrow lymphoplasmacytic infiltration equal to or greater than 10%, but with no evidence of end-organ damage (anemia, constitutional symptoms, hyperviscosity, lymphadenopathy (swollen/enlarged lymph nodes), or hepatosplenomegaly).

Somatic hypermutation: A cellular mechanism occurring during B-cell maturation and involving a programmed process of mutations affecting the variable regions of immunoglobulin genes. The process permits refinement of antibody specificity.

Specificity: As in diagnostic specificity, this is the conditional probability that a person not having a disease will be correctly identified by a clinical test, i.e., the number of true negative results divided by the number of true negative and false positive results. In other words, this is the percentage of patients without disease who have a negative test for the disease in question.

Spleen: The largest structure in the lymphoid system, the spleen is a gland-like organ situated in the left upper abdomen. It serves as a reservoir of blood, produces lymphocytes and plasma cells, and functions as a “filter” for the blood by removing damaged red blood cells from the circulation.

Splenectomy: Surgical removal of the spleen.

Stem cells: The immature cells that can differentiate into other diversified cell types and can self-renew to produce more stem cells.

Stem cell mobilization: The process of using certain drugs to increase the movement of stem cells from the bone marrow into the peripheral blood so that they can be collected for a stem cell transplant.

Stem cell transplant (SCT): A stem cell transplant is the infusion of healthy stem cells into the body. A stem cell transplant may be necessary if the bone marrow stops working and doesn't produce enough healthy stem cells. A stem cell transplant can help the body make enough healthy white blood cells, red blood cells or platelets, and reduce the risk of life-threatening infections, anemia and bleeding.

Stenosis: Narrowing or stricture of a duct or canal (e.g. aortic stenosis is a narrowing of the aortic artery orifice of the heart or of the aorta itself; carotid artery stenosis is atherosclerotic stenosis of the carotid arteries).

Subcutaneous: Under the skin.

Symptom(s): Subjective evidence of a disease, usually observed by the patient. (See Sign(s).)

Symptomatic: Of, relating to, or based on symptoms.

Syngeneic transplantation: A procedure in which a patient receives bone marrow or blood-forming stem cells from a genetically identical donor (such as an identical twin).

T (thymus-derived)-cells / T-lymphocytes / T-cells: T-cells are probably the most complex cells of the immune system, given the diversity of T-cell types, the wide range of cytokines, growth factors.
and immune modulators produced by activated T-cells, the complexity of T-cell interaction with antigens, and the complexity of T-cell maturation in the thymus. In general, they are white blood cells that mature in the thymus and attack viruses.

**T-cell receptors:** Structurally related to antibodies, the T-cell receptors on the surface of T-cells interact with class I or class II major histocompatibility complex molecules and antigens presented to them by antigen-presenting cells of the immune system. Activation of the T-cell receptors leads to various functions performed by T-cells. T-cell receptors are unable to recognize free unbound antigen. The T-cell receptors share many similarities with immunoglobulins insofar as their genes are concerned.

**T-cytotoxic cells:** CD8 T-cells that respond to class I major histocompatibility complex molecule presentation of viral or tumor antigens on the surface of a target cell, leading to the destruction or lysis of the infected target cell by the T-cytotoxic cell.

**T-helper-1 cells:** CD4 T-cells that produce cytokines which are associated with cell-mediated inflammatory reactions, activation of complement and/or macrophages, as well as antibody-dependent cell-mediated cytotoxicity.

**T-helper-2 cells:** CD4 T-cells that produce cytokines which provide optimal help for strong antibody and allergic responses.

**Targeted therapy:** A type of treatment that uses drugs or other substances, such as monoclonal antibodies, to identify and attack specific cancer cells. Targeted therapy may have fewer side effects than other types of cancer treatments.

**Terminally differentiated:** A term referring to the last step in differentiation, or maturation, of an immune system cell. Plasma cells are the terminally differentiated form of antibody producing B-cells.

**Thalidomide (Thalomid):** A drug that is used to treat multiple myeloma in patients who have just been diagnosed and to treat a painful skin disease related to leprosy. It is also being studied in the treatment of other types of cancer. Thalidomide is an angiogenesis inhibitor as well as belonging to a class of agents called immunomodulatory drugs (IMIDs).

**Thrombin:** Thrombin is a "trypsin-like" serine protease protein that in humans is encoded by the F2 gene. Prothrombin (coagulation factor II) is proteolytically cleaved to form thrombin in the coagulation cascade, which ultimately results in the stemming of blood loss. Thrombin in turn acts as a serine protease that converts soluble fibrinogen into insoluble strands of fibrin, as well as catalyzing many other coagulation-related reactions.

**Thrombocyte:** See Platelet.

**Thrombocytopenia:** An abnormally low number of platelets in the blood.

**Thymus:** The major site of T-cell differentiation, the thymus is considered a primary lymphoid organ and is located in the thoracic cavity over the heart.

**Thyroid-stimulating hormone:** A glycopeptide hormone produced by the anterior hypophysis (pituitary gland) in response to thyroid-releasing hormone, which is released by the hypothalamus.
Thyroid-stimulating hormone controls thyroid growth, development and secretion. Its production is regulated by thyroxine levels in the blood and by thyroid-releasing hormone.

**Thyroxine:** A hormone that stimulates metabolism and oxygen consumption and which is secreted by the thyroid gland in response to thyroid-stimulating hormone produced in the anterior pituitary gland.

**Toll-like receptors:** These are proteins that play a critical role in the early innate immune response to pathogens by sensing the presence of microorganisms.

**Toxicity:** Having to do with poison or something harmful to the body. Toxic substances usually cause unwanted side effects.

**Transcription:** The first step of gene expression, in which a particular segment of DNA is copied into messenger RNA. The messenger RNA will in turn serve as a template for protein synthesis.

**Transformation:** Indolent lymphomas generally grow slowly, can sometimes remain stable for a long while, or can even regress spontaneously. However, sometimes a more aggressive cell emerges from the population of indolent cells (which soon outnumber the indolent cells) leading to symptoms and the need to treat. This process is called transformation. When an indolent lymphoma transforms, there will be a mix of indolent and aggressive cells, and the goal of therapy is to cure the aggressive component. Following successful therapy, the indolent lymphoma can remain and remain challenging to cure. Follicular lymphomas are more prone to transformation to more aggressive clones than other indolent types.

**Transforming growth factors:** A group of cytokines identified by their ability to promote the growth of certain cells. Transforming growth factors are also generally immunosuppressive.

**Transfusion:** The process of receiving blood products into one’s circulation intravenously.

**Transfusion reaction:** A severe hemolytic reaction when an individual receives the wrong ABO blood group during a transfusion. The plasma contains red blood cell isohemagglutinins that destroy the transfused red blood cells. Theoretically, group O donor blood should be safe for any recipient, because group O cells possess neither the A nor the B antigen and, therefore will not be destroyed by either anti-A or anti-B antibodies in a recipient’s plasma. (See isohemagglutinins, ABO incompatibility.)

**Transposition:** A genetic event where a segment of DNA is moved to another position, or is replaced and / or exchanged for another genetic segment.

**Treatment:** Any of several methods of fighting disease, for instance, chemotherapy, radiation, surgery, transplantation, and others. It is synonymous with the word therapy.

**Tumor:** An abnormal mass of tissue, either benign or malignant.

**Tumor necrosis factor (TNF):** A cytokine released by activated macrophages; it is important in mediating inflammation and cytotoxic reactions.

**Tyrosine kinase:** An enzyme that can transfer a phosphate group from the energy molecule ATP to a protein in a cell. It functions as an “on” or “off” switch in many cellular functions, including
communication signals within a cell and regulating cellular activity, such as cell division. These enzymes can become mutated, stuck in the “on” position, and cause unregulated growth of the cell, which is a necessary step for the development of cancer. Therefore, inhibitors of tyrosine kinase are often effective cancer treatments. One example of a tyrosine kinase is BTK, and ibrutinib is an inhibitor of BTK.

**Ultrasound (ultrasonography):** A diagnostic method that generates images based on the differences in the ability of tissues of various densities to slow ultrasound waves.

**Uric acid:** A small breakdown product of purines, which are part of DNA. Uric acid is excreted primarily by the kidneys, as well as by the gastrointestinal tract. Increased uric acid crystals are deposited in various tissues; knee, elbow, ankle and particularly the “big toe” joint are favored areas. “Gout” is the general term used for the inflammatory and very painful condition caused by uric acid crystal deposition in joints. Uric acid increases with rapid cell turnover, such as occurs in cancer (particularly during chemotherapy for cancer where there is large amount of cell death), as a result of drug therapy (diuretics in particular), and in many other conditions.

**Urinalysis (UA):** A low-cost test in which a urine specimen is examined in order to screen for various diseases.

**Vaccination:** The deliberate induction of acquired immunity to a pathogen by injecting a vaccine, a dead or weakened form of the pathogen.

**Variable region:** The portion of the immunoglobulin’s light and heavy chains that are primarily responsible for antigen binding. This region is subject to frequent genetic manipulation / mutation.

**Varicella-zoster virus:** Also known as chicken pox. A virus that belongs to the herpes family of viruses; it is classified as human herpes virus-3. The primary or childhood form, chicken pox, presents in characteristic fashion, commonly as a wave of itchy vesicles that spread over the entire body, healing within three to five days. Of greater concern is first-time exposure to the varicella-zoster virus as an adult who lacks protective antibodies. Antibodies can be detected within one to four days of acute infection.

**Vascular endothelium:** The vascular endothelium is the thin layer of cells that lines the interior surface of blood vessels and lymphatic vessels, forming an interface between circulating blood and lymph in the lumen and the rest of the vessel wall. The cells that form the endothelium are called endothelial cells. Endothelial cells in direct contact with blood are called vascular endothelial cells whereas those in direct contact with lymph are known as lymphatic endothelial cells. Vascular endothelial cells line the entire circulatory system, from the heart to the smallest capillaries. These cells have very distinct and unique functions that are paramount to vascular biology. These functions include fluid filtration, such as in the glomeruli of the kidney (filtering blood to form urine), blood vessel tone, hemostasis (blood clotting), neutrophil recruitment, and hormone trafficking. Endothelium of the interior surfaces of the heart chambers is called endocardium.

**VDJ joining:** The event whereby the variable, diversity, and joining gene segments combine during the synthesis of an immunoglobulin heavy chain from genetic material. The precise positions at which these genes are spliced together are not constant, leading to different antigen-binding sites and therefore increased variability and diversity. The completed VDJ segment then binds to the immunoglobulin’s heavy chain constant gene segments.
Vertebrates: Vertebrates make up about 5% of all described animal species; the rest are invertebrates, which lack backbones. All vertebrates are built along the basic chordate body plan. This is a stiff rod running through the length of the animal (vertebral column or notochord), with a hollow tube of nervous tissue (the spinal cord) above it and the gastrointestinal tract below.

Very good partial response: In Waldenstrom's macroglobulinemia, a very good partial response following treatment is characterized by a detectable monoclonal IgM protein, a reduction in serum IgM level equal to or greater than 90% from baseline, complete resolution of enlarged lymph nodes and enlarged spleen if present at baseline, and no new signs or symptoms of active disease.

Viscosity: The resistance to the flow of a fluid, e.g. the thickness of the blood, or the ease with which it flows in the circulation.

Von Willebrand factor: A large protein, composed of multiple subunits, which is synthesized by blood vessels and platelets and is critical to the initial stages of blood clotting. This glue-like protein, produced by the cells that line the blood vessel walls, interacts with blood cells called platelets to form a plug which prevents the blood from flowing at the site of injury. People with von Willebrand disease are unable to make this plug because they do not have enough von Willebrand factor or their factor is abnormal. The efficiency of clotting is linked to the size of the subunits (ristocetin cofactor, von Willebrand’s factor; clotting factor VIII, the protein that's missing or doesn't work well in people who have hemophilia; and von Willebrand’s antigen) and to the vascular endothelium, megakaryocytes (a bone marrow cell responsible for the production of blood thrombocytes), and platelets. Von Willebrand's disease is a relatively rare inherited bleeding disorder.

Waldenstrom’s macroglobulinemia (WM): Waldenstrom's macroglobulinemia is a rare, indolent non-Hodgkin's lymphoma that begins in white blood cells called B-lymphocytes or B-cells. These B-cells mature in the lymph nodes, spleen, bone marrow, and other tissues. Lymphoplasmacytic cells are cells that are in the process of maturing from B-cells to plasma cells. In Waldenstrom's macroglobulinemia, abnormal lymphoplasmacytic cells multiply out of control, producing large amounts of a protein called monoclonal immunoglobulin M (also known as “macroglobulin”). High levels of immunoglobulin M in the blood cause hyperviscosity (blood thickness), which leads to many of the symptoms of Waldenstrom's macroglobulinemia.

WM mass: Agglomeration of lymphoplasmacytic lymphoma / Waldenstrom's macroglobulinemia cells occurring anywhere in the body, even outside the lymphatic system.

Watch and wait (W&W): Watch and wait (or watchful waiting) is often used with indolent or incurable cancers and means that a doctor does not actively treat a patient, but rather monitors the disease. This is desirable because treating asymptomatic patients does not cure the disease, improve quality of life, or change the outcome, plus many treatments have adverse side effects. The watch and wait method is used to ensure that treatment is begun when it is necessary to alleviate symptoms and improve quality of life. During this time, the patient will undergo regular medical testing to determine the current status of his or her disease.

Western blot (immunoblot): An immune assay that identifies the presence of proteins of specific molecular weights. It is commonly used to confirm human immunodeficiency virus after an enzyme-linked immunosorbent assay is positive. Western blotting is also used to identify proteins in Lyme disease. The proteins are separated by electrophoresis, then transferred (blotted) to a nitrocellulose or nylon membrane that is then exposed to a labeled antibody, which detects the antigen (i.e. protein) of interest.
White blood cells (WBCs): See Leukocytes.

Zinc: Zinc is a trace mineral that is essential for growth and development, and required for more than 200 enzymes (e.g. carbonic anhydrase, carboxy-peptidase, DNA- and RNA-polymerases, reverse transcriptase) and proteins involved in gene expression. Zinc is present in seafood, animal proteins, unrefined grains, legumes, and nuts. Approximately 20% of dietary zinc is absorbed; its absorption is enhanced by protein-rich foods. Of the zinc in the body, 50-60% is in muscle and 30% is in bone. The recommended daily allowance is 5-15 mg.
Abbreviations for Waldenstrom’s Macroglobulinemia
Patients and Caregivers

2CdA: Cladribine chemotherapy
Abs: Antibodies
ADCC: Antibody-Dependent Cell-mediated Cytotoxicity
AFP: Alpha-Fetal Protein
AIHA: AutoImmune Hemolytic Anemia
APRs: Acute Phase Reactants
BCR: B-Cell Receptor
BDR: Bortezomib, Dexamethasone, and Rituximab
BMB: Bone Marrow Biopsy
BMT: Bone Marrow Transplant
B-R: Bendamustine and Rituximab
BTK: Bruton’s Tyrosine Kinase
CaRD: Carfilzomib, Rituximab, and Dexamethasone
CAR-T: Chimeric Antigen Receptor T-Cells
CAT / CT: Computerized Axial Tomography
CBC: Complete Blood Count
CD markers: Cluster of Differentiation
CDC: Complement-Dependent Cytotoxicity (not Centers for Disease Control)
CHOP: Cytoxan, Hydroxydoxorubicin (also called Doxorubincin or Adriamycin), Oncovin (vincristine), and Prednisone
Class I MHC: (MHC Class I) Class I Major Histocompatibility Complex molecules
Class II MHC: (MHC Class II) Class II Major Histocompatibility Complex molecules
CLL: Chronic Lymphocytic Leukemia
**CPR**: Cytoxan, Prednisone, and Rituxan (not Cardio-Pulmonary Resuscitation)

**CR**: Complete Response

**CSFs**: Colony-Stimulating Factors

**CVP**: same as CHOP but without the Hydroxydoxorubicin

**DLBCL**: Diffuse Large B-Cell Lymphoma

**DNA**: Deoxyribonucleic Acid

**DRC**: Dexamethasone, Rituximab, and Cyclophosphamide

**Dx**: Diagnosis

**ENT**: Ear, Nose, and Throat

**EPO**: Erythropoietin

**ESR**: Erythrocyte Sedimentation Rate

**FCR**: Fludarabine, Cytoxan, and Rituxan chemotherapy

**FCM**: Flow CytoMetry

**G-CSF**: Granulocyte-Colony Stimulating Factor

**GERD**: GastroEsophageal Reflux Disease

**GGT**: Gamma Glutamyl Transferase

**GI**: GastroIntestinal

**GP**: General Practitioner

**HCT**: HematoCriT

**HAV**: Hepatitis A Virus (also known as Hep A)

**HBV**: Hepatitis B Virus (also known as Hep B)

**HCV**: Hepatitis C Virus (also known as Hep C)

**HDAC**: Histone DeACetylase

**HDV**: Hepatitis D Virus (also known as Hep D)

**Hem**: Hematologist
**Hem-Onc**: a Hematology and Oncology specialist

**HGB / HB**: HemoGloBin

**HSCs**: Hematopoietic Stem Cells

**HSM**: HepatoSplenoMegaly

**HHV**: Human Herpes Viruses

**IgA**: Immunoglobulin A

**IgD**: Immunoglobulin D

**IgE**: Immunoglobulin E

**IgG**: Immunoglobulin G

**IgM**: Immunoglobulin M

**Igs**: Immunoglobulins

**IFNs**: InterFeroNs

**ILs**: InterLeukins

**IMIDs**: ImmunoModulatory Drugs

**IV**: IntraVenous

**IVIG**: IntraVenous Immunoglobulin G

**LCDD**: Light Chain Deposition Disease

**LDH**: Lactate DeHydrogenase

**LPL**: LymphoPlasmacytic Lymphoma

**LSDs**: Lysosomal Storage Diseases

**MALT**: Mucosa-Associated Lymphoid Tissue

**MC**: Mixed Cryoglobulinemia

**MDS**: MyeloDysplastic Syndrome

**MfMN / MMN**: Multi-focal Motor Neuropathy

**MGUS**: Monoclonal Gammopathy of Undetermined Significance
**MHC**: Major Histocompatibility Complex
**MM**: Multiple Myeloma
**MR / RM**: Maintenance Rituxan
**MRI**: Magnetic Resonance Imaging
**MYD88**: MYeloid primary response Differentiation gene 88
**NHL**: Non-Hodgkin’s Lymphoma
**NK cells**: Natural Killer cells
**Onc**: Oncologist
**OS**: Overall Survival
**PCP**: Primary Care Provider
**PCR**: Polymerase Chain Reaction
**PET scan**: Positron Emission Tomography
**PFS**: Progression-Free Survival
**PLTs**: PLaTelets
**PN**: Peripheral Neuropathy
**PP**: PlasmaPheresis
**PR**: Partial Response
**PTH**: ParaThyroid Hormone

**R-CHOP**: Rituxan, Cytoxan, Hydroxydoxorubicin (or Doxorubicin or Adriamycin), Oncovin (or Vincristine), and Prednisone

**R-CVP**: R-CHOP without Hydroxydoxorubicin
**RBC**: Red Blood Cell
**RF**: Rheumatoid Factor(s)
**RFLP**: Restriction Fragment Length Polymorphism
**Rx**: a medical prescription
**SCT**: Stem Cell Transplant
**SFN**: Small Fiber Neuropathy

**SPEP**: Serum Protein ElectroPhoresis

**SV**: Serum Viscosity

**SW / SWM**: Smoldering Waldenstrom's Macroglobulinemia

**T4**: Thyroxine

**TC cells**: T-Cytotoxic cells

**TCRs**: T-Cell Receptors

**TGFs**: Transforming Growth Factors

**TH1 cells**: T-Helper-1 cells

**TH2 cells**: T-Helper-2 cells

**TNF**: Tumor Necrosis Factor

**TSH**: Thyroid-Stimulating Hormone

**Tx**: Treatment

**VGPR**: Very Good Partial Response

**VZV**: Varicella-Zoster Virus

**W&W**: Watch and Wait

**WBC**: White Blood Cell

**WM**: Waldenstrom's Macroglobulinemia

**X4**: 4 infusions
IWMF Vision Statement
Support everyone affected by Waldenstrom’s macroglobulinemia while advancing the search for a cure.

IWMF Mission Statement
To offer mutual support and encouragement to the Waldenstrom’s macroglobulinemia community and others with an interest in the disease.

To provide information and educational programs that address patients’ concerns.

To promote and support research leading to better treatments and ultimately, a cure.

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