

Immunoglobulins Explained

by Dr. Guy Sherwood

Immunology is the branch of biomedical science concerned with the body's response and protection against environmental agents that are foreign to the organism; it is also concerned with the body's recognition of self and not self. Immunology encompasses the study and function of the immune system, immunization, organ transplantation, blood banking, and immunopathology (diseases of the immune system).

A foreign molecule (i.e. pollen) or molecules on the surface of an infectious agent (i.e. bacteria, virus) that elicits an immune response is called an immunogen. These are also referred to as antigens. Antibodies are one of nature's most brilliant solutions to the problem of antigens or "foreign" material.

Acquired immunity (relatively new in evolutionary terms - present only in vertebrates) is initiated, as the name implies, by initial contact with the foreign agent (immunization). The initial contact triggers a chain of events that leads to the activation of certain cells (lymphocytes) and the production of proteins (antibodies) with specificity against the foreign agent. Antibodies attach themselves to antigens and start the immune response cascade that leads ultimately to the neutralization of the foreign agent.

B lymphocytes proliferate in response to a particular antigen and differentiate into nonproliferating antibody secreting plasma cells. Waldenstrom's is a disorder of unregulated proliferation of cells from the B cell lineage (lymphoplasmacytoid cells). Antibody proteins are often called immunoglobulins (Ig). All immunoglobulin molecules have many common structural features. The antibodies are made of protein "chains" linked together by chemical bonds. There are "heavy" chains and "light" chains.

I will spare you the intricacies of the detailed description of these chains; suffice to say that there are five different classes of heavy chains termed G, M, A, E, and D. Based on the differences in their heavy chains, immunoglobulin molecules are divided into five major classes: IgG, IgM, IgA, IgE, and IgD.

IgG is the predominant immunoglobulin of internal components such as blood, cerebrospinal fluid, and peritoneal fluid (fluid present in the abdominal cavity). IgG is the only class of immunoglobulin that crosses the placenta, conferring the mother's immunity on the fetus. IgG makes up 80% of the total immunoglobulins. It is the smallest immunoglobulin, with a molecular weight of 150,000 Daltons. Thus it can readily diffuse out of the body's circulation into the tissues. Rituxan is classified as an IgG.

Plasmapheresis cannot remove all the Rituxan because as an IgG some of it has diffused into the tissues. PP can only theoretically remove some of the IgG present in the blood. The synthesis of IgG is largely governed by antigen stimulation, so that in germ free animals, IgG levels are very low but rise rapidly on transfer to a normal environment.

IgM is often referred to as the macroglobulin (i.e. Waldenstrom's macroglobulinemia) because of its size. It is the largest immunoglobulin at 900,000 Daltons. Because of its size, it is essentially "trapped" in the circulation. PP can remove it quite readily. IgM makes up 6% of the total immunoglobulins in normal individuals. IgM is a very powerful antibody in the fight against foreign invaders. Elevated levels of IgM in normal individuals usually indicate recent infection or recent exposure to antigen. Large numbers of IgM in the blood serum, as in Waldenstrom's, can result in an increase in the viscosity of the serum, slower blood flow, etc.

IgA weighs in at 160,000. It makes up 13% of the Ig's. IgA is mainly concerned with defending the exposed external surfaces of the body against attack by micro-organisms. It is found selectively in the secretions of saliva, tears, nasal fluids, sweat, genito-urinary and gastro-intestinal tracts, secretions of the lungs, etc.

IgE is the “miserable” antibody responsible for most allergic reactions (eg. hay fever). It only makes up 0.002% of total immunoglobulins, but it is a very reagenic and efficacious antibody. The size of the IgE is 200,000 Daltons.

IgD is a bizarre and not fully understood immunoglobulin. It is present in small amounts, 0-1% of Ig's, and has a weight of 185,000 Daltons. It is not secreted by plasma cells, and has no known function in the serum. It is known to be a major surface component of many B cells. Its presence on the B cells serves as a marker of the differentiation of B cells, and it may serve in the control of lymphocyte activation and suppression. I am not sure if CD-20 and CD-59 are IgD molecules.

IgG, IgM, IgA, IgE, and IgD can be subdivided into subclasses as well. They can differ from one another in that portion of the molecule that binds specifically to the respective antigen. You can therefore have IgG that bind only to a specific bacteria and IgG's that bind to another type of bacteria or antigen. This of course can apply to IgM, IgA, IgE.