Antigen—Antibody Reaction in Various Aspects of Life

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SCIENTISTS have known for a long time that the white blood cells formed the force of defence of the body. These are small amoeboid cells. The smaller ones are called " Polymorphonuclear leucocytes " and the bigger ones are called " Macrophages." They swim around, actively patrolling in the blood and trying to swallow up all foreign particles, bacteria etc. But these leucocytes and macrophages are as good as an army without ammunition. There is something else in the blood that does the real fighting and gets the bacteria ready to be swallowed up. This " something " is what scientists call " *Antibody.*"

Similar other phenomena are observed in the realm of life at microscopic level, for example, a virus " fertilizing " a bacterium a sperm fertilizing an egg, a parasite exploiting a host cell. Although their final outcome is different, all these phenomena have one feature in common: two units of living matter interact or combine chemically to create something new. In a general way we can think of all these interactions as diverse expressions of one basic biological transaction—*Antigen-Antibody reaction.*

Antibodies are protein bodies belonging to a special class of proteins called, " gamma globulins." They are manufactured and liberated by the body cells in response to and by the action of all foreign proteins (with the exception of gelatin) or any invading organism like a bacterium, or even a part of its body which itself is composed of proteins. These agents or invaders which cause the production of specific antibodies are called " *Antigens.*" Although the antigenic character is always truly associated with the protein bodies, sometimes even the carbohydrate type of compounds or lipids derived from metabolic activity of microorganism or even simple synthetic chemicals exhibit specific antigenic character and in that case they are called "Haptens." Haptens, by themselves alone have no true capacity to behave antigenically, but when attached or combined with a protein, bestow a specificity upon the antigenic character of the protein. The capsular sheath of cholera bacteria, for instance, although of carbohydrate type (a polysaccharide) has specific antigenic character.

Antibodies in Immunology:

The interaction of an antigen with an antibody results in either " agglutination " (precipitation) or " lysis " (dissolution) of the antigen. Thus the agglutinated or lysed antigen is rendered susceptible to the phagocytic action of the white blood cells. It is well known that after a person had typhoid fever, the white cells in his blood, which before had not been able to do much good against the typhoid bacteria are suddenly able to swallow them up. In fact, the first attack of typhoid has caused the production of a large number of antibodies against typhoid bacteria and his blood serum could now be actually injected into people sick with typhoid to help them get well. Following the same principle, antitoxins or sera are prepared. The so called antitoxins or sera are actually blood sera full of anti-

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bodies which are called " lysins " when they dissolve the microbe as a whole, or " antitoxins " when they neutralise the toxins produced by the microbe.

Antitoxins are usually prepared by injecting in some sturdy animal like a horse, the antigens which commonly include toxins, toxoids and bacterial vaccines. The presence of antigens induces the formation of specific antibodies in the blood of the animal. After a specified time the blood of the animal becomes very rich in its antibody content, and then it is tapped out from its jugular vein, and processed to obtain a serum which is called " antitoxin." As against antitoxins, vaccines are suspensions of either live but attentuated bacteria or viruses or dead ones. Their function is to give a dummy, or if real, a subclinical attack of the disease, which serves as a sample lesson to the body cells as to what type of antibodies they should form if in future they happened to get the real attack. Thus antitoxins and vaccines, impart immunity against specific disease. However, immunity imparted by antitoxins or sera is called " Passive Immunity." No fresh antibody formation is induced by the antibody injected in to the blood in the form of antitoxin and the immunity is only temporary and short lasting. It is gradually lost as the antibodies introduced in the form of antitoxin are slowly metabolised and eliminated by the body. On the other hand immunity acquired by vaccination or by having the disease is called " Active Immunity " as it is long lasting. Some people have immunity to certain disease without " apparently " even having had the disease. Thirty seven per cent of the children and ninety-seven per cent of adults, for instance, have natural immunity to Diphtheria. This so called natural immunity is imparted either by the specific antibodies received from the mother's blood during the embryonic stage of a child or inadvertently by the subclinical attack of the disease during the infancy.

Natural antibodies and Blood groups

Some antibodies are natural, ever present components of the body. They are the antibodies present in the human blood plasma to which the existing systems of different blood groups owe their recognition. The antibodies most important in the blood classification are called " Anti A " and " anti B." The corresponding antigens are called antigen 'A' and antigen 'B' and are associated with red blood cells. Obviously the complimentary antigen and the antibody of such type cannot exist simultaneously in the blood of an individual. Hence human blood falls in one of the following four classes:—

Type of blood	*Antigen in Red blood cells*	*Antiobody in blood palsma*
'A'	'A'	'Anti B'
'B'	'B'	'Anti A'
'AB'	—	'Anti A') 'Anti B')
'O'	'A' 'B'	—

These antibodies are not formed in response to any foreign stimulus; they owe their existence to the individual genes.

If 'A' type of blood is injected into a 'B' type of individual, the red blood cells or " erythrocytes " of injected blood are agglutinated by the antibodies in the plasma of the 'B' blood. This is the reason why in blood transfusion, the ideal is to have the "donor" and the "recipient" of exactly the same blood group. However, a little deviation from the ideal is safely

possible. Generally, the antibodies present in the donor's blood plasma are not of great concern as they are harmlessly inactivated by the antigens which have diffused in to blood plasma from red blood cells of the recipient. Antigens in donor's red blood cells are, however, of great concern, as red blood cells can be agglutinated even when greatly diluted. When it is not possible to match the recipient's blood with that of a donor, a donor of 'O' type is unhesitatingly preferred, as 'O' type of blood has neither antigen 'A' nor antigen 'B' in red blood cells, and therefore, such donor is called a " Universal donor." Practical application of this discovery of blood antibodies and their doubtless inheritance has opened up new possibilities of settling cases of " doubtful paternity." It sometimes happens that infants belonging to different families are accidentally exchanged or that a child reputed to be legitimate is not so. For example, a man of type 'AB' married to a woman of type 'O', questions the legitmacy of her child, type 'O'. Obviously the child cannot be his, as he can produce only two types of sperm cells ('A' sperm and 'B'sperm) and consequently cannot father any 'OO' child. But even this test has its limitations.

In addition to 'A' and 'B' antigens, another principal one is the " Rhesus antigen," symbolised by Rh, so named because it is found in rhesus monkey. This antigen is also found in some human erythreocytes. Particular interest in Rhesus antigen is occasioned by its role in causing some of the natural abortions and miscarriages of human embryo. Rhesus negative persons are " rh, rh " or (Rh-), rhesus positive persons (Rh+) are either " Rh, rh " or " Rh, Rh." If a woman of type " rh, rh " (Rh-) marries a man of " Rh, Rh " or " Rh, rh " (Rh+) constitution, her child may be Rhesus positive, *i.e.* " Rh, rh." If some of the child's red blood cells which contain Rhesus antigen get through the placenta and into the mother's blood system, the foreign protein will stimulate the production of an antibody (Antirhesus). The antibody being soluble, can go through the placenta back to the infant's blood circulation. If it does, it causes destruction of the red blood cells of the infant and the damage may be so extensive as to cause death and abortion of the child, or if less severe, the child is born with a serious case of jaundice, the yellow colour being due to the presence of erythrocyte-breakdown products in the blood. In such jaundice there is a " compensatory " increase in the rate of release of red blood cells from bone marrow which may even release " erythroblasts " (the immature erythrocytes), hence the name of the ailment " erythroblastosis fetalis." However, the cases of union of Rh- females and Rh+ males are not always complicated and usually the first child is seldom affected.

Fertilisation and Antibodies:

The ancient problem of the fertilisation of an egg has found a new and inviting approach in the light of antigen-antibody reaction. That the substances of an egg and a sperm combine in the manner of antigen-antibody,was first discovered by the noted embryologist Frank R Lillie. He found that when he put the sperms of sea urchin in sea water which had been in contact with sea urchin eggs, the sperms clumped. He concluded that the eggs had released an agglutinating substance which he called " fertilizin." It has now been established that fertilizin forms the gelatinous coat of sea urchin eggs which gradually dissolves in water and combines with a substance " antifertilizin " present on the surface of sperms, causing the latter to agglutinate. The sperm

agglutination reaction is now known to occur in many species of animals. Sperms of some animals fail to show the reaction, but this does not necessarily mean that their eggs lack a fertilizin. According to the modern concept of serological agglutination reaction developed by J. R. Marrack, M. Heidilberger and L. Pauling mass clumping can occur only when the antigen and antibody possess two or more reactive sites *i.e.* each is multivalent. The concept of univalent antibodies explains why the fertilizin of some species of animals and certain other antibodies such as those in most type of anti-Rh blood, fail to cause agglutination of cells. The reaction between egg's fertilizin and the sperm's antifertilizin enables the sperm to attach itself to the surface of the egg. The reaction, like any antigen-antibody reaction is highly specific; the fertilizin of one species will not react with the antifertilizin of another species except that a weak reaction may occur when species are closely related. That seems one of the main reasons why different species cannot cross-breed; the sperm cannot even get foot-hold on the egg.

Chemically, fertilizins belong to a special class of proteins called " Glycoproteins " —proteins containing sugar. This class of substances are assuming incresing importance in biology. It includes, for example, the pituitory gonadotrophic hormones, the antigen contained in the 'A', 'B' and 'O' type of human blood and the receptor substances by which viruses attach to cells. Human blood group antigens and antibody contain a rather special type of sugar " Fucose." Fertilizin of sea urchin also contains the same sugar. Whatever the explanation may be, it is certainly striking that much the same type of substance is involved in such diverse reactions as the human blood group reaction, infection by virus and agglutination of a sea urchin's sperm.

Auto-Antibodies:

Another surprising discovery is that antifertitizin is also found in the interior of an egg itself and that its solution can agglutinate the egg itself. It is a remarkable fact that a single cell should contain within itself two substances which react with each other in the manner of an antigen and an antibody. The situation is true of many other cells, tissues and organisms. One such example is an individual's blood which is found to contain substances which agglutinate his own red blood cells, usually only below normal temperatures. It was supposed that such agglutinating substances were formed during certain diseases such as hoemolytic anaemea, virus pneumonia etc. as a reaction to the infection. But in the light of the finding that an antigen and an antibody may occur normaly in the same cell, it is considered more reasonable that these natural antibodies are formed by red blood cells during either their formation or breakdown. Another illustration of the phenomenon is the Wasserman Test used to diagnose syphillis. The antibody indicating the syphillitic infection is peculiar in that it does not react with the spirochete (bacteria causing syphillis) itself but with some fatty substances. Many different explanations for this are put forth. One such is that the fatty substance resembles the spirochete antigen. A different explanation is offered by Albert Tyler. He thinks that when spirochete destroys the body tissues, it liberates in the blood, a protein and a fatty substance which fit structurally like an antibody and an antigen respectively. Fatty molecules being smaller, are relatively more rapidly eliminated from the body whereas protein moiety (antibody) being larger, goes on accumulating in the blood. Samples of such blood serum can then react with the fatty antigen in a test tube. If this theory is correct other tissue destroy-

ing agents should also liberate same kind of antibodies in the blood. As a matter of fact, it is now well known that various other infections like malaria, leprosy and tuberculosis give false positive Wasserman Test. To add to the list of autoantibody phenomenon, mention must be made of the recent observations that a virus is a part of normal bacterial cell and that it can be formed by the latter's irradiation by X'rays etc. The autoantibody concept also explains why venomous snakes and scorpions are immune to their venoms.

Naturally, the autoantibody concept suggests the possibilities of fighting infections with the substances extracted from the infecting organisms themselves.

To sum up it should be said that the autoantibody concept is extended to all cells and as it is suggested by some, the large molecules which form the basis of their structure and function are made up of pairs of structurally complimentary substances that act like antigen antibody.

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