IMMUNITY

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IMMUNITY

The subject of immunity covers a vast field of work, a work that I will endeavor to narrate in an elementary manner the doings of the beneficial and injurious microbes and incidentally man's struggle to obtain mastery over his microscopic friends and foes.

If one examines a drop of stagnant water under the microscope, it is found to contain minute forms of animal life, amoeba, and minute forms of plant life, bacteria. On careful examination, the amoeba are seen infesting and digesting the bacteria. Now, if one killed the amoeba and again examined them, the living bacteria are observed decomposing the dead amoeba. It is evident that there was something inherent within the living naked mass of amoebic protoplasm which protected them against the bacteria. If a living plant be carefully examined microscopically, its surfaces are found covered with myriads of microorganisms, yet the living plant is uninjured by them. If this same plant is killed and left in a moist place, the same bacteria quickly tear it to pieces. On the skin, in the upper respiratory passages, and in the alimentary canal of man and animals are millions of different microorganisms, yet during life they do not attack. Something happens--we call it death-- and the microorganisms quickly enter all the tissues. If it is a friend who is thus attacked and we are far distant, we have to hurry to obtain a last fond look before the wrecking crew tears the body to pieces.

Then too, the germs which attack man during life are often not the ones which attack the lower animals. Animals can drink with impunity water infected with typhoid and cholera, yet man on drink-

ing similar water becomes infected. Fowls do not sicken with Asiatic cholera, nor men with fowl cholera. Whooping cough and diphtheria are unknown among the lower animals; and hog cholera and Texas fever are not among the human diseases. This power of resisting infection in varying degrees is universal and is known as immunity. As may be seen from the above examples, this power is not absolute and varies with different plants and animals and under different conditions, but is possessed by all life in some degree; for the absence of immunity like the absence of bacteria, is incompatible with life on this planet.

HISTORY OF IMMUNITY

Historically, the first reference to any attempt at protection against disease by the use of biological prodects was made by Mithiridates, who, it was alleged took small quantities daily of certain poisons in order to render himself immune. It has also been a custom of hunters of certain wild tribes to inoculate themselves systematically with snake venom to safequard the effects of snake bites.

Immunization, however was not placed on a truly practical basis until the eighteenth century, although practice existed in the East many years previously. Lady Montagu, the wife of the Ambassador to Constantinople permitted her son to be inoculated against small pox with matter from variola pustules and subsequently in 1721, introduced the method in England. Despite brilliant results that followed, owing to the fact that although it protected the inoculated it did not prevent the conveyance of the disease in a virulent form to the uninoculated and it was finally prohibited by law.

Sixty years later the attention of Jenner was directed to a peculiar disease of the udders of cows, the hands of milk-men becoming infected, would render them immune to small pox. As a result of his investigations, in 1796, he inoculated a boy with "cow pox" which inoculation with small pox showed him to be immune. In 1798, Jenner published his classical report, which was followed by a systematic and universal vaccination against the world's greatest scourge.

Almost a century passed before any further notable advance occurred in immunology. It was a stimulus in the field of bacteriology which promoted research along this line.

Schwann showed the relationship between decomposition of organic bodies and microorganisms. Supplementing this was Pasteurs work on fermentation and yeast fungus. In 1863, Davaine demonstrated that certain bacilli described in the blood thirteen years before were the causative factors in anthrax. Thirteen years later Koch succeeded in growing these bacilli on artificial medium in pure culture and anthrax was reporduced in animals.

The next problem was to attenuate the bacteria, that is, preserve their identity and life, at the same time reducing their virulence, so that inoculation would not result fatally. In 1881, Pasteur inoculated sheep and rendered them immune with a vaccine prepared from attenuated anthrax bacilli. It was not until 1885, however, after much animal experimentation that Pasteur inoculated the first human subject against rabies. The antirabic inoculation has undergone no material change, although the etiological microorganism of the virus of this disease is still undetermined. As a supplement to the work of Traube and Gescheidlen, in 1887, Buchner showed the specificity of the bactericidal properties of blood serum.

In 1888, Roux and Yersin, and Kitasato discovered the toxins respectively of diphtheria and tetanus. Antitoxin in the serum of animals immunized against the toxin of diphtheria was discovered in 1890 by Behring. In the same year, with the collaboration of Kitasato, immunity was conferred on mice from the serum of rabbits inoculated with tetanus.toxin. Wernicke in the following year, immunized other animals with antidiphtheric serum. Behring, however discovered the whole principle underlying serum therapy and became thereby its honored founder.

In the following year, Ehrlich demonstrated antibodies in the serum of animals inoculated with vegetable poisons, as ricin, abrin and crotin, and three years later, Calmette had similar results with snake venom.

It was recognized, even before Behring's discovery, that the serum of animals inoculated with certain bacteria possessed a specific anti-infectious effect or protection. In 1892, Metchnikoff noticed a particular substance which he called "stimulin", in antibacterial sera, capable of stimulating leucocytes to increased ingestion and destruction of bacteria. Upon this property of phagocytosis, Metchnikoff claimed that immunity depended.

During this time numerous foreign albuminous substances utilized for the production of antibodies and conceptions of the nature of immunity definitely distinguished two types active and passive. Besides this, it was found that exotoxic bacteria were adaptable chiefly to passive and endotoxic bacteria and to active immunization.

In 1895, the phenomenon of bacteriolysis as demonstrated by Pfeiffer dealt a severe blow to Metchnikoff"s doctrine. The following year, Gruber and Durham brought attention to the diagnostical value of "agglutination of bacteria in their specific antiserum. At this time Widal described the use of sera in the diagnosis of typhoid. This was followed up the next year by antityphoid inoculation by Wright. Previously, Ferran and Haffkine had employed attenuated living cultures, prophylactically against cholera. The work of Wright was significant however, as he demonstrated that antibodies may be produced by inoculation with dead bacteria. Wright therefore enjoys the distinction of being the first to realize that any bacterium responsible for a local disease and capable

of isolation in a pure culture may be employed in the form of bacterial suspension or bacterin to cure the disease it causes.

Seven years later Wright and Douglas showed that phagocytosis does not occur save in the presence of serum, thus claiming a specific sensitization of bacteria by certain substances to which the name "opsonins" was given.

The advances in serology at this time were remarkable. In 1898, Belfanti and Carbone discovered that the serum of horses immunized with blood of rabbits was very toxic for these animals. The analogy between these cytotoxins or cytolysins and the specific antibodies formed after bacterial inoculations was immediately recognized. Bordet, Ehrlich and Morgenroth by their experiments demonstrated the presence of haemolysins in the serum of animals inoculated with red blood cells and the interesting and important phenomenon of haemolysis or solution of erythrocytes was demonstrated.

Almost all tissue cells were employed in research work for the porduction of their specific antibodies. The name antigen was applied to these various heterogenous substances. Thus, leucotoxins, spermotoxins, trichotoxins, hepatolysins, nephrolysisn, and neurotoxins, were produced and their indluence as a causative agent in certain diseases became a subject of much scientific reserch. In 1900, Uhlenhuth employed therapeutically the specific cytotoxins for sarcoma and carcinoma in patients.

The year 1902 is memorable in seroloty as it marks the discovery of the complement-fixation reaction by Bordet and Gengau. They demonstrated that no haemolysis can occur if the thermolabile element of haemolysin by absorbed or fixed in the interaction between antigen and antibody.

After the discovery of the Treponema pallidum, Wasserman, in 1906, put the complement fixation to a practical and successful test for the diagnosis of syphilis, resulting in the Wasserman reaction. Subsequently, the principles employed in Wasserman technic have been applies to many other infectious diseases, notable gonorrhea.

THEORIES OF IMMUNITY

Various explanations of the causes and processes of natural and acquired immunity have been attempted. Analyses of the body tissues and fluids have been made and numerous theories formulated for the explanation of the phenomena. Some of these are:

1. The Exhaustion Theory -- this theory was formulated by Klebs, Koch, and Pasteur. These men tried to explain the changes that occur in the acquisition of immunity by assuming that during immunization certain substances necessary as food for the parasites are used up. If the food necessary for the micro-organisms is consumed, the individuals acquire an immunity to these organisms. The immunity lasts as long as the food necessary for the parasites existence and production of the disease is absent from the body.

2. The Noxious Retention Theory -- Chaveau assumed that in immunization, bacteria produce substances that are retained in the body of the immunized animal and individual and prevent further multiplication of these organisms. These products protect the body tistues from further in by that particular species of parasite as long as the noxious substances remain.

3. The Chemical Theory -- In 1887, several scientists, among whom were Salmon and Smith, Foa and Bonome, Roux and Chamberlain, claimed that immunity could be produced not only by the injection of bacteria but also by the injection of the products of bacterial metabolism. This resulted in the assumption of the chemical theory according to which the tissues of the body are chemically changed during immunization.

4. The Humeral Theory -- In 1887, Fodor observed that the body fluids, expecially the blood of the normal individual or animal,

animal, contain certain elements by which they are able to destroy bacteria. Buchner, Behring, and Nutthal later discovered that certain sera are able to destroy some species of bacteria while leaving others unharmed. Nutthal further discovered that heating blood to 60°C. or above, destroyed this germicidal power of fresh normal blood. These substances are called alexins. In 1888, Hericourt and Richet and in 1889, Babes and Lepp demonstrated that blood serum from animals that had acquired immunity to certain diseases was injected into other animals, an immunity to the same disease was conferred.

Behring and Kitasato in 1890 reported successful immunization of rats to tetanus by injection of blood serum from rats immunized to tetanus. From the work of these investigators developed the humeral theory of immunity.

In 1891, Philsalix and Vertrand discovered that if a large animal was injected with sublethal doses of cobra venom, this animal produced substances that neutralized venom of the cobra. This protective substance was called antivenin.

5. Ehrlich Side Chain Theory -- this theory is the basis for our present view of the mechanism of the defenses of the body against disease. It is supported almost entirely by experimental evidence. It is important to realize that the interaction between antigens and antibodies is of chemical nature, that is, the antibody does not destroy the antigen but forms a chemical combination with it.

Ehrlich conceived of a body cell consisting of a nucleus upon which its life depends and a number of processes or "side chains" capable of combining with foodstuffs for the nutrition of the cell

and with foreign substances that might prove injurious to it. These side chains or processes were termed receptors. Each receptor had a special affinity for a certain kind of foodstuff or toxin. Certain receptors are common to all cells while others are found only in special cells. It is also believed that certain receptors are not normally present but are formed by the stimulation of certain toxins.

The toxic molecule consists of two groups, the haptophore group which binds it to the cell receptor and the toxophore group which bears the toxic properties. When the receptor combines with the toxin molecule, the cell throws it off into circulation and similar receptors are formed to take its place. But these receptors are formed in excess and the cell throws these off into the circulation where they unite with corresponding toxic molecules in the circulation.

There is a receptor for each particular for of toxin molecul e Thus the tetanus toxin combines only with the specific receptor provided for it and will not unite with those intended for the diphtheria toxin.

Ehrlich's theory at first only covered the simple union of toxin with antitoxin but was later extended to explain the action of more complex antibodies and is now believed to completely cover all forms of antigen-antibody action.

6. Metchnikoff's Theory of Phagocytosis -- The French school of immunologists headed by Metchnikoff believed the whole process of ingestion and destruction of invading disease producing agents by leucocytes and certain other body cells. This is known as the phagocytic or cellular theory of immunity. At first this theory

was believed to oppose that of Ehrlich's side chain theory but they are not considered so now because it has been found that to some degree one process depends on the other, and that in some diseases both processes are very active while in others one may take the leading role. Some diseases do not stimulate any activity on the part of the other, that is, they are not followed by a condition of immunity.

TYPES OF IMMUNITY

Immunity can be either natural or acquired. I will first discuss natural immunity or that immunity acquired at birth.

Natural immunity is of two types: Congenital Immunity or that acquired from the mother; and Inherited Immunity or that which is a part of the germ composition of the living embryo.

Many infants show a resistance toward certain diseases because of antibodies acquired from the mother during uterine life. For example, babies often have considerable amounts of diphtheria antitoxin in their blood passed to them from the blood of their mother. Similarily infants may possess a specific resistance to other diseases to which the mother is immune. This type of immunity tends to disappear after one years age.

Inherited natural immunity concerns those individuals, who, apart from this natural immunity acquired from the mother inherit as a part of their constitution varying degrees of natural resistance towards infection. If we find that there are marked differences among different races and groups of some species and among individuals of the same race.

Inherited natural immunity is further subdivided into species immunity, racial and group immunity, and group immunity.

Species immunity is the difference in the susceptibility of various species. In general, cold blooded animals such as fish, frogs turtles, are not susceptible to diseases common to warm blooded animals.

Physical imperfections such as deviated nasal septum, flat chest increase liability to infection. Our normal resistance is af-

fected by physiological state of the body. Any infection is likely to be more severe during pregnancy, for example. Malnutrition, fatigue, worry, overexertion, exposure to wet and cold, alcoholism, preexisting weakening diseases such as cancer, diabetes, leukemia, measles, influenza, or tuberculosis also exert an influence over susceptibility. Age is an important factor, most diseases occurring between the ages of one to ten and among the very old.

Acquired Immunity: successful resistance against germ diseases depends upon the development of a specific immunity, associated with the appearance in the blood of so called antibodies which act upon the germ or its toxin. This special resistance is acquired as a result of natural infection or by one of the artificial methods of immunization and is probably never inherited.

Acquired immunity, whether caused by a previous natural attack of the disease, or artificially by the inoculation of bacteria is always strictly specific, that is, the protection extends only to the particular disease which has previously occurred or whose germs have previously been injected. An attack of scarlet fever, protects only against scarlet fever but not against measles or any other disease. Inoculating an individual with typhoid bacilli protects him only against typhoid fever, but not against dysentery, plague, cholera, etc.

Before examining into the nature of this very specific form of immunity, it will be well to call attention to certain important means by which the body defends itself against bacterial invasion in general.

Many of these are so commplace that their significance is of-

ten overlooked:

(1) The protection afforded to the body by the unbroken skin is undoubtedly one of the most important means of defence. It is well to remember this, and especially to bear in mind that we say "unbroken" skin. In the sterilization of the skin prior to a surgical operation a great deal of harm is sometimes done by too vigorous scrubbing or the application of too concentrated disinfectants.

(2) A similar protection, though less powerful is afforded by intact and healthy mucous membranes. Any condition injurious affecting these renders the body more liable to bacterial invasion. This is well illustrated by the frequency with which an attack of measles (which affects the mucous membranes to a marked degree) is the starting point of other infections.

(3) The acid gastric juice undoubtedly destroys large numbers of bacteria which are swallowed. Disorders of digestion may, therefore constitute the deciding factor in determining a bacterial invasion especially of the intestinal tract.

(4) Fresh blood serum is able to kill a considerable number of bacteria, and this, therefore, constitutes another mode of defense against bacterial invasions.

(5) The white blood cells, or leukocytes as they are called, appear to be designed especially to destroy invading bacteria. This process has already been discussed under phagocytoses.

(6) Still another mode of defense is seen in what takes place in abscesses. When these are examined, it is found that the body has built a wall around the infected area, thus shutting off the

bacteria and their poisonous products from the rest of the body.

(6) The body temperature is a factor in resistance to disease. Fowls whose temperatures are higher than that of human beings ($42^{\circ}C.$) are normally resistant to microorganisms causing plague and anthrax. However, if a hen were chilled by immersion into cold water, it would become very susceptible to anthrax.

Variation in susceptibility to diseases have been observed in different races and groups of the same species. This is known as racial immunity. It is claimed that Algerian sheep may be pasteured with impunity on land so thoroughly infected with anthrax bacilli as to be deadly for the common breeds of sheep. Field mice are very susceptible to glanders whereas white mice are immune. The black rat is more resistant to anthrax than the white rat.

Racial immunity is also perceptible in man. It is generally believed that the negro, Eskimo, and American Indian are more susceptible to tuberculosis than the white man. However, according to Carrol, the white race is more susceptible to yellow fever than the negro and that among the latter, those living nearest the equator are less susceptible than the more northern races.

Smallpox which is so highly fatal among some races, is considered a relatively mild disease in Mexico.

Differences of susceptibility of different species to tuberculosis is especially interesting. Fish have a form of tuberculosis which is not transmissable to human nor will the human tubercle infect fish. Hens and other birds have a spontaneous disease very much like tuberculosis in man but avian tubercle bacilli probably never infect human beings. Man is susceptible however, to tuberculosis infecting animals but not to such a degree as to the human type of germ. Rabbits and guinea pigs are both susceptibel to bov-

vine type but rabbits are more resistant than guinea pigs to human type.

It is general knowledge that some families or members of a family contract all communicable diseases which they come in contact whereas other individuals of the same family or race escape. When a town's water supply becomes infected, some individuals contract disease while others escape. This is known as individual immunity. Some individuals seem to be naturally resistant to skin disorders common colds and other familiar diseases. This natural resistance of some individuals may also vary from time to time depending upon the season of the year and changes in the physical body.

Laboratory animals such as rabbits, guinea pigs, etc., on which most experiments are conducted show very slight in individual variation. In fact, the uniformity of reaction on part of the guinea pigs of similar age and weight against measured quantities of bacterial toxins make it possible to use these animals to standardize antitoxins. This has led some scientists to believe that there is no individual immunity. What is claimed by some as natural individual immunity, they believe is really an acquired immunity resulting probably from a earlier slight unrecognized attack of the disease. Recent work has proved that individual immunity in cases of dysentery and typhoid comes from a previous attack. It is quite likely that as the subject of immunity becomes better understood it will be found that the majority of all reported cases of individual immunity to the communicable diseases come from missed mild cases.

There are, however, clear cut cases of individual immunity due to age. There are certain diseases classed as children's diseases

to which the individual shows greater immunity at one age than at another, such as ringworm, diphtheria, and scarlet fever.

VACCINES AND IMMUNE SERUMS

Physicians and nurses have a tendency to confuse the terms "vaccine" and "immune serum," any produce of this nature being spoken of as a "serum". Vaccines and immune serums differ in their fundamental basis, method of production, and type of immunity that they bring about.

A vaccine is the causative agent of a disease (bacterium, toxin, or virus) modified in such a manner that it is incapable of producing the disease but is able when introduced into the body to elicit the production of specific antibodies against the disease.

The use of vaccine for the purpose of causing people to have mild attacks of a disease began among the ancient Chinese whose custom it was to place in their nostrils a scab from a smallpox sore thus vaccinating themselves against the disease in its regular form. In England in the 18th century, Dr. Jenner developed the method of using the scab from a person who had the cowpox and it is from this source that we get the name, vaccine coming from the Latin "vaccinia" meaning cowpox.

Vaccines are always antigens; i.e. they always produce an active immunity. They find their greatest usefulness in the prevention of disease. Important vaccines are those for the prevention of smallpox typhoid fever, and rabies; toxin-antitoxin and toxoid to prevent diphtheria, toxin to prevent scarlet fever, and the recently introduced toxoid for bringing about a more or less permanent immunity to tetanus. All of these except scarlet fever toxin are the causative agents of their respective diseases so modified that they are no longer able to cause the disease but are still capable of producing anti-

bodies against it. Instead of modifying scarlet fever toxin itself the dose is modified, that is, it is given in a series of doses so small that they are not injurious.

Vaccines are prepared in a number of different ways depending upon the type of vaccine. A bacterial vaccine is a suspension of killed bacteria in normal salt solution, killed by heat or by a chemical disinfectant and preserved by a weak germicidal agent, such as 0.5% phenol or 0.25% tricresol. A culture of the bacteria is grown for a short time (twenty-four to forty-eight hours). If grown on slants the bacteria are washed off by swab and sterile solution of saline. The number of bacteria in each cubic centimeter of the washings is determined and salt solution is added until the desired number per cubic centimeter is obtained. The bacteria are killed and cultures are made from the finished product to see that the bacteria are dead. The theory underlying the use of bacterial vaccine is that they increase phagocytosis and cause tissues not involved in the disease to produce antibodies. Bacterial vaccines are of three types, autogenous, stock, and mixed stock vaccines.

Autogenous vaccines are prepared from cultures of bacteria isolated from the patient to be treated and are far more effective than stock vaccines for many conditions having the advantage of using the particular infecting strain of that individual and community. They have the disadvantage at times of being more virulent cultures with a greater chance of a pronounced reaction and hence require the use of smaller initial dosage than in the use of stock vaccines. They also have the disadvantage of the delay required for preparation.

Stock vaccines are vaccines made from laboratory stock cultures

The best known and probably most efficient in use is the typhoid vaccine used in the prophylactic inoculation against typhoid fever, known as the Rawling strain of the typhoid bacillus. The Park strain of diphtheria bacillus has for years been used in the production of immunizing agents against diphtheria. Among the various types of stock vaccines are those prepared for the prevention of whooping cough, cholera, plague, and the pyogenic cocci (staphylococcus and streptococcus), pneumococcus, colon bacillus, influenza bacillus, gonococcus, meninogococcus, etc. The stock vaccines are declining in favor and only one is now widely and successfully used typhoid vaccine.

Smallpox vaccine is prepared by the inoculation of female calves with cowpox virus. The abdomen is shaved and rendered sterile. It is then scratched with a needle in many places just deep enough to bring a little blood. The virus is rubbed into these scratches. At the end of about six days the abdomen will be thickly broken out with vesicles which contain the modified virus used for vaccination. These vesicles are opened, using aseptic technic and a sticky exudate is removed, mixed with four times its weight of equal parts of glycerin and water containing 1% phenol for preservation. The vaccine is purified, tested to determine if it is of sufficient potency and sterility and is ready for use.

Rabies vaccine is prepared from the brain and spinal cord of rabbits suffering with rabies. The rabbit is inoculated with rabies and kept under the best of sanitary conditions. Just before its death it is chloroformed and spinal cord removed under aseptic conditions. The cord is cut into pieces and dried over an appropriate drying agent or subjected to chemical treatment. Parts of it are

so treated for one day, other parts for three days and so forth up to eighteen days. Pieces of cord which have dried or been treated long are injected hypodermically (after they have been mixed with water) to the patient, followed at daily intervals by cord which has been dried for shorter time until eventually the patient is receiving cord which has been dried for only one day.

An immune serum is the serum of an animal that has been highly immunized to an infectious disease. Its characteristic feature is the antibodies that it contains. Immune serums bring about only passive immunity, this being due to the antibodies they contain. Immune serums are specific in their action bringing about an immunity to no other disease than the one for which they are prepared.

Antitoxins are immune serums prepared against extra-cellular toxins. They have no action of the bacteria that produce the toxins. The antitoxins that have been used longest and have saved most lives are those against diphtheria and tetanus. Both are prepared in the same general way. The bacteria are allowed to grow in a liquid medium until the medium contains a large amount of exotoxin that has been thrown off by the bacteria. They are then separated from the toxin is found to be of suitable strength, horses are immunized against it by beginning with a small dose and giving several injections increasing the dose at each injection. When the antitoxin production is at its height, the horse is bled and the antitoxin strength of the blood serum is tested. If the serum is of sufficient strength it is further refined and purfied for use.

Since antitoxin can be prepared only against organisms producing exotoxins and since few organisms produce exotoxins, the

number of antitoxins is limited. An antitoxin against the toxin of scarlet fever streptococcus is being used with considerable success. The unit of measurement of scarlet fever streptococcus toxin is known as the "skin test dose" (S.T.D.) which is the smallest amount that will cause a reaction when injected intradermally into a susceptible person.

Botulinus antitoxin has been used with good results. Reports seem to indicate the erysipelas streptococcus antitoxin is of benefit. All antitoxins should be given early and in sufficient amount because they cannot repair injury already done.

Toxin-antitoxin is a mixture of diphtheria toxin and antitoxin with a slight excess of the former. It is used for producing a permanent immunity to diphtheria but cannot be used to prevent the disease in those already exposed as it takes three months or more for the immunity to become completely established. The treatment consists of three injections given at weekly intervals.

Another type of serum used in the treatment of disease is that used in convalescent serum therapy. It consists of injecting the whole blood or serum of a person who has recently recovered from a disease, into one ill of the disease (as a therapeutic measure) or one exposed to the disease (as a preventive measure). The theory on which this type of therapy is based is that the blood of the convalescent patient contains antibodies, and these antibodies confer a passive immunity upon a person to whom the blood is given. This type of therapy has been used with good results in measles, poliomyelitis, scarlet fever, and probably mumps.

HYPERSENSITIVENESS

Allergy and anaphylaxis have a very definite connection with immunity. If a small amount of foreign protein (blood serum, egg white, etc.) which within itself is not poisonous, is injected into a suitable animal, the dose will be without noticeable effect; but if a second injection is given after an interval of ten to fourteen days severe symptons or even death may occur. This condition is known as anaphylaxis. The first dose is known as the sensitizing dose, the second dose is known as the provocative dose. When the injections are given at closer intervals, immunity instead of anaphylaxis results.

Certain people exhibit unusual manifestations upon coming in contact with substances, usually of a protein nature, that have no effect on the average person. For instance certain persons have asthma upon coming in contact with horse dander, feathers, etc. A great many have hay fever upon coming in contact with pollens and others have skin eruptions or asthma after eating certain foods. Such diseases are known as allergic diseases and the condition of increased susceptibility underlying their occurrence is known as allergy. Substances that are capable of bringing about the allergic state are known as allergens.

Anaphylaxis and allergy are fundamentally much alike if not identical. For this reason the term hypersensitiveness, which includes both anaphylaxis and allergy has come into general use. By hypersensitiveness is meant a condition in which the affected person exhibits a marked reaction to substances that have no noticeable effect on a normal individual of the same species.

The phenomenon of anaphylaxis may be best demonstrated by giving a guinea pig a small injection of horse serum and at the end of ten to fourteen days giving a second but larger injection. Within one or two minutes the pig will become restless and exhibit difficulty in breathing which progresses to frantic activity with extreme dyspnea, followed by death from respiratory failure. The autopsy reveals the lungs of the animal to show a remarkable resemblance to those of a person with asthma. If a rabbit is used as the test animal, death is due to circulatory failure, and in the dog, the symptons are referable to the gastro-intestinal tract failure. The symptoms of anaphylaxis depend on the species of the affected animal and not on the substance that brings about the anaphylactic state.

Another phenomenon relating to anaphylaxis which is significant and important in the relation to blood transfusions. If the blood serum of an animal sensitive to some foreign protein be injected into a normal animal and after an interval of from five to eight hours the normal animal is injected with some of the material to which the first animal is sensitive, anaphylactic symptoms will occur. This is known as passive anaphylaxis. The passive transfer of the hypersensitive state assumes considerable importance when it is realized that the use of a hypersensitive donor for blood transfusion may render the recipient hypersensitive. Since several days must elapse after;the sensitizing material must be of a protein nature; and since anaphylaxis is specific and may be passively transferred; does it not seem reasonable to believe that anaphylaxis is due to antibody formation and is closely related to immunity? Such is believed to be the case.

Several theories have been formulated as to the reason anaphy-

lactic shock develops in one case and immunity defelops in another case under very similar circumstances. According to one theory, the antibodies responsible for anaphylaxis split the antigen into a poisonous and a nonpoisonous portion, and the poisonous portion brings the anaphylactic symptons. According to another theory, the antibodies responsible for anaphylaxis are not cast into the blood stream, as are those responsible for immunity, but remain attached to the body cells where the combination with antigen takes place and the injury to cells brought about by the combination leads to the anaphylactic manifestations. According to still another theory, whether immunity or anaphylaxis will occur is a matter of speed, a slow combination of antibody and antigen leading to immunity while a rapid one leads to anaphylaxis. Whatever the mechanism may be it is believed that the sensitizing dose of antigen leads to the production of antibodies remarkable alike if not identical with those responsible for immunity, and when the antigen is again introduced into the body the antibodies combine with it to produce anaphylactic manifestations.

Many conditions such as asthma, hayfever, serum sickness, urticaria, and other allergic skin diseases, angioneurotic edema, and certain drug idiosyncrasies are believed to be of allergic origin. The fundamental origin of allergies differs in no way from anaphylactic reactions excepting that sensitization occurs naturally instead of being induced artificially. The tendency to allergic diseases is not inherited as may be seen by the individuals on one family all of whom may be allergic to different proteins, but the state of hypersensitiveness may be inherited.

Allergens may reach the body by way of the respiratory or digestive tracts or by transmission through the placenta. The respiratory tract is the most common method. In some cases, passive sensitization may be transmitted the mother to the child in utero via the placenta. Like immunity of the newborn this type of sensitization does not last long.

Asthma is an allergic condition that is most often due to animal hair, feathers, or dander, house dust, food bacteria and certain insects.

Hayfever is due to sensitiveness to pollens. To be of importance as a hay fever producer a plant must porduce a light dry pollen that is easily carried a long distance by the wind. This excuses both goldenrod and roses which have been accorded an unearned distinction as cause of hayfever. Early spring and early summer hayfever is most often due to tree pollen and the more late summer type is due to grass pollens.

Serum sickness is a type of allergy res lting after the administration of immune serums. It is common and its manifestations are unpleasant but seldom dangerous to life. It usually begins from eight to twelve days after the injection of an immune serum and is characterized by a skin eruption, swollen, painful and stiff joints enlargement of the lymph nodes, leucopenia, and decreased coagulation of the blood. It is believed to be due to the action of antibodies formed in the early days after the injection on a part of the serum still remaining in the body.

Hypersensitive reactions are of use in the diagnosis of susceptibility to various diseases. This may be demonstrated in the use of the Schick test for diphtheria, the Dick test for Scarlet

Fever, and the Tuberculin test for Tuberculosis.

The purpose of the Schick test is to determine whether a person has sufficient diphtheria antitoxin in his blood to render him immune. It is used to detect those who need active immunization and to determine whether active immunization has been effective. The test is performed by injecting a minute amount of diphtheria toxin intracutaneously.

If the person's blood contains sufficient antitoxin to protect him against diphtheria no reaction will occur. If insufficient antitoxin is present, a reddened area will appear at the site of inoculation within twenty-four to thirty-six hours, and persisting for four or five days.

The Dick test is to determine susceptibility to scarlet fever. It is performed by injecting between the layers of the skin of the forearm a small amount of scarlet fever toxin so diluted that one S.T.D. (skin test dose or the amount that will cause an inflammatory reaction when injected into the skin of a susceptible person) is injected. In the immune persons the antitoxin in the blood neutralizes the injected toxin and no reaction occurs. In susceptible persons no antitoxin is present, and the toxin attacks the cells aroung the site of injection, producing within twenty-four hours to thirty hours an area of inflammation and redness of the skin.

The tuberculin test is occasionally used in human beings but is almost exclusively used in the testing of cattle for tuberculosis. A small amount of tuberculin is injected subcutaneously into the individual or the animal and careful record of the temperature is kept for the following hours. If there is a significant rise in

temperature, it indicates that the individual is tuberculous.

The Von Pirquet test consists of the introduction into the abraded skin of a small amount of "Old Tuberculin", a product made by extracting and concentrating an old culture of tubercle bacilli in glycerin broth. If the skin where the test is made turns red, while the control test spot remains essentially unchanged, it means that the person has or has had tuberculosis infection of some grade. If both spots are unchanged, it means that the patient has not had the disease. The test must be considered as being of value but as not being final in accuracy.

The Mantoux test is being used more and more for the purpose of diagnosing early tuberculosis in children. It consists of injecting a small quantity of a dilute solution of "Old Tuberculin" into the superficial layer of the skin. Redness and swelling about the site of injection indicates a positive reaction.

IMMUNITY

Immunity plays a vital role in the life of every individual whether he or she may realize it or not. Constantly each one of us is coming in contact with destructive organisms , which were it not for the immune bodies and properties of the body would probably cause severe illness if not death.

The mortality of those diseases treated with vaccines a nd serums has been reduced unbelievingly and with the advent of new serums and bacterial products of immunization, scientists are coming nearer that goal of "prevention or a cure for every disease".