

SERUM THERAPY.

HOW SERUMS ARE EMPLOYED IN MODERN MEDICINE.

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SERUM therapy is the treatment of disease by injecting into the blood the serum, or watery part, of the blood of an animal that has been made immune to that disease. Something similar to serum therapy appears to have been practised in antiquity. Mithridates, king of Pontus, fearing that he would be poisoned, caused repeated small doses of various poisons to be administered, for long periods, to ducks, the blood of which he drank, with the astonishing presentiment that it must contain effective antidotes to the poisons. The members of an ancient priestly caste in India allowed themselves to be bitten frequently by snakes which had been deprived of their poison glands. These priests claimed that their saliva thus acquired power to save the lives of persons who had been bitten by venomous serpents. These methods of treatment undoubtedly originated in the mind of some man of genius and were afterward practised ignorantly and according to tradition. Many centuries later a very important science was founded on the same basis.

In 1888 the French physiologists Richet and Héricourt, inspired by Pasteur's theory of vaccination, made the surprising discovery that rabbits survived injections of ordinarily deadly doses of certain bacteria if they had recently received injections of the blood of dogs which had been treated with increasing doses of the same bacteria until they had become immune to the action of doses normally fatal to dogs. In other words, Richet and Héricourt discovered the possibility of communicating to another animal the immunity which Pasteur had succeeded in producing in the individual by repeated and increasing doses of the disease germ.

Two years later Behring expressed the conviction that acquired immunity is due to the presence of definite protective substances in the blood, and that this condition can be transferred to other individuals by injections of serum.

Diseases of three classes are caused by bacteria. In the first class, represented by diphtheria, dysentery and tetanus, the bacteria settle in one part of the body, where they multiply and produce poisonous substances, or toxins. The toxins enter the circulation of the blood, but the bacteria do not. In the second class, represented by erysipelas, puerperal fever, pneumonia, meningitis and diseases resulting from the infection of wounds, the bacteria enter the circulation of the blood and invade every part of the body. Diseases of this class are called septic diseases and are very often fatal. In none of them has any true toxin, or soluble poison, been discovered. In the third class, represented by typhoid fever, cholera and plague, both the bacteria and their toxins enter the general circulation.

Tuberculosis, the disease which causes more deaths than any other, has not yet been satisfactorily classified or explained. Although countless autopsies and other investigations are continually being made, we do not know whether Koch's bacillus kills by producing toxins or directly by its multiplication in the blood and tissues of the body. As the forms of disease caused by bacteria differ, so must the protective or immunizing influences which their germs develop in the blood. Ehrlich and Behring distinguish three classes of protective serums: serums containing antitoxins, or substances which neutralize the toxins of diseases of the first class; anti-bacterial serums, which check the multiplication of bacteria, in diseases of the second class; and serums which combine both of these properties and are efficacious in diseases of the third class. Hence, in view of our ignorance of the precise character of tuberculosis, it is not surprising that no efficient serum for that disease has yet been produced.

In France, Austria and some other countries, therapeutic serums are prepared in government establishments, called Pasteur institutes. In Germany, a few great chemical firms have taken up the work. The serum is obtained from the blood of horses. The weight of the animal having been determined, a minimum dose of a toxin or a bacterial culture is injected, according as the object is to produce an antitoxin serum or an antibacterial serum. The horse reacts to the injection with slight fever and other symptoms of ill health. After these have passed and the initial weight has been regained a second dose, twice as large as the first, is injected. In this way the injections are repeated and increased for a few months, until the horse finally fails to react to a dose large enough to kill 1,000 unprepared horses. Three weeks after this condition of immunity has been attained about two gallons of blood are drawn from the horse's veins. After

the blood has coagulated, the clear serum is separated from the clot and its curative power is tested by injecting it into the circulation of mice, guinea pigs, monkeys and other small animals, which have previously received injections of the toxin or the bacterial culture of the disease in question. This examination in the factory is followed by rigid official tests applied at the Ehrlich Institute in Frankfurt. The serum cannot be sold for use on human beings until its potency has been officially determined and stamped upon the bottles. In the case of diphtheria serum, the only one for which the system of gradation adopted can be regarded as final, the unit is a quantity of antitoxin sufficient to protect a guinea pig against 100 times the normally deadly dose of the toxin of diphtheria. A serum which contains one unit of antitoxin in each cubic centimeter, is called a normal serum and its potency is 1. A serum 1,000 times as strong is of potency 1,000, and so on.

The most successful results have been obtained with antitoxin serums, especially in diphtheria, tetanus and dysentery. In all of these diseases the serum exerts a curative action and abates the distressing symptoms. The statistics of diphtheria clearly demonstrate the importance of Behring's discovery. Only sixteen years ago the diagnosis "diphtheria" created panic in the family of the patient. Tracheotomy was frequently practised and many children died of suffocation. Now, if the serum is administered promptly at the outbreak of the disease, the suffering child becomes quiet, the temperature falls and the pulse regains strength in eight or ten hours. The morbid accumulation is expelled from the throat, sleep becomes possible and 36 hours later the child is convalescent. The result which nature can accomplish only in weeks, by slowly producing antitoxin in the body of the patient, modern science effects in a few hours, by administering antitoxin which has been formed in the blood of horses.

The antibacterial serums, which are employed to check the propagation of living germs and their dissemination through the body, work in far less favorable conditions, for every one of the host of microbes already produced is a fresh source of infection and even those which have been killed by the serum may cause serious organic injury. Hence these serums are efficacious chiefly, or only, when they are administered while the bacteria are still at the point of entrance and before they have become disseminated through the body. This is especially true in infected wounds, puerperal fever, pneumonia and splenic fever. For all of these diseases we possess serums which prevent the dissemination of the germs and protect the organism from fresh infection, but it is seldom possible to cure a patient whose blood is already poisoned by the disease germs.

In diseases of the third class, which includes typhoid fever, cholera, and plague, the serum is required both to neutralize toxins and to check the multiplication of bacteria. The serum therapy of these diseases is still in its infancy, but experience has convinced me that success will ultimately be attained.

In tuberculosis the prospect is less bright. No effective immunizing agent is yet known. A serum prepared by Marmoreck has recently attracted much attention, but its curative value must still be regarded as doubtful.

The statistics of diphtheria, on the other hand, show that the mortality in this disease has been reduced, by the introduction of the serum treatment, from between 30 and 41 per cent to 16 per cent, and to between 2 and 6 per cent of the cases in which the serum is employed in the first two days of illness. In an epidemic of diphtheria in Berlin in 1895 the mortality was 32 per cent in a hospital in which the serum was not used, and only 8 per cent in a hospital in which it was used. Behring was fully justified in asserting that the serum treatment of diphtheria annually saves 20,000 human lives, in Germany alone.

In every disease to which serum therapy is applicable, the benefit derived from the treatment increases with the promptness of its application. The rule should be, not to wait until the disease has appeared, but to begin the serum treatment at the first sign of danger. Hence diphtheria serum is administered to all the children of a family in which a case of diphtheria occurs, tetanus serum is administered when a wound has been contaminated with earth (for the germ of tetanus lurks in the soil), and puerperal fever is prevented by injecting streptococcus serum at the first appearance of fever in childbed.

This employment of serum is destined to revolutionize all therapeutics. The more fully convinced of its harmlessness physicians become, the more will they be inclined to employ it, even at the risk of taking an unnecessary precaution. The excellence of the results obtained by this early employment of serums is due to the fact that all the toxins or bacteria that subsequently invade the body are attacked and destroyed immediately upon their entrance, before they can reach important organs.

In contrast to this preventive serum treatment is the curative treatment, employed after the disease has actually appeared. In the latter case the objects of the treatment are to check the multiplication of the bacteria and their production of toxins, and to free the cells of the body from the toxins which have already become attached to them. It is not certain that the second object can be accomplished. There is good reason to believe that a cell, once poisoned, is incurable and doomed to death. But if the general organism is freed from poison, it easily survives the loss of a few cells, and replaces them by new ones. If the injury is extensive a scar is formed by the substitution of useless connective tissue for active cells, but if the disease is quickly checked and the general vitality little impaired no permanent lesion is produced. Hence the action of serums is essentially preventive, even when it appears to be curative, for it is the protection of the tissues which have not yet been attacked that assures the replacement of the parts which have been destroyed.

The principal reason why the employment of serum treatment is so often delayed is to be found in the attitude of the public. The physician is often induced, by the violent opposition of the family, to wait until the favorable moment has passed. Many cases of diphtheria and puerperal fever are lost in this way. Furthermore, the older physicians are not very familiar with the theory and practice of the method and are not inclined to employ it except in desperate cases. But these obstacles are gradually being removed as the increasing success of the continually improved serums gains new advocates of serum treatment.

The popular opposition to the new method finds some apparent justification in the unpleasant effects which it often produces. In about one case in five, the injection of serum is followed, in a week or so, by eruption and itching of the skin, slight fever and pains in the joints. These symptoms are justly attributed to the injection of serum, but recent experiments prove that they are caused, not by the antitoxin, but by the action which certain substances, formed in the human organism under the influence of the serum, exert upon the albuminous constituents of the equine serum. The eruption is harmless and no patient has lost his life because of it.

Which diseases appear most likely to find effective serum treatment within a reasonable time? Unquestionably diphtheria and dysentery, in both of which a very gratifying degree of success have already been attained. Although tetanus is a disease of the same class, the toxin class, serum treatment of tetanus has met with little success. An effective method cannot be developed until improved methods of diagnosis enable us to detect the disease before the beginning of the convulsions. So long as tetanus can be diagnosed with certainty only from the convulsions the majority of patients will die, though treated with the best of serums.

In the second, or septic, class of diseases, the situation is very similar. With the same serum, results a hundredfold better are obtained by a good diagnostician than by a poor one, and success in treatment must wait for improvement in diagnosis. A new field, however, has been opened for the employment of antibacterial serums in these diseases—the field of local application. Recent investigations encourage the hope that peritonitis and meningitis can be checked in their first stages and quickly cured by the influence exerted upon the white corpuscles of the blood by antibacterial serums applied at the point of initial infection.

There is also good reason to hope that more efficient serums than those now known will soon be obtained, by a double immunizing process, for the diseases of the third class, typhoid, cholera and plague.

In tuberculosis, however, there is no immediate prospect of finding a method in any way superior to the rational and natural treatment with fresh air, sunlight and abundant food. We must continue our studies until we learn more of the nature of the specific poison and the germ which produces it.—Umschau.