The Control of Scarlet Fever

Medicine

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The first part of this article, in which Dr. Dick told how she and her husband established the nature of scarlet fever, was printed in the March (1928) issue of *Medical Progress*, the publication of the American Association for Medical Progress that is now merged with the SCIENCE NEWS-LETTER. For the convenience of those who wish to read the first installment, a limited number of copies have been secured and will be sent upon request for 10 cents in stamps to cover handling and postage.

This second part relates the development and application of a scarlet fever antitoxin.

While the determination of the cause of scarlet fever was important scientifically, it would not have been of much practical value without the discovery of the specific toxin of the disease. It was the discovery of the toxin which enabled us to develop:

First, a skin test to determine which individuals are susceptible to scarlet fever and which are immune.

Second, a method of immunizing susceptible persons against scarlet fever so that they do not contract the disease on exposure to it.

Third, an antitoxin specific for scarlet fever which is used therapeutically to treat persons who are already sick with scarlet fever, and prophylactically as temporary emergency protection after exposure, in suitable cases.

Fourth, a method of recognizing scarlet fever streptococci and distinguishing them from other streptococci, such as are found in erysipelas and puerperal sepsis.

These four applications of the discovery of the specific toxin of scarlet fever furnish the means of controlling the disease. Sufficient time has now elapsed to permit the determination of their practical value.

Until the results of this work were available, there had been no way of distinguishing the streptococci associated with scarlet fever from the hemolytic streptococci found in other diseases. There is nothing characteristic about their appearance or manner of growth that distinguishes them. Attempts to differentiate them by means of immune reactions had not been successful. But the discovery that hemolytic streptococci are capable of producing potent toxins specific for certain diseases enabled us to develop a method of identifying the streptococci by means of their toxins and corresponding antitoxins. The toxin in question is mixed with a known antitoxin, such as scarlet fever antitoxin. If it is neutralized by scarlet fever antitoxin, the toxin

DR. GLADYS DICK, co-originator of the Dick test for scarlet fever susceptibility, and of scarlet fever antitoxin

is shown to be scarlet fever toxin and the hemolytic streptococcus which produced it is identified as a scarlet fever streptococcus. This method of identifying hemolytic streptococci by means of their toxins has opened up a new field for medical research, in which many investigators are now working. By applying this method, Birkhaug and Amoss have been able to show that the hemolytic streptococcus of erysipelas produces a specific toxin and they have been able to obtain the corresponding antitoxin. Others have reported that the hemolytic streptococci found in child-bed fever produce a specific toxin for this disease. Thus the whole problem of hemolytic streptococcus infections, in which so little progress had been made, is apparently in the process of being solved by application of the new methods developed in the research on scarlet fever.

Scarlet fever antitoxin is produced artificially by injecting human beings or horses hypodermically with the sterile toxin in gradually increasing doses. If properly carried out, this treatment stimulates the production of scarlet fever antitoxin and confers immunity against scarlet fever without inconvenience or danger to the individual immunized.

For the production of antitoxin on a large scale to be used in the treatment of scarlet fever patients, horses are employed because it is possible to obtain larger amounts of antitoxin from them. Gradually increasing doses of the toxin are given until it is found that the horse is producing a good antitoxin. He is then bled and the serum, or fluid portion of the blood, which contains the antitoxin, is separated from the blood cells. This serum is subjected to a chemical process which concentrates and refines it. It is then standardized against the toxin and is ready for use in the treatment of scarlet fever patients.

There is considerable variation in the severity of scarlet fever. There are mild forms in which the chief object in giving antitoxin is to reduce the chances of complications to a minimum. From such mild forms there are all possible gradations to the fulminating, toxic type in which the patient may die in a few days of the toxemia. The therapeutic dose of antitoxin adopted by the Scarlet Fever Committee is adequate for the ordinary mild to moderately severe attack. Within 12 to 18 hours after the antitoxin is given in an early case there is an improvement in the general condition of the patient. The fever subsides and the rash begins to fade. In more severe cases, especially in those complicated by sinus infections, it is sometimes necessary to give a second dose of antitoxin 18 to 24 hours after the first dose. In extremely toxic cases, with high fever and delirium, it is advisable to give two therapeutic doses at once. Occasionally one sees cases of scarlet fever of several days' duration in which the streptococci have found their way into the blood and the heart and kidneys are so badly damaged that no method of treatment can be expected to effect a cure. An effort should be made to administer scarlet fever antitoxin early enough to prevent such conditions.

It has been shown that properly prepared and standardized scarlet fever antitoxin, given in adequate dosage early in the disease, shortens the course of scarlet fever and reduces the frequency and severity of complications. In order to be most effective, the antitoxin should be given as soon as the rash begins to appear. With every day of delay in administering the antitoxin its benefits diminish.

In a series of three hundred scarlet fever patients treated with antitoxin and compared (*Turn to next page*)

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with a similar series of three hundred cases treated without antitoxin, the incidence of complications was 8 per cent. in the antitoxin series and 38 per cent. in the series which received no antitoxin. Gordon has reported another series of 500 cases treated with antitoxin and 500 treated without antitoxin. He found a similar reduction in the number and severity of complications in those treated with antitoxin.

In addition to its use in the treatment of scarlet fever, the antitoxin may be given prophylactically in selected cases as an emergency measure to prevent the development of scarlet fever in susceptible persons already exposed to the disease and infected with scarlet fever streptococci as shown by nose and throat cultures. Such passive protection with antitoxin is purely an emergency measure and it must be kept in mind that the protection is only temporary, lasting at the most two or three weeks. As soon as the foreign serum is eliminated from the body, the individual again becomes susceptible to scarlet fever and may contract the disease again.

The Only Permanent Protection

The only permanent form of protection is that furnished by active immunization with graduated doses of scarlet fever toxin which stimulates the individual to produce his own antitoxin.

Not everyone is susceptible to scarlet fever. Some have spontaneously acquired immunity to the disease through having had an attack or by repeated exposure. To learn which individuals in any group are susceptible so that they need to be immunized and which ones are immune and do not require immunization, skin tests are made. This is accomplished by injecting just beneath the upper layer of the skin exactly one-tenth of a cubic centimeter of a dilute and accurately standardized solution of scarlet fever toxin. The injection should be made on the anterior surface of the forearm, at the junction of the upper and middle thirds. The result of the test is observed between twenty and twenty-four hours later. This observation should be made in a bright light in order not to overlook slightly positive reactions.

An area of reddening one centimeter in any diameter constitutes a positive reaction and indicates some degree of susceptibility to scarlet fever. There is no induration in the positive tests—only reddening with slight superficial swelling and positive reactions have usually disappeared in 30 to 48 hours so that the results of observations made more than 24 hours after the test would not be reliable. On the other hand, the observations should not be made too soon—not earlier than 20 hours. According to the degree of susceptibility of the individual, the skin reaction may vary in color from faint pink to intense red; in size up to five centimeters in diameter.

Incidence of Susceptibility

In a series of skin tests made in thirty thousand persons, it was found that infants under 6 months showed less frequent and less strongly positive reactions than older children. During the first year there is apparently a gradual increase in susceptibility. Between one and six years of age, 90 per cent. of children living under good conditions may show positive reactions indicating that they have not yet had scarlet fever. After the children start to go to school they are exposed to scarlet fever from time to time and some of them contract the disease. This results in a decrease in the incidence of susceptibility with increasing age. The more crowded the schools and living conditions, the more rapidly this spontaneous immunization takes place due to the fact that crowding favors the spread of infection. Extremes of susceptibility due to differences in living conditions are illustrated by two institutions. The first is an orphanage of 3,000 where the children live in cottages and are out doors most of the time when they are not in school. In this orphanage 63 per cent. were found susceptible to scarlet fever, indicating that 37 per cent. had had the disease in some form. The other institution was one of 3,000 feeble-minded children who were kept indoors in crowded buildings. Here only 13 per cent. were found susceptible, showing that 87 per cent. had had scarlet fever.

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Footnote on Scarlet Fever

Medicine

Editorial comment on Dr. Dick's article, prepared by the American Association for Medical Progress.

In the article on the Control of Scarlet Fever, by Dr. Gladys H. Dick, the second installment of which appears in this number of SCIENCE NEWS-LETTER, no attempt was made to indicate the many important ramifications which the study of this disease has had to pursue, since experimental methods were systematically applied to it.

Earlier experimenters had succeeded in obtaining a pure culture of streptococcus germs which produced the characteristic toxic symptoms of scarlet fever. Others had used both the toxic filtrate from a culture and the bacteria themselves for the immunization of horses in such manner that the serum would neutralize the poisons of scarlet fever or destroy the bacteria supposed to cause the disease. Moser of Vienna in 1902 inoculated a horse with a mixture containing both bacteria and the toxic products formed by the bacteria growing in broth. Serum subsequently produced from the horse's blood was found to have excellent therapeutic value in treating scarlet fever.

Savchenko a few years later showed that in scarlet fever there are present both the local action of bacteria and the diffusion of a poison or toxin. In 1907 Dabritschewsky, another Russian, developed an experimental vaccine for immunizing against scarlet fever by using a combination of the poison and killed streptococcus bacteria.

In spite of these successes with vaccine and therapeutic serums, there still remained doubts in many minds as to the specific nature of the bacteria responsible for scarlet fever and as to other details in the disease process. It had not been possible to produce the disease by inoculating experimental animals. Doctors George and Gladys Dick were the first to subject volunteers to deliberate infection, and they developed the use of minute quantities of pure scarlet fever toxin, injected into the skin, as a test of susceptibility to the disease.

Parallel with the work of the Dicks in this country was the experimental research of A. R. Dochez and associates, which resulted in the production of a scarlet fever antitoxin by injecting into horses successive small amounts of melted nutrient agar carrying scarlet fever streptococcus. The serum produced in this manner was found to be remarkably effective in clearing up scarlet fever within a few hours, even when highly diluted.

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