according to the published reports, leaves behind by many hours the curves of the production of hemolysin, of leucocydin and of the X substances of Zinsser, et al.

In the tests in rabbits we have been able to show so far that while convalescent scarlet fever serum seems to neutralize the filtrates of the growth of the hemolytic streptococci from scarlet fever, as shown by the intracutaneous reaction, it has not yet neutralized toxic filtrates obtained in the same way from *Staphylococcus pyogenes* or from *Escherichia coli.* Neither has it neutralized a toxic filtrate obtained from a hemolytic streptococcus from endocarditis while it has neutralized one (strain F) isolated from a wound infection, which we included by absorption of agglutinins in our agglutinative group of hemolytic streptococci obtained from scarlet fever. Young rabbits (about 1500 gm.) of the type giving a good skin reaction with vaccine virus and depilated as we depilate for that test seem to be especially suitable for this test and in the many questions of interest that are coming up in connection with this work they promise to be a great help.

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Results obtained with the Dick test in normal individuals and in acute and convalescent cases of scarlet fever.

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Studies have been made with the Dick test among normal individuals along lines similar to those carried out with the Schick test. The susceptibility by age groups from birth to adult life has been investigated and found to correspond closely to the percentage susceptibility to diphtheria, as shown by the Schick test. Comparative studies have been made with the reaction on mothers and their offspring. The results indicate that the reactions are similar in the mother and offspring during the first six months of life. The antibodies are transmitted through the placenta

and persist in most infants for a period of about six to nine months. The blood sera of individuals who gave positive or negative Dick reactions have been studied for their properties in causing the extinction test of Schultz-Charlton in a fresh scarlet fever rash; also for their power to neutralize the test fluid for the Dick reaction.

The blood serum of a person giving a "negative" or a "pseudo" Dick reaction causes blanching of the rash and neutralizes the test toxin; that of a "positive or a combined" reaction causes no blanching of the rash and does not neutralize the test toxin. The Dick test is positive as a rule during the first two days of scarlet fever but becomes less positive toward the end of seven days and negative toward the end of ten to fifteen days, when the antitoxic properties begin to appear in the patient's serum. This can be shown by its power to blanch the scarlet fever rash and neutralize the Dick test toxin. The neutralization of the test toxin is a more delicate index of the presence of antibodies in a serum than its property to cause blanching of a scarlet fever rash. The blanching or Schultz-Charlton test is a fairly crude phenomenon and depends on too many variable factors such as the character of the rash and its duration before the serum injection, the accuracy of the intradermal injection, etc. In spite of these drawbacks the test is of some value in showing whether a suspicious rash may be scarlet fever or not, especially when the test is made during the early stage of the disease.

Quantitative studies have been made with increasing concentrations of the test fluid to determine the approximate amount of antibodies that develop during the convalescence from scarlet fever, the antibody content of the serum of normal negative Dick reactors and of the antitoxic horse serum prepared by Dochez. The antibody content is determined by one of two methods: (1) By testing the individual directly with increasing concentrations of the test toxin, beginning as Dick recommended with a dilution of 1:1000 or indirectly; (2) By diluting equal volumes of the test toxin (1:500) with increasing dilutions of the serum, undiluted, 50, 33, 25, 20, 10, 5, 2.5 and 1 per cent, allowing the two mixtures to remain preferably at room temperature for 30 minutes and then injecting either all of these test mixtures or alternating ones into an individual who has shown a good positive reaction with the 1:1000 dilution. If the

standard toxin dilution is 1:500, then the serum is added to a toxin dilution of 1:250, so that the ultimate dilution of the toxin in the mixture is 1:500. Another Dick test is made at the same time to serve for purposes of comparison. A measure of the antibody content will give valuable data in showing the suitability of donors of blood serum for prophylaxis and for treatment. Normal or "naturally" immune donors can thus become available for this purpose. Another very important result of our ability to measure the antibody content of a serum is that it will enable us to determine one of the important characteristics of extracellular toxins, which is so well recognized in the case of diphtheria toxin, *i. e.*, the property of a toxin to be neutralized in multiple proportions by an antitoxic serum. Such studies are being conducted at the present time.

We have applied the Dick test to nearly one hundred cases of scarlet fever during the first four days of the disease and found them to be positive in all but three. As the patients progress into convalescence they nearly always show a negative or a pseudo reaction.

Two of the patients tested gave doubtful and one a negative reaction. The blood serum of the latter patient, taken on the fifth day of illness, showed strong blanching of a scarlet rash. The patient's history also indicates great doubt as to the diagnosis of scarlet fever. He had a marked rash, frequently described by the term "boiled lobster rash", but at no time did he have a sore throat. The fauces and tonsils were not congested. The rash began with a marked general pruritus. There was a heavy desquemation, which did not begin on the hands and soles of the feet, but in large flakes all around the neck. It gradually extended over the rest of the body.

There are four different reactions that can be distinguished with the Dick test and these reactions correspond closely to the similar four reactions that are noted with the Schick test. There is a positive, a negative, a pseudo and a combined reaction.

The positive reaction closely resembles at the end of 24 hours a positive Schick test which has reached its maximum on the third or fourth day. It appears within 6 to 12 hours, reaches its height at the end of 24 hours, and fades fairly rapidly; a good positive reaction is followed by pigmentation, with very slight or no scaling. The pigmentation may persist for a week or longer.

The pseudo reactions are due to the autolyzed bacterial substance of the streptococcus and other proteins in the test fluid. These reactions are not specific, as individuals who show a pseudo reaction will show similar reactions with the autolyzed protein of streptococci from different sources, such as abscesses, etc. To separate the pseudo reactions from the positive reactions I am using as a control a test toxin neutralized with an equal amount of 50 per cent convalescent serum or of normal serum from negative Dick reactors. In individuals giving pseudo reactions the local effect of the test fluid is not neutralized by the convalescent serum, the reactions on the two forearms, in the test and in the control, being of the same appearance. The pseudo reactions were seen in older children and especially in adults. They were also noted in some of those who gave a previous history of scarlet fever. *The results of the test become very confusing unless a control is made; then the results can be interpreted with little difficulty.* The combined reaction shows a much more pronounced redness at the site of the Dick test as compared with the control test. The positive and combined reactors are probably susceptible, the negative and pseudo reactors are probably immune to scarlet fever. The test is being applied now in institutions and homes where scarlet fever has developed and the actual experience will soon prove whether the clinical test and the corresponding serum findings (blanching of a scarlet fever rash and neutralization of the test toxin) can be depended upon.

The presence of varying amounts of antitoxic bodies in the serum of different individuals accounts probably for variations in the intensity of the clinical symptoms seen in cases of scarlet fever.

The toxin has been studied as to its ability to resist destruction by heat. At 100° C. for 45 minutes the toxin is destroyed in dilutions of 1 :100. The pseudo-action of the protein is not interfered with by the heat. We will probably use the heated toxin for purposes of control, just as we have recommended the use of heated diphtheria toxin as a control in the Schick test.

The toxin does not seem to have as intense a local effect as the diphtheria toxin. The local reactions, however, seem to be in proportion to the dilutions of the toxin when compared with an arbitrary standard. Such a standard will have to be more definitely fixed before long to enable the work to be carried out everywhere in a more uniform manner.

The guinea pig showed only a slight effect and the mouse practically no effect to the intradermal or subcutaneous injection of the undiluted toxin. The rabbit reacts with rapidly diminishing intensity and shows only a slight reaction to a dilution of 1:100. Standardization on this animal may be subsequently worked out in a more satisfactory manner. At the present time the standardization of a toxin is most satisfactorily carried out by testing it intradermally in different dilutions in susceptible individuals.

The local effect of the toxin in the skin cannot be counteracted by a subsequent injection of an antitoxin containing serum. After a positive reaction has fully manifested itself at the end of 24 hours it cannot be blanched out by the injection of convalescent serum into the local reaction.

The positive reaction noted in all early cases of scarlet fever and the subsequent negative or pseudo reaction during convalescence in nearly all these patients would indicate that the different agglutinative strains of hemolytic streptococci found in the throats of scarlet fever patients produce the same antitoxic antibodies. Dr. Anna W. Williams and her co-workers in the Research Laboratory have found that only 35 per cent of strains could be put by their agglutination characteristics into one group. This is important as similar observations on the unity of toxin have been made in connection with different agglutinative strains of the bacilli of diphtheria and tetanus.

The Dick test has been found very valuable for diagnostic purposes, as a positive reaction obtained during the first day or two of a suspicious scarlet like rash and again two weeks or more after the fading of the rash will indicate that the patient did not have scarlet fever. The test is of great value and will find, like the Schick test, an increasing field of application in the selection of susceptible individuals for passive and active immunization; for passive immunization with convalescent serum from human beings or antitoxic serum from animals and for active immunization with increasing doses of the toxin itself. The negative retest would indicate the development of antitoxic immunity. Such studies in active immunization with diluted toxin are being carried out at the present time. I am using the following doses of toxin for active immunization, *i. e.*, 25, 50, 100 and 200 skin test doses, the injections being given

intramuscularly about a week apart. The retest to determine the development of antitoxic immunity should be made after two to three months. The local reactions are only slight in positive reactors, but more marked in pseudo and combined reactors.

With the discovery of the toxin producing power of the hemolytic streptococcus a wide field of productive research has been thrown open to the investigator. Many problems will, no doubt, very soon be solved, such as the identity or lack of indentity of toxins produced by different strains of hemolytic streptococci obtained from a variety of sources. The subject of erysipelas and the possibility of producing an effective antitoxic serum will have to be reinvestigated. Eight years ago I used, with striking results, the convalescent whole blood from a case of erysipelas in the treatment of a young child, intensely ill with erysipelas.

The diagnosis of varying forms of sinus disease, such as ethmoid, sphenoid, antrum, ear infections, etc., will be facilitated as regards a doubtful scarlet fever etiology, if the strain of hemolytic streptococcus causing the local condition is obtained, a toxin produced and it is subsequently determined whether the toxin can be neutralized with convalescent scarlet fever serum.

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The influence of thyroid substances on the absorption of pleural effusions.

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A good many patients suffering with pneumonia develop during the course of their disease pleural effusions. Some of these effusions are small and assume no clinical importance since they are usually absorbed at or soon after the crisis. Others are large and manifest themselves by physical and röntgenological signs. They last for a number of weeks, are accompanied by moderate fever prolonged convalescence and sometimes undergo purulent metamorphosis. The gross appearance of the fluid is usually straw-colored, of varying transparency and usually bacteria-free on culture.