

SCIENTIFIC PROCEEDINGS.

ABSTRACTS OF THE COMMUNICATIONS.

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The value of the conglutination reaction as a means of diagnosis of acute bacterial infections.

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In connection with the work on the relation of sensitizers to the alexin in 1906, Bordet and Gay described the presence in bovine serum of a substance to which the name of "colloid" was given. This colloidal substance had the property of producing a characteristic clumping of red blood cells and of accelerating their lysis when they had been treated with both a sensitizer and an alexin; its action was possible under no other circumstance. To this substance the name of "conglutinin" was subsequently given by Bordet and Streng, perhaps somewhat inadvisedly as the term had been used to describe the agglutination of blood cells by ricin. At about the same time a probably similar substance was described in goat serum by Manwaring to which the name of "auxilysin" was given, but the description of its mode of action has remained insufficient for identifying it with the colloidal substance of Bordet and Gay. In 1908 Streng was able to reproduce the phenomenon of conglutination in bacteria that had been treated with a specific sensitizer and an alexin, on the addition of bovine serum from which the normal agglutinins had been removed, if such were present. He further suggests the possible use of this reaction in the diagnosis of infections such as typhoid fever, in which case the blood of the patient would serve as the sensitizing serum.

During the past summer the matter was thoroughly considered by one of us (Lucas) in collaboration with Drs. Schorer and Fitzgerald in a comparative study which was made of methods of serum diagnosis in acute bacillary dysentery in infants. In this series of cases, shortly to be reported in full, a bacteriological examination was made of the stools for the presence of one or more types of *Bacillus dysenteriae* and a comparative study of the reactions of agglutination, fixation, and conglutination made with the serum of each case, and usually at intervals in the course of a given case. From 45 cases of infantile dysentery, dysentery bacilli were isolated in 84.4 per cent. and in 35 of these bacteriologically positive cases, mannit fermenting organisms alone were present. In every case the three reactions with the serum were tested both with a mannit fermenting (Flexner) and a mannit non-fermenting (Shiga) strain of the dysentery bacillus. Positive reactions with the Flexner strain were much more frequent than with the Shiga strain; this may be due not only to a direct relation of the organisms concerned in producing the infection, but also, in all probability, to a greater susceptibility of the Flexner organism to the action of serum. Fifteen control cases which gave no evidence of having suffered from dysentery were also studied both bacteriologically and from the standpoint of serum diagnosis.

A positive reaction of agglutination was obtained with the serum of one control case to the Flexner organism, but in none of them to the Shiga organism. A positive agglutination reaction with the Flexner strain was obtained in 55.5 per cent. of the positive cases ranging from 9 per cent. during the first four days of the disease, to 75 per cent. in the third week. In about half as many cases a reaction was obtained with the Shiga organism. Fixation reactions were obtained with the Flexner, but not with the Shiga strain in over a quarter of the control cases (28.5 per cent.). The reaction occurred with both Flexner and Shiga organisms about equally in from 50 to 60 per cent. of the positive cases subsequent to the first week. No positive conglutination reaction was obtained in control cases, although in a few instances a reaction in a dilution of 1-40 did occur which was arbitrarily chosen as the limit of a doubtful reaction, beyond which a reaction was called "positive." The conglutination reaction appeared in 63.1 per cent. of the

positive cases with the Flexner organism. In addition, conglutination was obtained with this organism in *50 per cent. of the cases during the first four days of the disease*. Reactions of conglutination with the Shiga type were absolutely and relatively fewer than by the other methods, which would seem to indicate a more absolute specificity for this reaction. The reaction, when present, occurs usually in very high dilutions (up to 1-800) and is not to be confused with agglutination, as it frequently occurs when agglutination is absent in dilutions of 1-20, and may fail to occur when agglutinations are positive. Inasmuch as bovine serum contains a normal agglutinin for the dysentery bacillus, it is necessary to work with a preparation from bovine serum obtained by saturating with dysentery bacilli or by separating out by dialysis the insoluble proteids which contain the conglutinin but not the agglutinin (Streng).

As complementary to this work on infantile dysentery, a number of convalescent cases of dysentery from the Danvers State Hospital have recently been examined by Dr. M. M. Canavan under our direction. Dr. Canavan found that in these cases which had suffered from dysentery from one and a half years to one month previously, the agglutination reaction was present with the Flexner strain in 10 of 14 cases and with the Shiga organism in 3 cases. The conglutination reaction was present with the Flexner organism in the same number of cases (10) although not in the same cases in which the agglutination was positive. Conglutination reaction with the Shiga organism was present in one case only. It is interesting to note that in one case which had had an attack of dysentery one and a half years previously, the conglutination reaction was present with the Flexner organism, although agglutination was negative. Agglutination reactions had been obtained a month previously in this case with both organisms in low dilutions. In 8 control cases from the same institution no conglutination reaction was obtained with either organism.

We have recently considered this reaction as a means of diagnosis in typhoid fever. We have met with a number of technical difficulties and for this reason are not able to recommend the reaction as yet as thoroughly serviceable. Our findings, however,

have been constantly indicative of its ultimate value. In every set of experiments we have controlled our tests by determining the limit of agglutination with the typhoid serum and by testing for conglutination with alexin plus conglutinin alone, and also with various dilutions of a normal serum. In certain of our experiments we have obtained positive reactions without the presence of a typhoid serum, owing either to a great susceptibility of the organism used as a reagent, or else to the presence of a normal sensitizor as well as an alexin in the fresh serum of the guinea-pig employed. In many of our experiments, however, we have met with clear cut positive reactions with typhoid sera alone which, in point of dilution, ran far higher than the control agglutination reactions and which failed to occur in the controls without serum or with dilutions of normal serum. It seems at the present moment unwise to use a formolinized culture of the typhoid bacillus as we did with dysentery, as it tends to sediment spontaneously. It may be mentioned that in one case of typhoid fever a conglutination reaction was obtained on the second and third days, whereas a blood culture was negative on the fifth day and the Widal reaction did not appear until the ninth day.

A few preliminary results with cases of acute tuberculosis offer hope that the reaction may also be of value in the diagnosis of at least certain forms of this disease. Our results on this subject, however, are not sufficient to warrant a communication.

It would seem to be indicated, then, that the reaction of conglutination may prove of superior value to the agglutination reaction in the diagnosis of acute bacterial infections, both on account of its greater constancy and its early occurrence in the disease.

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Analysis of the cleavage products of the nucleoprotein of the mammary glands.

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Many theories as to the origin of casein in milk have been discussed in the past and for the present we have no positive ex-