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Preliminary studies on the antigenic properties of different strains of *bacillus typhosus*.

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A search through the literature reveals no report of special work upon antigenic differences among typhoid strains, although serologic methods have frequently been used in differentiating typhoid from closely allied organisms. The demonstration of the severally specific antigenic individualities, notably of strains of pneumococci, streptococci, gonococci, meningococci, and influenza bacilli; the fluctuant epidemiologic severity of typhoid fever from time to time; the observation that antityphoid inoculation confers no protection against paratyphoid infection; the growing list of instances in which antityphoid inoculation has been unsuccessful, the previously known and personally confirmed fact that a polyvalent antigen is essential for good alexin fixation reactions in typhoid fever are the main facts which have led to this investigation.

Attention has been focused chiefly upon the delicately specific method of alexin fixation as a means of detecting antigenic differences. A considerable number of confirmatory agglutinin absorption experiments have also been performed.

Materials and Technic.—Of the 48 strains which have been used 21 are laboratory strains two to fifteen years old, and the rest have been isolated and authenticated during the past year by Gay and Chickering in the course of studies of local cases of typhoid fever.

The antigens used were washed, formalized suspensions of typhoid bacilli. These suspensions have been used also for immunizing rabbits, being eminently satisfactory for this purpose as agglutinogens for agglutination and absorption tests. The total volume of the fixation test has been one cubic centimeter, one fifth that of the classical Wassermann. Sheep cells, rabbit anti-sheep hemolysin, and guinea-pig serum make up the hemolytic system

which has daily been balanced by simultaneous alexin and hemolysin titrations. Pooled serum from six or more guinea pigs has been preserved by salting for alexin, a method which has many advantages.

Serum cross-titrations with standardized antigens have developed the fact that different strains of typhoid bacilli fall into different groups, somewhat analogous to the groupings of pneumococci. This is evidence which must be seriously considered in the explanation of the causes of failure in typhoid vaccination, since it is not unlikely that subjects may have been infected with strains dissimilar to those used for prophylactic inoculation. The strains tentatively placed in Group I cross-fix with all antigens; those in Group II cross-fix with each other but not with Group I strains. Group I-A strains give irregular results. There is no apparent relation between the virulence of the organisms as indicated by the severity of the disease which they caused, or between their toxicity as indicated by the reactions produced in immunizing rabbits, and this grouping. All of the Group II strains, however, have been under artificial cultivation for a number of years. Number 13 is the Rawlins strain, so extensively used in prophylactic immunization. It seems to possess a lesser antigenic complexity than does any organism in the other groups. On this evidence it would seem to be theoretically of less value as an immunizing strain.

The results of absorption tests, while somewhat less consistent, are confirmatory of the findings obtained with the alexin fixation reaction. Group I and Group II serum absorbed respectively with Group I and Group II strains give usually negative results with all organisms. Absorption of Group I sera with Group II strains results in the removal of all agglutinins for Group II while agglutinins for Group I still remain.

It is considered that the evidence of antigenic differences thus far discovered among typhoid strains is sufficiently valid to warrant the presentation of these data, and sufficiently encouraging to justify similar more extensive work, especially with regard to the comparative protection which is aroused by strains of different character. Although the principle of polyvalency has been used empirically in the past, it would seem advisable now on more

certain data to employ a polyvalent typhoid vaccine for immunizing and therapeutic purposes compounded in accordance with these groups as tentatively suggested and which may be confirmed or extended in the future.

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Note on "Salt fever."

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About six years ago one of us¹ published a short account of the rise of temperature which follows the injection of sodium chloride into rabbits, either intravenously or subcutaneously. This fact seems to have been completely overlooked by subsequent investigators, of whom there are many (Bingel, Freund, Samelson, Hort and Penfold, McIntosh, Fildes and Dearborn, and others). Samelson² claims that the rise of temperature is due to bacterial toxins contained in the distilled water, and not to the sodium chloride. The observations were made on nursing children. Freund,³ on the other hand, maintains that the sodium chloride is the cause of the rise of temperature, at the same time admitting the fact that contaminated water may also cause fever.

As we wished to make use of this fact in another connection, it became necessary for us to be sure that the rise of temperature was due to the injection of the salt, and to that end we have repeated the earlier work. Sterile sodium chloride was put in a flask that had been thoroughly sterilized, and the water, redistilled in glass, was received directly into the flask from the condenser. The mouth of the flask was closed with sterile cotton, and the solution ($m/6$ concentration) was used as soon as it had cooled down to the proper temperature. There can be no doubt, therefore, of the purity of the solution as far as bacterial contamination is concerned. Antiseptic precautions were observed in making the injections.

¹ Burnett, Univ. Calif. Publ., Vol. 4, 1910, p. 5.

² Samelson, *Monatsch. f. Kinderheilk*, Vol. 11, p. 3.

³ Freund, *Arch. f. exp. Path. u. Pharm.*, Vol. 74, 1913, p. 311.