tration, but practically no change during the remainder. The variations in plasma proteins during acid periods were slight and inconsistent.

The action of alkali in accentuating edema has been noticed by Falta and Quittner[1] in severe undernourished cases of diabetes mellitus and by Albright and Bauer[2] in a case of chronic nephritis of the nephrotic type. The former authors also attempted to produce edema by large doses of sodium bicarbonate in normal individuals without success. The diuretic effect of acids and acid-producing salts like ammonium chloride is well known and has been used in the treatment of various types of edema.

It is surmised here that the ease with which the water balance is so easily influenced by alkali and acid in cases of nutritional edema, nephrosis and severe diabetes with poor nutrition is probably related to the low level of plasma proteins found in such conditions. However, it can not be said that alkali or acid acts directly by altering the level of plasma proteins, as the changes in the latter accompanying alkalosis or acidosis are slight and not consistent.

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Small-Flaking or "O" Agglutinin After Intravenous Injections of Typhoid Vaccine.

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Since the introduction of the use of prophylactic typhoid vaccine, confusion has risen in interpreting the Widal agglutination reaction in the diagnosis of typhoid fever. Recently Felix[1] introduced the technic of demonstrating the presence of small-flaking or "O" agglutinin, which he claimed to occur only in infection but not after subcutaneous inoculation of the vaccine. Gardner[2] found that while "O" agglutinin can be produced by subcutaneous inoculation of the vaccine, it very rarely reaches a titer higher than 1 :200. We wished to know whether this "O" agglutinin can be produced by re-

[1] Falta, W., and Quittner, M., *Wien. klin. Wchnschr.*, 1917, **30**, 1189.

[2] Albright, F., and Bauer, W., *J. Clin. Invest.*, 1929, **7**, 465.

[1] Felix, A., *J. Hyg.*, 1929, **28**, 418.

[2] Gardner, A. D., *J. Hyg.*, 1929, **28**, 376.

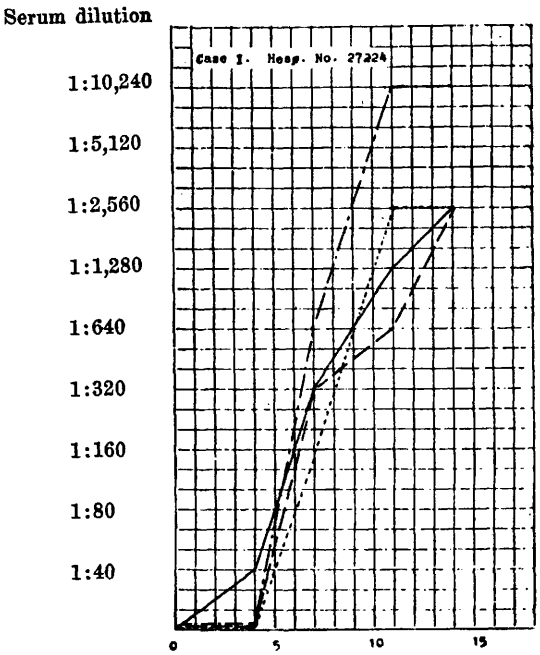
Serum dilution
1:10,240
1:5,120
1:2,560
1:1,280
1:640
1:320
1:160
1:80
1:40
Case I. Hosp. No. 27224
0
5
10
15
Number of days after treatment.

FIG. 1.

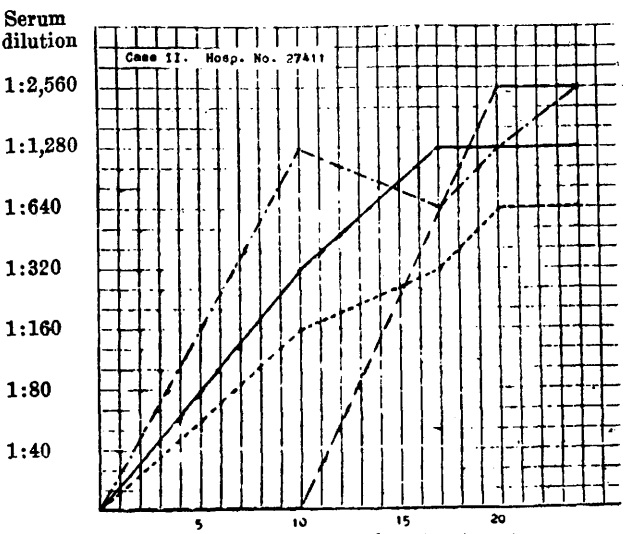
Serum dilution
1:2,560
1:1,280
1:640
1:320
1:160
1:80
1:40
Case II. Hosp. No. 27411
5
10
15
20
Number of days after treatment.
B. typhosus "H" agglutination
B. typhosus "O" agglutination
B. paratyphosus A agglutination
B. paratyphosus B agglutination

FIG. 2.

peated intravenous injections of the vaccine and whether its titer would be higher than that occurring after subcutaneous injections. After this work was begun, we noticed that Pijper and Dau had reported the finding of high titer "O" agglutination after oral ingestion of typhoid vaccine.[3]

Large-flaking or "H" antigens were prepared by the usual method, namely, agar washings in saline or broth of *B. typhosus, B. paratyphosus A* and *B. paratyphosus B* preserved with 0.1% formalin, and used with suitable dilution. Small-flaking or "O" antigen was prepared from *B. typhosus* (Rawlin's strain) treated with alcohol; a modified Bien's method[4] was used which will be described in detail later.

Sera were obtained from patients undergoing treatment for various conditions. These patients all received standard triple typhoid vaccine intravenously with varying numbers of organisms and doses. The first dose was usually 25 million organisms and the usual increase was 25 million with each subsequent injection. All patients showed a systemic reaction with fever and chills. In several instances serum was obtained before the commencement of the treatment and after each injection. In others only single specimens were obtained during treatment.

Dreyer's macroscopic agglutination technic was followed in all the tests. The tubes containing the serum dilutions and the bacterial suspensions were incubated in the water-bath at 37°C. for 18 to 24 hours. In a number of instances incubation at 56°C. over-night was also used and the results with these 2 methods were identical. In every instance the "O" agglutination gave a typical granular flocculation.

The findings of 2 illustrative cases are presented in the accompanying charts. While it is too early to make any definite statement, it is significant that in every case after intravenous injection of the typhoid vaccine, "O" agglutinin was produced in a titer approaching fairly closely to that of the "H" agglutinin. It is therefore reasonable to conclude that "O" agglutinin is readily produced by intravenous stimulation.

[3] Bien, Z., *Centr. f. Bakteriol*, 1 Abt. Orig., 1925, **98**, 196.

[4] Pijper, A., and Dau, H., *Brit. J. Exp. Path.*, 1930, **11**, 112.