ificity between the nondialysates and the immune substances present in typhus serum. Still, the flocculation tests seemed to exhibit more specificity than was found in agglutination tests with typhus serum. Such a degree of specificity was not found in the flocculations between the nondialysates of the other cultures here used and the other immune sera. Instead, the results paralleled the behavior of agglutinating reactions between these immune sera and related organisms (Table II). Under these conditions and with these organisms, flocculation with nondialysates and immune serum seem to be no more specific than the group agglutinations commonly observed between the species used. It seems reasonable to conclude, therefore, that the *in vitro* reactions of the nondialysable growth products of microorganisms studied are without a strict degree of specificity.

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## Vitamin-C Inhibition of Agglutinin Production.

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In a previous paper it was shown that ascorbic acid added to or injected simultaneously with horse serum hastens and augments specific-precipitin production in rabbits. A 10- to 30-fold increase in precipitin-titer is readily produced by optimal doses (about 50 mg) of this enzyme-activator. We have extended the study of the potentiating action of ascorbic acid to other antigens. The present paper summarizes our experimental data with bacterial vaccines and sheep erythrocytes (Forssmann antigen).

About 200 two kg rabbits were divided into groups of 6. Each group was injected intravenously with an arbitrary dose of sheep erythrocytes, or of living, heat-killed or formalin-killed suspensions of *B. proteus, B. coli* or *B. typhosus.* One minute after each injection, 3 members of each group were given an intravenous injection with 50 mg ascorbic acid dissolved in 1 cc NaCl-solution.

Very low antibody-titers were obtained as a result of these single injections. Within the limits of the experimental error ascorbic acid had only border-line effects on antibody-yield, except on the yield of

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specific agglutinin. In 3 groups injected with *B. typhosus,* for example, the yield of specific agglutinins was reduced about 50%.

In order to magnify these border-line effects, additional groups of 6 rabbits were given from 7 to 13 multiple injections with the same antigens, followed in half of the members of each group by our routine therapeutic dose (50 mg) of ascorbic acid. In addition to the erythrocytes and bacterial vaccines above tested, 3 groups of rabbits were injected with partially autolysed or 'phage-lysed *B. typhosus* and 2 groups with staphylococcal proteins obtained by grinding staphylococci in a ball-mill. For the staphylococcal proteins used in these tests we are indebted to Dr. A. P. Krueger, of the University of California. Typical data from these multiple injections are recorded in Table I.

TABLE I.

Multiple Injections of 'Phage-lysed *B. typhosus* and Ascorbic Acid.

Intravenous injections with 1 cc of a 10-hour 'phage-lysed *B. typhosus* culture at 3- to 5-day intervals, followed immediately with 50 mg ascorbic acid also given intravenously. Half of the members of each group (controls) were given no ascorbic acid. Bleedings were made at irregular intervals, usually at least 5 days after the previous injection. (Number of previous injections shown by the Roman numerals.) The resulting antiserums were titrated for specific precipitins (ring test) and specific agglutinins. The low precipitin-titers recorded are due to the use of a very dilute Berkefeld-filtrate of 'phage-lysed *B. typhosus* as the test-antigen. The recorded precipitin-titers should be multiplied by at least 1000 to make them quantitatively comparable with the specific agglutinin titers.

Almost identical average titers were obtained in the 2 series of rabbits injected with staphylococcal proteins.

| | 25th day VI | 45th day XI | 53d day XII | 60th day XIII | 67th day XIII | 74th day XIII | Avg % |
|---|---|---|---|---|---|---|---|
| Precipitin-titer | | | | | | | |
| Ascorbic acid group | 0 | 1:4 | 1:9 | 1:8 | 1:10 | 1:5 | 130 |
| Control group | 0 | 1:3 | 1:6 | 1:7 | 1:8 | 1:4 | 100 |
| Agglutinin-titer | | | | | | | |
| Ascorbic acid group | 0 | 1:1800 | 1:4500 | 1:1500 | 1:1000 | 1:500 | 40 |
| Control group | 0 | 1:4700 | 1:7500 | 1:6400 | 1:2500 | 1:1500 | 100 |

From this table it is seen that multiple doses of ascorbic acid increase specific-precipitin production against bacterial vaccines about 30%. This increase, however, is negligible when compared with the 10- to 30-fold increase previously obtained with horse serum. This border-line beneficial effect, however, is more than offset by the 60% reduction in the average yield of specific agglutinins.

While ascorbic acid is thus without apparent clinical promise as a potentiator of bacterial vaccines, the above dual effect is of basic theoretical interest. The slight but distinct increase in specific-

precipitin production coupled with a marked decrease in the yield of specific agglutinins, is conclusive evidence of the existence of at least 2 different physiological mechanisms for specific-antibody production.

A plausible explanation would be furnished by the hypothesis that there are 2 competitive defensive mechanisms operative in humoral immunity: (i) an extracellular synthesizing process mainly operative against relatively non-toxic alien proteins and responsible for specific-precipitin production, and (ii) an intracellular lytic process mainly operative against phagocyted microörganisms or microbic fragments. Vitamin-C activation of tissue enzymes, therefore, might conceivably increase precipitin-production while reducing the yield of specific agglutinins by causing a more rapid intracellular destruction of phagocyted antigens.

If this is true, vitamin C therapy would have a predictable clinical value in the treatment of specific infectious diseases, even though it is of no apparent clinical promise as an adjuvant in vaccine therapy. Recent reported successes of vitamin C therapy in the treatment of experimental poliomyelitis and tuberculosis are in line with this prediction.

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## Cerebrospinal Pressure, Hydrocephalus and Blood Pressure in the Cat Following Intracisternal Injection of Colloidal Kaolin.

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Certain animals develop an increased intracranial pressure associated with vascular hypertension following the intracisternal injection of colloidal kaolin. This syndrome was first described in the dog by Heller[1] and his associates, and recently confirmed by Jeffers, Lindauer and Lukens.[2] A similar response in the white rat

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1 Dixon, W. E., and Heller, H., *Arch. f. exp. path. u. pharm.*, 1932, **166**, 265.

2 Jeffers, W. A., Lindauer, M. A., and Lukens, F. D. W., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 260.