

tion rather than the obstruction itself is responsible for the fatal outcome in some cases of biliary surgery. 2. The hepatic changes always present in biliary disease are aggravated in some cases by the surgery instituted to relieve it, which imposes upon an already damaged liver an intolerable burden. As a result of the degenerative hepatic changes, there is released into the circulation a toxic substance which is presumed to be a water-soluble foreign protein. 3. When, after liver function fails, the kidney takes up the function of detoxification, there is resulting damage to its convoluted tubules, through which foreign proteins are excreted. 4. The liver-kidney syndrome is a single pathologic process, of which the kidney pathology represents the second stage.

Further experiments are at present being undertaken to support the hypothesis herein set forth.

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## Precipitation and Complement-Fixation Reactions with Pneumococcus Soluble Specific Substance.

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The following observations, while but part of a broader investigation of the complement-fixation test with specific bacterial antigens in the diagnosis of infection,<sup>1-4</sup> have, nevertheless, a special significance in that they indicate the relative sensitivity of precipitation and of complement fixation with a highly purified bacterial antigen. The reports of other observers have been based upon studies with more complex antigens.<sup>5-7</sup>

<sup>1</sup> Wadsworth, Augustus, Maltaner, Frank, and Maltaner, Elizabeth, *J. Immunol.*, 1925, **10**, 241.

<sup>2</sup> Wadsworth, Augustus. In: *The Newer Knowledge of Bacteriology and Immunology*, Jordan and Falk, editors, Chicago, University of Chicago Press, 1928, p. 831.

<sup>3</sup> Wadsworth, A. B., van Amstel, J. E., and Brigham, M. W., *J. Immunol.*, 1930, **19**, 289.

<sup>4</sup> Rice, C. E., *J. Immunol.*, 1932, **22**, 67.

<sup>5</sup> Dean, H. R., *Z. f. Immunitäts.*, 1912, **13**, 84.

<sup>6</sup> Parker, J. T., *J. Immunol.*, 1923, **8**, 223.

<sup>7</sup> Goldsworthy, N. E., *J. Path. and Bact.*, 1928, **31**, 220.

In both the precipitation and complement-fixation experiments, the soluble specific substance of the pneumococcus, Type I, was used as antigen with the pooled sera of 3 rabbits which had been immunized with formalinized Type I pneumococcus vaccine. The antigen was diluted 1:1000, 1:10,000, 1:100,000, 1:1,000,000, and 1:10,000,000. The serum was used undiluted and diluted with physiological salt solution 1:5, 1:10, 1:20, 1:40, and 1:80, with all of the antigen dilutions. For the precipitation tests, 0.3 cc. of antigen was mixed with 0.3 cc. of antiserum, and the reactions recorded according to the bulk of the precipitate after 2 hours' incubation at 37°C., followed by 24 hours' at ice-box temperature. The complement titrations were performed and the data calculated according to the method of Wadsworth, Maltaner, and Maltaner.<sup>8</sup> The tests were repeated 3 times, the complement-fixation with 3 different pools of complement.

For convenience, the precipitation and complement-fixation data are presented in one figure, although the units are not comparable.

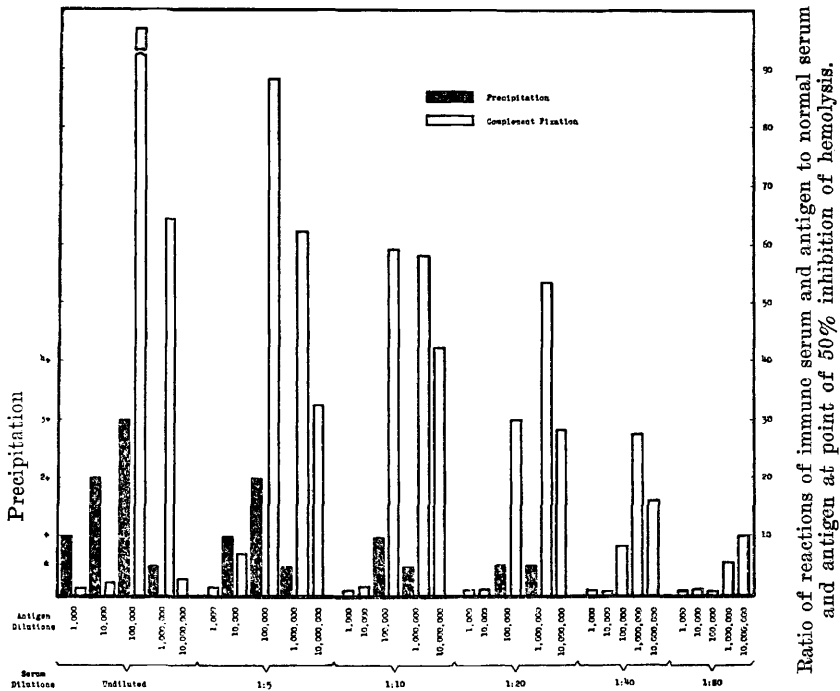


FIG. 1.  
Relative sensitivity of precipitation and of complement fixation with pneumococcus soluble specific substance.

<sup>8</sup> Wadsworth, Augustus, Maltaner, Elizabeth, and Maltaner, Frank, *J. Immunol.*, 1931, **21**, 313.

The precipitation reaction was recorded as 4+, 3+, 2+, +, ±, and —. As the basis of comparison for the complement-fixation reactions, the ratio of the amount of complement necessary to give 50% inhibition of hemolysis in the presence of immune serum and antigen to the amount of complement giving the same reaction in the presence of normal serum and antigen, was used. In one instance (antigen dilution 1:100,000 and undiluted antiserum), such a ratio could not be determined as fixation was almost complete with the largest amount of complement used, namely 0.1 cc.

When the precipitation and complement-fixation data are compared, it is apparent that under the conditions of the tests the maximum reactivity occurred with the same antigen and antibody dilutions in both tests, namely, 1:100,000 with undiluted antiserum. The sensitivity of the complement-fixation reaction, however, exceeded that of the precipitation. With any one dilution of serum a broader range of antigen dilutions reacted strongly in titrations of complement than in precipitation tests. The direct proportionality between the amounts of serum and complement fixed in the specific reaction with tubercle-bacillus antigen and antiserum recorded by Wadsworth, Maltaner, and Maltaner was also observed in this reaction between pneumococcus soluble specific substance and anti-pneumococcus serum within the zone of optimum reactivity.

*Summary.* The results of the 2 tests, precipitation and complement-fixation, paralleled one another so closely with this highly purified soluble specific substance of Type I pneumococcus that the reactions appear to represent union of the same antigen and antibody. The comparative titration of complement, however, is the more sensitive measure of the specific activity of an immune serum. Within the zone of optimum reactivity the amount of complement fixed was directly proportional to the amount of immune serum present.