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On non-specific complement fixation.

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Complement is fixable by various substances. It is fixed by different extracts containing certain proteins. Fixation in this case is direct and *non-specific*. On the other hand, complement is also fixed by a combination of *specific* antigens and antibodies (Bordet-Gengou). In the last instance, fixation is accomplished by the coöperation of the antigen and antibodies, the latter being inert without the aid of each other. From this observation the deduction was formed that whenever complement is fixed by a mixture of two substances, it is an expression of a specific reaction taking place in such a mixture. This assumption, however, is permissible only when the above phenomenon can be produced by none but the specific antigens and antibodies.

Recently I encountered a peculiar phenomenon which resembles very closely the true Bordet-Gengou reactions, differing from the latter in the non-specific nature of the substances serving as antigen. Working on the sera of tuberculous patients, using tuberculin and the nucleoprotein of tubercle bacilli as antigen, I found that twenty out of twenty-five cases gave complement fixation in varying degrees when tested in unheated state. Encouraged by this result, I examined thirty-five control cases without tuberculosis and found, to my surprise, that twenty-eight of these gave positive reactions with the same antigen.

A subsequent study revealed that pepton, albumoses, glycogen, various extracts of bacteria, tissues and organs, and certain cleavage products of protein[1] gave similar fixation phenomena. Thus the phenomenon is found to be non-specific and is due to the addition of these substances to active human sera and it is present in a majority of human sera.

[1] I am greatly indebted to Dr. P. A. Levene who placed these substances at my disposal. Among these may be mentioned allanin, glycil-glycin, leucin, tyrosin, glycocoll; these have, however, less fixing power than higher protein molecules and glycogen.

This non-specific fixation of complement can be avoided by inactivating the sera before testing. *From the above finding it follows that no complement fixation test, with a view of obtaining a specific reaction, should be made with unheated serum. On the other hand, the Wassermann reaction can be carried out with active human sera when the antigen does not contain those substances which are found to give a non-specific reaction with the active sera.*

I usually use in my system of the Wassermann reaction active sera and pure lipoids free from proteins and have never obtained the so-called *non-specific reaction.* It is not possible, however, to obtain reliable results if one uses aqueous or alcoholic extracts of liver as antigen, because these extracts contain the disturbing proteins already referred to. When one intends to use aqueous or alcoholic extracts as antigen, the patient's serum should be inactivated before using. In a recent article by Swift, I noticed that he obtained positive reactions in certain non-syphilitic cases by employing my method and he states that this can be avoided by using inactivated sera. I would like to call attention to the fact that he used alcoholic extracts and not pure lipoids (acetone-insoluble fractions as recommended by me) in the former of which there exist large quantities of proteins capable of producing false fixation with the active sera. Hence his results.

For the sake of clarity, I propose to call the non-specific reaction caused by active serum and these proteins *proteotropic fixation,* and the Wassermann reaction caused by syphilitic and leprous sera in the presence of lipoids *lipotropic.*

No parallelism is found to exist between the proteotropic and the lipotropic properties of a given specimen of serum. Inactivation removes the proteotropic property almost entirely, while it only reduces the lipotropic titre to about one-fourth of the original strength.