# SCIENTIFIC PROCEEDINGS.

ABSTRACTS OF COMMUNICATIONS.

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*President Jackson in the chair.*

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### The Reticulo-endothelial system in relation to antibody formation.

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The general lines of inquiry to determine the seat of antibody formation have been to seek the tissue where a given antigen is fixed; to determine the locality where the corresponding antibody may first be detected; or to prevent the formation of antibody either by specific injury (benzol, x-ray) or by extirpation of an organ. It has also been claimed that antibodies may be produced in tissue culture. With the evidence obtained by these methods it has been variously concluded that the essential antibody formers are the leucocytes; the leucocyte forming organs, spleen, bone marrow and lymph nodes; the liver; and the capillary endothelium.

We have probably been led astray by the expectation that some particular organ like the spleen, or some strictly localized cell group, rather than a more universal tissue, is responsible. Many of the phenomena of general immunity can be better explained on the assumption that some widely distributed cell-type is the essential antibody producer. The condition of strictly local immunity

in various parts of the body, which we believe has now been proved to exist, can be understood only on such an assumption.

The reticulo-endothelial system of cells (Aschoff) fulfills this criterion of wide distribution throughout the body including as it does one of the constituent elements of connective tissue and the capillary and lymph space endothelium, and being related to adult endothelium and the monocytes of the blood. It includes, moreover, the most markedly phagocytic and resistant cells of the body; indeed its differentiation depends on its ability to take up rapidly and to retain particulate matter and colloidal substances. The undoubted importance of spleen, lymph nodes and liver in the disposal of foreign cells and in antibody-formation, that has already been mentioned, would depend on their content of elements that make up the reticulo-endothelial system; and the failure of removal of one of these organs (*e. g.* spleen) to prevent antibody formation entirely, would depend on the vicarious or increased functioning of other parts of the same system.

It has occurred to others recently, as well as to ourselves, that a crucial experiment to prove the importance of the reticulo-endothelium in antibody formation might be effected by "plugging" or "blocking" the vacuolar segregation apparatus of these cells (clasmatocytes and capillary endothelium) with some indifferent non-protein colloid, and then attempting antibody formation. There are recent experiments which show that one colloidal substance when taken up by the clasmatocytes prevents absorption of a second colloidal substance, thus indicating that the segregation apparatus in these cells is a single one. Therefore, if this reticulo-endothelial apparatus is the antibody producer, saturation with any indifferent colloid should prevent antibody formation.

Standenath[1] and Vanucci[2] have recently published some such experiments on antibody formation. Standenath, who tested precipitin formation in rabbits after the use of China ink, found it was increased rather than diminished. Vanucci, who used both carmine and Wasserblau dye, thought subsequent agglutinin formation was decreased. These experiments not only disagree but are each in themselves wholly inconclusive when viewed in detail from the extremely small number of animals involved, and

[1] Standenath, *Zeit für Immunitats Firsch*, 1923, xxxviii, 19.

[2] Vanucci, *Lo Sperimentale*, 1924, lxxxviii, 23.

the relatively slight differences in antibody strength between treated and controls.

Our own experiments on the effect of vital staining on hemolysin and bacteriolysin production are unequivocal. Rabbits and rats were saturated with Trypan Blue for about two weeks and then given three injections of sheep blood cells on successive days. In rats tested five days after the blood injections, during which period the Trypan Blue injections were continued, the serum of control animals untreated with Trypan Blue but given similar injections of blood, gave hemolysis in dilutions of 1-2500 to 1-10,000, whereas in the Trypan Blue animals it was negative at 1-10 in two animals and positive at 1-160 only in two others. In rabbits the hemolysin formation was followed more fully and showed similar differences between control and Trypan Blue animals. In controls the hemolysin titer was 1-1666 on the average in nine days, whereas the maximum production, reached only on the fourteenth day, in Trypan Blue animals was only 1-140.

Similar results have been obtained in the formation of bacteriolysins and agglutinins to the Cholera Vibrio. Our results on precipitin formation to horse serum after vital staining are as yet variable. It is possible that another mechanism is involved in the formation of this antibody.

The question naturally arises as to whether our success in preventing antibody formation by the use of a colloidal dyestuff has not been due to the injury of all the cells in the body, rather than to the specific "plugging" of the cells responsible for antibody formation. In view of the apparent harmlessness of Trypan Blue we do not believe that this explanation can be invoked, but further controls are necessary to check this possibility.

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