3237

Newer Concepts as to the Origin and Nature of Antibodies.

W. H. MANWARING.

From the Laboratory of Bacteriology and Experimental Pathology, Stanford University, California.

Practically the only complete and consistent theory as to the origin and nature of immunological antibodies is the theory based on the specific receptor hypothesis. Physiological data collected in our laboratory during recent years are sufficient to my mind to prove this theory wholly untenable. I believe the wide acceptance of the specific receptor hypothesis by clinicians and practical serologists constitutes today our most serious handicap to immunological progress, and that the theory should be replaced by concepts more nearly in accord with accepted facts of biochemistry. The following are some of our typical findings:

(a) The assumed multiplication of sessile receptors in hypersensitive and immune tissues should increase the specific affinity of these tissues for soluble antigens. Yet, in our hands, perfusions of isolated blood-free organs of normal, hypersensitive and immune animals with soluble antigens have shown no demonstrable differences in their specific tissue-antigen affinities.[1]

(b) The blood-free tissues of immune animals should be specifically hypersensitive, due to an increased number of sessile receptors. Yet the isolated blood-free organs of immune dogs show no suggestion whatsoever of specific hypersensitiveness.[2]

(c) The blood of immune animals should serve as a portal defense to the fixed tissues by shunting the injected specific antigen from the fixed tissues. Yet a hypersensitive dog, three-quarters of whose blood had been replaced by transfusion from an immune donor, is typically hypersensitive on immediate physiological test.

(d) Circulating antibodies should be *qualitatively* identical at all stages of sensitization and immunization with the same antigen. Yet the blood of a hypersensitive dog will invariably render a normal dog passively hypersensitive, while no demonstrable hypersensitiveness is transferred to a normal dog by fractional transfusion from an immune donor.[3]

It would be comparatively easy to replace the discarded specific

receptor hypothesis with a theory based on the assumption that fixed and circulating intibodies are slowly formed in the body as a result of the interplay between injected antigens and extracellular and intracellular, hydrolyzing and synthesizing enzymes, and by these enzymes specifically adapted to the antigens or to the primary or secondary products of antigen hydrolysis.

[1] Manwaring, W. H., Kusama, Y., and Crowe, H. E., *J. Immunol.*, 1917, ii, 511.

[2] Manwaring, W. H., O'Neill, F. I., Thompson, K. W., and Dobson, L. G., *J. Am. Med. Assn.*, 1925, lxxxv, 1729.

[3] Manwaring, W. H., Wright, R. W., and Shumaker, P. W., *J. Am. Med. Assn.*, 1926, lxxxvi, 1271.