

peutic injection, and in increasing amounts thereafter, for at least two to three weeks. As a rule, antibody can be demonstrated either at the onset of the serum sickness or within one or two days thereafter. Thus, these two factors coexist in the blood throughout the serum sickness, and even for some days after its subsidence.

The bearing of these facts upon the interpretation of serum sickness is not easy to determine. In the first place, it is not probable that the coëxisting antigen and antibody correspond to one another; in all likelihood they represent different fractions of the complex antigen, namely horse serum. According to present conceptions, the antigen is progressively neutralized by the antibody, both of the cells and of the circulating blood. Reasoning by analogy, this neutralization, when it takes place within the blood, produces no symptoms of any kind. When it takes place within the cells, it produces a multiform group of symptoms, summarized under the name of anaphylaxis. It is probable, therefore, that the serum sickness represents the progressive combination of cellular antibody with antigen. Why the symptoms should cease while the antigen is still in the blood, is perhaps explainable upon the theory that the desensitized cells failed to react further.

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#### Some suggestions for rational auto-serum therapy.

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Assuming that certain dermatoses as well as intestinal and respiratory disturbances may be due to hypersensitiveness of certain individuals to various proteins, a number of investigators suggested that the onset of acute pathologic phenomena in such cases may be due to the appearance in the circulation of specific protein, causing anaphylactic reaction. On the basis of this assumption various authors have successfully applied the method of immunization in the treatment of such conditions. In cases

where the identity of protein in question was obvious from the history of the case, or where the different methods have permitted to disclose its nature by a special investigation, the treatment consists in immunization of patient by repeated injections of the specific protein. In those cases where the nature of protein could not be determined, it was suggested to use the blood of the patient, as a carrier of antigen. If the presence of antigen in the blood of a sensitized individual causes anaphylactic phenomena, it is evident that during the periods of freedom from symptoms the patient's blood is probably free from circulating antigen. This fact is lost sight of by many authors who in applying the auto-serum therapy presumably on the basis of the above described theoretical considerations collect the blood at regular intervals without any regard as to whether such blood contains free circulating antigen or not.

Much has been written of late on therapy by parenteral introduction of nonspecific proteins<sup>1</sup> and it is possible, if the observations of the clinicians are correct, that the therapeutic effects of promiscuous injections of patient's own serum are due to some other phenomena than that of immunization by the circulating antigen.<sup>2</sup> Though in such cases apparently injections of normal horse serum can be expected to give just as good results, human serum is evidently to be preferred in order to avoid an additional sensitization to a horse protein. In so much, however, as the authors base their therapy on hypothesis that serum contains the circulating antigen, it seems essential to withdraw the blood at the time when antigen is present in it.

On the other hand, should the removed portion of the blood contain the circulating antigen, what is the rationale of injecting it back practically immediately (as some authors do), when the remaining blood of the patient contains at the time considerably larger amount of antigen already. On the basis of our experimental data we wish to suggest that the blood be withdrawn immediately preceding, during, or immediately after the anaphylactic reaction;

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<sup>1</sup> Miller and Lusk; Smith; Jobling and Petersen. *Journ. A. M. A.*, 1916, p. 1753-58.

<sup>2</sup> M. H. Kahn and H. W. Emsheimer, *Arch. of Internal Medicine*, Vol. xviii., pp. 445.

that the presence of circulating antigen in the blood be determined either by titration of its complement<sup>1</sup> or by antitryptic index,<sup>2</sup> and finally that the serum containing the circulating antigen be properly preserved and injected into patients between the anaphylactic attacks. The time of injections will be determined by antitryptic index, as the animal experiments have shown that such injections give best results at the time when antitryptic index is lowest.

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**Note on a toxic nucleoprotein obtained from rat carcinoma.**

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Flexner-Jobling rat carcinomata of the strain used by Robertson and the author<sup>3</sup> were ground in a mortar with sand, extracted with M/6 NaCl solution, filtered and centrifuged to remove all foreign particles. The supernatant fluid was poured off, diluted with ten times its volume of NaCl solution, and CO<sub>2</sub> allowed to bubble through it for half an hour. A flocculent precipitate which settled in a few hours was the result. Phenol was added to make the suspension 0.5 per cent.

The original problem was to ascertain if such a substance, assumed to be cell globulin, would prove to be specific, using complement fixation as a test. An attempt was made to immunize a rabbit by intravenous injection, but the rabbit died within five

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<sup>1</sup> Bronfenbrenner and Schlesinger, in press, these *Proceedings*.

<sup>2</sup> Bronfenbrenner, *PROC. SOC. EXPER. BIOL. AND MED.*, 1915, xiii., p. 42.

<sup>3</sup> Robertson and Burnett, *Jour. Exper. Med.*, Vol. 21, 1915, p. 281.