jected animal is complete within 5 minutes and that the injected precipitin is retained quantitatively in the blood stream for at least 15 minutes after its introduction. The method here described seems to be a reasonable procedure for blood plasma volume determination and to possess certain advantages over other methods. A more extensive report of this work will be made elsewhere.

6378

Tobacco Sensitiveness in Thrombo-Angiitis Obliterans.

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(Introduced by George Baehr.)

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The etiology of thrombo-angiitis obliterans is unknown. The current theories as to the cause are specific infections, endocrine disturbances, toxic factors, such as ergotism and tobacco. Thus far there is no decisive evidence in favor of specific infection. The rôle of tobacco has been stressed by Buerger, Erb, Meyer, L. F. Barker, Silbert and others. Statistically Barker has shown that the excessive use of tobacco is much more common in patients with thrombo-angiitis than in a control group of similar ages. The disease has been reported in individuals who do not use any tobacco. In the large experience of Silbert, however, no typical instances of thrombo-angiitis obliterans have ever been observed in non-smokers. Silbert has noted clinically that cessation in the use of tobacco has often definitely arrested the progress of the disease. While it is a fact that patients suffering from thrombo-angiitis are almost universally excessive smokers, it is also true that many equally extensive users of tobacco never develop thrombo-angiitis obliterans. If, therefore, tobacco plays an etiologic rôle, the question arises why this agent should affect one group of individuals, and not all others.

It occurred to one of us (J. H.) to investigate this problem from the point of view of specific hypersensitiveness to tobacco. Typical cases of thrombo-angiitis observed for a number of years in the Thrombo-angiitis Clinic were selected for investigation. This report gives the results obtained in 68 cases of thrombo-angiitis varying between the ages of 24 and 56, and 122 controls. All the control

cases were males addicted to the use of tobacco, 47 healthy college students between the ages of 16 and 21, and 75 adults, chiefly Russian Jews, between the ages of 26 and 68. In this control group are 15 cases, suffering from circulatory disturbances of their extremities, atherosclerotic in nature; 5 of infectious asthma, and 15 cases of hay fever. These 75 controls were comparable in race, in the duration and amount of tobacco used, with the thrombo-angiitis patients.

Extracts of tobacco were prepared after the method of Coca. The tobacco used consisted of the uncured leaf furnished by the American Tobacco Co. Separate extracts were made from the following varieties: Burley, Maryland, Virginia and Xanthis (Turkish). A tobacco extract representing a mixture of various tobaccos obtained from the Allergy Department of the New York Hospital through the courtesy of Dr. Cooke, which we labelled "Coca" extract, was also employed. Five different extracts were tested on every case of thrombo-angiitis obliterans and every control. All the extracts were diluted 1-10, because the original solution was irritating and produced false positives. The technique used was the one employed in the testing of hay fever or asthma patients. The outer arm was injected intracutaneously with approximately 0.01 cc. of the tobacco extract and reactions read within 15-20 minutes. The results were as follows:

Out of 68 cases of thrombo-angiitis 58 or 83% reacted to one or another tobacco extract. Ten or 17% were negative. The reactions just as in other allergics varied in intensity. "Coca" extract which was a mixture of tobaccos naturally gave the largest number of positives.

Of 107 controls, all cigarette smokers, 97 were negative and 10 reacted to tobacco. or about 10%. In none of the 10% positives were the reactions marked, being at the most 2+. Analysis of this control group indicates that of the 47 college students 5 or about 10% reacted positively. Of the 55 individuals between the ages of 26 and 68, 5 also reacted. Fifteen patients included in this group who suffered from circulatory disturbances in their lower extremities of an arteriosclerotic nature were negative, although all of them were excessive cigarette smokers.

The five cases of infectious asthma were negative. A. Brown reports that 1% of asthmatics react to tobacco. All of the 15 cases of ragweed hay fever, however, reacted positively to tobacco. Whether these reactions were merely indications of the multiple sensitization observed in atopic individuals, or whether these patients were also tobacco sensitive, must be investigated further.

In contrast to this observation is the fact that only 2 out of the 68 thrombo-angiitis patients reacted to ragweed. One of these was a ragweed hayfever patient and the other had a father who was ragweed sensitive although he himself was free of symptoms. All of the other 66 were negative. They gave no atopic history.

A search for sensitization to substances other than ragweed and tobacco in 15 cases of thrombo-angiitis revealed definite reactions to foods and other inhalants. Thus 10 patients reacted to horse epithelium; 9 to tomato; 6 to rice; 5 to halibut; 4 to almond, beef, kapok, and cabbage; 3 to oats; 2 to cottonseed, lima bean and ragweed; one each to chicken, orange, eggwhite, lamb, black pepper, and pyrethrum.

While it is interesting to note that thrombo-angiitis patients, like allergic patients in general, also show multiple sensitization, no other antigen seems to be as dominant as tobacco. The importance of the simultaneous sensitization to foods, etc., however, is not to be disregarded. Further study may reveal some collateral significance.

Study of the character of the reactions to tobacco was made in 20 of the positively reacting patients with thrombo-angiitis to determine whether their reactions were dependent upon the presence of atopic reagins. The passive transfer technique of Prausnitz and Küstner was employed. Ten cc. of blood was drawn from the arm vein, clotted, and 0.1 cc. of the serum injected into various sites of the forearm of normal individuals. Three days later these sites were reinjected with the tobacco to which the patient had originally reacted. Out of 20 sera thus tested 13 gave positive passive transfers. The presence of reagins to tobacco in these thrombo-angiitis cases indicates that we are dealing with individuals who were in all probability atopic, and that the positive phenomena are true antigen-antibody reactions.

Summary. 1. 58 out of 68 cases of thrombo-angiitis or 83% were found to be hypersensitive to tobacco by means of positive skin reactions to various tobacco extracts. 2. The presence of atopic reagins to tobacco was demonstrated in 13 out of 20 patients by means of passive transfer. 3. Multiple sensitization characteristically prevalent in allergic individuals was also found in thrombo-angiitis patients. 4. Out of 102 control smokers only 10, or about 10%, reacted to tobacco. These reactions were at most 2+. In this group 15 cases with circulatory disturbances on an atherosclerotic basis were completely negative. 5. Ragweed patients usually reacted to tobacco, whereas only 2 patients in the entire group of 68 thrombo-angiitis sufferers reacted to ragweed.

Final conclusions cannot be drawn. Further investigation of other diseases for the occurrence of tobacco hypersensitiveness must be carried out before its importance in thrombo-angiitis can be definitely established. It has been clearly demonstrated, however, that a large percentage of patients suffering from thrombo-angiitis obliterans belong to the category of allergic individuals and that this allergy is essentially characterized by a hypersensitiveness to tobacco.

6379

Oral Immunization of Rabbits Against Pneumococcus Pneumonia and Septicemia.*

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As shown by Ross[1] it is possible to actively immunize rats against Type I pneumococcus septicemia by the oral administration of tissues carrying this organism as well as by feeding acid-killed, bile dissolved and mechanically disrupted organisms and the specific polysaccharide. Kolmer and Amano[2] found that rabbits could be sometimes immunized against highly fatal pneumococcus meningitis and septicemia, especially that produced by Type I pneumococcus, by the oral administration of heat killed and living vaccines. We have thought it worth while to ascertain if rabbits could be vaccinated against the pneumococcus pneumonia and septicemia induced by the intratracheal injection of living cultures as employed by Cecil and Steffen[3] in the production of pneumococcus pneumonia of monkeys. Cecil[4] reported that 3 subcutaneous injections of Type I pneumococcus vaccine protected these animals against pneumonia when inoculated intratracheally 3 weeks later.

Since it may be that the oral administration of pneumococcus vaccines may engender an equal or even higher degree of immunity

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[3] Cecil, R. L., and Steffen, G. I., *J. Exp. Med.*, 1921, **34**, 245; 1923, **38**, 149.

[4] Cecil, R. L., *Arch. Int. Med.*, 1928, **41**, 295.