

ovary then we would have to assume, that whenever sufficient ovary regenerates it would prohibit complete sex-reversal in all its characters and it may cause a reversal of some of the already formed male characters in the female direction. This statement is made with some reserve since it is not known at the present time what the internal findings will reveal. However, if ovarian tissue should be found it would seem to show that complete sex-reversal is not possible in cases of pathological reduction or natural ovariectomy unless the ovary be completely destroyed or removed.

Our results indicate that the female in the Brown Leghorn fowl has many potentialities of the male, which are normally inhibited by the presence of the ovary, and that these potentialities can assert themselves approximately fully after the complete removal of the ovary at an early age.

## 16 (2539)

### **Bacterial allergy and tissue reactions.**

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The bacterial allergies, though they are phenomena of relatively specific hypersusceptibility, differ in certain fundamental respects from true protein anaphylaxis. Our own investigations on this subject have dealt chiefly with the tuberculin reaction in regard to which it seems safe to state that:

1. Tuberculin allergy as manifested by the intracutaneous reaction may occur without general anaphylaxis to tuberculo-protein, and vice versa.

2. The active principle of tuberculin which elicits reactions in the sensitive subject is not a protein.

3. Tuberculin sensitiveness seems inseparably associated with the reactions of the animal tissues to the tubercle bacilli or their constituents; in other words, after prolonged experimentation, we arrive again at the recognition that there is no tuberculin sensitiveness without a tubercle. Here again the fact that the

tuberculin reaction is merely the classical example of the bacterial allergies in general is apparent in that our own work with other bacteria as well as especially that of Fleischner and Meyer with *bacillus abortus* has indicated that bacterial allergy is associated with infection rather than with the type of immunization with soluble bacterial substances which leads to antibody formation without necessarily active focal inflammatory reactions.

In the case of the tubercle bacillus Petroff and the writer have shown that the injection of the dead bacilli induces tuberculin allergy quite effectively, probably because of the insolubility of these organisms, in consequence of which the dead organisms lead to tubercle formation essentially analogous to that induced by the living. This point, apart from its possible practical interest, is theoretically significant in that it indicates that, in the association of bacterial allergy with infection rather than with immunization, it is the tissue reaction which is of importance rather than any differences in the products which pass into the infected animal from dead and living bacteria respectively.

Our present experiments were aimed more particularly at an inquiry into the relationship of antibodies to bacterial allergy. The problem was approached by two separate lines of investigation. In the first series of experiments pneumococcus antigen and anti-serum were employed because it was relatively easy to obtain large quantities of both substances. Considerable amounts of anti-pneumococcus serum were injected into a large series of guinea pigs by various routes and by both single and repeated injections. Subsequently, at intervals ranging from several hours to several weeks, skin reactions were done upon these animals with various forms of pneumococcus extracts, all of which were powerfully precipitable by the anti-pneumococcus serum employed for the preliminary injection. In the large majority of these animals no characteristic delayed skin reactions were obtained. In many of them mildly positive reactions appeared and in only four or five was anything approaching a tuberculin reaction observed. In other words, these experiments showed that allergy, as indicated by the delayed skin reaction, could not be produced passively in guinea pigs with any degree of certainty or regularity by the injection of highly potent specific precipitating sera, and that there was, in other words, no relationship between antibodies and allergic reactions of the tuberculin type.

In the second series of experiments tuberculin and the sera of rabbits containing precipitating antibodies for tuberculin were used. The sera were produced in various ways by the prolonged treatment of rabbits with tubercle bacilli and their products. At the same time similar passive transfers were attempted with the sera of rabbits and guinea pigs in which multiple tuberculous lesions had been produced by the injection of living tubercle bacilli, usually bovine in the cases in which rabbits were used.

The results of these experiments may be briefly summarized as follows:

1. Many of the sera containing potent precipitating properties for tuberculin and tubercle bacillus residues conveyed little or no allergy to subsequent intracutaneous administration of O. T.

2. Some of these sera did convey such allergy, which appeared four or five days after the serum injection.

3. A number of the rabbit sera obtained from rabbits which were suffering from multiple tuberculous lesions but which possessed no precipitating properties, or almost none, conveyed allergy in a typical way, so that subsequent tests with tuberculin four to eight days later resulted in + + + to + + + + (characteristic, though never necrotic) tuberculin reactions.

In a few cases in which this happened, similar allergy could be induced by the injection of the filtrates of the ground tissues of the lesions themselves.

It may be concluded that passive transfer of tuberculin allergy to normal guinea pigs can be accomplished by the injection of tissue filtrates from tuberculous lesions of rabbits and, in many cases, with the serum of such rabbits, indicating that the substance which conveys allergy is probably given off from the tissues to the serum. The presence of such substances that convey the allergy is dependent upon the existence of inflammatory foci, and varies in quantity according to factors that we have not yet ascertained. These substances, however, do not run parallel to the ordinary precipitating antibodies and can not be identified with them.

We are inclined to suggest from these experiments that allergic hypersusceptibility of the tuberculin type is dependent upon substances in the production of which tissue reactions are essential.

When dissolved or soluble bacterial materials are injected into an animal, antibodies of the classical type result which may, just as when horse serum or egg albumen are injected, lead to anaphylaxis. These antibodies in the case of bacteria are probably concerned with protection, in that by agglutination of the bacteria and the sensitization of the bacteria to phagocytic action they aid in the removal of the organism from the blood stream of the tissue spaces. No typical allergy, however, need result.

When the living bacteria are injected or, as in the case of the tubercle bacillus, dead bacteria in a more or less insoluble state, inflammatory reactions occur and, as a result of these tissue activities, other substances, not antibodies in the ordinary sense, are produced which lead to allergy.

Other work going on in this laboratory on tuberculosis indicates the correctness of the suspicion expressed by many previous workers, that tuberculin hypersensitiveness and resistance to infection are parallel processes, and these allergic substances, as we may call them for the present, therefore, may also possess a perhaps deeper protective significance.

If we remember the fact that the tuberculin reaction in its main characteristics shows close analogy with similar phenomena occurring in connection with other infections such as, for instance, the Mallein reaction, the typhoidin reaction and such work as that of Fleischner and Meyer with *bacillus abortus*, it seems more than likely that we are faced with a fundamental principle. In all of these reactions the association of the allergy with actual infection rather than with treatment with dead bacteria appears fairly clear.

Thus we cannot avoid the thought that there is a basic difference in the occurrences which result in the animal body from the injection of dissolved or soluble dead bacterial substances on the one hand, and those which are consequent upon actual inflammatory response to the living invaders. Such a conception, furthermore, is in harmony with a great many heretofore unexplained facts, such as, for instance, the difference between the results of immunization with living and with dead bacteria; the protective effects of convalescent serum in conditions in which artificially produced immune sera are relatively ineffective in spite of high antibody contents; the relatively limited protective effects of antibody containing sera in many bacterial diseases; the fre-

quent and curious lack of parallelism between antibody contents and protective functions generally. The obvious direction indicated to us for further experimentation by these results is to include attempts to produce inflammatory foci in the processes of active immunization for the production of protective sera.

## 17 (2540)

### Estimations of blood sugar in decerebrate animals.

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Figures for blood sugar following decerebration have been given by J. Mellanby,<sup>1</sup> but he used an injection of starch for decerebration and the actual area of brain damage remained very uncertain. He found a hyperglycemia lasting as long as six and a half hours and supposed that this high sugar level might be maintained indefinitely. On the other hand, Bazett and Penfield found a disappearance of sugar from the urine in decerebrate cats within two days.

A few observations on blood sugar have been made on cats decerebrated aseptically by a scooping out method under chloroform anesthesia. The blood has been obtained from a cut in the ear and the sugar estimated by Maclean's method. In one such animal a blood sugar of 0.256 per cent was obtained 24 hours after operation, and the urine secreted during the night contained sugar. In another animal the blood sugar 24 hours after operation was found to be 0.19 per cent. In both of the above animals the pituitary was left intact. In an animal decerebrated acutely with the Sherrington guillotine and chloroform anesthesia in which the whole of the hypophysis was removed and also any accessory pituitary tissue in the pharynx a blood sugar of 0.37 per cent was obtained one half hour after decerebration and the level gradually fell until 7 hours after operation it was 0.20 per cent and finally reached 0.165 eleven and a half hours after the operation. At this time the animal began to have difficulty in

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<sup>1</sup> Mellanby, J., *J. Physiol.*, 1919, liii, 1.