8498 P

Influence of Allergy on Development of Early Tuberculous Lesions.

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Quantitative considerations of the amount of lipoid in a few hundred tubercle bacilli compared to the amount of tubercular or other lipoid required to produce a noticeable foreign body reaction obviously render inadequate the present more or less generally accepted hypothesis purporting to explain the histogenesis of the tubercle. Moreover, such a theory completely fails to explain the development of closely similar, sometimes almost indistinguishable lesions in other infectious granulomata such as syphilis, typhoid, glanders, or brucellosis.

In a previous paper[1] concerned with the histologic reactions in hypersensitive states, the authors pointed out that bacterial allergy—defined as the first stage of the immune response to parenterally injected antigen, characteristic only of active as contrasted with passive immunity—develops much more rapidly than has generally been believed and determines on the part of the host a tissue reaction characterized by a marked infiltration with large mononuclear phagocytes. Attention was called to the fact that bacterial allergy is particularly well marked in that group of diseases in which focal mononuclear reactions characterize the histologic picture and the suggestion was made that the relationship between the two states might better be explained by the assumption that the allergy determined the type of histologic response than by the more conventional theory that the granulomatous response provoked the allergy. The present experiments were designed to test this hypothesis by a study of the time relationships of the development of allergy and the character of the histologic reactions.

Approximately 50 guinea pigs were infected with large doses of tubercle bacilli (5 to 20 mg.), strains of both low and high virulence being used, in order to insure the rapid and intensive development of generalized hypersensitiveness. The sites of primary inoculation were varied, 2 groups of animals being infected intratesticularly, one group intraperitoneally, and one both intratesticularly and subcutaneously. Tuberculin sensitiveness was tested with the

[1] Dienes, L., and Mallory, T. B., *Am. J. Path.*, 1932, **8**, 689.

intracutaneous injection of tuberculin and also by the injection of small doses of living tubercle bacilli into the skin. The animals were killed on successive days and the sites of infection and the skin tests were examined microscopically. In all groups the development of the lesions and the appearance of sensitivity were so uniform that a summary description is adequate.

Grossly, tuberculin sensitiveness was first noticeable in skin tests made 96 hours after infection. Microscopically, however, skin tests made 72 hours after infection showed a marked infiltration of the tissues with mononuclear cells—a finding which in a former paper[1] we have shown is not only a reliable indication of bacterial allergy but is distinctly more sensitive than gross examination.

When living tubercle bacilli were substituted for tuberculin and 24-hour-old skin lesions produced on successive days after the primary infection were examined histologically, it was found that a marked polymorphonuclear reaction was always present. When the skin injection was made simultaneously with the primary infection or followed it by only 24 hours, practically no other reacting cells were visible, but when 48 hours intervened between the injections some of the animals began to show significant mononuclear infiltration and after 72 and 96 hours this became constant and extensive.

It is realized that the rate of replacement of polymorphonuclears by mononuclear cells varies with the size of the infecting dose but since the dosages were uniform, it seemed not unreasonable that this should be interpreted as evidence of early tuberculin sensitivity—the relatively persistent antigen depot supplied by the bacilli making it evident that an earlier period than was possible with tuberculin.

The primary lesions—subcutaneous, testicular, and intraperitoneal—were closely compared with the skin tests. Within a few hours the bacteria were surrounded by polymorphonuclears, which rapidly led to abscess formation in the course of 48 hours. By 72 hours the abscess was surrounded by a well defined zone of large mononuclears which in succeeding days spread centrally and gradually replaced the great majority of the granulocytes. At the same time rapid fibroblastic proliferation at the periphery of the lesion resulted in true fibrous encapsulation.

Under these conditions of massive infection, it appears fair to conclude that bacterial allergy appears coincidentally with the histologic change from a simple pyogenic to a granulomatous response. That general sensitivity would occur so early with small localized infections is of course out of the question, but the possibility of the earlier development of sensitivity at the site of the lesion sug-

gested by Stewart[2] has recently received strong inferential support from the demonstration of localized antibody formation by McMasters and Hudack.[3]

8499 C

Influence of Ethyl Alcohol on Energy Metabolism of the Mammalian Heart.*

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(Introduced by Maurice B. Visscher.)

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The use of the older methods of studying the isolated heart led to contradictory conclusions regarding the effect of alcohol on cardiac contraction. Sulzer,[1] using the Starling heart-lung preparation, at present the most sensitive and reliable method for this purpose, found no stimulating effect in any concentration and showed that concentrations commonly reached in the human blood stream in alcoholic intoxication produce dilatation without an increase in the work of the heart. We have confirmed this effect and studied the changes in energy metabolism associated with it.

We have used a modified heart-lung preparation, which has been previously described.[2] In some experiments the diastolic volume was allowed to increase when alcohol was added (Table I), while in others (Table II) the external diastolic volume was maintained constant throughout the experiment by adjustment of the venous return. In all cases the venous pressure had to be lowered in order to keep diastolic volume constant after alcohol. A piston recorder was used for ventricular volume recording and the heart was held in a glass cardiometer, following the technique of Starling and Visscher.[3]

After a control period of 15 to 30 minutes, during which the volume output and oxygen usage remained constant, the desired

2 Stewart, F. W., *Am. J. Path.*, 1925, **1**, 495.

3 McMasters, P. D., and Hudack, S. S., *J. Exp. Med.*, 1935, **61**, 783.

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1 Sulzer, *Heart*, 1924, **11**, 141.

2 Peters, Rea and Visscher, PROC. SOC. EXP. BIOL. AND MED., 1934, **32**, 268.

3 Starling and Visscher, *J. Physiol.*, 1927, **62**, 243.