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On the production of generalized syphilis in the rabbit by local inoculation.

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Two of the most striking features of the infection usually produced in rabbits by testicular or scrotal inoculations of well-adapted strains of *Treponema pallidum* are the marked reaction at the site of inoculation and the total absence of generalized lesions. In fact, these features of the reaction to infection are so conspicuous as to suggest a casual connection between the two, especially when it has been shown that the failure to produce generalized lesions can in no wise be attributed to the absence of a generalized infection or to an insusceptibility on the part of the animal's tissues to react to such organisms. Specifically, it appeared to us that in all probability, the failure to produce generalized lesions was due in a large measure to an inhibitory influence arising from the reaction at the primary focus of infection and that the reduction or suppression of this reaction might be sufficient in itself to permit the development of generalized lesions.

In order to test this hypothesis, three types of experiments were carried out which were intended to compare the effects produced by unilateral and bilateral inoculations, the effects of castration and the effect of suppression of the primary lesions by the use of therapeutic agents. The castrations were done under ether anesthesia.

Effects of Unilateral and Bilateral Inoculation and of Castration. —In the first series of experiments, there were 27 rabbits inoculated in one testicle and 20 inoculated in both testicles, giving a total of 47 rabbits. These were divided into two groups, one of which was castrated soon after the appearance of the primary lesion and the other held as controls. Both groups were kept under observation for a period of 4 months after inoculation.

Of the 27 rabbits inoculated in one testicle, 14 were castrated

and 13 were held as controls. Generalized lesions developed in 8 of the 13 controls and 13 of the 14 castrated animals.

Of 20 rabbits inoculated in both testicles, 6 were held as controls and 14 were castrated. Generalized lesions occurred in 1 of the 6 controls and in 13 of the 14 castrated animals.

Several other experiments of a similar character gave essentially the same results. In one of these, 46 rabbits were given a heavy inoculation with a testicular emulsion—half of them unilaterally and the other half bilaterally. With these animals, the influence of castration at different periods of the infection was studied and the effects of suppression of the local infection by the use of a therapeutic agent. Only the results of the therapeutic experiments can be given here.

Effects of Suppression of Primary Lesions by Therapeutic Agents.—In carrying out these experiments, a drug was chosen from among those studied by us in collaboration with Dr. W. A. Jacobs and Dr. Michael Heidelberger whose effect in inducing resolution of lesions was much greater than its spirocheticidal action. This substance was arsenophenylglycyl dichloro-*m*-aminophenol.

Twelve rabbits, 6 of them inoculated unilaterally and 6 bilaterally, were given a single intravenous injection of this drug 14 days after inoculation and the results were controlled by 6 untreated rabbits from each of the respective groups.

In the unilateral series, the lesions present were almost completely resolved and the local reaction suppressed for between 2 and 3 weeks. At the end of 3 months, all of these animals had developed generalized lesions as contrasted with 3 of the 6 controls. The effect of the drug upon the animals inoculated in both testicles was less marked and lasted for only 7 to 10 days. At the end of 3 months, generalized lesions had developed in 4 of the 6 treated animals and in 1 of the 5 surviving controls.

Effects of Complete Prevention of a Primary Reaction and Early Removal of the Medium of Inoculation.—An experiment originally carried out for the purpose of determining the time at which a true generalized infection became established in the rabbit proved to be a remarkable demonstration of the effects which might be obtained from complete prevention of the develop-

ment of a primary lesion plus an effect which appeared to be attributable to the early removal of even the small bit of syphilitic tissue used in the process of inoculation by the implantation of a small piece of infected testicle beneath the skin of the right scrotum. 48 hours later, the entire scrotum and testicle were amputated under ether anesthesia. By the end of the 7th week, 8 of the 10 rabbits had developed marked generalized syphilis while the other 2 showed a definite lymphadenitis. One of these developed slight generalized lesions at the end of 2 months and the other 2½ months after inoculation. As a whole, however, the generalized infection was the most pronounced which we have seen in any single group of animals.

Conclusions.—The conclusions to be drawn from these experiments are: That the marked character of the reaction which takes place in the rabbit following local inoculation of old strains of *Treponema pallidum* is in a large measure responsible for the absence of generalized lesions; that an inhibitory influence is exerted upon the development of other lesions which is proportionate to the reaction taking place at the site of inoculation and that the reduction, suppression or prevention of this reaction will remove this influence to a sufficient extent to permit the development of a generalized disease analogous to that which occurs in man.

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Blood changes in ether anesthesia.

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During light ether anesthesia the bicarbonate content of the arterial blood falls, the carbon dioxide tension (determined directly by the tonometric method on the blood) rises, as does the hydrogen ion concentration. These phenomena indicate a state of uncompensated acidosis. The oxygen saturation increases, indicating that ventilation is accelerated in response to the stimulus