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Multiple infections with Treponema pallidum in the rabbit.

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Once it has been demonstrated that under appropriate conditions superinoculation of a rabbit with an advanced syphilitic infection may give rise to a typical primary lesion,[1] the question naturally arises as to whether this second infection is limited in its effects to the local reaction or is capable of further participation in the disease produced.

The problem was approached by a number of experiments. Rabbits infected with strains of low virulence were reinoculated with strains of high virulence after the original infection had become well established. In general, the primary inoculation was made in one or both testicles while the second was intracutaneous on the sheath or at the base of one ear, using equivalent amounts of a testicular emulsion. The infections thus produced were compared with those in a series of control animals. The interpretation of the experimental results was based upon the usual course of the disease produced by each strain with particular reference to the type and severity of lesions and to their time and sequence of occurrence since at a given time and under given conditions these are comparatively constant properties of any given strain.

The experiments up to the present time have yielded a number of instances in which the nature of the infection differs from that ordinarily seen with any one of the several strains employed and this may be illustrated by citing a single example. The two strains used in this experiment have been studied in a large series of animals. The less virulent strain (III) used for the primary inoculation was isolated in the fall of 1919. It has always produced a mild infection with slight primary lesions of short duration and generalized lesions of a minor character consisting of occasional small diffuse or papular lesions of the skin, slight infiltrations about the sheath, a few cases of keratitis and two in-

[1] Brown, W. H., and Pearce, L., PROC. SOC. EXPER. BIOL. AND MED., 1921, xviii, 200.

stances of slight periostitis of the nasal bones. The infection produced by the Nichols strain, which was isolated in 1912, has been much more severe with pronounced primary lesions and the frequent occurrence of extensive lesions of the bones, large cutaneous granulomata, lesions of the mucous membranes and of the eyes. The time of occurrence of generalized lesions with both strains is subject to wide variations but in general, is from 2 to 3 months after inoculation. In the vast majority of instances, lesions of the periosteum and bone, skin, and eyes appear in the order given.

The rabbit was inoculated into the right testicle with Strain III on December 2, 1920, with the production of an orchitis, which pursued a normal course. On January 26, 1921, 55 days after inoculation, the rabbit was reinoculated in the sheath with the Nichols strain; at this time, resolution of the testicular lesions was well advanced and the inguinal lymph nodes were barely palpable.

During the following week, a definite papule developed on the sheath; the inguinal lymph nodes became enlarged and indurated and activity of the orchitis was resumed. 19 days after reinoculation, the lesion on the sheath was much larger than in any of the controls and dark field examination showed actively motile spirochetes. In addition, marked metastatic lesions were present in the left testicle.

3 weeks after reinoculation, or 2½ months after the primary inoculation, there was a large actively growing chancre, an intense metastatic orchitis, marked popliteal adenitis, a keratitis of the right eye, and a number of bone lesions which resulted in extensive necrosis of the nasal and tarsal bones and slight necrosis of the distal end of the right ulna. The animal also showed pronounced emaciation and weakness. During the next few weeks, the keratitis completely disappeared and has not recurred and the nasal lesions were also healed. The destruction of the tarsal bones, however, was more extensive than has been observed in any other animal infected with any strain of *Treponema pallidum* and during the 2 months since the appearance of the lesions, very little repair has been accomplished, a condition never before observed. The chancre showed irregular periods of growth and

resolution with a pronounced tendency to necrosis and central softening.

This was the condition of the animal 2 months after reinoculation at which time a second group of lesions developed beginning with a reinduration of the chancre and an increase of the lesions in the left testicle. These were followed by the appearance of a granuloma of the left tendo-Achillis and of large cutaneous granulomata on the tail, on the left hind foot and a little later in both scrota. All of these lesions are still present.

The outstanding features of the infection in this animal are the sequence of events and the type and destructiveness of the lesions. The first unusual feature was the remarkably rapid development of the chancre at approximately the same time with a keratitis and extensive bone lesions. Obviously, the occurrence of the chancre can be attributed to the reinoculation. If the keratitis is also referred to the Nichols strain, its time of appearance, 3 weeks after reinoculation, is the first instance of this kind we have so far observed. On the other hand, if it is attributed to the original inoculation, its occurrence 2½ months later, is more in accord with our experience of the time relation of generalized lesions. The subsequent development of a number of prominent cutaneous and tendon sheath lesions some weeks after the keratitis, is another peculiar feature of this experiment, since eye manifestations are usually terminal events of an infection. The only bone lesions observed with the strain used for the primary inoculation have been two instances of slight periosteal lesions of the nasal bones and while destructive bone lesions are comparatively common with the Nichols strain of *Treponema pallidum*, they have never reached the proportions of those observed in this instance. In point of time, moreover, the occurrence of such bone lesions 3 weeks after inoculation is unprecedented in our experience.

The large cutaneous lesions which appeared some 2 months after reinoculation are of the usual type observed with the Nichols strain but differed markedly from the comparatively rare cutaneous lesions of Strain III, which are of the papular or infiltrative type. Moreover, if these granulomata were due to the original inoculation, they should have occurred some time before the keratitis. In their type, time of occurrence and sequence rela-

tionship, therefore, these lesions are more closely related to the second than to the first inoculation.

Viewed in this light, it would be difficult to attribute the infection produced in this animal to either of the strains of *Treponema pallidum* with which it was inoculated and although the outstanding manifestations of disease conformed more to the general character of the infection produced by the second than by the first organism, it would seem to be more logical to regard the infection as one produced by the combined action of the two organisms. These results are presented as a means of directing attention to the possibilities of double or multiple infection where appropriate conditions exist rather than to the probabilities of their occurrence.

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Report on anaphylactic deaths in guinea pigs from intracutaneous injection of small amounts of egg albumin.

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In view of the importance of the many problems arising in regard to the relationship between intracutaneous skin reactions and true anaphylaxis, the following laboratory "accident" would seem well worth reporting. It seems especially interesting in connection with the account of a human case of anaphylaxis following the intradermal injection of egg protein which was published by Goestenberger and Davis, and which bears out certain views concerning the relationship of bronchial musculature and anaphylaxis brought out by Wells[1] in his recent critical articles in the *Physiological Reviews*. The occurrence which is unique in our experience with anaphylactic guinea pigs, was as follows:

Six guinea pigs, 341, 349, 62, 568, 1122, and 1119, three males and three females ranging in weight from 235 grams to 265 grams, were treated on February 9 with intraperitoneal injections of 2 c.c. of a solution of crystallized egg albumin, representing about

[1] Wells, *Physiological Reviews*, 1921, i, 44.