EXPERIMENTAL SYPHILIS IN THE RABBIT PRODUCED
BY THE BRAIN SUBSTANCE OF THE
LIVING PARETIC.

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In 1913 Forster and Tomaszewski reported a method for demonstrating Spirochaeta pallida in the living brain of patients suffering from general paresis. Their method, embodying a modification of the Neisser-Pollak trephining operation, was described by me in 1913.

Forster and Tomaszewski inoculated rabbits with the cortex thus obtained, but their results were negative. In 1913 Noguchi reported two successful inoculations of thirty-six rabbits inoculated with material obtained at autopsy from paretic brains. In the first case, after 97 days, typical nodules appeared in the testes and the scrotal skin. In the second, 102 days elapsed before the nodules appeared. In one case there were extremely few spirochetes, but a large number were demonstrable in the second. An attempt at inoculation into a second generation of the rabbits resulted in a very small lesion. This also appeared only after three months' time.

Berger reported very few spirochetes in the lesions of three out of twenty inoculations, and he made no attempt to prolong the strain. The small number of organisms found in his case makes it probable that these were survivals.

Nichols and Hough reported sixteen inoculations of brain substance from eight cases with slight success in two instances. In their cases, however, small testicular lesions resulted, with striking eye manifestations, but no spirochetes were demonstrable in the lesions, nor were they able to reinoculate other rabbits from the lesions.

All the experiments mentioned above, except those of Forster and Tomaszewski, were made from material recovered at autopsy soon after death.


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During the past year I have repeated the inoculation experiments of Forster and Tomaszewski, using living material for the inoculation. It seemed to me that the lack of success of previous observers might be due to the small number of organisms present, and I therefore inoculated the brain substance of several cases into a single rabbit. Moreover, it seemed possible that the organisms from a living subject would be more likely to infect than those taken at autopsy.

For my series of experiments six cases were chosen from a large number of paretics. The diagnosis from the clinical findings and from the spinal fluid was frank general paralysis. All the cases had been under the observation of Dr. Edmund A. Christian at the Pontiac State Hospital for a long time, and in each case there were marked manifestations of advanced paresis.

The material was obtained from the brain. The site was prepared with tincture of iodine, with ethyl chloride as a local anesthetic. The skull was trephined over the frontal convolution at a point about one-half to one inch from the midline and well forward of the course of the middle meningeal artery. By means of a long thin trocar needle connected to a syringe a small cylinder of gray and white matter with some fluid from the ventricle was removed. The material was transferred to a sterile Petri dish, containing a few drops of normal salt solution and was at once examined for spirochaetes under the dark-field microscope. In five of the six cases spirochaetes were demonstrable; in one case they were extremely numerous, and in the remaining four it required from ten minutes' to half an hour's search to demonstrate them.

The major portion of the material thus obtained was at once injected into the testes of a large rabbit (June 11, 1915). The material from five cases was injected into the left organ and that from one case into the right. About two weeks after the inoculation, small hard nodules could be felt in both organs. Aspiration of the nodules after four weeks (July 10, 1915) showed large numbers of active, motile spirochaetes. These continued to be demonstrable up to the eleventh week after inoculation, when the animal died from an accidental trypanosome infection, the nature of which was not determined. When the organisms were first demonstrable a second rabbit was inoculated (July 11, 1915) from the aspirated testicular juice of
the first animal. On August 1, 1915, twenty-one days later, both testes were found to be the sites of hard nodules, from which again, on aspiration, large numbers of spirochetes were demonstrable. These continued to be demonstrable in the second rabbit for five weeks, up to the time of the death of this animal from the same accidental infection. A third rabbit was inoculated (August 2, 1915) with the aspirated testicular juice of the second, and fifteen days after inoculation (August 17, 1915) small nodules appeared in both testes, in which again large numbers of organisms could be found on repeated examinations.

Thirty-three days after spirochetes were found in the first rabbit (August 12, 1915), the testis of one side was castrated. The organ was cut into small pieces and a mash made with normal saline solution. A portion of this material was used for cultural work and a small portion for inoculation into a fourth rabbit. At the present writing (October 28, 1915) viable organisms are still present in the cultures made from this mash. Rabbit 4 is still alive (October 28, 1915), and although no nodes are palpable in the testes, pallidae in moderate numbers are still demonstrable by aspiration from both organs.

The work of Noguchi, Nichols and Hough, and Uhlenhuth and Mulzer seems to indicate the existence of a neurotropic strain of spirochetes. Slight differences in morphology are ascribed to this strain. According to Nichols, the organism is thicker than is ordinarily found, and the curves are not so deep as in the finer variety, the organism being almost as coarse as Spirocheta refringens.

The spirochetes in these experiments differ in morphology from those ordinarily seen in mucous and cutaneous lesions. They were similar to those described by Nichols, being shorter and thicker. In all cases, moreover, they seemed to be less actively motile. This may have been partly due to the physical properties of the fluid in which they were studied.

Nichols and Hough reported in their inoculations the occurrence of keratitis and choroiditis from the testicular inoculations. These


lesions were identical with those found in acquired syphilis, but the most careful search on their part failed to demonstrate the spirochaetes in their cases. None of the rabbits inoculated by me showed either the development of keratitis or other eye symptoms. The rabbit at present living, however, the fourth one inoculated, shows a patchy alopecia, particularly of the head and neck, which is strikingly like that seen in early syphilis.

Noguchi's inoculations required 97 to 102 days of incubation before the development of lesions. His inoculations in the second generation required three months before development. He concludes, therefore, that the infectiousness of general paresis for rabbits is weak and that the virulence of the spirochaete from this source to rabbits is also weak.

In my experiments the first rabbit to be inoculated was found to be infected four weeks from the time of the inoculation and undoubtedly would have proven positive before this time, as nodules were discovered two weeks earlier. The second and third generation showed an increasing virulence as exhibited by the larger numbers of organisms and by the incubation period of three weeks and fifteen days, respectively.

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CONCLUSIONS.

1. Spirochaetes from the living paretic brain easily infect rabbits with experimental syphilis.

2. They constitute a virulent strain with a shorter period of incubation for the rabbit than exists with other strains.