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## Testicular Lesions in Rabbits Following Intraspinal Syphilitic Infection.

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In the course of an investigation concerning the therapeutic efficiency of various chemical compounds in neurosyphilis, it became necessary for us to determine their trypanocidal and spirocheticidal effects in the cerebrospinal system. The central nervous system of animals was infected by the introduction of either trypanosomes or spirochetes into the intraspinal canal. After complete anesthesia of the rabbit is effected, a small incision is made in the parietal region of the skull and the animal then trephined with a small bore.* After trephination, a special capillary pipette is introduced into the opening, and the spirochetes or trypanosomes injected into the fourth ventricle by means of a syringe. After the introduction of the microorganisms the incision is sutured, and after complete recovery from the anesthesia, which usually requires two or three hours, the chemical compounds are introduced intravenously into the animals. Our plan was to destroy the trypanosomes or spirochetes after they were introduced into the cerebrospinal system, by the action of small amounts of chemical compounds which were able to penetrate the choroid plexuses and reach the central nervous system. In this manner we were able to sterilize the spinal fluid by the use of various compounds.

The problem consisted in the selection of the most penetrative and at the same time the most effective spirocheticidal substance. It was necessary to develop a technic for the production of a definite infection of the cerebrospinal system, particularly the spinal fluid. In this article we will describe our results with spirochetic infections, while our experiences with trypanosome infections will be reported elsewhere.

Various investigators attempted to infect the central nervous system of rabbits with syphilis. Thus, Uhlenhut[1] tried to inoculate the brains of healthy animals with syphilis, but obtained no positive results. The attempts of Noguchi and Bartarelli[2] failed too. Plaut[3] inoculated rabbits intratesticularly with spirochetes obtained from the brain of a paretic, and observed certain changes in the

* Description of pipette and details of method, see *J. Chemotherapy*, 1927, April.

cerebrospinal fluids of the animals which, in his opinion, furnished definite evidence of a syphilitic infection. Brown and Pearce[4] inoculated rabbits with spirochetes through the testicles, and were subsequently able to demonstrate the penetration of the spirochetes into the spinal canal by injecting some of the spinal fluid into the testicles of healthy animals and producing typical syphilitic lesions.

In our investigation it was necessary to secure definite evidence of syphilitic infection of the cerebrospinal system after the introduction of spirochetes into the fourth ventricle of rabbits. Incidentally, interesting observations were made, which clearly indicate that such an infection takes place in the majority of cases. Of particular importance is our observation that in the greater number of animals the lesions appear in the testicles. The spirochetes, after their introduction into the intraspinal canal, apparently soon disappear from the spinal fluid, enter the body and are probably carried by the lymphatic system or the blood stream into various parts of the animal body, finally producing skin lesions.

In our inoculations we always used numerous spirochetes which were motile, as confirmed by preliminary dark field examinations. In some cases in which the spinal fluid was examined three to five days after the inoculation, no spirochetes could be found by dark field examinations. Experiences with trypanosomes and spirochetes convinced us that the mere examination of the blood stream or spinal fluid does not always reveal the presence of trypanosomes or spirochetes. More exact methods are necessary in such cases.

The next procedure, therefore, is to inoculate healthy animals with the spinal fluid supposedly containing spirochetes and observe the development of testicular lesions. This was done by us in various instances with negative results thus far. The results obtained with rabbit No. 1155 are particularly interesting. It was inoculated intraspinally on January 25th, 1927, killed on January 28th, and some of the spinal fluid injected into the testicle of rabbit No. 1163. This animal was observed until May 2, 1927 (a period of 89 days) but no testicular lesions appeared. This rabbit is still under observation.

Finally, we decided to study the systemic manifestations of syphilis in rabbits infected intraspinally with spirochetes. This resulted in the striking observation that the majority of animals develop syphilitic manifestations when infected by the intraspinal route only. Of even greater interest is the fact that practically all of the rabbits which exhibited systemic infections developed testicular lesions.

Thus, rabbit No. 781 which received spirochetes intraspinally on 10-8-25 exhibited a medium node in the left testicle 53 days after the inoculation. The dark field examination of the testicular tissue showed a large number of very active spirochetes. Rabbit No. 1069, inoculated intraspinally showed a small node in the right testicle 120 days after inoculation. The left testicle exhibited a very hard medium sized node. This was observed 166 days after the intraspinal infection. The right testicle on examination in the dark field showed numerous very active spirochetes. It is interesting to note that in these animals the lesions disappeared from both testicles 187 days after intraspinal inoculation. Rabbit No. 1070, infected by the intraspinal route, showed a small scrotal chancre on the right side 47 days later, 11-15-26. The scrotum then became normal and remained so for nine weeks. On 1-24-27, 117 days after intraspinal inoculation, a small node appeared. On the scrotum of the left testicle a small chancre was evident. Examination of the scrotal tissue in this case again showed numerous very motile spirochetes. All the lesions disappeared on 3-28-27, 80 days after intraspinal infection. Rabbit No. 1068 was inoculated on 9-29-26. A small node was observed in the right testicle on 3-14-27, 166 days after intraspinal inoculation. On 4-4-27, 187 days later, a large superficial chancre appeared on the scrotum of the right testicle. The left testicle showed a small node. Examination of the testicular tissue showed the presence of very numerous and active spirochetes. In this animal, 187 days after intraspinal inoculation, we also observed an ulcer about the size of a ten cent piece in the middle of the ventral part of the tail, and a small, very hard, pea-sized node on the right leg. Both contained numerous motile spirochetes.

From the above it is safe to conclude that the introduction of spirochetes into the cerebrospinal system through the fourth ventricle produces a syphilitic infection in a majority of cases in the rabbit. The presence of spirochetes cannot be proved by a mere dark field examination of the spinal fluid. It cannot always be confirmed by inoculation of the supposedly infected spinal fluid into the testicles of healthy rabbits, a procedure usually employed for such investigations. The best method is to observe the animals after the intraspinal inoculation of spirochetes over a long period of time. In our opinion this period should last from six to eight months. The animals should be examined very carefully because the lesions may be small and therefore overlooked. All lesions and even the tiniest node should be viewed under the dark field for spirochetes. The findings are usually positive. It is significant to

note that in the majority of cases the intraspinal inoculation of rabbits results in the development of testicular lesions. The investigations of others, especially Brown and Pearce,[4] indicate that the spirochetes migrate from the site of the testicular inoculation into the intraspinal canal and generally to the cerebrospinal system. Our experiments, however, definitely establish the fact that they travel from the cerebrospinal system to the superficial tissues, particularly the testicles.

[1] Uhlenhut, P., *Med. Klinik*, 1922, xviii, 1210, 1246.

[2] Noguchi, H., *Berl. Klin. Wchnschr.*, 1913, xli, 1884; Bartarelli, E., *Zntrlbl. f. Bakt. and Parasitenk*, 1907, xliii, 238.

[3] Plaut, F., and Mulzer, P., *Muench. med. Wchnschr.*, 1922, lxix, 1779.

[4] Brown, W., and Pearce, L., *Arch of Derm. and Syph.*, 1920, ii, 635.

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## The Antirachitic Activity of Monochromatic and Regional Ultraviolet Radiations.

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In a communication published some years ago it was shown that ultra-violet rays longer than about 324$\mu\mu$ exert no antirachitic potency, and that waves 302$\mu\mu$ are of great value in this respect.[1] Somewhat later we suggested, as the results of experiments with selective filters, "that the intense line of the mercury vapor spectrum 302$\mu\mu$ in length conferred definite protection and that the 313$\mu\mu$ waves exerted probably a feeble action in this respect."[2] The question as to whether antirachitic potency ceases at the 313$\mu\mu$ or the 302$\mu\mu$ level is of both theoretical and clinical importance, as the shorter rays are present to but a small extent and in low intensity in the solar radiations which reach the surface of the earth. This is especially the case where the rays are intercepted by moisture or smoke. It, therefore, seemed worth while to make a more minute dissection of the spectrum in this region. This has been accomplished by means of the isolation of these two lines of the mercury vapor spectrum and testing their power to activate cholesterol. The radiations were of equal intensity, and the same amounts (2.5 mg. per capita daily) of the irradiated cholesterol were fed to