

It was found that morphin, in both large and small doses, impaired the memory and the behavior of the rats. In the case of only one of the animals was there an excitation or stimulation noted after small doses of the drug. After large doses of morphin, the impairment was long-lasting, continuing for several days. In most cases, however, the animals eventually completely recovered from the effects of the narcotic.

In regard to the comparative effects of morphin alone and morphin given in combination in the form of pantopon or narcophin, the following interesting observations were made: Out of 26 experiments with pantopon and morphin, in 22 the effects of morphin were found to be more depressant than those of pantopon.

Out of 9 experiments with morphin and narcophin on the same animals, 7 experiments showed that morphin was more depressant than narcophin. In all the experiments with the opium alkaloids, the effects were noted on both the time in which the rats went through the maze and the total distance traversed or the number of errors made.

Codein, in 9 experiments out of 11, produced impairment, as indicated by both the time and the distance. Narcotin, in 5 experiments out of 7, produced also a depression. Narcein, out of a total number of 10 experiments, produced a slight depression in 4, and no effect in 6. Thebain indicated a slight retardation in 10 experiments out of 11. In the case of papaverin, it was found that very little effect was produced by small doses of the drug, but that after large doses (10 or 15 mgs.), a depression was noted. The complete data of this research will appear in due time in the *Journal of Pharmacology and Experimental Therapeutics*.

88 (1548)

On the generalization of *Treponema pallidum* in the rabbit following local inoculation.

By **LOUISE PEARCE** and **WADE H. BROWN**.

[From the Laboratories of the Rockefeller Institute for Medical Research, New York.]

That a widespread dissemination of *Treponema pallidum* may be produced in the rabbit by local inoculation has been shown

by the recovery of the organisms in isolated instances from the blood, lymphnodes or other organs as well as by the occasional occurrence of generalized lesions in infected animals. However, there is no evidence to show either the time or frequency with which this dissemination occurs or whether the organisms thus distributed over the body are capable of sustaining the infection in these animals.

With these questions in mind, a series of experiments was undertaken, the object of which was to determine the frequency of invasion of the regional lymphatics and the general circulation following inoculation in the scrotum or testicles and how soon a self-sustaining generalized infection might be established.

Time and Frequency of Invasion of Regional Lymphatics.—An examination was made of the inguinal lymphnodes in a series of 29 rabbits which had been inoculated by the introduction of a bit of infected tissue beneath the skin of the scrotum. The nodes were excised under ether anesthesia at intervals of from 61 days down to 48 hours after inoculation and the presence or absence of *Treponema pallidum* determined by dark field examination or by animal inoculation.

The first group of nodes studied included those showing well marked enlargement and induration and these gave positive results in all cases. Nodes were then taken 5 days after inoculation and after the lapse of only 48 hours. Positive results were again obtained in all cases.

Invasion of the Blood Stream.—A similar series of experiments was carried out to determine the time and frequency of blood stream invasion and something of the character of the blood stream infection with relation to processes of reaction in the primary lesions. With a few exceptions, the animals used for these experiments were inoculated in the testicles. The mode of determining the presence of *Treponema pallidum* in the blood of infected animals was by bleeding from the heart, defibrinating and injecting 0.5 c.c. of blood into each testicle of 2 normal rabbits.

A total of 81 bleedings was made on a series of 37 rabbits at intervals of from 7 to 99 days after inoculation. The earlier bleedings were all spaced with reference to some phase of the testicular infection and from these it was found that organisms

could be recovered from the circulating blood from the time an infection could first be detected clinically (12 to 14 days) until regression of the primary lesions took place. The number or the virulence of the organisms as indicated by the incubation period and the constancy of infection in subinoculated animals varied, however, according to the stage of development and the state of the reaction in the primary lesions.

A small series of animals was then bled arbitrarily one week after inoculation and it was found that even as early as this, the number of organisms in the circulating blood was sufficiently great for each 0.5 c.c. of blood to constitute an infecting dose. In view of these facts, there seemed to be no immediate object in further reducing the time limits.

The Establishment of a (True) Generalized Infection.—When it had been shown that *Treponema pallidum* appeared to be widely distributed through the body within a very short time after inoculation, it was considered necessary to determine whether a true generalized infection had been established in these animals or whether the organisms proved viable only because they were transferred to such a favorable medium as the testicles of normal rabbits. For this purpose, 10 rabbits were inoculated in the right scrotum only (using implants), and 48 hours later, the entire right scrotum and testicle were amputated under ether anesthesia. In spite of the complete removal of a wide zone surrounding the area of inoculation, 9 of the 10 rabbits showed well-marked infections by the end of the seventh week and the tenth developed lesions at the end of 2½ months after inoculation.

Conclusions.—These experiments show that following a local inoculation of well adapted strains of *Treponema pallidum*, there is an immediate invasion of the tissues of the animal and that within a very short time, organisms may be recovered from both the regional lymphatics and the circulating blood. They also show that the blood stream infection tends to pursue a course parallel with that of the primary lesions. Finally it was shown that within 48 hours or less, a true generalized infection had been established which was capable of maintaining the infection in the animal independent of that at the site of inoculation.