# INOCULATION OF MONKEYS WITH HUMAN LEPROSY MATERIAL*

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The account of animal experimentation by Cochrane, Menon, and Pandit described the investigations to September 1940. This article further summarizes the work to date.

Table I gives a summary of the experimental work undertaken on a total of 38 animals. It is unnecessary to give minute details on these experiments, and therefore only the most important results will be summarized briefly. In the previous article the development of a high power of resistance to infection with *M. leprae* by monkeys has been indicated, and the experiments which endeavored to produce leprosy by blockage of the reticulo-endothelial system by injection of a 5 per cent suspension of solid India ink were referred to. The interesting observation was made that while no infection resulted in those animals which received the India ink, the lepromin reaction in 2 of the 3 animals failed to become positive after inoculation, and in the third animal, number 14, it showed only a slight positive and then became negative.

Since this experiment our clinical investigations have suggested that leprosy might be possible of development only when the reticulo-endothelial system is intact and that it seems probable that *M. leprae* cannot parasitize the reticulo-endothelial system unless it multiplies in the corium of the skin. If this hypothesis be correct, then the endeavor to block the reticulo-endothelial system with India ink would not result in the development of progressive leprosy.

From this study and the previous work it seemed that a positive lepromin reaction could be obtained in an animal only after a primary focus had been established (in this case an intra-abdominal nodule), and without such a focus it was impossible to elicit a positive response in spite of daily intradermal injections of lepromin (See Table I).

Work was then carried on in an endeavor to enhance the lepromin reaction, first by intra-abdominal inoculation and then by

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* Before publication of the previous article, it was returned to Dr. Cochrane, February 1946, for approval. This further note brings the results of this animal experimentation up to date.

Fig. 1

Fig. 2

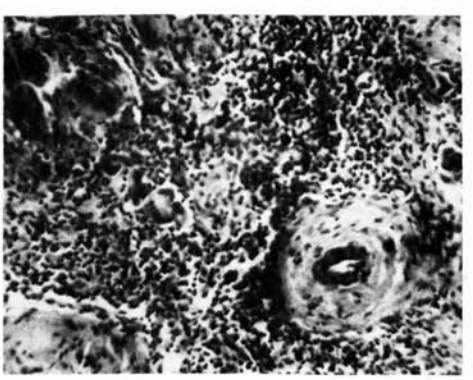

Fig. 3

FIG. 1. Lesion on forehead of monkey. This infiltrated erythematous lesion appeared 10 months after second inoculation and persisted while intradermal lepromin was injected elsewhere.

FIG. 2. Enhancement of lepromin reaction showing hemorrhagic lesions on abdomen (monkey 21).

FIG. 3. Photomicrograph (x 200) of lesion on forehead of monkey 21 showing intense round cell infiltration and in one area giant cells and epitheloid cells suggestive of a tuberculoid lesion.

daily injections of lepromin. While several monkeys were injected daily for varying periods of time with lepromin intra-abdominally (See Table II), only monkey 21 presented features of exceptional interest. Monkeys 31 and 34 were not inoculated, and the lepromin reaction remained consistently negative. Monkeys 37 and 38 died. Monkeys which were inoculated and injected daily with lepromin all developed a positive reaction; in monkeys 21 and 30 this reaction became enhanced. This was especially marked in monkey 21, and a more detailed history is herewith given. Number 21, a Rhesus monkey, was splenectomized on November 25, 1940, and infected in the usual fashion. For a short while it was given a Vitamin C free diet, but as monkeys 18 and 20 died on such a diet the usual diet was restored in this animal. This monkey was reinfected on December 1, 1941, and again on March 20, 1943. Between October 5, 1942, and February 2, 1945, erythematous lesions appeared between the eyebrows, and erythematous patches were seen extending from the inside of the thigh down the leg (Figures 1 and 2). These patches, especially the one on the forehead, were much more prominent when daily injections of lepromin were continued. The patches on the inside of the thigh were not investigated by biopsy because the area was in the vicinity where intradermal lepromin had been injected. The forehead, however, had received no intradermal injections and therefore was of particular interest. On December 17, 1942, the lesion on the forehead was biopsied and revealed round cell infiltrations with giant cell formation in one field (Figure 3). The biopsy of the lepromin nodules on February 2, 1945, also showed giant-cell formation, but this was considered of little significance as such a reaction is known to occur in positive lepromin lesions in man.

## DISCUSSION

While animal inoculation has been pursued for 6 years, we feel, since we were unable to conduct these experiments systematically because of lack of time, that definite conclusions can hardly be drawn. First, if it be correct that it is impossible to produce a positive lepromin reaction without a previous inoculation, then it may be legitimate to conclude that a lesion of tuberculoid leprosy can appear only as a result of a primary focus and that even a single lesion may indicate not the site of a primary injection but that the individual has been previously infected with *M. leprae*. Further, our histopathological studies indicate that active tissue defense can be developed only in the corium of the skin, and in tuberculoid leprosy we believe that the formation of epitheloid foci results in anchoring the bacilli and prevents their dissemination throughout

the reticulo-endothelial system. Lepromatous leprosy on the other hand is a manifestation of an effective tissue defense resulting in widespread dissemination and multiplication of the bacilli. It is tempting, therefore, to conclude that in monkey 21 we succeeded in producing what would be analogous to a tuberculoid lesion in man and the reason that we were unable to get progressive disease is that active tissue immunity developed. Further work will be continued in the endeavor to break down tissue defense, for we believe that success will be attained only if this tissue defense reaction can be abolished allowing free multiplication of the bacilli in the corium of the skin. While we cannot claim to have produced progressive disease in a monkey we feel that further light has been thrown on the pathology of the disease and new avenues of investigation opened.