THE FAILURE OF DIPHTHERIA TOXOID TO INFLUENCE THE COURSE OF EXPERIMENTAL MURINE LEPROSY*

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In 1940, Collier and McKean (1) reported that patients with leprosy improved following the administration of diphtheria antitoxin and toxoid. Later reports by these authors (2, 3, 4, 5), describing further success with diphtheria toxoid, attracted considerable attention among leprologists throughout the world. The last of these reports (5) is more conservative and points out that the method of treatment is less effective than first reported. The evaluation of any type of therapy in a chronic disease like leprosy is obviously difficult and requires many years of observation. Because murine and human leprosy have many similarities, but the murine disease runs a much shorter course, a study was undertaken to determine whether diphtheria toxoid had a beneficial effect on the infection in rats.

MATERIALS AND METHODS

Two strains of murine leprosy were used in the present experiments. One was received in rats from the laboratory of Dr. A. W. Sellards of the Harvard Medical School, the other strain was sent to us in mice by Dr. C. Krakower of the School of Tropical Medicine at San Juan, P. R. This strain was originally isolated from a wild mouse by Krakower and Gonzales (6). We have been unable to observe any differences in the disease caused by the two strains, both of which have been carried through several serial passages in white rats.

The method of serial transfer was as follows: one gram of lepromatous tissue from a subcutaneous nodule was minced with scissors and ground in a sterile mortar with 5 ml. of an 0.85 per cent NaCl solution. Before inoculation, films were prepared and examined microscopically to ascertain the presence of large numbers of acid-fast bacilli. Then, 0.2 ml. of the inoculum was injected into young white rats weighing from 150 to 200 gm. in the region of the right precrural lymph node. In most instances, nodules developed at the point of inoculation within 2 or 3 months. As the lesions progressed the animals gradually became emaciated. Subsequently, extensive ulceration developed over the lepromatous masses and

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along the adjacent abdominal wall. Death usually occurred about one year after inoculation.

The diphtheria toxoid used in the present experiments was prepared in the Division of Laboratories and Research of the New York State Department of Health, Albany, New York.

Experimental

Twenty-nine rats were used. Seventeen were infected with the "Puerto Rican" strain, and 12 with the "Harvard" strain. Six of each group were untreated and served as controls. Six rats inoculated with each strain of leprosy were treated with diphtheria toxoid as follows: 0.2 ml. of toxoid was injected at weekly intervals for 3 weeks beginning a week after inoculation of the infectious material. Six months later, when it became evident that the toxoid therapy had been ineffective, treatment was resumed and injections of 0.5 ml. of toxoid were given weekly until it was evident that the animals were moribund. The remaining 5 rats infected with the "Puerto Rican" strain received no treatment until 4 months after inoculation, at which time they showed advanced lesions of the disease. An injection of 0.2 ml. of toxoid was given weekly for 3 weeks. Seven months later another series of treatment was given consisting of one injection of 0.5 ml. of toxoid each week for two months.

Results

The subcutaneous injection of diphtheria toxoid failed to influence the character of the lesions, the course of the disease, or the length of time the animals survived after inoculation. The 6 rats inoculated with the "Puerto Rican" strain, in which group treatment was initiated within a week after inoculation, survived for a total period of 58 months; whereas, the controls lived for a total of 61 months. The 5 rats treated with diphtheria toxoid late in the disease survived a total of 52 months. Death followed inoculation by from 7 to 12 months.

Of the rats inoculated with the "'Harvard" strain, the treated group survived for a total of 40 months, while the controls survived for a total of 43 months. In the case of the treated group, death occurred between 3 and 11 months after inoculation, whereas in the controls it occurred between 7 and 9 months (Table 1).

TABLE I. *Results of the treatment of murine leprosy with diphtheria toxoid.*

Strain	Rats treated with diphtheria toxoid			Rats untreated		
	No.	Total no. months of survival after inoculation	Av. no. months of survival after inoculation	No.	Total no. months of survival after inoculation	Av. no. months of survival after inoculation
"Puerto Rican"	6 5*	58 52	9.6 10.4	6	61	10.1
"Harvard"	6	40	6.6	6	43	7.1

* No toxoid administered until 4 months after inoculation.

SUMMARY

The subcutaneous injection of diphtheria toxoid failed to produce a beneficial effect on the course of murine leprosy in white rats. This was true whether the toxoid was injected early or late in the course of the disease.

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