EFFECT OF BCG VACCINATION UPON THE EVOLUTIVE RATE OF MURINE LEPROSY

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The reported results concerning the influence of BCG vaccination on the evolutive rate of experimental murine leprosy are in disagreement. Certain reports, by Valtis and Markianos ([12]), Azulay ([1, 2]), Kawaguchi ([10]), and Hanks and Fernandez ([9]), suggest slower development of the disease when rats previously vaccinated with BCG were afterwards inoculated with *M. leprae murium*. Such an effect of BCG would indicate a partial inhibition of the evolution of the leprous lesions and a lesser degree of dissemination of the bacillus ([1, 2, 10]). Both effects would probably be correlated with the development of some degree of resistance.

On the other hand, reports by Muir and Henderson ([11]) and by Hadler and Ziti ([4]) showed that previous vaccination with BCG does not produce any alteration of the development of the disease or of the histologic structure of the murine leprosy lesions. They suggest, on the contrary, that BCG vaccination is not effective in modifying the evolutive rate of murine leprosy.

The present paper results from an attempt to investigate this matter.

MATERIAL AND METHODS

Wistar rats of both sexes, weighing 85-90 gm. at the beginning of the experiment, received 20 mgm. of fresh BCG as specified below:

(1) 30 animals injected intramuscularly;

(2) 30 animals injected intraperitoneally;

(3) 30 animals given BCG orally, by means of a stomach tube;

(4) 30 untreated animals as controls.

Thirty days after the BCG vaccination the animals of all groups were inoculated intraperitoneally with 0.5 cc. of a suspension containing approximately 5.3 mgm. of *M. leprae murium*.

The evolution of the disease was studied in the four groups, on the basis of the mean survival times of the animals and the pathologic aspects of the lesions. The survival time for each group was determined with reference to 20 animals; the mean of survival, and the regression of the number of living animals in time were calculated. The differences among the means of survival in the 4 groups were statistically analyzed (analysis of variance).

The other 10 animals of each group were killed at intervals of 30 or 60 days, providing material for the pathologic study of the leprous lesions. Besides the macroscopic

examination, pieces of liver, spleen, omentum, lymph nodes and lungs were fixed in 10 per cent formalin, and paraffin sections were stained by the hematoxylin-eosin and the Ziehl-Neelsen methods.

RESULTS

Table 1 shows the means of the survival times and the coefficient of regression of the number of living animals on time, for the four experimental groups. Table 2 indicates the results of the analysis of variance concerning the means of the survival times.

TABLE 1.—*Means of survival and coefficients of regression of the survival on time, in the four experimental groups.*

Mode of administration of BCG	Mean of survival (days)	Coefficient of regression of survival on time
Intramuscular	255.9	—0.04244
Intraperitoneal	282.2	—0.03954
Oral	215.7	—0.11204
Controls	241.8	—0.06805

TABLE 2.—*Analysis of variance of the survival means of the four experimental groups.*

Source of variation	d. f.	S sq	m. s. q.	F
Treatments	3	125.657	41.886	2.71 N. S.
Error	76	1.176.345	15.478	
Total	79	1.302.002		

The results indicate that BCG, under the conditions of the experiment, is ineffective in modifying the evolutive rate of murine leprosy.

The means of the survival times of the animals previously vaccinated with BCG, by the routes used, do not differ significantly from that of the unvaccinated control rats, when the same dose of *M. leprae murium* is inoculated intraperitoneally.

The development and evolution of the lesions, and their histologic structure, observed throughout the experiment, did not indicate any difference between the animals previously vaccinated with BCG and the unvaccinated controls.

DISCUSSION

In previous work ([7]) we have shown, on the basis of the survival times of rats inoculated intraperitoneally with *M. leprae murium*, that there exists an intimate correlation between the evolutive rate of the disease and the dose of bacilli used ([7]).

On the other hand, eventual influences on the evolutive rate of murine leprosy can be easily investigated with the aid of the mean of survival of treated animal groups, compared with untreated ones taken as control. This method has proved to be entirely suitable for testing the antileprosy activity of drugs ([6]). In such a way the eventual

influence of BCG vaccination on the evolutive rate of murine leprosy can be estimated.

As shown by the results obtained, BCG vaccination does not modify either the survival time or the structure of the lesions of rats inoculated with approximately 5.3 mgm. of the *M. leprae murium* bacillus. This is in agreement with a previous report by Hadler and Ziti ([4]), in which the results concerned animals inoculated with a small dose of bacilli. These results demonstrate the ineffectiveness of BCG either in modifying the evolutive rate of rat leprosy lesions, or in altering the behavior of the inflammatory macrophage of the normal rat ([5]). Under such experimental conditions, however, information on the evolutive rate of murine leprosy could not be obtained. The dose of mycobacteria used in the present experiment provides such information.

Vaccination of hamsters with dead BCG increases the evolutive rate of the disease produced by the inoculation of *M. leprae murium*, by decreasing the length of the early period of the disease ([8]). In this period the unvaccinated animals show evidences suggesting some degree of resistance against the infection, as far as the tissue reaction is concerned, which is inhibited by BCG vaccination.

SUMMARY

The influence of BCG vaccination on the evolution of murine leprosy was investigated on the basis of the animal survival and the histologic structure of the lesions observed in rats inoculated intraperitoneally with approximately 5.3 mgm. of *M. leprae murium*.

The BCG vaccination, with 20 mgm. of the bacilli, was carried out by intramuscular and intraperitoneal injection and by oral administration.

Statistical analysis of the survival of treated and control animals shows that BCG vaccination is ineffective in modifying the evolutive rate of murine leprosy; nor does the histologic structure of the leprous lesions show any effect achieved by vaccination.

RESUMEN

Los autores investigaron la influencia de la vacunación por el BCG sobre la evolución de la lepra murina, basándose en la curva de supervivencia y en la estructura de las lesiones encontrades en ratones "Wistar" inoculados con aproximadamente 5,3 mgr. de *M. leprae murium* por via intraperitoneal.

La vacunación con BCG se hizo con 20 mgr. de bacilos por las siguientes vias: intramuscular, intraperitoneal y oral.

El estudio estadistico de la vacunación con BCG no modifica la evolución de la lepra murina. La observación histológica reveló que la vacunación no produce alteración de la estructura de las lesiones leprosas.

RESUMÉ

L'influence de la vaccination par le B.C.G. sur l'évolution de la lèpre murine a été étudiée d'après le temps de survie et la structure histologique des lésions, chez des rats inoculés par voie intra-péritonéale avec environ 5.3 mg de *M. leprae murium*.

La vaccination par le B.C.G., comportant l'administration de 20 mg de bacilles, a été effectuée par injection intramusculaire, par injection intra-péritonéale, et par voie buccale.

L'analyse statistique du temps de survie chez les animaux traités et chez les animaux témoins a montré que la vaccination par le B.C.G. n'est pas capable de modifier le cours de l'évolution de la lèpre murine. De même, la structure histologique des lésions de lèpre ne témoigne pas en faveur d'une action quelconque de la vaccination par le B.C.G.

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