

Research on Spirochaetal Strains isolated in Jordan

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While one of us was carrying out a survey of relapsing fever in Jordan, a number of spirochaetal strains were isolated from the blood of patients and from *Ornithodoros tholozani* ticks.^a We subsequently decided to use these strains, which, in accordance with our ideas on nomenclature, we classified as *Treponema persicum*,^b in a series of laboratory studies designed to clarify certain aspects of relapsing fever.

The first task we set ourselves was to determine whether the recrudescence of the febrile state and the reappearance of spirochaetes in the blood-stream after apparent clinical recovery were due to relapse or to reinfection. In the former case, it might be assumed that spirochaetes linger in the brain or other organs and that some aspecific cause fosters their development and subsequent invasion of the blood-stream. If, on the other hand, reinfection does indeed occur, then it would seem that infection with one strain of *T. persicum* does not confer immunity to other strains present in the area where the patient is living.

From the results of a series of experiments with mice, we were able to establish that spirochaetes persist in the brain of mice for as long as 50 days or more after their disappearance from the blood-stream. However, the survival rate is not constant, and individual animals show variations in response.^c If these results in mice are applicable to man, one might well assume that the spells of fever which occur some time after the original onset of the disease are authentic relapses.

Since this finding did not necessarily invalidate the second hypothesis—that of reinfection—we decided to carry out a series of cross immunity tests using various strains of *T. persicum*. For this purpose we selected the Nablus strain (isolated from the blood of a patient); the Husn, Irbid and Saham strains (isolated from *O. tholozani* ticks captured in the area); and the Itete strain of *T. duttoni* (isolated by R. Geigy in Central Africa and made available to us in *O. moubata* specimens).

Batches of mice were inoculated, each with a different strain. Twenty to forty days after the outbreak of infection, the precise date of which was determined by daily blood examinations, we subcutaneously inoculated all the mice with 500 mg of chloramphenicol succinate per kg of body-weight

^a Babudieri, B. (1957) *Bull. Wild Hlth Org.*, 16, 911

^b Babudieri, B. (1953) *Proposta di una nuova sistematica dell'Ordine delle Spirochaetales*. In: *Atti del VI Congresso Internazionale di Microbiologia, Roma, 6-12 Settembre 1953*, Rome, 5 (Sez. XIII), p. 46

^c Our thanks are due to Dr G. Marchis, of the Health Laboratory, Amman (Jordan), who co-operated in these investigations.

in order to rid them completely of the invading spirochaetes. Every batch of mice was then subdivided into five lots, each containing at least seven specimens. One of the lots was reinoculated with the homologous strain and the others with the heterologous strains. The mice were observed for a minimum period of 10 days, and daily microscopical examinations were made of their blood. It was observed that in the large majority of cases infection broke out only among those mice which had been reinoculated with heterologous strains. These results would seem to prove that recovery from the infection leaves the subject immune to reinfection from a homologous strain, but liable to succumb to reinfection from heterologous strains, even though these latter may be of local origin.

In cross immunity tests between the Irbid and Husn strains, we noted an example of "asymmetric immunity"—a phenomenon already observed by Geigy in experiments with *T. duttoni* strains.^d It was found that the mice which recovered from infection with the Irbid strain were protected against reinfection with the Husn strain, whereas those originally inoculated with the Husn strain succumbed to infection with the Irbid strain.

The results of these laboratory experiments are confirmed by the disease picture to be observed in areas where *T. persicum* infections are endemic. For example, it seems that the nomadic Bedouins, being exposed to a greater variety of strains, are more susceptible to reinfection than are the more stable tribes, who remain in one locality for a lengthy period.

Even if treatment succeeds in completely freeing the organism from the invading spirochaetes, it must be remembered that the patient will still be virtually unprotected from new infections. For this reason, tick-control must play an important part in the campaign to combat relapsing fever.

In an effort to find a suitable remedy for the disease, we decided to try out the following drugs on mice experimentally infected with the Irbid and Nablus strains of *T. persicum*: an arsenobenzene (Neojacol of the Istituto Sieroterapico Milanese); penicillin (G. K. Squibb); streptomycin (Lepetit's Anastropto); chlortetracycline (Lederle's Aureomycin); oxytetracycline hydrochloride (Pfizer's Terramycin); tetracycline hydrochloride (Lederle's Acromycin); and chloramphenicol (Erba's Chemicetina succinato). Batches of mice, each consisting of at least 5 specimens, were injected subcutaneously with mouse-blood containing spirochaetes. As soon as spirochaetemia became evident—generally on the 3rd or 4th day—the drugs, dissolved either in saline or in distilled water, were inoculated subcutaneously in amounts varying according to medicament. In assessing the efficacy of each drug, two criteria were borne in mind: (a) the capacity for speedy elimination of spirochaetes from the blood-stream; and (b) efficacy in preventing relapses.

To test these two effects, the blood was examined on three successive occasions—namely, 3 hours, 24 hours and 7 days after administration of the drug. If no spirochaetes were revealed during the last examination, the mouse was sacrificed. Its brain was ground, suspended in saline, and inoculated into another mouse. The blood of the latter animal was then

^d Geigy, R. (1951) In: *Atti del 3° Congresso di Igiene e Medicina Mediterranea, 14-15-16 maggio 1951, Palermo*, p. 93

examined for 10 days running. Only if the last of these tests gave negative results did we consider the drug to be effective in preventing relapses.

As far as therapeutic action was concerned, penicillin, administered in regular doses, proved to be more satisfactory than either streptomycin or arsenobenzene; over the long term, however, all three drugs were discovered to be almost powerless to prevent relapses. Chloramphenicol had an immediate and complete therapeutic effect, but its spirochaetal action was insufficient to prevent relapses. In the tetracycline group, the effect of Acromycin on infections produced by the two strains of *T. persicum* was very different; its use does not therefore guarantee recovery in every case. On the other hand, Aureomycin and Terramycin gave first-class results in both respects, and, despite their high cost, may be considered as the drugs *par excellence* for Jordanian tick-borne relapsing fever.

Leprosy and Yaws: Points of Contact *

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Although the causative agents of yaws and leprosy are entirely distinct, the two diseases have a number of points of contact as regards clinical appearances, epidemiology, and control. These similarities are interesting and may occasionally be of importance. The matter has received very little notice in the past, but has recently forced itself upon the attention of workers in Eastern Nigeria, where during the past 20 years massive yaws infection in a dense rural population has been accompanied by an outbreak of leprosy of unusual magnitude. Since the two diseases have flourished side by side, there have been unusual opportunities for observing similarities both in their epidemiology and, what is more important, in their clinical appearances. In an investigation of control methods, lessons have been learned which are of common importance to workers in the prevention of both diseases.

Usually the differential diagnosis of yaws and leprosy presents little difficulty. The typical case of either disease is not likely to be confused with that of the other, and even with only simple laboratory facilities mistakes should not be made. The two diseases may, however, be present in the same patient, and in the course of survey work, especially where yaws treatment has been inadequate and leprosy is common, a variety of skin manifestations may be encountered in which the one disease can simulate the other very closely. Such lesions are usually localized and are often atypical.

* The author wishes to acknowledge the assistance given by Mr S. E. Drewett, Senior Laboratory Superintendent, in the preparation of clinical photographs, and to thank the Director of Medical Services, Eastern Region, Nigeria, for permission to publish this paper.