## REVIEWS

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The original articles are as follows:

N. Souza Campos and P. R. de Souza write on "Reactional States in Leprosy." They apply the term "lepra reaction" to only "erythema nodosum leprosum" which occurs in lepromatous leprosy. They distinguish between (a) tuberculoid reactivation (tuberculoid lepra reaction), (b) reactional tuberculoid leprosy, which they hold to be a distinct variety, and (c) the *limitantes* or "border line" condition. The clinical and histological features of these conditions are described and illustrated. (The reviewer did not find it easy to understand this paper.)

R. S. Ginto, J. A. Doull and Laurentino De Guia write on "The Mortality of Persons with Leprosy prior to Sulphone Therapy," based on accurate studies carried on in the Cordova, Talisay, Cebu Provinces, Philippines, from 1933 till 1951. Sulphone treatment was not used at all commonly until 1951; most of the patients had been treated for some years with hydnocarpus injections. Standardised death rates are combined for the total population and for persons suffering from (a) lepromatous and (b) non-lepromatous leprosy. The mortality in lepromatous patients was five times that of the general population; in non-lepromatous leprosy the mortality rate was little higher than in the general population.

In the period 1941-48, covering the Japanese occupation, the mortality in the general population rose by 64.5 per cent, but in the leprosy patients it was less, probably because many returned

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to the leprosarium and were thus safeguarded from malaria, malnutrition and other hazards.

The study should give valuable data for comparison with similar data collected during the post-sulphone era from 1951 onwards.

J. L. Buyers and R. R. Wolcott write on "M. leprae in skin and nasal scrapings during Sulphone Treatment." 146 cases were studied. They found that within one year, the nasal scrapings became negative in 50 per cent and in 5-10 years over 90 per cent. The skin scrapings became negative in less than 10 per cent of patients treated from one to ten years. The nasal scrapings were studied because, from the public health point of view, the nasal mucosa may be more important than the skin which is usually free from ulcers.

Montestruc et al. write on "Child Leprosy in Martinique." They record a high incidence in children, and a high proportion of lepromatous cases in children. The difficulty in tracing the source of infection, frequently extrafamilial, is discussed. The limitations of chaulmoogra treatment are emphasised; it has been abandoned. Sulphones are now in general use. It is proposed that all newborn babies and all anergic leprosy contacts shall be compulsorily vaccinated with BCG, and compulsory hospitalisation of all lepromatous children is recommended.

- J. H. Hale, B. D. Molesworth, D. A. Russell and L. H. Lee write on "Isonicotinic Hydrazide in the Treatment of Leprosy." Their own summary is as follows:
- A trial on isonicotinic hydrazide treatment of leprosy in Malaya is reported.
- 2. Only 26 patients out of a total of 83 showed any improvement at the end of an eight-month period.
- 3. Eighteen of the patients showing improvement were from the group classified as atypical. Since spontaneous changes take place frequently in cases of this group, it is difficult to assess the effect of the drug.
- 4. Because only 24 per cent of the whole series became progressively worse under the treatment, we believe that the drug is not without some limited therapeutic effect. It is not, however, comparable in efficiency to the sulfones.
- J. Convit and E. Rassi write on "Lepromin and Tuberculin Tests in Venezuelan Leprosy Foci and the Induction of Lepromin Reactivity by BGC Vaccination." Their own summary is as follows:

The reactions to tuberculin and lepromin were studied in 8,353 inhabitants of leprosy foci in rural areas in Venezuela. Of this general group, a total of 1,356 (16.2 per cent) proved to be negative to the Mitsuda test, while 5,205 (62.5 per cent) were Mantoux-negative. In the group of Mitsuda-positive persons 44.8 per cent were also Mantoux-positive, while in the Mitsuda-negative group on 3 per cent were Mantoux-positive.

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In the Mantoux-positive group 99.5 per cent were Mitsuda-positive,

while in the Mantoux-negative group 74.4 per cent were Mitsuda-positive.

Considering that 16.2 per cent of the persons examined were found to be without protection against leprosy in the first tests, and taking into account that almost all lepromatous and indeterminate cases come from the lepromin negatives, which form the endemic matrix of the disease, there can be no doubt but that BGC vaccination will be an effective phophylaxis, at least in rural areas, when it can reduce the percentage of Mitsuda negative from 16.2 to 1.3 per cent.

Dharmendra, N. Mukerjee and P. N. Khoshoo write on "A Comparative Study of three Antigens for the Lepromin Test," (a) the Wade modification of the Mitsuda antigen, (b) the original Dharmendra antigen (long extraction with chloroform and long grinding), and (c) modified Dharmendra antigen (I hour's chloroform extraction and short grinding, 5 minutes. Tests with all three antigens were made on 110 patients, some being lepromatous, and tuberculoid and some intermediate. Early (24-48 hours) reactions and late reactions, 2-5 weeks, are recorded. With all three antigens the findings are summarised:

The Wade-Mitsuda antigen produced the highest number of positive late reactions and a fair number of early reactions. The Dharmendra original caused the highest number of positive early reactions, and the lowest number of late reactions. The Dharmendra variant gave results which were intermediate.

In the lepromatous cases both the early and the late reactions were negative with all the antigens. In the maculoanesthetic cases the early reactions was positive in 82 per cent and 56 per cent with the Dharmendra and the Wade antigens, respectively, and the late reaction was positive in 34 per cent and 96 per cent with these antigens. In the tuberculoid

cases the corresponding figures were 95 per cent and 92 per cent for the early reaction, and 74 per cent and 100 per cent for the late one.

In general the early reactions with the Dharmendra antigen and the late reactions with the Wade-Mitsuda antigen were in agreement. There was, however, disagreement in 5 of the 91 cases—4 of the 29 maculoanesthetics and 1 of the 36 tuberculoids.

The Dharmendra variant gave stronger late reactions than the Dharmendra original, but this increase was far below the strength and frequency of the late positive reactions with the Wade Mitsuda antigen. A better way of attempting to remove the disagreement between early reaction with Dharmendra's antigen and late reaction with Wade's antigen may perhaps be to try to increase the potency of the former.

J. Emibl, et al., report failure in an attempt to demonstrate multiplication of Hansen's bacilli in the yolk sac of the duck embryo.

Sister Hilary Ross writes on 'An Evaluation of the Maillard-Gagliardo Complement Fixation Test in Leprosy' in 100 cases. This test uses sheep red cells sensitized with old tuberculin, and, as a complement, reconstituted dried guinea-pig serum. The test is characterised by the hemolytic reaction resulting from the fixation of complement. The summary is as follows:

- 1. The Maillard Gagliardo complement fixation test was performed on sera obtained from 100 cases of leprosy in which a diagnosis of tuberculosis had been excluded.
  - 2. Normal controls showed titers up to 10.

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3. Titers above normal were found in  $_{44}$  (44 per cent) of the roo cases of leprosy.

- 4. Titers above normal were found in 33 (58.9 per cent) of the 56 bacteriologically positive cases of lepromatus leprosy.
- Y. T. Chang reports on studies of Nicotinamide and Pyrazinamide (Aldinamide) on Mouse Leprosy. His own summary is as follows:

A brief review of the pharmacological actions of nicotinamide and allied compounds in relation to the mycobacterial infections has been presented.

The activity of nicotinamide and pyrazinamide (Aldinamide) in mouse leprosy has been studied, employing the intraperitoneal route for infection. Compartive studies of the activities of these compounds with that of the known effective drugs—isoniazid, streptomycin and DDS—were made in animals treated immediately after inoculation or after delays of one or two months. The duration of the experiments was three months.

Both nicotinamide and pyrazinamide were found to be highly effective in the suppression of the leprous infection. Nicotinamide was found to have a degree of activity similar to that of pyrazinamide and of isoniazid, and superior to that of streptomycin; DDS was the least active.

All these five compounds were most effective when the administration was started immediately after the inoculation and continued for three months, proportionately less effective when the treatment was delayed for one or two months. Only nicotinamide, pyrazinamide and isoniazid possessed any significant activity when the treatment was delayed for two months and then carried out for only one month.

The Editor (H. W. Wade) discusses bacteriological improvement in the chemotherapy of leprosy. He mentions the fabulous number of bacilli present in untreated lepromatus lesions, the shrinkage in the size of the lesions produced by treatment, as well as the reduction in the density of the bacilli. He thinks that considering the tremendous number of bacilli that were present at the outset to be disposed of, and considering the resistance of even dead acid-fast bacilli to such deleterious influences as exist in the tissues of normal animals, let alone lepromatus patients, the wonder is that leprosy lesions ever clear up at all. At any rate, we should seriously ask ourselves if the current attitude that the bacilli in the lesions do not decrease as they should under sulfone treatment should not be reconsidered. The situation may be viewed with an attitude less discouraging to the physician and to the patient.

The Editor also discusses certain differences of opinion between research workers about cellular reaction to microbacteria. This discussion is difficult to summarise; the finding of Suter that monocytes cultured from immune guinea-pigs were able to inhibit multiplication of tubercule bacilli, whereas normal monocytes could not, has been challenged and discussed by Mackaness and others.