

REVIEWS

International Journal of Leprosy, Vol. 21, No. 3 (July-Sept. 1953).

Leprosy in Children in French West Africa, by Laviron and Lauret.

The problem of leprosy is a serious one in French West Africa and the disease seems to be on the increase. The total number of children with leprosy is estimated as 30,000. Familial infection is the rule, and it appears that not only are lepromatous cases responsible for the spread, but also tuberculoid and indeterminate cases as well. The majority of cases start between the ages of 5-15. The onset is usually indeterminate, and later one of the polar forms develops. Only 10-15% are lepromatous. Treatment with sulphones combined with chaulmoogra oil is confined to the lepromatous cases. The only practical form of prophylaxis possible is medical inspection of schools with the segregation and treatment of all children with leprosy.

B.C.G. in the Prophylaxis of Leprosy. A preliminary report, by Nelson de Souza Campos.

The writer is convinced that a BCG induced positive lepromin reaction has the same significance as the natural reaction, and that persons who have had no contact with leprosy and show a positive lepromin reaction undoubtedly have had a primary infection with tuberculosis. There may, however, be congenital conditions, intrinsic or constitutional, which render a person positive or permanently negative to lepromin.

In Sao Paolo from Feb.-Dec. 1952, 1,658 contacts were given 3 weekly doses of 200 mgm BCG by mouth while 3,329 contacts had no BCG. Up to Jan. 1953 10 cases of leprosy, all tuberculoid, had appeared amongst the vaccinated (0.6%), whereas amongst the unvaccinated 179 (5.4%) cases of leprosy had occurred—47 lepromatous, 84 undifferentiated, and 48 tuberculoid.

As this is only a preliminary report; the writer agrees that later reports may alter the picture.

The value of the Lepromin reaction in the diagnosis of clinical forms of leprosy, by Salomon Schujman.

The writer holds that whereas the classification of a case of leprosy should be based on combined clinical, bacteriological, histopathological and immunological criteria, yet the last is the most important as the lepromin reaction is the most stable. Other factors change with the progress of the disease but the lepromin, especially the late Mitsuda phenomenon, remains practically fixed throughout. It is of the greatest value in indeterminate cases, where a negative lepromin nearly always indicates that the case will become lepromatous.

Study of the morphological modifications of Mycobacterium leprae during chemotherapy, by M. G. Malfatti and E. D. L. Jonquieres.

Using the electron microscope with direct and shadow casting technique, the writers noted changes in the *M. leprae* after treatment with sulphones, isoniazid and thiacetazone. They found that swelling of the cytoplasm and the granular state are signs of the first modification of morphology, and also the disappearance of the peripheral halo which is apparently dependent upon the normal bacillary metabolism. They believe that modern chemotherapy holds out great hope in the eradication of leprosy.

Staining of M. leprae by the Rio Hortega Silver method in frozen and paraffin sections, by Jose Sanchez.

Rio Hortega's method of double impregnation with silver without reduction is described in detail. Owing to the argentaffinia

of leprosy bacilli, the writer claims that many more bacilli are seen after such staining than by the regular Z.N. or Gram Weigert techniques.

A Review of recent animal inoculation studies with human and murine leprosy bacilli, by T. Tanimura and S. Nishimura.

Ten years of experimentation failed to produce any infection in fowls or other animals with human leprosy bacilli. Repeated attempts to infect fowls with murine bacilli also failed. The human bacillus finds only the human being a favourable host, and the murine bacillus is limited to rats, mice and hamsters. The ocular tissue which has an affinity for many pathogenic organisms could not be made to react differently to the race specificity. All attempts to alter the constitution of animals failed to induce infection with leprosy.

G. O. TEICHMANN.

Modern Concepts of Leprosy by Harry L. Arnold, Jr.

This small book is by a dermatologist with a wide experience of leprosy. Written primarily for doctors who are not familiar with the disease, it will nevertheless prove useful to workers in leprosy institutions. Because of its primary purpose, the greater part of the book is devoted to diagnosis and pathology, and only two very short chapters to treatment and prevention. He urges the great importance of certainty in diagnosis owing to the serious social implications involved, and lays down the minimal diagnostic criteria required:—(1) Either the presence of acid-fast bacilli morphologically consistent with *M. leprae* obtained by Wade's scraped incision method from lesions, and not obtained only from nasal scrapings, ulcers, or skin surfaces where other acid-fast bacilli are commonly found; or (2) evidence of nerve damage which cannot be attributed to trauma or non-leprous peripheral neuritis. He stresses that in early cases as a rule only one of these criteria, not both, can be satisfied. It is often taught that leprosy attacks either the skin or the nerves, but in both types both are affected in almost all cases.

With regard to epidemiology, very few positive statements can be made, as it is full of curious contradictions and paradoxes. It is generally accepted that leprosy is only mildly contagious and is usually contracted in childhood after prolonged contact with lepromatous cases. However, many cases can remember no known contact with the disease, and numerous instances have occurred in individuals clearly exposed for the first time in adult life. Also, attempts to transmit leprosy by inoculating human volunteers with

fresh presumably infective material have almost uniformly failed. Perhaps the open case of leprosy does not play as vital a role as has been supposed, and casual contact may occasionally suffice to cause infection.

His statement that nodular leprosy is the commonest variety is not the experience of workers in India or Africa where the tuberculoid type greatly predominates.

Dealing with pathology, he says that one can best understand the lepromatous type if one recalls that they are not true inflammatory but rather foreign-body granulomas, in which the *M. leprae* grow and multiply. They represent a passive phagocytic process rather than an active defensive one. In distribution and configuration they clinically resemble lymphoblastomas, as both are composed of reticuloendothelial cells, and they tend to develop in cool areas of the body. For this reason lesions are usually found on the face, ears, outer limb surfaces, and internally in the nose, larynx and testicles.

The histological changes in tuberculoid leprosy are very similar to those in Boeck's sarcoid. Diagnosis should depend not on biopsy but on nerve damage, the lepromin test and the absence of hyperglobinaemia. The last present in sarcoid and the first absent.

He stresses the importance of the positive lepromin test in differentiating tuberculoid cases. Negative reactions should relegate a case to either the intermediate, borderline or lepromatous type.

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International Journal of Leprosy, Vol. 21, No. 4 (Oct.-Dec. 1953).

Original Articles:

Laviron, P. Lauret, L. et Jardin, C. Contribution a l'etude de la chimiotherapie-retard dans la lutte antilepreuse en Afrique Occidentale Francaise.

Wolcott, R. R. and Ross, Sr. Hilary. Exacerbation of leprosy during present day treatment.

Contreras, F., Guillen, J., Ponziani, J. and Terencio, J. Hemoterapia en las leproorreacciones.

Vilanova, X. and Catusus, J. M. La prueba da Nelson-Mayer (Inmovilizacion Treponemica) aplicada al suero do los enfermos de lepra. (Nota previa).

Sagher, F., Liban, E., Zuckerman, A. and Kocsard, E. Specific tissue alteration in leprous skin. V. Preliminary note on specific reactions following the inoculation of living micro-organisms ("isopathic phenomenon").

Traversa, E. L'etat actuel de lutte contre la lepre en Italie.

Bushby, S. R. M. and Barnett, M. Isonazid resistance in murine leprosy.

Lavale Aguilar, P., Iturribarria, F. M. y Middlebrook, G. Un caso de infeccion humana por *Mycobacterium ulcerans* en al hemisferio occidental. Nota previa.

Editorials: Wade, H. W. Report on the Madrid Congress.

News and Notes.

Current Literature.

This is the Madrid Congress number of the Journal. The original articles here printed were all presented at the Madrid Congress; the Editorial consists of the Editor's report on the Congress; the Leprosy News and Notes Section runs to twenty-three pages devoted entirely to an account of the Congress, a list of those attending, and its proceedings, the reports of the various technical committees, and to the minutes of the General Meeting of the International Leprosy Association held in Madrid; the Current Literature section gives the titles, and usually an abstract, of all the papers officially presented at the Madrid Congress; they number 166.

Laviron, Lauret and Jardin's article is summarised as follows:—

In French West Africa, where each medical officer has to cover a very large area, the number of leprosy cases that can be treated is the greater the less frequent the treatments, and efforts have been made to develop a satisfactory deposit (retard) method that calls for injections only once in two weeks. It is shown that when DDS in fine crystalline form is suspended in peanut oil—the dose 1.25 gm in 5 cc.—there is rapid absorption, with correspondingly high blood and urine levels for a few days and only traces in the latter part of the period. When chaulmoogra preparations are used, however, there is a more satisfactory deposit effect, with slower absorption of the drug and prolonged maintenance of a useful blood level. The ethyl esters (with 4% guicol) are rather painful, while chaulmoogra oil itself is too viscid for convenience, so in practice a mixture of equal parts of the two is used. The results obtained have been more satisfactory than with other methods of administering DDS. Too little chaulmoogra is used to regard the treatment as one of therapeutic 'association' or 'synergy,' but it is nevertheless regarded as rational to use it rather than an inert vehicle. It would be possible to combine the deposit sulfone therapy with chaulmoogra treatment. 'thus realizing an effective association of medicaments.' "

Walcott and Ross's article is summarised as follows:—

" Since 1948 exacerbations of leprosy have been observed in hospitalized patients receiving sulfone and other present-day treatments. Case histories and clinical photographs illustrate typical cases of aggravation of lepromatous leprosy. The cause of the exacerbation is not apparent. Erythema nodosum is usually absent before exacerbation. The possibility of clinical and bacteriologic exacerbation must be considered in evaluating the prognosis of patients undergoing present day treatment."

The article by Contreras, Guillen, Ponziani and Terencio is summarised as follows:—

" The authors relate their experience with transfusions of various blood products in the treatment of lepra reaction and certain other conditions, beginning with heterologous plasma (a proprietary calf-plasma

product which gave good results although with frequent untoward reactions), homologous plasma (lyophilized, used on a small scale with no intolerance), autohemotherapy (of limited usefulness), and finally whole blood obtained mostly from blood banks. On the basis of over 400 whole-blood transfusions the results in the various conditions treated are stated in percentages. For example, in severe general lepra reaction some 83% of the cases were cured within three days, and many of them in from 12 to 48 hours. All cases of the erysipelatoid form of reaction cleared up rapidly. On the other hand, in reactions of long duration and moderate severity there was only transitory improvement in 90%. Summaries of several of the more striking cases are given. There were only slight post-transfusion reactions in 20% of the cases, and no severe ones. The procedure is regarded as of great value."

The article by Vilanova and Catusis is summarised as follows:—

"Previous reports of results of the treponema immobilization test on sera from leprosy patients are reviewed, and it is pointed out that they do not permit any conclusion as to whether positive results are obtained more frequently in lepromatous than in tuberculoid cases, the former of which give more nonspecific reactions than the latter with the ordinary tests for syphilis.

Eighteen cases were submitted to various serological tests and the treponema immobilization test, 8 of them lepromatous, 9 tuberculoid, and 1 indeterminate. The data are given in the table (somewhat condensed to conserve space). They had all received considerable treatment, and even those still classed as active were definitely improved. That fact is held to explain why the ordinary serum tests gave positive results in only two cases. In one of them the T.P.I. was definitely positive, while in the other the result was uncertain although the patient was a gypsy who might well have once had syphilis. The results are held to be in favour of the specificity of the test. The study is to be continued."

Sagher, Liban, Zuckerman and Kocsard in previous papers had recorded that in leprosy (lepromatous?) patients, the injection of tuberculin, leishmanin, milk and peptone elicited a histological reaction characteristic of lepromatous leprosy, while in normal persons the histological reaction was non-specific. In the present paper the reaction of leprosy skin to living organisms was studied, B.C.G. living vaccine and *Leishmania tropica* cultures being used. In practically all those injected with B.C.G., and in most of those injected with *Leishmania*, the histological reaction was "lepromatous or prelepromatous." This phenomenon is called the "isopathic phenomenon." Further studies are being made of its possible usefulness "in detecting leprosy in contacts and in determining the effectiveness of chemotherapy."

The article of Traversa is summarised as follows:—

"There were 391 known leprosy cases in Italy at the end of 1952, of which 190 were hospitalized as contagious. The disease exists in coastal regions where there is much maritime traffic and movements of migration. Special attention is given returning emigrants, for early diagnosis. No secondary case has been found in the families of cases discovered early, but there are some in families of such people who had not been diagnosed until late."

"For isolation, there are four special pavilions, connected with dermatological clinics in Bari, Genes, Messina and Cagliari, three of them being enlarged and improved. There is also being built at Pouilles an agricultural colony, on an area of 43 hectares located quite distant from centres of habitation, with a section composed of cottages in which mem-

bers of the same family may live together. Here there may be effected voluntary isolation of patients who are bacteriologically negative and classified as noncontagious.

"It is planned to provide financial aid for both the patients and their families during the period of hospitalization. This measure is expected to aid in the discovery of cases which now avoid detection because of the fear of economic dislocation."

The article of Bushby and Barnett follows on their previous report that isoniazid has a marked effect in suppressing murine leprosy infections. They now find that in mice the suppressive action of INH is only temporary, and that this is due to the development of resistant organisms. The resistance was shown by the fact that isoniazid failed to protect further mice infected with spleen emulsions from the original treated animals. It is considered possible that in human leprosy a similar resistance develops, and that this may explain the poor late results of treatment. A plea is made for the trial of isoniazid in conjunction with known anti-leprosy drugs, and not alone.

The article of Aguilar, Iturribarria and Middlebrook describes a case of infection of a finger with *M. ulcerans* with necrosis. Histopathological examination revealed nothing specific. An acid-fast bacillus corresponding on culture to *M. ulcerans* was isolated. The condition had progressed for two years in spite of treatment. Treatment with DDS, 100 mg. a day for 15 days, and then 200 mg. a day for 8 months. Improvement was slow and steady. Terramycin was necessary to control secondary infection. At the end of eight months, activity of the lesion had almost gone.

The **Reports** of the Technical Committees, as adopted by the plenary session of the Madrid Congress, are reproduced elsewhere in this issue.

Modern Trends in Dermatology (Series 2) Chap. 9 "A Critical appraisal of Modern Trends in Leprosy with particular reference to advances in Immunology, Histopathology and Treatment." By R. G. Cochrane.

This critical appraisal contains some assertions that have not gained universal acceptance at present. The author accepts the results of Khanolkar's work in Bombay in which 20% of healthy contacts of leprosy patients were found to harbour *M. lepræ* in the skin, and states that his concentration method of demonstrating bacilli in so-called closed cases of leprosy has opened up the whole question of the infectivity of these cases, but he considers this should not affect the well-established methods of public health control, as the likelihood of infection is very slight. However, the statement that a positive lepromin reaction indicates that the person is probably harbouring *M. lepræ*, dead or alive, within the tissues is difficult to reconcile with the fact that many people living

in countries where leprosy is absent give a positive reaction. He believes that all persons who come into contact with leprosy and everyone who is infected at first develop a positive lepromin reaction which corresponds with Khanolkar's " Silent phase." From this one of three developments can take place—(1) the tissues may become hypersensitized and give a strongly positive reaction; (2) they may become desensitized and give a negative reaction, or (3) they may remain in an unstable condition—not fully sensitized or desensitized. In Khanolkar's cases, however, all those healthy contacts that give a positive lepromin reaction and later developed leprosy developed, as one might expect, the tuberculoid type.

These three developments lead to the three primary groups or types of leprosy—(1) Tuberculoid (lepride), (2) lepromatous and (3) Dimorphous (Borderline). Taking the lepromin test as guide to grouping, the author considers the disease, according to its clinical manifestations, as Macular, Infiltrative and Polyneuritic. Macules giving a strongly positive lepromin reaction may be simple inflammatory or definitely tuberculoid; those with a negative reaction form the typical uncharacteristic or indeterminate macules of the S. American classification, or form the prelepromatous or lepromatous macules. In sections the bacilli show a " fish swimming up-stream " appearance; and those giving a weak positive are not easy to describe and form the dimorphous group. Infiltrations are similarly divided into (1) Minor and major tuberculoid; (2) lepromatous and (3) Atypical tuberculoid and atypical lepromas. Histological characteristics of the three groups are shown in tabular form.

Polyneuritic lesions. These are not the lesions found in normal lepromatous or tuberculoid cases, but those in which no macules or infiltrations are seen, but in which bacilli remain in the nerves and have not burst into the corium of the skin. Such cases are divided into three groups but no clinical symptoms are given.

In the section on diagnosis details are given of Wade's slit smear method and of the staining of slides.

Under therapy there is no mention of Hydnocarpus oil. Of the Sulphones the author prefers the parenteral use of 50% aqueous solution of sulphetrone, but also gives details of the oral use of Dapsone. He advises great care in the use of sulphones in dimorphous cases, as serious nerve damage is likely if they go into reaction. The sulphones appear to interfere with the metabolism of the *M. lepræ*, which undergo fragmentation. Khanolkar has shown that as the bacilli first attack the nerves, so finally the nerves act as reservoirs of the granular bacilli, and as the disease may recrudescence from these maintenance doses of sulphones are advised for a prolonged period.

G. O. TEICHMANN.