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Abstracts

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1. **The treatment of leprosy with the sulfones. 1. Faget's original 22 patients. A thirty-year follow-up on sulfone therapy for leprosy**, by R. R. JACOBSON and J. R. TRAUTMAN. *Int. J. Lepr.* 1971, **39**, 726-737.

This interesting and informative report from Carville, U.S.A., gives the case histories of the first 22 patients to have received sulphone therapy for leprosy (Faget *et al.*, *Trop. Dis. Bull.* 1944, v. **41**, 494) and describes their subsequent progress. Disappointingly, it shows that 30 years after commencing treatment, or at the time of death, 13 patients had active lepromatous leprosy (but 2 of these patients can be excluded as they died prematurely). The three most important facts emerging from this report are: (1) all (excepting the 2 who died prematurely) had their disease arrested after taking treatment regularly for varying numbers of years; (2) sulphone resistance tended to develop in those who suffered reactivation of their disease due to stopping treatment or to becoming irregular with treatment; (3) sulphone resistance did not develop in those who continued treatment regularly.

The authors rightly conclude that, in lepromatous leprosy, regular therapy for life is the wisest course to follow.

W. H. Jopling

2. **Controlled drug trial of B663 compared with DDS. Preliminary (48-week) report, by J. G.** TOLENTINO, J. N. RODRIGUEZ, and R. M. ABALOS. *Int. J. Lepr.* 1971, **39**, 738-741.

In a controlled drug trial in the Philippines, lasting 48 weeks, the progress of 16 patients taking clofazimine (Lamprene; B663) was compared with that of an equal number taking dapsone (DDS). Dosage of clofazimine was 200 mg daily six times a week, and of dapsone was 50 mg given twice a week increasing to 600 mg weekly. Clinical and bacteriological progress was equally good in both groups, but erythema nodosum leprosum reaction and acute neuritis occurred less frequently and with less severity in the patients taking clofazimine.

[The controlling effect of clofazimine on lepra reaction in this trial was due to the fact that the drug was given in the high dosage usually reserved for the treatment of lepra reaction; it is highly doubtful if this effect would have occurred with the much smaller, but therapeutically effective, dosage of 100 mg twice a week.]

W. H. Jopling

3. **Traitement de la lèpre lépromateuse par l'ethionamide. (Treatment of lepromatous leprosy with ethionamide)**, by R. ROLLIER and M. ROLLIER. *Maroc méd.* 1972, **52**, 148-166.

This well-documented account of a trial of ethionamide in leprosy attempts an objective reappraisal of the efficacy of this neglected drug, and thus complements the experimental work of Shepard (*Trop. Dis. Bull.* 1971, v. **68**, abstr. 1013). The trial concerned 102 patients and extended over 10 years. Laboratory investigations were inadequate, including examinations of skin biopsy specimens and material obtained from the skin (by the slit-smear technique) and from the "nasal mucus".

All the patients, except one, had lepromatous leprosy. The drug was first given at a dose of 1 g daily; because of side-effects (mainly digestive) the dose was reduced to 0.50 g daily for an adult, and 0.25 g for an adolescent. Bacilli disappeared from the "nasal mucus" and from the skin at a regular rate, and at the end of 4 years of treatment, in the majority of patients, the Bacillary Index had fallen to zero. [The morphology is not indicated.]

Clinical amelioration was also impressive. Early signs of improvement could be seen after 6 months of treatment, and after 2 years 75% of the patients could be classified clinically as "disease arrested". Special attention was paid to lesions of the upper respiratory tract (nasal mucosa, palatal mucosa and the tongue), and to the occurrence of erythema nodosum leprosum. Some evidence is given that the latter might on several occasions have been precipitated by the drug when given in the higher initial dose of 1 g daily.

The authors conclude that ethionamide is active in leprosy and that its activity resembles that of dapsone. Given at the dose recommended, it is relatively free from side-effects. Its price militates against it ever being more than a second-line drug.

S. G. Browne

4. A comparison of the growth curves of the NQ bacillus (*Mycobacterium* sp.) derived by photometric turbidity, microscopic counting, and viability in a tube-dilution-series, by C. V. REICH. *Int. J. Lepr.*, 1971, **39**, 25-33.

This study "was designed to investigate the existence of the unstained, microscopically invisible state in a cultivable species of mycobacteria and to determine whether the state can be associated with biologic activity." The NQ bacillus is a mycobacterium isolated from the ear and testis of hamsters inoculated with material from patients with leprosy. The growth medium was Dubos medium at pH 6.8, but without Tween 80 and with 20% bovine serum. 15 tubes of culture were read daily for turbidity, and the tube which was nearest the daily mean was selected to provide the sample aliquots for viability and microscopic counts. These latter were made by the procedure of Shepard and McRae (*Int. J. Lepr.* 1968, v. **36**,78). The cultures were sampled for 46 days, and viability counts were made using ten 10-fold dilutions. The number of acid-fast bacilli increased rapidly for 10 days reaching a level of 10^8/ml. They remained at this level for a further 15 days and then rose to nearly 7×10^8/ml by the thirtieth day. However, the number of viable units increased for 20 days up to 10^{10}/ml. The "turbidity" increased more slowly to give an estimated 10^8 bacteria/ml after 40 days. The author discusses reasons for the difference between the count of acid-fast bacilli and the viability count, but dismisses clumping as a possible cause. It is suggested that mycobacteria which did not stain by the Ziehl-Neelsen method appeared in the medium after 10 days. The extremely rapid initial rate of growth of almost two logs that occurred in the first 3 days is explained by the author as "inter-conversion from nonstaining to acid-fast [forms]". He concludes that "in the active reproductive phase of a mycobacterial culture, a significant proportion of the population remained unstained by the Ziehl-Neelsen procedure". The author states that his study "is directed ultimately to *Mycobacterium leprae*". [This study poses significant questions, but whether the bacterial population in a leprosy patient after many years of the disease is in "an active reproductive phase" seems doubtful.]

C. S. Goodwin

5. Attempts to establish the armadillo (*Dasypus novemcinctus Linn.*) as a model for the study of leprosy. 1. Report of lepromatoid leprosy in an experimentally infected armadillo, by W. F. KIRCHHEIMER and E. E. STORRS. *Int. J. Lepr.* 1971, **39**, 693-702.

It is reported that an armadillo (*Dasypus novemcinctus*) has developed lepromatoid infection with *Myco. leprae* approximately 14 months after inoculation of leprosy bacilli, from an untreated case of lepromatous leprosy, into the skin of its abdomen and ear lobes. The diagnosis of lepromatoid leprosy is supported bacteriologically by over 1000-fold increase in the inoculation sites of acid-fast bacteria, which do not grow on mycobacterial culture media and which oxidize D-dopa. In addition, these acid-fast bacteria have been found in great numbers at a skin site remote from the inoculated area. The remote skin site was of normal appearance. The inoculated skin sites were converted into massive nodular lesions. The acid-fast bacteria were intracellular, and typical lepra cells made up much of the lepromas. Bacilli were also seen in cutaneous nerves. It is too early yet to evaluate the results of the mouse footpad inoculations of the bacilli. So far, however, sections of the footpads show what one would expect of *Myco. leprae* after one month.

The reasons for attempting transfer of leprosy to the armadillo and the possible future significance of the armadillo in leprosy research have been discussed.

6. **Etude clinique et épidémiologique de 56 cas de lèpre suivis à la Clinique Dermatologique de Bordeaux depuis 1947. (A clinical and epidemiological study of 56 cases of leprosy seen at the Bordeaux Skin Clinic since 1947),** by L. TEXIER. *Med. Afr. Noire,* 1972, **19,** 193-196.

In the 23 years from 1947 to 1969 inclusive, the author made the diagnosis of leprosy on 56 occasions in patients attending his skin clinic. All except 7 had contracted the disease outside Europe; 4 were from Spain, and 3 had caught leprosy in France. Among the 31 patients born in metropolitan France, 10 had been in Government service, 7 in commerce, 5 in the armed services and 5 were missionaries. The 25 immigrant patients were mainly students (8), or workmen (8), or wives and children (6).

The presenting signs that brought patients for diagnosis were confined to the skin in 44, in both skin and peripheral nerves in 8, and in peripheral nerves only in 4. 33 were classified as having tuberculoid leprosy, 20 as lepromatous, and 3 as indeterminate. It is noteworthy that of the 20 patients with lepromatous leprosy, 15 were from metropolitan France. The average minimum "silent" period before signs of leprosy appeared would be under 2 years.

All patients were admitted initially to hospital, and those with lepromatous leprosy were kept in hospital until the nasal mucus no longer harboured *Mycobacterium leprae* (the morphology not being indicated). Patients with tuberculoid leprosy are discharged from hospital after stabilization of treatment has been achieved, and continue taking dapsone at home under medical supervision, reporting to the clinic each month. The standard treatment is dapsone, with a starting dose of 25 mg daily, increasing to a maximum maintenance dose of 200 mg daily. No untoward complications attributable to this dose of dapsone are noted.

Most patients are correctly diagnosed within 2 years of the appearance of the first signs, but 1 patient had to wait 12 years before the diagnosis of leprosy was entertained.

Details are given of the 3 patients who contracted leprosy in France itself. One was a boy in boarding school, 2 of whose classmates (both immigrants) had leprosy. Another was a woman who had looked after a civil servant known to have had lepromatous leprosy. In the third instance, a hotel maid, there is no suggestion of any contact with anyone suffering from leprosy, and the source of her infection remains quite unknown.

S. G. Browne

7. **Immunological phenomena in leprosy and related diseases,** by J. L. TURK and A. D. M. BRYCESON. *Adv. Immunol.,* 1971, **13,** 209-266.

The following is an extract from the authors' introduction:

"Failure of host resistance frequently results from a defect in cell-mediated immunity (CMI). However, hypersensitivity reactions resulting in tissue damage can occur as readily from CMI as from the deposition of immune complexes involving humoral antibody. Such an interaction between immune procedures and a given microorganism can display a wide spectrum of pathological processes, which, in turn, leads to markedly different clinical manifestations.

Such a spectrum is particularly well demonstrated by the recent elaboration of the varied clinical patterns in leprosy. Postulations from time to time related these differences to variations in the host's resistance, yet experimental and clinical evidence has been available only during the last few years. With elucidation of the immunological basis for the disease spectrum in leprosy, a parallel has been sought and found in other infectious diseases. These include especially certain protozoal diseases such as leishmaniasis and others caused by yeasts and fungi such as candidiasis and the systemic mycoses. This review is, therefore, concerned with immunological concepts in leprosy leading to a discussion of analogous states now recognized in other infectious diseases."

[There are 214 references.]

8. **WHO co-ordinated short-term double-blind trial with thalidomide in the treatment of acute lepra reactions in male lepromatous patients,** by C. G. S *et al. Bull. Wld Hlth Org.* 1971, **45,** 719-732.

This is a report of a WHO short-term double-blind trial on male patients suffering from lepromatous leprosy carried out to compare the effect of thalidomide with that of acetylsalicyclic acid in the control of lepra reaction. 214 lepra reactions were treated during a period of 9 months, 116 with thalidomide and 98 with acetylsalicylic acid, and treatment was given for 7 days. Dosage of thalidomide was one tablet (100 mg) 4 times daily for patients over

50 kg in weight, with a reduced dosage for lighter patients, and those on acetylsalicylic acid received an equal number of tablets of 400 mg strength.

Although acetylsalicylic acid had a beneficial effect on some of the symptoms, thalidomide was more effective; its effect on skin lesions and body temperature was greater than on acute nerve and eye manifestations. In the very short period of the trial, side-effects of a serious nature were not encountered in either group, but thalidomide had a tendency to induce leucopenia.

W. H. Jopling

9. **Infection of murine striated muscle with *Mycobacterium leprae*: a study by light and electron microscopy**, by M. M. ESIRI, A. G. M. WEDDELL and R. J. W. REES. *J. Path.* 1972, **106**, 73-80

It has already been shown that in murine infections with *Mycobacterium leprae* the striated muscle fibres are colonized at a very early stage, whether the mice are intact or thymectomized (Rees and Weddell, *Ann. N.Y. Acad. Sci.* 1968, v. **154**, 214). The present paper examines the distribution of *Myco. leprae* in striated muscle over a 2-year period of the infection, and the pathological changes that result.

Bacilli in footpads increased steadily in number from the sixth to the tenth months, the number being about 100 times greater in the thymectomized animals. Microcolonies were almost always intracellular in muscle fibres (in disorganized sarcoplasm), or macrophages. In the footpad they were nearly all in muscle but in the nose they were nearly all macrophages. This might be associated with the fact that mitochondria are more numerous in the muscle fibres of the nose, which have the characteristics of red muscle. It is possible that *Myco. leprae* preferentially colonizes white muscle fibres.

In intact mice the infection produced after several months of low-grade inflammation with only slight patchy damage to muscle fibres. In thymectomized-irradiated mice the greater number of bacilli was associated with more widespread inflammation and damage, which was attributed directly to the bacilli and not secondarily to nerve damage. The nature of the damage to muscle fibres is described and illustrated with electronmicrographs.

D. S. Ridley