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Abstracts

A rational view of world leprosy. S. G. BROWNE, *Without the Camp*, Apr.–Jun. 1966, **278,** p. 32.

The author describes that the world leprosy problem, far from diminishing, is most probably increasing. The world population is increasing, particularly in countries where leprosy is prevalent. Everybody is living longer, including those who suffer from leprosy. Many people travel further afield in search of work. Overcrowding and low standards of hygiene affect more people than ever before, especially in those countries where leprosy is prevalent.

The proportion of leprosy patients under treatment remains low: in the world as a whole, only 1 leprosy patient out of every 5 has any chance of treatment for leprosy. For some years now, enough knowledge to control leprosy has been available, but this knowledge has not been applied. It is quite premature, and grossly misleading, to speak of leprosy as being 'on the way out'. A higher priority must be given to leprosy. There are two new reasons for hope: (1) Dr DHARMENDRA of Chingleput, S. India, has reported that the standard leprosy drug DDS will prevent the signs of leprosy developing in a high proportion of family contacts when given regularly by mouth over long periods. Welcome work is in hand to develop and confirm this finding: (2) KINNEAR BROWN has been studying BCG protection against leprosy in a high proportion of East African children. This work is being continued, as the test must be carried further in time. (Lepra has a leprosy control project just started in Malawi to show that this and other knowledge can be used to control leprosy in a reasonable period of time, and orthopaedic surgery and physiotherapy and rehabilitation have an important role in modern control in leprosy). There is a continuing challenge to constant reappraisal by all workers. Facile optimism is out of place, but hope and hard work are called for because of the recent advances and present trends.

2. **Absorption, Metabolism and Excretion of di-p-aminophenyl Sulphone (Dapsone) and di-p-aminophenyl Sulphoxide in Man,** by G. A. ELLARD, *Brit. J. of Pharmacology and Chemotherapy*, Jan. 1966, **22,** No. 1, p. 212.

The excretion in the urine of leprosy patients of di-p-aminophenyl sulphone (dapsone), di-p-aminophenyl sulphoxide, their acid-labile metabolites, and other diazotizable compounds was measured.

About 41% of the dapsone given is excreted as the free compound plus acid-labile conjugates, and 27% as compounds which are hydrolysed to dapsone-like substances by boiling with dilute acid. The absorption of the sulphoxide appears to be less complete than that of dapsone only about 55% of the dose being excreted in the urine as diazotizable compounds compared with 75% for dapsone. Considerable oxidation of di-p-aminophenyl sulphoxide to dapsone occurs in the human body and about a quarter of free amines excreted in the urine after dosage with the sulphoxide are due to dapsone.

The excellent absorption of dapsone previously reported by other workers is confirmed (75% and may be rather more). The author's findings suggest it is relatively slowly metabolized in man and that its anti-leprotic activity is due to the presence of the unchanged drug in the body. The chromatographic studies of JARDIN (1958) suggest that some of the antileprotic activity of the sulphoxide, but not necessarily all, is due to its conversion in the human body to dapsone.

3. **Recent Bact. Immunolog. and Pathol. Studies on Experimental Human Leprosy in the Mouse Foot Pad.** R. J. W. REES, of the National Institute for Medical Research, Mill Hill, London, N.W.7, Proceedings of LWM—AFIP Conference reported in *Internat. J. Leprosy*, 1965, **33,** 3, pt. 2, 646—655.

The author has demonstrated conclusively that human leprosy can be transmitted to the mouse foot pad. Multiplication of *M. leprae* depends on the size of the inoculum and is confined to the foot pad. So far identical infections have been produced with 35 strains of *M. leprae* obtained from previously intreated patients from different parts of the world; 27 from Malaysia, 6 from Burma, 1 from East Africa, 1 from the West Indies. Lepromatous patients provided 29, borderline 5, and reactional tuberculoid 1. Bacilli from patients treated 12 to 16 months with DDS nearly always failed to multiply in the mouse foot pad. A very high proportion of bacilli from these patients were degenerate and yielded irregular staining with carbol fuchsin. The foot pad infection can be inhibited by DDS, phenazine: B 663, Fanasil, and Madribon, and almost completely with Ciba 1906 and TB1. There is suggestive evidence that some *M. leprae* derived from patients on 2 years or more of treatment with Ciba 1906 are partially resistant to Ciba 1906 and show cross resistance to thiosemicarbazone. There has been definite confirmation that a very few patients with progressive leprosy, even after many years of treatment with DDS, are infected with DDS-resistant strains of *M. leprae.*

Detailed analysis of the histology of infected foot pads has revealed a very high proportion of healthy-looking bacilli are sited within striated muscle fibres, appearing as 'microcolonies'. This may be the main site of multiplication of *M. leprae* within the mouse foot pad. It has been shown that *M. leprae* inoculated into mouse thigh muscle can produce a similar picture of multiplication of the bacilli within striated muscle fibres. Studies with other strains of mycobacteria have shown no predilection for muscle fibres. Attempts have been made to diminish the

immunological response and preliminary findings are of significant enhancement in previously thymectomized mice and irradiated CBA mice. This perhaps may lead to a much more progressive and generalized infection with *M. leprae* in the mouse.

This paper by R. J. W. REES is fascinating for what it finds and the lines it suggests. He gives 25 references which suggest his valuable collaborators in this work, and it is hoped in the future they will continue their collaboration.

4. **Influencia de la Talidomida en la Reacción Leprosa.** (**Influence of Thalidomide in Lepra Reaction**) by Dr J. SHESKIN, of the Dermatological Department of the Hadassah University Hospital and its daughter hospital Jerusalem, Israel, whose Director is Prof. E. Sagher, *Revista Dermatologia Venezolana*, 1965, **4,** Nos. 3 and 4, p. 210—21.

The author gives the symptomatology of lepra reaction as follows:— pyrexia up to 40°C, shivering, sleeplessness, lack of appetite, vomiting, joint pains, muscle pains, bone pains, headache, abdominal pains, oedoma of the limbs and glottis, nephritis and enlargement of liver and spleen, orchitis, rhinitis and/or epistaxis, iritis and iridicyclitis, neuritis or polyneuritis, swelling of the lymphatic glands, skin lesions in the form of reactivation of pre-existing lesions and appearance of lesions similar to nodose erythema and/or multiform erythema, accompanied at times by vesicles and/or necrosis and/or ulceration. He reports 11 patients with lepra reactions who received treatment with thalidomide since 6 months ago. They all had lepromatous leprosy and had been under observation 3 months to 22 years. Thalidomide was given on 19 occasions to these 11 patients and placebo treatment on 10 occasions. There was rapid response in lepra reactions in all patients, both subjectively and objectively, and the improvement began within 8 to 48 hours of exhibition of thalidomide. By contract, placebo treatment was ineffective. Since the thalidomide treatment 7 patients appear to have improved in active lepromatous lesions: in one of these there had been no improvement with 19 months of sulphones. Studies of the lesions which seem to have improved in lepromatous patients will be carried on in bacteriology, histology, and immuno-allergy. The dosage given of Thalidomide was usually 400 mgm. daily. Duration and minimum effective dose will require study of a larger number of patients. Secondary effects of thalidomide were noted in a few patients, but did not necessitate cessation of treatment. The dangers of thalidomide in pregnancy are well known. Care was taken to exclude pregnancy. The author recommends the use of Thalidomide in the treatment of lepra reactions. (See 'Further Observation with Thalidomide,' by J. SHESKIN, *Leprosy Review*, Oct. 1965, **4,** p. 183 and comments p. 186—187.)

5. **Prophylactic value of DDS against leprosy – an interim report,** by DHARMENDRA, P. MAHAMEDALI, S. K. NORDEEN, and K. RAMANUJAM, *Leprosy in India*, Oct. 1965, **38,** No. 4.

The prophylactic value of DDS among intra-familial child contacts exposed to lepromatous and bacilliferous non-lepromatous cases is being investigated at the Central Leprosy Teaching and Research Institute, Chingleput, India, which is situated in the midst of a large belt of high endemicity of leprosy.

To begin with, a preliminary house to house survey was done in an area adjoining the Institute, covering a total population of a little over 213,000. This took about 1 year. A prevalance rate of 21 per thousand, and a lepromatous rate of a little over 14% was found. The total number of 'source' cases was 362, including 330 lepromatous cases and 32 bacilliferous non-lepromatous cases. A little over 700 healthy intra-familial child contacts (below 15 years of age) of these cases were recorded.

The healthy child contacts were divided into two comparable groups – the 'prophylaxis' and the 'control' groups.

The prophylaxis group has been receiving DDS in scheduled doses, and the control group, similar looking placebo tablets. The study has been conducted by the 'double blind method'.

All the 'source' cases have also been treated with therapeutic doses of DDS.

The study proper (after the survey which took a year to complete, and after some preparatory work) has now (August, 1965) been in progress for 2½ years, during which all the contacts of both the groups have been examined periodically and regularly.

During the course of study there had been certain deletions and additions in the number of contacts. The number of healthy contacts at the start of the study was 689. Of these, (291 belonging to the prophylaxis group, and 294 to the control group) had been treated for the full period of observation. The present report is based on an analysis of the findings in these 585 contacts.

During the period of observation, 43 patients with leprosy have been recorded in the 585 contacts. Of these cases, 14 have been in the 291 contacts in the prophylaxis group, giving an incidence of 4.81%; and 29 in the 294 contacts in the control group, giving an incidence of 9.86%. This difference is found to be statistically significant at 2% level.

It is therefore tentatively concluded that, under the conditions of the present investigations, administration of DDS to healthy child contacts of leprosy patients has been found to have a protective value against the disease.

The protective value is, however, apparent only after 9 months of the prophylactic treatment; during the first 9 months there was no difference between the prophylaxis and the control groups regarding the incidence of the disease.

Further, there appears to be a relationship between the protective value of DDS and the age of the contact at which the prophylaxis treatment is first started. In the study under report, the prophylactic treatment was found to be of definite value in the contacts up to 10 years of age, but it had no value in contacts above that age. This would emphasise the need for starting prophylaxis treatment soon after exposure to infection; in intra-familial contacts it would mean starting the treatment at as early an age as possible.

There is some evidence to suggest that in the contacts developing the disease, the prognosis may be better in those under DDS prophylaxis than in others.

DDS prophylaxis was also found to be more effective among males. The reason for this observed difference is not clear and no inference can be drawn from this particular finding.

It is proposed to continue the present study for a little longer, and then to analyse the findings from the various aspects before coming to a final conclusion.

Once the effectiveness of prophylactic treatment with DDS is finally established, further studies will have to be planned to get information on various practical points regarding its general application in the control of the disease, and regarding other related matters.

Since the 2¼ years the findings of an additional period of 28 to 30 months have become available and the results strengthen the finding of the value of prophylactic DD in contacts.

This paper is of great value and its intimate study is recommended. There are 10 informative tables and 3 maps and one table in the addendum which extends the period of observation by 28–30 months.

6. **Antigenic Studies of Other Fungi and Mycobacterium Leprae,** by R. J. W. REES, K. R. CHATTERJEE, J. PEPYS, and ROSEMARY D. TEE, *Amer. Review of Respirat Diseases*, Dec. 1965, **92**, Part 2, pp. 139—149.

This report has 9 illustrative figures, 1 table, and 1 diagram. The present studies of the authors indicate the special types of problem which arise during the investigation of the immunological aspects of an infection such as leprosy, in which the causal organism cannot be cultured *in vitro*. Nevertheless it has been possible to use a whole-bacillus antigen, isolated from infected tissues, and also possible, by absorption tests, to distinguish the mycobacterial constituents from the contaminating tissue antigen constituents. Their present studies on leprosy patients were confined to serological tests with culture filtrates, in which it has been shown that circulating precipitating antibodies can be detected, and that these antibodies are predominantly anti-polysaccharide. In future it will be possible to test these sera against disintegrated *M. leprae*, and also investigate whether antigens are produced by protein constituents of mycobacteria.

The serological studies on *M. lepraemurium* multiplying in cell culture have shown for the first time that intracellular mycobacteria release a soluble mycobacterial antigen, polysaccharide in nature, which can readily escape from the host cells into the culture medium. The sera used in these present studies were provided by Dr M. F. R. WATERS from his patients at the Sungei Buloh Leprosy Research Unit, Malaysia.

7. **Observations on the Inoculation of M. leprae in the Foot Pad of the White Rat,** G. R. F. HILSON, M.D., St George's Hospital Medical School, London, S.W.1., L.W.M.—A.F.I.P. Conference, *Internat. J. of Leprosy*, 1965, **33**, No. 3, pt. 2, p. 662..

The author used the Shepard technique and inoculated the foot pads of white rats with human bacilli from two different human sources of leprosy. Methods of microbial enumeration showed that limited multiplication of the acid fast mycobacteria occurred in the two cases, generally similar to mouse foot pads and the histopathology was also similar. Also carried out were two further serial passages of the isolates.

8. **Studies on M. lepraemurium and M. leprae in Tissue Culture,** ELIZABETH W. GARBUTT, M.S., National Institute for Medical Research, Mill Hill, London N.W.7., present address, Dept. of Biochemistry, University of Alberta, Edmonton, Alberta, Canada, L.W.M.—A.F.I.P. Conference, *Internat. J. of Leprosy*, 1965, **33**, No. 3, pt. 2, p. 578.

The author's studies showed that continuous multiplication of *M. lepraemurium* can occur in rat fibroblasts that are subcultured regularly, and there is also some evidence that *M. leprae* will grow in such regularly subcultured cells, both human and rat, provided the cultures are kept a sufficiently long time to overcome an apparent bacillary lag phase of between two and four months.

The cell type used for growing rat leprosy bacilli may be important, for the author found that multiplication did not occur in mouse monocytes, mouse fibroblasts (L strain), HeLa cells, nor monkey kidney cells. Growth of *M. lepraemurium* was achieved only in cells derived from animal species susceptible to the infection. The medium is also of importance in growth requirements, for bacilli were destroyed in cultures of 14pf cells in cell serum and peptone while bacilli in 14pf grown in cord serum and Hank's solution ($CS_{50}H_{50}$) are capable of continuous multiplication.

With *M. leprae* some multiplication has been obtained in rat fibroblasts and human diploid cells, and tissue culture-grown bacilli from the fibroblasts have been passaged successfully in mouse foot pads. The common denominator in these experiments has been a human element, either human cells grown in medium containing non-human serum, or rat cells grown in human cord serum. This raises the possibility that growth of *M. lepraemurium* might be obtained in cells other than these from rats or mice. Grown in tissue culture *M. lepraemurium* has shown all the characteristics of its parent organism and it is suggested that tissue-culture *M. leprae* would do the same.