LEPROSY REVIEW

Volume 50, Number 4, December 1979

Published Quarterly for the
British Leprosy Relief Association
By Academic Press
ISSN 0305-7518

Leprosy Review

The Clinical and Research Quarterly of the British Leprosy Association LEPRA

Published Quarterly (Mar., June, Sept., Dec.) at 24–28 Oval Road, London NW1 7DX, England by Academic Press Inc. (London) Limited (on behalf of the British Leprosy Relief Association).

1979: Volume 50, 4 issues. Inland, £11.00 inclusive of postage and packing; abroad, $29.00 inclusive of postage and packing. Subscription orders should be sent to Academic Press Inc. (London) Limited, 24–28 Oval Road, London NW1 7DX, with the exception of those originating in the U.S.A., Canada, Central America and South America; these should be sent to Academic Press Inc., 111 Fifth Avenue, New York, N.Y. 10003, U.S.A. Second-class postage paid at Jamaica, New York 11431, U.S.A. Air freight and mailing in the U.S.A. by Publications Expediting Services Inc., 200 Meacham Avenue, Elmont, N.Y. 11003, U.S.A.

British Leprosy Relief Association
Registered Offices: Fairfax House, Causton Road, Colchester CO1 1PU

Editorial

THE SAGA OF THE SKIN SMEAR

Three methods of bacteriological investigation of leprosy patients were in vogue by the time the "scraped incision" method became generally accepted as the most practical. There was the very first one, described by L. J. Alvarez at the 1st International Leprosy Congress, held in Berlin in 1897; this was to remove a small piece of skin surgically, grind it up in a mortar with a few drops of saline, and make smears of the resultant fluid. The second was the "skin-clip" method, favoured by the late Ernest Muir (1921), which involved clamping the surface of a skin lesion with curved haemostatic forceps and snipping off a small piece of skin with curved scissors; the raw surface of the clipping was then rubbed or squeezed onto a slide. The third was the puncture method which the late H. W. Wade found in routine use in Manila when he was appointed to the official Leper Examining Committee of the Bureau of Health in 1916. Here are his own words (Wade, 1963):

> "The main function of the Committee was the examination of smears for bacilli. The expression often used in those days was 'examinar el sangre', and it was truly blood that was examined. Before the Committee convened, the resident staff had prepared the smears. Usually selecting a single lesion of each patient, it was punctured deeply with a surgical needle. The blood that exuded, or was expressed, was smeared more or less widely and thickly on a slide. When lesions contained an abundance of bacilli there was no difficulty in the examination, but it was otherwise when they contained few or none. In such cases it was required that each member of the Committee should, in turn, spend a certain number of minutes on each slide before a patient could be declared negative and eligible for release. That was very time-consuming, and exquisitely boresome."

In the following year (1917) Wade replaced this puncture method by his "scraped incision" method, but it was not until ten years later that it was published in a booklet written with Rodriguez (1927), and it was not contributed to the periodical literature until nearly another decade had elapsed; this was a revised description of the method by Wade (1935), so detailed and clear that it could be copied verbatim into any modern leprosy textbook. At that time it was usual for smears to be taken exclusively from skin lesions, as is modern practice in non-lepromatous leprosy, and time had to pass before earlobes were included in routine smears in lepromatous leprosy, and for many years it has been generally accepted that bacilli are likely to be found in earlobes, in long-treated patients, when they have disappeared from other sites. The wheel of progress has made a further turn, and the earlobe has now been

0305–7518/79/040271 + 03/$02.00/0

replaced by the finger as the richest site for bacilli in such patients, and also the skin site from which the earliest intimation of relapse can be obtained by finding solid-staining bacilli whereas such (living) bacilli had been absent previously. It was at the Hospital for Tropical Diseases in London that the original work was done on the inclusion of skin smears from fingers in follow-up tests on lepromatous patients under treatment (Ridley *et al.,* 1976). The idea came from Mrs Marian Ridley and was prompted by a conversation she had with Dr John Pearson in which the latter queried why fingers should so often appear oedematous even when there are no clinical lesions there. After discussing the programme with her I began to include two finger smears in all lepromatous patients reporting for follow-up examination, and I decided to use the dorsum of each middle finger. The first phalanx was chosen as it seemed easier to make a good smear because there was enough skin to grip between thumb and index finger of the left hand. The following smears were taken from each of 30 patients reporting consecutively in 1975: 2 from earlobes, 2 from healing or healed lesions on trunk or limbs, and 2 from fingers. Additional smears were from toes and nasal mucosa in some patients. Our results showed that the mean Bacterial Index (BI) was a little higher, and the mean SFG Index was much higher, in fingers. In four patients the fingers were the sole skin site for bacilli. Toes gave results which were less informative than fingers, and as would be expected in long-treated patients, nasal mucosa was generally unrewarding, but the nose gave early intimation of impending relapse in one patient as the few bacilli seen were all solid-staining; finger smears gave supporting evidence in this case as some solid-staining bacilli were present among the fragmented and granular bacilli. No solids were found at other sites.

The next report (Hiramalini *et al.,* 1978) was on 41 lepromatous patients receiving treatment at Karigiri, India. Smears were taken from both middle fingers, both second toes, right earlobe, left forehead, right chin, left buttock, and nasal mucosa. All patients wore sandals. The authors found fingers and toes consistently more informative than the other sites, with higher BI and MI, but with no significant difference between them, excepting that the terminal phalanx of the finger harboured more solid-staining bacilli than the middle phalanx. Three patients with negative smears from earlobes and nose had granular bacilli in fingers and toes, and in one patient who was negative at all routine sites after 10 years of treatment, granular bacilli were found only in the terminal phalanges of fingers and toes.

The paper by Haidar Abu Ahmed *et al.* in the present Number of this Journal compares smears from eight different skin sites in 18 new (untreated lepromatous patients. They found that mean values of BI were highest in earlobes and fingers (4.5 + in each), and as regards MI the figure for earlobes was slightly higher than that for fingers (14.3 as against 13.0). We are not told which phalanx was chosen. The authors recommend 6 smears from all new lepromatous patients and during follow-up tests: 2 from earlobes, 1 from face, 1 from buttock, and 2 from fingers.

In another paper in this Number, Jopling *et al.* take the story of finger smears a stage further. They describe two patients, under treatment with dapsone, and showing no clinical signs of relapse, who were found on routine testing to have solid-staining bacilli in fingers. Mouse foot-pad inoculation gave

positive results in both cases (proving that viable bacilli were present in the fingers), and in the second patient tests for dapsone resistance were carried out; these confirmed the presence of dapsone-resistant organisms.

These four papers leave no doubt that smears from fingers should be included in the assessment of all new lepromatous patients and in all follow-up examinations, and I would go so far as to suggest that no more than 4 smears are necessary: one from each earlobe and one from the terminal phalanx of each middle finger.

At this stage in our knowledge we can do no more than surmise as to the reasons why in lepromatous leprosy the skin of fingers is so rich in bacilli, and there are three likely explanations, working in concert: *firstly,* fingers are among the coolest skin sites, and it is well known that leprosy bacilli prefer cooler sites; *secondly,* the dermis of fingers has a good supply of sensory nerves, much favoured by bacilli; *thirdly,* these dermal nerves on the dorsal aspects of fingers are close to the surface because of the thinness of the dermis, and therefore an incision with a scalpel blade can readily collect bacilli from them; this applies particularly to the middle and distal phalanges. The role of repeated minor trauma is more speculative.

W. H. JOPLING

References

Hiramalini, S., Joseph, N. A. and Chacko, C. J. G. (1978). Concentration and persistence of bacilli in the fingers and toes of patients with lepromatous leprosy. *Lepr. Rev.* **49,** 223.

Muir, E. (1921). Handbook on leprosy: its diagnosis, treatment and prevention. Cuttack: R. J. Grundy.

Ridley, M. J., Jopling, W. H. and Ridley, D. S. (1976). Acid-fast bacilli in the fingers of long-treated lepromatous patients. *Lepr. Rev.* **47,** 93.

Wade, H. W. and Rodriguez, J. N. (1927). A description of leprosy: its etiology, pathology, diagnosis and treatment. Manila: Bureau of Printing.

Wade, H. W. (1935). The bacteriological examination in leprosy. *Lepr. Rev.* **6,** 54.

Wade, H. W. (1963). The examination of skin lesions for bacilli. *Int. J. Lepr.* **31,** 242.

Subscriptions to *Leprosy Review,* 1980 onwards

At a meeting of the Editorial Board of *Leprosy Review* in August 1979, it was decided that the yearly subscription, from Number 1, *51,* (1980) would be £15 for the four issues; or £4 per copy, inclusive of postage and packing (UK and abroad). Subscription orders or enquiries should be sent to the British Leprosy Relief Association (LEPRA), Fairfax House, Causton Road, Colchester, CO1 1PU, England.At its own discretion, LEPRA will continue, and also expand, its policy of sending free issues of this journal to people in various parts of the world; this will include doctors working directly with leprosy who cannot afford the above subscription, or obtain foreign currency, together with selected libraries covering tropical medicine.

Lepr. Rev. (1979) **50,** 275–281

ELISA Inhibition Technique for the Demonstration of Sulphones in Body Fluids I. Sulphones Specific Antibody-enzyme Conjugate*

HAN HUIKESHOVEN, MADELEINE de WIT, ANYA SOETERS, TEUNIS A. EGGELTE, J. E. LANDHEER and D. L. LEIKER

Royal Tropical Institute, Amsterdam, The Netherlands

A sulphones specific antibody-enzyme conjugate was developed as a basic tool for an enzyme linked immunosorbent assay (ELISA) for dapsone. The conjugate was found to be specific for sulphones without significant cross-reactions with sulphonamides. The sensitivity for dapsone is in the ng/ml range. This may lead to a simple and sensitive ELISA inhibition technique for the qualitative demonstration of sulphones in body fluids.

Introduction

From the first therapeutic experiments with dapsone in 1937 techniques were needed to determine or quantify sulphones in biological fluids or pharmaceutical preparations. Methods have been used, ranging from simple colour tests (Buttle *et al.,* 1937; Balakrishnan, 1968) to the sophisticated high performance liquid chromatography (HPLC) techniques (Murray *et al.,* 1971, 1975; Carr *et al.,* 1978; Mannan *et al.,* 1978). Whereas the latter are quite satisfactory for work in advanced laboratories, the former do not fully satisfy the needs of the man in the field. The WHO Expert Committee on Leprosy (1977) asks for "simpler methods for analysing urine for dapsone content" in order to monitor patient compliance with treatment in leprosy.

Our time is witnessing an explosive development of enzyme immunoassays for qualitative and quantitative estimations of all kinds of substances in biological fluids (Wisdom, 1976). These methods often pair high sensitivity

* This investigation received support from the Chemotherapy of Leprosy (THELEP) component of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases.

Received for publication 18 May, 1979.
0305–7518/79/040275 + 07/$02.00/0

to simplicity, also when applied to the determination of drugs (Brattin and Sunshine, 1973; Mulé *et al.,* 1974). We have therefore engaged in the development of a sulphones specific antibody-enzyme conjugate as a basic tool for an enzyme linked immunosorbent assay (ELISA) for dapsone. Initial studies have shown the feasibility of such an assay (Huikeshoven *et al.,* 1978).

Materials and Methods

ANTISERUM TO DAPSONE

Using equimolar amounts of dapsone (DDS) and nitrous acid, monodiazotized DDS was prepared and coupled to horseshoecrab hemocyanin (Williams and Chase, 1976). The resulting hemocyanin-DDS conjugate was purified by gel filtration on a Sephadex G 25 column. The number of DDS residues introduced into a protein molecule (molecular weight 70,000) was estimated by colorimetry to be between 15 and 20 (Bratton and Marshall, 1939).

Rabbits received intramuscularly 3 mg of hemocyanin-DDS in 1 ml Freund's Complete Adjuvant. Booster injections with 3 mg of conjugate in Freund's Incomplete Adjuvant were given after 6 weeks and at three-weekly intervals thereafter (for over 1 year now). One week after each booster injection 25 ml blood was taken by venapuncture to yield about 12 ml antiserum at a time.

ISOLATION OF SULPHONES SPECIFIC ANTIBODY

The Ig fraction of the antiserum was precipitated with 50% saturated ammonium sulphate. After washing, dialysis and lyophilization the yield was 25 mg Ig per ml serum.

Of this product 50 mg was dissolved in 10 ml 0.01 M phosphate buffered saline of pH 7.2 (PBS) and mixed (16 h, 4°C) with a 50 ml batch of immunosorbent prepared by conjugating horseshoecrab hemocyanin to activated Sepharose 4B. The mixed immunosorbent was filtrated with suction and the filtrate was mixed (4 h, 4°C) with a 50 ml batch of a second immunosorbent prepared by coupling DDS to activated CH-Sepharose 4B (Affinity Chromatography. Principles and Methods, Pharmacia, 1976). Also this mixed immunosorbent was filtrated with suction and then washed with PBS. The washed immunosorbent was mixed with 25 ml 0.1 N glycine HCl buffer of pH 2.8 and immediately filtrated with suction, followed by a wash with 25 ml PBS to neutralize the filtrate as quickly as possible. The filtrate was dialysed (16 h, 4°C) against distilled water (adjusted to pH 7 by a drop of diluted ammonia solution) and finally lyophilized. The yield was about 2 mg sulphones specific immunoglobulins.

CONJUGATION OF ANTIBODY AND PEROXIDASE

Horseradish peroxidase (10 mg) was conjugated to sulphones specific Ig (20 mg) according to the method of Nakane and Kawaoi (1974), but without removal of free peroxidase on a Sephadex G 200 column. Instead the enzyme–immunoglobulin conjugate (E-Ig) was precipitated with 50%

saturated aqueous ammonium sulphate solution. The product, taken up in 2 ml water, was dialyzed against PBS (16 h, 4°C) and stored at + 4°C in a final volume of 2.5 ml.

E-Ig DOSE-RESPONSE CURVE

A bovine serum albumin DDS conjugate (BSA-DDS) was prepared in the same way as the hemocyanin-DDS described above. Each well of a polystyrene microlitre tray (Cooke F) was incubated with a solution of 0.2 µg BSA-DDS in 100 µl carbonate buffer of pH 9.6 (15 min, 56°C). The tray was washed 4 times with PBS containing 0.05% Tween 20 (PBS/Tween), each time leaving the fluid in the wells for 1 min.

The E-Ig dialyzate was diluted fivefold with PBS/Tween containing 5% normal horse serum (PBS/Tween/Serum). Starting from this dilution 12 twofold serial dilutions in PBS/Tween/Serum were prepared. PBS/Tween (50 µl) was added to each well, followed by 50 µl of one of the 12 E-Ig dilutions. The tray was incubated (15 min, 56°C) and washed with PBS/Tween as above.

The enzyme substrate 5-amino-salicylic acid (5AS) was purified according to the method of Ellens and Gielkens (personal communication). 12 g 5AS was dissolved in 1500 ml water of 80°C together with 12 g sodium bisulphite. After filtration over active carbon and cooling to 4°C the precipitate was washed and dried in the air. Portions of 10 mg were dissolved in 10 ml PBS of pH 7.0 containing 0.0001 M EDTA. Each portion was lyophilized, and dissolved in 9 ml distilled water when needed. Immediately before use 1 ml of 0.05% H_2O_2 was added. Each well of the tray was incubated with 100 µl of the 5AS/H_2O_2 solution (1 h, room temperature). The reaction was stopped by the addition of 25 µl of 2 N NaOH.

Relative quantification of this ELISA was done by measurement of the optical density at 449 nm (O.D. 449) in a spectrophotometer. A dose-response curve was obtained by plotting O.D. 449 as a function of the logarithm of the E-Ig dilution factor.

INHIBITION BY SULPHONES AND ANALOGUES

From the dose-response curve a point was chosen where relatively maximal slope was paired to relatively maximal O.D. 449. The corresponding E-Ig

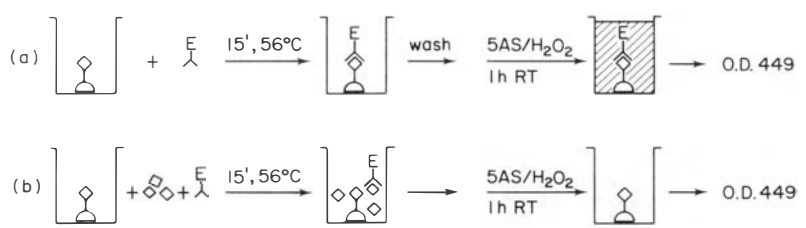


Fig. 1. The ELISA (a) is inhibited by sulphones (b).
Symbols: ◇ = DDS (◇) conjugated to BSA (⌓); E = E-Ig; ◇ = sulphones.

dilution was used to study the inhibitory action of sulphones and analogues on the ELISA. For this purpose 50 µl of serial dilutions in PBS/Tween/Serum of the compounds under test were added to the wells before 50 µl of the E-Ig solution was added and incubated (15 min, 56°C). The substrate was added after washing and the product was measured as above.

The principle of the ELISA and the inhibition tests is illustrated in Fig. 1.

Results

Fig. 2 is a photograph of the ELISA results on which the dose-response curve for the sulphones specific E-Ig conjugate was based. From this curve (Fig. 3) an E-Ig dilution factor of 5×10^{-3} was chosen for the inhibition tests with sulphones and analogues.

Fig. 4 is a photograph of the ELISA inhibition tests on which the graphs of Fig. 5 were based. Table 1 gives the sensitivities of E-Ig for the compounds tested, expressed in molarity of the solutions used at 50% response. The table moreover gives the relative specificities of E-Ig for the compounds, expressed as percentage cross-reaction towards DDS.

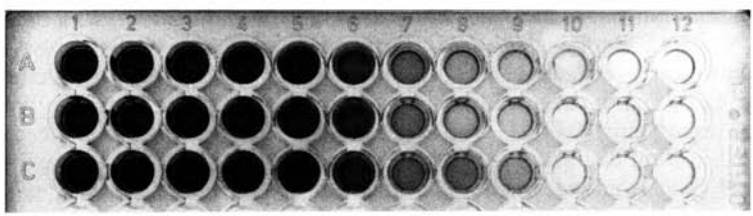


Fig. 2. ELISA of sulphones specific E-Ig. Twofold serial dilutions in triplicate.

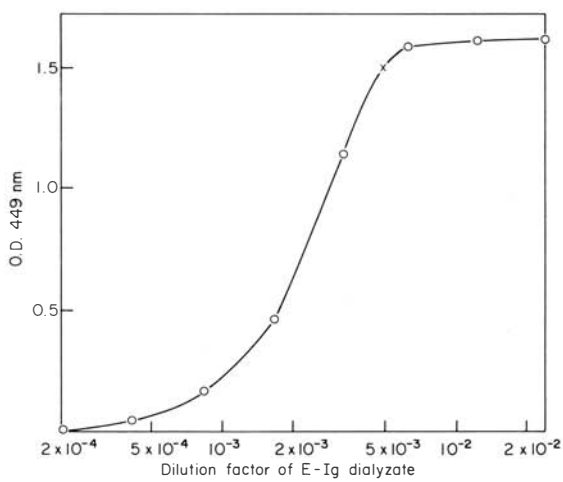


Fig. 3. Dose-response curve for sulphones specific E-Ig in ELISA. From the curve an E-Ig dilution factor of 5×10^{-3} (×) was chosen for the inhibition tests.

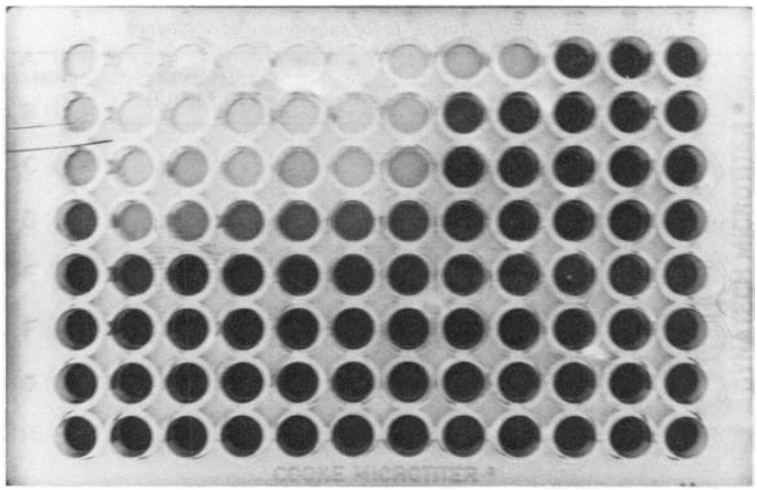


Fig. 4. ELISA inhibition tests of sulphones and analogues. A–H are fourfold serial dilutions of the compounds tested. Row numbers correspond to compound numbers in table 1. Row 12 contains blank controls (E-Ig without additional compound).

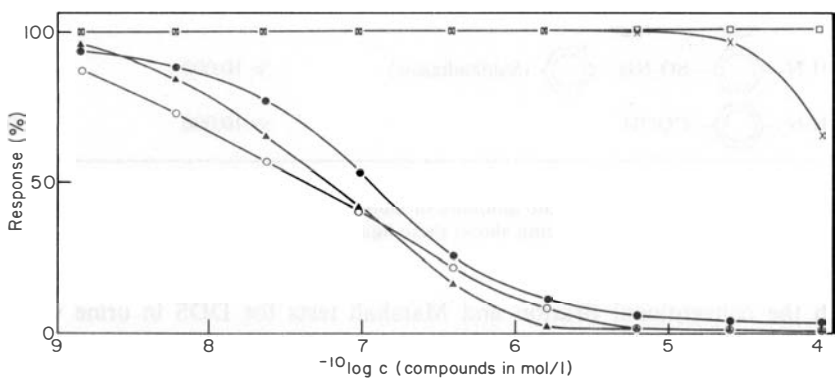


Fig. 5. ELISA inhibition curves for some sulphones and one sulphonamide.
●, DDS; ○, DADDS; ▲, MADDS; ×, Diphenylsulphone; □, Sulphadiazine. (100% response = no inhibition).

Discussion

Our final goal is to develop a simple and sensitive ELISA inhibition technique for the demonstration of dapsone in fluids. Pilot experiments with 44 urines of Kenyan leprosy patients have shown the feasibility of such a technique (Huikeshoven *et al.*, 1978). Results of the present study indicate that an ELISA inhibition technique with the E-Ig conjugate might be sensitive to 10^{-7} mmol DDS per ml, which is equal to 25 ng/ml. This compares favourably

TABLE 1
Sensitivity and specificity of E-Ig for sulphones and analogues

Compound	50% response (10^{-8} mol/l)	cross reaction (%)
1. $H_2N-C_6H_4-SO_2-C_6H_4-NH_2$ (DDS)	11	100
2. $CH_3CONH-C_6H_4-SO_2-C_6H_4-NHCOCH_3$ (DADDS)	4	275
3. $H_2H-C_6H_4-SO_2-C_6H_4-NHCOCH_3$ (MADDS)	6	183
4. $H_2N-C_6H_4-SO_2-C_6H_4-NHSO_3K$	6	183
5. $H_2N-C_6H_4-SO_2-C_6H_4-NO_2$	7	157
6. $H_2N-C_6H_4-SO_2-C_6H_4-NHOH$	10	110
7. $H_2N-C_6H_4-SO_2-C_6H_4$	10	110
8. $C_6H_5-SO_2-C_6H_5$ (Diphenylsulphone)	> 10,000	< 0.1
9. $H_2N-C_6H_4-S-C_6H_4-NH_2$	> 10,000	< 0.1
10. $H_2N-C_6H_4-SO_2NH-C_4H_3N_2$ (Sulphadiazine)	≫ 10,000	≪ 0.1
11. $H_2N-C_6H_4-COOH$	≫ 10,000	≪ 0.1

The 100% response value is the O.D. 449 measured when no sulphone or analogue was added. The first column of figures indicates the amounts of sulphones or analogues needed to reduce the response to 50%. The second column shows these figures relative to the one for DDS (= 100% cross reaction).

with the conventional Bratton and Marshall tests for DDS in urine with a sensitivity in the μg/ml order (Ellard *et al.*, 1974). Neither the Bratton and Marshall reagent nor our E-Ig are absolutely specific for DDS. They cross-react with other sulphones. This is no real problem as long as there is no need for a test that distinguishes between DDS and its metabolites or conjugates. Cross-reaction with sulphonamides however, one of the real problems of the Bratton and Marshall test, is negligible with the E-Ig conjugate. The conclusion must be that an ELISA inhibition technique for DDS may be a useful development for the man in the field, if workload, cost, and shelf-life of the reagents all prove to be satisfactory. According to Voller and his colleagues (1977) ELISA stands a fair chance in these regards. If however exact information about quantities of DDS, distinguished from its metabolites and conjugates, is wanted, separation methods will be needed with unavoidable loss of simplicity and therefore loss of attractiveness for the fieldworker. Yet in sophisticated laboratories sulphones specific E-Ig might profitably be used in parallel with other sensitive analytical tools.

References

Affinity Chromatography. Principles and Methods. (1976). Pharmacia Fine Chemicals. Uppsala, Sweden.

Balakrishnan, S. (1968). Application of a spot test for detection of DDS in urine. *Lepr. India* **40,** 1.

Brattin, W. J. and Sunshine, I. (1973). Immunological assays for drugs in biological samples. *Am. J. Med. Techn.* **39,** 223.

Bratton, A. C. and Marshall, E. K. (1939). A new coupling component for sulfanilamide determination. *J. Biol. Chem.* **128,** 537.

Buttle, G. A. H., Stephenson, D., Smith, S., Dewing, T. and Foster, G. E. (1937). The treatment of streptococcal infections in mice with 4:4′ diaminophenylsulphone. *Lancet,* **i,** 1331.

Carr, K., Oates, J. A., Nies, A. S. and Woosley, R. L. (1978). Simultaneous analysis of dapsone and monoacetyldapsone employing high performance liquid chromatography: a rapid method for determination of acetylator phenotype. *Br. J. clin. Pharmac.* **6,** 421.

Ellard, G. A., Gammon, P. T., Helmy, H. S. and Rees, R. J. W. (1974). Urine tests to monitor the self-administration of dapsone by leprosy patients. *Am. J. trop. Med. Hyg.* **23,** 464.

Huikeshoven, H., Landheer, J. E., v. Denderen, A. C., Vlasman, M., Leiker, D. L., Das, P. K., Goldring, O. L., and Pondman, K. W. (1978). Demonstration of dapsone in urine and serum by ELISA inhibition. *Lancet,* **i,** 280.

Mannan, C. A., Krol, G. J. and Kho, B. T. (1977). High-speed liquid chromatographic analysis of dapsone and related compounds. *J. Pharm. Sci.* **66,** 1618.

Mulé, S. J., Bastos, M. L. and Jukofsky, D. (1974). Evaluation of immunoassay methods for detection, in urine, of drugs subject to abuse. *Clin. Chem.* **20,** 243.

Murray, J. F., Jr., Gordon, G. R. and Peters, J. H. (1971). A chromatographic-fluorometric procedure for the determination of nanogram quantities of antileprotic sulfones *J. Lab. Clin. Med.* **78,** 464.

Murray, J. F., Jr., Gordon, G. R., Gulledge, C. C. and Peters, J. H. (1975). Chromatographic-fluorometric analysis of antileprotic sulfones. *J. Chromatogr.* **107,** 67.

Nakane, P. K. and Kawaoi, A. (1974). Peroxidase-labeled antibody. A new method of conjugation. *J. Histochem. and Cytochem,* **22,** 1084.

Voller, A., Bidwell, D. E., Bartlett, A. and Edwards, R. (1977). A comparison of isotopic and enzyme immunoassays for tropical parasitic diseases. *Trans. R. Soc. trop. Med. Hyg.,* **71,** 431.

Willians, C. A. and Chase, M. W. (1967) *Methods in Immunology and Immunochemistry. Volume 1: Preparation of Antigens and Antibodies.* New York and London: Academic Press.

Wisdom, B. (1976). Enzyme-immunoassay. *Clin. Chem.* **22,** 1243.

World Health Organization (1977). WHO Expert Committee on Leprosy. *Bull. Wld. Hlth. Org. Tech. Rep. Ser.,* No. 607.

Lepr. Rev. (1979) **50,** 283–287

Selection of Sites for Slit-skin Smears

HAIDAR ABU AHMED*, AYELE BELEHU, GERALD STONER, JACOB TOUW and TSEHAI ATLAW

Armaeur Hansen Research Institute, P.O. Box 1005, Addis Ababa, Ethiopia

The results of slit-skin smears from 18 untreated lepromatous leprosy patients showed high bacteriological index (BI) and morphological index (MI) in the ears, fingers, face, buttocks and toes. Need for standardization of site of smearing is stressed. The ears, fingers, face and buttocks are suggested as standard sites for slit-skin smearing for diagnosis, follow-up and assessment of chemotherapy.

Introduction

The bacteriological status of leprosy patients is usually assessed by the slit-skin smear method introduced by Wade (1963). A detailed description of the method is given by Cochrane (1964). The bacteriological index (BI) is used as a semiquantitative assessment of the bacterial load in the sites from which smears are taken (Ridley 1964). The morphological index (MI) is the percentage of solid-stained (living bacilli) found in the smear (Waters and Rees, 1962). The MI is assumed to be a sensitive index for assessment of the efficiency of chemotherapy and for the detection of early mycobacterial resistance to antileprosy drugs. The viability of *Mycobacterium leprae* in slit-skin smears can also be estimated by the mouse footpad technique (Pearson, 1975). However, the MI, inspite of all its limitations (Chatterjee, 1973; Chang, 1977), remains the only method for routine estimation of viability of *M. leprae* in slit-skin smears.

With the increasing importance of dapsone resistance (Pearson *et al.* 1976, 1977; Waters, 1977), new antileprosy drugs and new combinations of the existing drugs are needed. To obtain a meaningful result from such drug trials there is real need for standardization of the methods of assessment of drug effectiveness.

This study was undertaken to determine the difference in BI and MI in the smears from different sites on lepromatous leprosy patients. Only untreated patients were studied because these are the ones who might usually be selected in drug trials (Rees, 1975). Six sites which showed the highest BI and MI are suggested as standard sites for slit-skin smearing.

* Present Address: Dr. Haidar Abu Ahmed, Ministry of Health, P.O. Box 303, Khartoum, Sudan.

Received for publication 3 March, 1979

0305–7518/79/040283 + 05/$02.00/0

Material and Method

Slit-skin smears are taken routinely from all new leprosy patients attending the outpatient clinic in the Addis Ababa Leprosy Hospital. Besides the six routine sites, namely, ear lobe, face, arm, back, buttock and legs, smears were taken from the dorsum of the index finger and the big toe. There was no selection of obvious lesions at the site of these smears. They were stained by a standard Ziehl-Neelsen technique (heat fixation, carbol fuchsin for 10 min, differentiation in 10% sulphuric acid for a few sec, counterstaining with brilliant green for 5 min). All smear preparation, staining and reading was done by the same technician who does the routine laboratory work. The BI is recorded for each site according to Ridley's scale (Ridley 1964) and the MI as the percentage of the morphologically solid-stained bacilli found in the smear.

Results from 18 newly diagnosed untreated lepromatous leprosy patients seen over the period May 1978 to January 1979 were examined. All the patients have an average BI of 2 or more.

TABLE 1

Bacteriological and Morphological Indices from 18 Untreated Lepromatous Leprosy Patients

Indices	Ears	Fingers	Faces	Buttocks	Toes	Legs	Arms	Backs
BI	4.5* ± 0.1	4.5 ± 0.1	4.2 ± 0.1	4.2 ± 0.1	4.0 ± 0.1	3.8 ± 0.1	3.5 ± 0.1	3.0 ± 0.2
MI	14.3 ± 0.5	13.0 ± 0.9	12.5 ± 1.0	11.8 ± 1.1	10.8 ± 0.9	10.2 ± 0.2	10.6 ± 1.0	8.3 ± 0.8

* Mean of 18 readings ± standard deviation.

Results

The mean values of BI and MI from the different sites of the 18 patients are shown in Table 1. Comparing all 8 sites the BI and MI were highest in the smears taken from the ears. The finger smears gave BI and MI results as high as the ears in most of the patients and were always higher than in the other sites. Smears from the face and buttocks showed similar BI and MI. The BI and MI of the smears from the toes were lower than those of the fingers but were always more than those from the back which gave the lowest results. There was a direct correlation between BI and MI in all sites in all the patients.

Discussion

Slit-skin smears have been used by different workers both for diagnosis and assessment of efficiency of drug therapy. There has been no uniformity in the selection of skin sites for slit-scraping or in the number of sites scraped. The nasal-scraping which was at one time used routinely (Browne, 1966, 1967;

Dharmendra, 1967; Doull, 1961) is no longer in general use. The main reasons for exclusion of the nasal smear are the possibility of contamination of smear by non-pathogenic acid fast bacilli (Cochrane, 1965) and hence the possibility of giving a false positive result, variation in the results from different areas within nasal cavity (Davey and Barton, 1973) and the inconvenience the nasal cavity smears caused to the patients.

The number of sites smeared by different leprologists vary widely. Davison (1961) used four sites for follow-up of his patients. Dharmendra (1967), Browne (1959, 1966), recommended six sites as routine for diagnosis. Six sites were also used by Leiker and Carling (1969) and Garrod and Ellard (1968) for assessment of efficiency of drug therapy. Jopling (1965) recommended eight sites as routine for diagnosis. Eight sites were also used by Doull (1961), Browne (1965, 1966, 1967) for drug assessment and follow-up of patients. Cochrane (1964) recommended eleven sites for diagnosis, while others (Bryceson and Pfaltzgraff, 1973) recommend six to eight sites without specification. Levy (1969) recommended only one site to be smeared.

As leprosy workers differ in their selection of the number of sites smeared, they also differ in the specific sites smeared. Dharmendra used the ear, cheek, chin, right arm, left thigh and nose. Browne (1959) used six sites including the ear lobe, the forehead, cheek, and three active lesions. Cochrane (1964) used two ear lobes, forehead, chin, cheeks and six smears from suspicious lesions. Jopling (1965) recommended two ear lobes and six active-looking lesions.

It has been noticed (Levy 1969) that there is a wide variation both in BI and MI from different sites. Browne (1967) stressed the variation of result due to the technique of taking the smear. In a study by Gideon and Job (1965) the ears were found to have the highest BI followed by the chin, with similar results for the buttocks in males and thighs in females. The arm, chest and back showed the lowest results. Similar findings were repeated by Padma (1965).

Although serial biopsies had been recommended for the assessment of bacteriological changes (Leiker, 1971), the direct skin-slit scrape method has been shown (Izumi, 1971) to be sensitive enough to be used for bacteriological and morphological indices.

The results in this study confirm the previous finding of Gideon and Job (1965) and Padma (1965). The ears, fingers, face, buttocks give the highest BI and MI. There is correlation between BI and MI which confirm the findings of Levy (1969). Smears from the fingers show approximately 30-fold more bacilli than the back smears (BI 4.5 vs 3) and the difference in number of viable bacilli is approximately 50-fold (MI 14.3 vs 8.3). The fingers provide uniformity of sites and are more likely to yield comparable results with repeated smearing. They have also been shown (Ridley *et al.,* 1976) to be the site at which bacilli were most frequently detected.

It is evident that the highest numbers of viable bacilli are in the ears, fingers, face and buttocks. These results provide a rational basis for the selection of standard sites for skin smears. However in relapses and drug resistant cases it is important to smear newly developing lesions which may be in unexpected sites. We recommend that if six sites are to be smeared they be routinely taken from the two ear lobes, the face, the buttocks and two fingers. The problem of variation in the technique of smear taking (McDougall, 1975)

and the staining problem (Ridley and Ridley, 1971) could be overcome by the use of a single well-trained technician for all patients under study. The use of the recommended standard sites for skin smears should make the BI and MI reliable indices for assessment of new patients and response to antileprosy drugs.

Acknowledgements

The Armauer Hansen Research Institute is supported by The Norwegian and Swedish Save The Children Organizations and is affiliated with The All Africa Leprosy and Rehabilitation Training Centre (ALERT).

We are grateful for Dr Bernard Naafs and the rest of ALERT clinicians for selecting the patients for this study. We would like also to thank Ato Muzeyin Mohamed for helping with the smears and the other staff of ALERT Laboratory for their co-operation. We are also grateful to W/ro Shitaye Wolde Kidane for typing the manuscript.

References

Browne, S. G. (1959). Some observations of the bacteriological index in leprosy. *Lepr. Rev.* **30,** 174.

Browne, S. G. (1965). Leprosy in Eastern Nigeria, Reflections on cases diagnosed at Uzuakoli 1959–64. *Lepr. Rev.* **36,** 133.

Browne, S. G. (1966). Some observations on the morphological index in lepromatous leprosy. *Int. J. Lepr.* **17,** 23.

Browne, S. G. (1967). Drug trials in leprosy. Some unemphasized factors. *Lepr. Rev.* **38,** 7.

Browne, S. G. (1971). The bases of chemotherapy and immunosuppression therapy in leprosy. *Int. J. Lepr.* **39,** 406.

Bryceson, A. and Pfaltzgraff, R. E. (1973). *Leprosy for Students of Medicine,* p. 32. Churchill-Livingstone.

Chang, Y. T. (1977). Are all non-solid *M. leprae* dead? Does a negative finding in the mouse foot pad indicate that there is actually no growth of *M. leprae* in the animals? *Int. J. Lepr.* **45,** 235.

Chatterjee, B. R. (1973). Non-uniform staining and viability in mycobacteria. *Lepr. India,* **45,** 4.

Cochrane, R. G. (1964). Technique of examination. In *Leprosy in Theory and Practice,* 2nd edit., p. 612. Cochrane, R. G. and Davey, T. F. eds. Bristol: John Wright.

Cochrane, R. G. (1965). The diagnosis of leprosy with special reference to tissue defence. *Lepr. Rev.* **36,** 189.

Davey, R. F. and Barton, R. P. E. (1973). Multiple nasal smears in early lepromatous leprosy. *Lepr. India,* **45,** 54.

Davison, A. R. (1961). Six year follow-up of diphenylthiourea treatment. *Lepr. Rev.* **36,** 145.

Dharmendra (1967). *Notes on Leprosy,* p. 254. Ministry of Health Government of India.

Doull, J. A., Tolentino, J. G., Rodriguez, J. N., Guinto, R. S., Rivera, J. N., Fernandez, J. V. and Mabalay, M. C. (1961). Clinical evaluation studies in lepromatous leprosy. *Int. J. Lep.* **29,** 291.

Garrod, J. M. B. and Ellard, G. A. (1968). Appearance of resistance during prolonged treatment of leprosy with thiambutosine. *Lepr. Rev.* **39,** 113.

Gideon, H. and Job, C. K. (1965). Skin smears in leprosy. *Lepr. India* **37,** 74.

Izumi, S. (1971). Statistical calculations of the confidence interval and significant difference ranges of the morphologic index. *Int. J. Lepr.* **39,** 852.

Jopling, W. H. (1971). *Handbook of Leprosy.* Heinemann.

Leiker, D. L. and Carling, D. (1969). Second trial of low dosage of DDS in lepromatous leprosy. *Lepr. Rev.* **40,** 54.

Leiker, D. L. (1971). Assessment of bacteriological changes in leprosy based on serial biopsies. *Lepr. Rev.* **42,** 121.

Levy, L. (1969). Uniformity of the solid ratio of *Mycobacterium leprae* from lesion to lesion. *Int. J. Lepr.* **37,** 416.

McDougall, A. C. (1975). The diagnosis of leprosy: Clinical and bacteriological. *Lepr. Rev.* **46,** 79.
Padma, M. N. (1965). Choice of site for routine smearing *Lepr. India* **37,** 87.
Pearson, J. M. H. (1975). A simplification of the mouse foot-pad infection using *Mycobacterium leprae* from skin scrapes. *Lepr. Rev.* **46,** 105.
Pearson, J. M. H., Ross, W. F. and Rees, R. J. W. (1976). DDS resistance in Ethiopia. A progress report. *Int. J. Lepr.* **44,** 140.
Pearson, J. M. H., Haile, G. S. and Rees, R. J. W. (1977). Primary dapsone resistant leprosy. *Lepr. Rev.* **48,** 129.
Rees, R. J. W. (1975). Chemotherapeutic trials and their assessments. *Lepr. Rev.* **46,** (Suppl.) 17.
Ridley, D. S. (1964). Bacterial indices. In *Leprosy in Theory and Practice,* 2nd edit., p. 620. Cochrane, R. G. and Davey, T. F., eds. Bristol: John Wright.
Ridley, M. J. and Ridley, D. S. (1971). Stain Techniques and the morphology of *Mycobacterium leprae. Lepr. Rev.* **42,** 88.
Ridley, M. J., Jopling, W. H. and Ridley, D. S. (1976). Acid fast bacilli in the fingers of long treated lepromatous patients. *Lepr. Rev.* **47,** 93.
Wade, H. W. (1963). The examination of skin lesions for bacilli. *Int. J. Lep.* **31,** 240.
Waters, M. F. R. and Rees, R. J. W. (1962). Changes in the morphology of *Mycobacterium leprae* in patients under treatment. *Int. J. Lep.* **30,** 266.
Waters, M. F. R. (1977). Management of complications of sulphone therapy. *The 1st International Workshop on Chemotherapy of Leprosy in Asia,* 37–52. Manila, Philippines.

Lepr. Rev. (1979) **50**, 289–292

The Fingers as Sites of Leprosy Bacilli in Pre-relapse Patients

W. H. JOPLING, R. J. W. REES, D. S. RIDLEY*,
M. J. RIDLEY AND N. M. SAMUEL

The Hospital for Tropical Diseases, London NW1 0PE, the National Institute for Medical Research, London NW7 and the Middlesex Hospital Medical School, London W1

Two dapsone treated patients with apparently quiescent lepromatous leprosy were found to have solid-staining acid-fast bacilli (AFB) in the fingers. The viability of the bacilli from both patients was proved and dapsone resistance was established in one patient by mouse foot-pad inoculation. Subsequently both patients relapsed bacteriologically, one clinically in addition. Thus solid-staining AFB in the fingers, though there may be none seen in skin lesions, may be the prelude to relapse.

It is suggested that the dorsum of fingers is a favourable site for persister bacilli because it is cool and nerve bundles are more superficial there than in most other areas.

INTRODUCTION

It has been found that acid-fast bacilli (AFB), sometimes solid-staining, may be found in slit-skin smears from the dorsum of the fingers of long-treated patients with lepromatous leprosy when other sites are bacteriologically negative. This was the more striking in that there were no lesions on the fingers (Ridley *et al.*, 1976). These results were confirmed by Hiramalini *et al.* (1978), who obtained similar results also from the dorsum of the toes of patients with open footwear. Follow-up studies were not performed.

The purpose of the present paper is to report two cases of relapse, confirmed by mouse foot-pad inoculation, in patients in whom solid-staining AFB had previously been detected in fingers.

Case Reports

CASE 1

Mr J. T. is a Nepalese who was examined in his home country in May 1973, at the age of 21, and was found to have 5 skin lesions which were insensitive.

* Requests for reprints at Hospital for Tropical Diseases.

Received for publication 4 May, 1979.
0305–7518/79/040289 + 04/$02.00/0

There is no record of nerve examination at this time. Skin smears were negative for AFB and a skin biopsy was reported as borderline leprosy.

Progress

Treatment with dapsone was instituted and was continued (with a break of 2 months) until he was seen in London in February 1976, when a clinical diagnosis of borderline-tuberculoid (BT) leprosy was made on the strength of a moderate number of purplish skin lesions, asymmetrically situated, all flat (macular), with a fairly dry surface, and all showing some degree of sensory impairment. Eyebrows and ears appeared normal. Several nerve trunks were thickened, and there was anaesthesia over the right forearm and over both legs and feet. The first intimation of a wrong clinical classification came from skin smears; these showed a BI of 3.5+ and an SFG index of 2.0. It is noteworthy that the only solid-staining bacilli were found in the normal-looking skin on the dorsum of fingers. Histology of two skin lesions was that of subpolar lepromatous leprosy in regression. Mitsuda reaction was negative.

Treatment with dapsone was continued, and 2 months later he underwent a type 2 lepra reaction with erythema nodosum leprosum (ENL) and nerve pain, recurring over the next 3 months and requiring treatment with prednisone; there was one bout of left-sided epididymo-orchitis. By the end of July 1976 all reaction had ceased, his skin lesions appeared the same as they had done 5 months previously, and there were no new lesions. Skin smears were as follows:

Rt. ear	BI	3+	SFG	1	Lt. thigh	BI	3+	SFG 2
Lt. ear		3+		1	Rt. finger		3+	3
Upper arm		3+		2	Lt. finger		3+	3
Forearm		4+		2				

Thus although there were no lesions on the fingers (unlike the arm, forearm and thigh), bacilli in smears from fingers were as numerous as those in smears from these lesions. Once again fingers were the only source of solid-staining AFB (SFG 3).

At this time a biopsy of skin was taken from the dorsum of one of the middle fingers. This specimen weighed 0.068 g and yielded a total of 7.3×10^4 AFB, of which 2.5×10^3 were inoculated into both hind footpads of 6 thymectomized-irradiated mice. Bacilli were too few for an adequate MI, but the majority were degenerate. However, 3 of 8 footpads harvested 8 to 9 months later showed significant multiplication (28 to 40 fold increase), confirming the presence of small numbers of viable bacilli in the fingers.

The patient was re-examined in January 1977. Although his skin lesions appeared to be unaltered and there was no sign of reaction, the skin smears showed deterioration, with solid-staining AFB now present in ear lobes. The evidence of relapse at this stage was considered to warrant a change of treatment, but progress could not be followed owing to the patient's return to Nepal.

CASE 2

Mr S. S. came to England as a Pakistani student in 1957. When he was first seen in London in October 1961, aged 24, he stated that for about 5 months he

had experienced nasal symptoms consisting of blocked airway and occasional epistaxis and for about 3 months he had noticed papules on face and ears. On examination there were many skin-coloured papules on face, mostly on chin and ears, and both ear lobes were thickened. Eyebrows appeared normal. Several nerve trunks were thickened. Skin smears showed large numbers of AFB, mostly solid-staining. The histology of a papule was that of active subpolar lepromatous leprosy.

Progress

He was treated with dapsone and all skin lesions slowly disappeared. By October 1969, 8 years after commencing treatment, he had the first set of completely negative smears. His skin continued to remain normal, and smears to remain negative, until 1976 (nearly 15 years after beginning treatment), when his fingers were examined for bacilli in the course of the research study to which reference has already been made. These smears gave a BI of 3+ and some solid-staining bacilli were present, although smears from ear lobes were negative and there were no skin lesions. Six months later (January, 1977), while continuing dapsone therapy, his skin was still clear of lesions but smears taken at random gave results as follows:

ear	BI	1 + (granular)
right upper arm		1 + (some solids)
left upper arm		3 + (some solids
two fingers		4 + (some solids)

At this time a biopsy of skin was taken from the dorsum of one of the middle fingers. This specimen weighed 0.037 g and yielded a total of 4.1×10^5 AFB, of which 1.2×10^4 were inoculated into both hind footpads of 3 thymectomised-irradiated mice. All footpads harvested 8 months later showed significant multiplication (130 to 750 fold increases), confirming the presence of viable bacilli in the fingers. Bacilli harvested from these mice were passaged to further groups of untreated and dapsone treated mice, to determine their dapsone sensitivity. The bacilli multiplied in the groups of mice fed levels of 0.0001% and 0.001% dapsone, thus indicating a significant but intermediate degree of dapsone resistance.

After a further 6 months, 1 year after the finding of bacilli in fingers, macules typical of borderline leprosy were found on his back and around the waist. They looked slightly erythematous and active, but not in reaction. A biopsy of skin from one of these lesions showed an active BL lesion, which indicated that some upgrading had occurred during the period of remission. Bacilli were most conspicuous in a Meissner corpuscle.

Scanty AFB were present in nasal secretions, singly and in globi (but insufficient for animal inoculation). Evidence of relapse was conclusive. The patient responded well to a change of treatment.

Discussion

Of the two patients presented here, one had become clinically quiescent and the second apparently cured as a result of dapsone therapy, when solid-

staining AFB were discovered as a result of examining smears from the dorsum of a finger. In each case the number of viable bacilli obtained on biopsy was sufficient to infect mice, and in the second case the bacilli were proved to be resistant to dapsone at two of the three dapsone levels at which sensitivity testing was carried out. There is some suggestion of dapsone resistance in the first case also, since there was evidence that the patient downgraded from BT to subpolar LL leprosy while on dapsone therapy. In both cases these findings were followed by a relapse of the infection with the reappearance of solid-staining bacilli at other sites and, in one case, of new skin lesions. It is apparent, therefore, that the dorsum of the fingers (or toes) is the site which produces the highest BI and the greatest chance of obtaining solid-staining bacilli (Ridley *et al.,* 1976; Hiramlini *et al.,* 1978); and also that the solid-staining bacilli so discovered may predict a clinical and bacteriological relapse.

In this study the skin smears were taken from the dorsum of the first phalanx. Hiramalini *et al.* (1978) found more solid-staining bacilli in the dorsum of the terminal than the middle phalanx. The pulp and palmar aspects of the fingers have not been investigated as sites of bacilli, because they are inconvenient sites for the patient for the taking of smears. However, it seems likely that the reason why the fingers are a site of predilection for persister bacilli, drug resistant or otherwise, is that they are a cool site, and also that on the dorsal surface the relatively large deep nerve bundles are more superficial than elsewhere because of the thinness of the dermis in this position. This would not apply so much to the palmar surface where the dermis is thicker. This hypothesis is supported by some unpublished observations on finger biopsies. The nerve bundles on the dorsum were convoluted, and AFB were present in the nerve bundles and sometimes in perineurial lepromatous granulomata. Expanded nerve endings (Meissner corpuscles only) were not conspicuous and they were not much involved by AFB. Thus the preponderance of these nerve endings is not likely to be the explanation for the predilection of leprosy bacilli for the fingers, as was suggested in the earlier study (Ridley *et al.,* 1976).

References

Hiramalini, S., Joseph, N. A. and Chacko, C J. G. (1978). Concentration and persistence of bacilli in the fingers and toes of patients with lepromatous leprosy. *Lepr. Rev.* **49,** 223.

Ridley, M. J., Jopling, W. H. and Ridley, D. S. (1976). Acid-fast bacilli in the fingers of long treated lepromatous patients. *Lepr. Rev.* **47,** 93.

Lepr. Rev. (1979) **50,** 293–296

Leprosy in Preschool Age

C. R. REVANKAR*, P. R. DEWARKER†, SINGH MULCHAND** & R. GANAPATI*.

**Acworth Leprosy Hospital Society for Research, Rehabilitation and Education in Leprosy, Wadala, Bombay-400 031, India and Bombay Leprosy Project, 6/27, Amar Bhuvan, Sion (East), Bombay-400 022, India*
*** Vimala Dermatological Centre, Versova, Bombay-400 061, India*
† Bombay Leprosy Project, 6/27, Amar Bhuvan, Sion (East), Bombay-400 022, India

Examination of 4235 preschool age (1–5 years) children from various slums in Bombay revealed 20 active leprosy cases (prevalence rate of 4.7 per 1000). An analysis of pooled figures from clinics showed that preschool children formed 1.3% of the total number of patients attending these clinics. 5% were smear positive; 45% had one or more family members with leprosy (25% of the latter being bacteriologically positive). The high proportion of associated infectious cases (as compared to corresponding data for school age) indicates a strong possibility of intrafamilial infection in children of preschool age.

Introduction

The focus of attention all over the world in this "International Year of the Child" on problems related to children prompted us to study the literature from the point of view of childhood leprosy. Though there have been several publications recently (Kurian *et al.*, 1975; Ganapati *et al.*, 1976; Noussitou *et al.*, 1976; Koticha 1976) on leprosy in school-going children, we did not find any large data on the prevalence of leprosy in preschool age, (1–5 years). Bechelli *et al.* (1966) found varying prevalence rates ranging from 1.5 (Cameroon) to 2.1 (N. Nigeria) for the population in the age group 1–4 years.

We have therefore analysed relevant figures obtained from surveys from two urban field projects as well as those from clinics where patients reported voluntarily.

Observations

(a) DATA FROM THE FIELD

The field data were collected from groups of slums situated in the northern suburbs of the city of Bombay in which 2 voluntary agencies namely the Bombay Leprosy Project and Vimala Dermatological Centre are active.

Received for publication 7 June, 1979

A population of 37,399 was enumerated of which 4403 (12%) were in the preschool age group (1–5 years).

TABLE 1
Prevalence rates in various age groups

Population	Enumeration	Examination	Leprosy cases	Prevalence rate/1000
Preschool (1–5 years)	4403 (12%)	4235 (96%)	20	4.7
School (5–14 years)	9441 (25%)	8416 (89%)	127	15.0
Above 14 years	23,495 (63%)	17,276 (74%)	426	24.7
TOTAL:	37,339 (100%)	29,927 (80%)	573	19.0

1. Twenty preschool children were found to be suffering from active leprosy (Prevalence rate of 4.7 per 1000); the overall prevalence rate in the total population was 19 per 1000.
2. The preschool leprosy cases formed 3.5% of the total of 573 leprosy cases and 13.6% of the total 147 (20 + 127) childhood cases (between 1 to 14 years).
3. Of the 20 children 13 were female (Male to female ratio was 1: 2).
4. Two (10%) had the N?L* type of disease (BT-BB-according to Ridley-Jopling classification); the remaining 18 (90%) were of N* type.
5. No smear positive case was found.

(b) DATA FROM THE CLINICS (POOLED FIGURES)

An analysis of pooled data from the records from various central and peripheral treatment centres in Bombay revealed 511 leprosy cases in the preschool group and these (including 20 cases described above) formed 1.3% of 38,478 leprosy patients attending these clinics.

As many household contacts of the 511 children with leprosy as were available were examined in the clinics. The results are tabulated below, and compared with corresponding data for school age children from a previous study.

1. Familial association of leprosy in the preschool and school age group was 45% and 14% respectively.
2. 126 (25%) of the preschool cases had a bacteriologically positive (potentially infectious) case in the family. In the school group study on the other hand only 1% of the associated family cases were infectious.

* See footnote to Table 2.

TABLE 2
Clinical features of the preschool cases from the clinics

Total preschool cases	N*	N?L*	L*	Smear positive cases	Polyneuritic involvement
511	407 (79.6%)	103 (20.2%)	1 (0.2%)	23 (5%)	3 (0.6%)

* Clinical typing (field classification)
N, Nonlepromatous (Indeterminate and tuberculoid).
N?L, Intermediate forms (Borderline–BT–BL according to Ridley-Jopling scale)
L, Lepromatous.
(Classified according to the Operational Guide and Guidelines of Assessment of leprosy work in India 1969).
N cases generally had only single lesions.

TABLE 3
Clinical types of associated cases in the families of the preschool cases

Cases	No. of preschool leprosy children		Clinical types	
	With associated cases	*With smear* + ve asso. cases	Of index cases	Of asso. cases
Preschool group (present analysis)	232/511 (45%)	126/511 (25%)	L-1 N?L-91 N-140	L-85 N?L-125 N-85
School group (Ganapati *et al.*, 1978)	27/190 (14%)	2/190 (1%)	L-1 N?L-2 N-24	L-2 N?L-1 N-38

Discussion

1. The field figures showed that the prevalence rate in preschool age is 1/3 of that in the school group and 1/6 of that found in the adult-group. It may be said that for every 1 preschool case, there were 3 school age cases and 6 adult cases in the community studied.
2. Advanced leprosy in preschool children was more likely to be seen at treatment clinics than in the field.
3. The high proportion of intra-familial case association for preschool children indicates a strong possibility of intrafamilial infection.
4. The importance of this study is that the presence of leprosy in preschool children indicates that the community is endemic for leprosy.

Acknowledgements

We thank the Regional Secretary for India, German Leprosy Relief Association for permission to study the data from sponsored projects. We are grateful to the President, Acworth Leprosy Hospital Society for Research, Rehabilitation and Education in Leprosy, for financial support for the analysis.

References

Bechelli, L. M., Dominguez, V. M. and Patway, K. M. (1966). WHO Epidemiological random sample surveys of leprosy in Northern Nigeria (Katsina), Cameroon and Thailand (Khonkaen). *Int. J. Lepr.* **34,** 223.

Ganapati, R., Naik, S. S., Acharekar, M. Y. and Pandya, S. S. (1976). Leprosy endemicity in Bombay: An assessment through surveys of municipal schools. *Lepr. Rev.* **47,** 127.

Ganapati, R., Revankar, C. R., Christina and Romano (1978). Associated Cases in the Families of school children with leprosy. *Lepr. Rev.* **49,** 43.

Koticha, K. K. (1976). Case detection through school surveys in Greater Bombay. *Lepr. India* **48,** 819.

Kurian, P. V., Vasundhara V. and Devanbu, D. (1975). School survey as an effective method for leprosy control in rural areas. *Lepr. India* **37,** 45.

Noussitou, F. M., Sansarricq, H. and Waeter, J. (1976). *Leprosy in children,* pp. 1–18. WHO Publication.

Operational Guide and Guidelines of Assessment of Leprosy Control work in India. (1969). Govt. of India Publication, p. 61.

Lepr. Rev. (1979) **50,** 297–302

Duration of Treatment for "Disease Arrest" of Non-Lepromatous cases and Relapse Rate in these Patients

V. EKAMBARAM

Elep Dharmapuri and Damien Foundation in India, Madras

This is a study of 1879 patients declared disease arrested in the Elep Leprosy Project, Dharmapuri. The study analyses the duration of treatment needed for rendering a patient disease inactive and disease arrested and the number of relapses occurring among these cases. The relapses have been analysed with references to the maintenance and total treatment the patients had before relapse, and the periodicity of relapse, after being declared disease arrested with a view to determining the minimum treatment needed for disease arrest, the surveillance needed after discharge from treatment, etc.

Introduction

When a person diagnosed of suffering from leprosy gets over the initial psychological shock, he then asks his physician whether the disease is curable and if so the duration of treatment needed. Hence the main objective of health education about leprosy is not only to assure the patients and the public that leprosy is curable but also to state the approximate duration of treatment needed. Though we always tell the public that leprosy is curable, still, we fight shy of using the word "cured" but use various expressions to denote the same viz., released from control, disease arrested and lesions resolved. But among the above, the most preferable is disease arrested and so this expression is used in this paper to denote cure. Since we want to give as accurate an answer as possible as to the period of treatment needed for disease arrest, we decided to find out from a study of patients declared disease arrested the period of treatment needed for rendering a non-lepromatous patient disease inactive, the maintenance therapy needed thereafter till they are declared disease arrested, and the total duration of treatment for being declared disease arrested, with reference to the number of patches, involvement of nerves and also the

Received for publication 7 June 1979.
0305–7518/79/040297 + 06/$02.00/0

regularity of treatment. We have also studied the relapse rate and the relationship of relapse to such variables as duration of maintenance therapy, regularity of treatment and number of patches in these patients.

Materials and Methods

This paper is based on the findings in the patients declared "disease arrested" in the Elep Leprosy Control Project, Dharmapuri.

SELECTION OF PATIENTS FOR STUDY

All the non-lepromatous patients (only 'T' or 'M.A.' cases) declared "disease arrested" in 18 subcentres, started on therapy between 1968 and 1974 and declared "disease arrested" till the end of 1977 have been analysed in this paper.

Drug for therapy in all these cases was D.D.S. given orally (400 mg a week).

Criteria for declaring "disease arrested" are those laid down in the operational guide of the Government of India (by a committee consisting of senior leprologists of India).

The criteria are as follows: 1. For non-lepromatous 'T' or 'M.A.' (1) one and a half years after the patient is declared "disease inactive" during which period treatment is continued in full dosage.

Treatment was by medical officers at monthly clinics at various subcentres.

ASSESSMENT OF CASES

Periodical assessment of cases was done every year for declaring a patient "disease inactive" or disease arrested. Quite a few patients became irregular or were absent for treatment after being declared inactive. In such cases, the condition of the patient at the end of the specified period after being declared "disease inactive", (one and a half years) was taken as a guide to declare him "disease arrested" and not the actual period of treatment taken. After being declared disease arrested and discharged from treatment, patients were examined periodically by the medical officer at the clinics for 2 years and thereafter, the para-medical worker kept them under observation by home visits.

DEFINITIONS

Few patches
Multiple patches: more than 2 but less than 5
Nerves involved : either one or more nerves
} at the time of start of therapy

Disease inactive is the stage at which no signs of activity of the disease are present.

Disease arrest is synonymous with release from control.

Maintenance therapy is treatment given after being declared "disease inactive" and before being disease arrested.

TABLE 1

Total non-lepromatous patients declared "disease arrested" till end of 1977	No. of these studied in 1978	No. among these with few patches	Patients with multiple patches
4990	1879	1441 or 76.6%	438 or 23.4% of the total declared "disease arrested"

FINDING OF STUDY

The total number of patients declared "disease arrested" ('T' and 'M.A.' cases) is given in Table 1.

COMMENTS

Out of the total cases declared "disease arrested" the majority 76.6% are those with few patches, whereas only 23.4% are those with multiple patches. It is of interest to state that among patients with multiple or few patches, if the nerves are involved, only few patients have become disease arrested.

Out of 1441 patients with few patches, 303 or 21% with nerve involvement have become disease arrested. Similarly, 177 out of 438 patients or 41% of patients with multiple patches and with nerve involvement have become disease arrested.

Duration of Treatment for becoming "Disease Inactive" (Sign Free).

As regards the period of treatment needed for a non-lepromatous case to become disease inactive, it is found that: (a) those with few patches need an average of 179 weeks of treatment; (b) those with multiple patches need an average of 200 weeks of treatment.

Even among these, it is seen that those with *nerve involvement* among patients with *few patches* need 181 weeks of treatment.

Those with *nerve involvement* among patients with multiple patches need *205* weeks of treatment.

So, involvement of nerve prolongs the duration of treatment needed for disease arrest.

Maintenance Therapy

It is of interest to study the duration of maintenance therapy the patients needed before being declared "disease arrested". (a) In total, a non-lepromatous case needs 106 weeks (a patient with few patches needs only 98 weeks whereas one with multiple patches needs 114 weeks of maintenance therapy.

Total Duration of Treatment for being Declared "Disease Arrested"

(a) Among those with few patches with or without nerve involvement duration of treatment is 277 weeks and (b) among those with multiple patches with or without nerve involvement 319 weeks.

On an average, a non-lepromatous case needs about 296 weeks for becoming "disease arrested".

COMMENTS

It is seen that an average of 6 years of treatment is needed for a non-lepromatous case for becoming disease arrested.

Regularity of Treatment with Reference to "Disease Arrest"

A study has also been made to find out the relationship of regularity for treatment with the number of those declared "disease arrested" about which information is given in Table 2.

TABLE 2

	Declared disease arrested among		
Total no. of patients declared "disease arrested" in non-lepromatous cases	Those who took very regular treatment i.e., above 50% of the total treatment	Irregular between 25% to 50% of the total treatment	Who were grossly irregular i.e., treatment below 25% of the total treatment or absent.
Adult: 1637 ChildrenL 242 Total: 1879	1185	355	339

COMMENTS

In general regularity of treatment has been found to help in "disease arrest" since the majority of patients declared "disease arrested" are those who have taken treatment regularly whereas among those that were irregular or absent, only a minority became "disease arrested".

Relapse Rate Among Patients

The total number of patients relapsed among the "disease arrested" is 34 consisting of 31 adults and 3 children.

The relationship of relapse with the number of lesions is given in Table 3.

COMMENTS

There has been in total a relapse rate of 1.8% in the non-lepromatous cases released from control as "disease arrested". The relapse rate among adults is

TABLE 3

Cases relapsed up to 1978			No. of cases relapsed according to no. of patches in non-lepromatous cases	
18 Adults	Children	Total	Those with few Patches	Those with Multiple Patches
0				
31	3	34	23	11

1.9% and among children slightly lower i.e., 1.2%.

Analysing it further, it is seen that among the 'N' cases, with few patches the relapse rate is 1.6% whereas the relapse rate in those with multiple patches is higher i.e., 2.5%.

Hence patients with multiple patches are at greater risk of relapse of the disease.

Time Factor in Relapse

A study has also been made to determine the period of time elapsing between being declared "disease arrested" and relapse, the findings of which are presented in Table 4.

TABLE 4

No. of cases relapsed	Time interval between being declared "disease arrested" and relapse.					
	After 1 y	After 2 y	After 3 y	After 4 y	After 5 y	After 6 y
34	4	15	6	5	3	1

COMMENTS

The maximum number of relapses have occurred in the first 2 years after discharge. Later on, there is a steady decline in the number of relapses. So, it is imperative that patients discharged from treatment should be under observation for at least 3 years after discharge from treatment.

It is also of interest to study the relationship between the duration of maintenance therapy and number of relapses in Table 5.

NOTE

Though the total patients declared "disease arrested" are 34, only 22 among them were regular for treatment (maintenance therapy) after being declared "disease inactive" for whom the duration of maintenance therapy with reference to relapse is presented in the Table 5.

TABLE 5
Relationship between maintenance therapy and release

Total no. of relapsed	No. of patients relapsed studied with reference to maintenance therapy	Average period of maintenance therapy of the patients declared disease arrested and who have relapsed in non-lepromatous cases					
		1½ yr	2 yr	2½ yr	3 yr	3½ yr	4 yr
34	22	14	4	2	2	—	—

COMMENTS

It is seen that the maximum relapses have occurred in those who had a maintenance therapy up to 2 years and the relapses reduce as the duration of maintenance therapy increases.

Certain Interesting Features about the Relapsed Cases

Among the 34 relapsed cases, 8 (only adults) have changed type, 3 to B.L. and 5 to B.T. It is gratifying to note that none of the child cases, who have relapsed changed type to 'B' or 'B.L'.

Conclusion

From the findings of this study in non-lepromatous cases, it is evident that patients with multiple lesions and involvement of nerves need longer treatment for disease arrest since they have greater likelihood of relapse. Also the relapses are more with shorter periods of maintenance therapy. Patients declared disease arrested need to be under surveillance for at least 3 years after discharge from treatment.

A non-lepromatous patient needs an average of 6 years of therapy to become disease arrested.

References

Parikh, A. C., Chulawala, R. G. and Ganapati, R. (1973). Criteria of discharge of leprosy patients from control. *Lepr. India* **45**, 206.

Vellut, C., Lechat, M. F. and Misson, C. B. (1979). Maintenance therapy in non-lepromatous leprosy. Paper XI, 281, Eleventh International Leprosy Congress, Mexico, November 1978. *Int. J. Lep.* (1979), **47** (suppl.), 432.

Lepr. Rev. (1979) **50,** 303–306

Leprosy and the Community

THIRTY-SECOND WORLD HEALTH ASSEMBLY

LEPROSY

The Thiry-second World Health Assembly,

Recalling resolutions WHA29.70 and WHA30.36 and previous other resolutions both of the World Health Assembly and the Executive Board;

Noting:

(a) the progress made throughout the world since the adoption of the above resolutions—particularly in studies of ultra-structure, histochemistry, bacteriology, immunology, chemotherapy and prophylaxis;

(b) that leprosy, in spite of such advances, is still a major public health and social problem in some countries of Africa, Asia, Latin America and Pacific Islands;

(c) that urgent and resolute steps will be necessary to control leprosy if the concept of Health for all by the year 2000 is to become a practical possibility, since the periods of incubation and infectivity of leprosy may extend up to a considerable number of years;

1. URGES Member States with endemic leprosy to:

(1) allocate adequate resources to carry out effective leprosy programmes, including training of their own personnel;

(2) support treatment, physical and social rehabilitation and vocational programmes for leprosy patients to make them self-reliant and self-supporting;

(3) review the current practices of isolation of leprosy patients in specialized institutions, where this exists, in order to achieve their progressive integration as active and fully accepted members of society;

2. REQUESTS the Director-General to:

(1) intensify the Organization's activities for leprosy control in the next decade, in contribution to the attainment of the objective: Health for all by the year 2000;

(2) cooperate with Member States with endemic leprosy to develop effective programmes for prevention and treatment of leprosy;

(3) continue to mobilize resources from extrabudgetary sources both for the leprosy control programme and for the Special Programme of Research and Training in Tropical Diseases, particularly for epidemiological surveys and chemotherapeutic trials, and to promote relevant research for the development of new drugs as well as in the field of immunology with the objective of producing a vaccine for prophylaxis; and

(4) report to the Thirty-fifth World Health Assembly on the steps taken.

Fourteenth plenary meeting, 25 May 1979

INTERNATIONAL CONFERENCE ON PRIMARY HEALTH CARE, ALMA-ATA, USSR, 6–12, SEPTEMBER, 1978

The full description of this important conference has already been circulated by WHO, but we nevertheless draw attention to a "runner-up" information sheet numbered PHC/3, 7 June, 1978, not previously reported in this journal, which gives an excellent account of the steps, from 1973, which have given such impetus to the concept of Primary Health Care. In May 1977, at the 30th World Health Assembly, WHO's Director General stated . . .

> ". . . I submit that the main target for WHO to aim at in the coming decades should be the enjoyment of a level of health by all citizens of the world by the year 2000 that will be conducive to a high social and economic productivity."

And in May of the following year, 1978, Unicef's Executive Director said. . .

> "In 1980, for the countries where UNICEF cooperates in programmes, we can assume that some 100 million children aged 0–6 will have access to health services—and some 400 million children will be without access."

(Anyone who has reservations about the physical effects on children without this access would be well advised to read—and to look at some of the pictures—in the most recently published Magazine of the World Health Organisation *"World Health"*, July, 1979)

WHO:

The use of formulated plans of action for national leprosy control programmes (a hypothetical plan for uniform strategy). WHO document LEP/79.1. Original: English.

This very practical document, recently issued by WHO, should be studied by all those concerned with leprosy control. It outlines in detail, and with great attention to the need for economy, appropriate to most of the areas concerned, how the job should be done with the knowledge and drugs currently at our disposal. There is an interesting, clear-cut recommendation on page 12 for the use of clofazimine with dapsone for all newly diagnosed lepromatous and borderline cases (rifampicin not being mentioned in this context). For proven or strongly suspected dapsone resistance,

> "combined therapy with two drugs other than dapsone is to be given. This should consist of 600mg of rifampicin with clofazimine 100 mg daily. This combination should be given for a duration of 2–3 months after which time clofazimine should be continued indefinitely with 100 mg three times a week."

NEWSLETTER
Special Programme for Research and Training in Tropical Diseases No 13. June 1979

THE SECOND ANNUAL REPORT of the Special Programme is now available for general distribution. It contains an Overview of the entire programme, as well as reports of the activities of each programme component up to 30 June 1978. The reports of the Scientific Working Group meetings held during the reporting period are available as annexes. To request a copy of the report please complete and return the form attached at the end of this Newletter.

The section reporting progress on leprosy has the following headings–
Continued Priority for Armadillo-derived *M. Leprae* Supply.
Standard Safety Requirements for Preparation of Lepromin.
Dapsone Resistance Surveys.

(The Annual Report referred to above can be obtained on application to the Office of the Director, Special Programme for Research and Training in Tropical Diseases, WHO, 1211, Geneva, 27, Switzerland. Bona-fide applicants may of course also obtain, from the same address, the *Newsletter,* which, for most of us, is by far the most readable way of following the progress on the 6 subjects of this programme.)

"Crusade against Leprosy". By P. K. J. Menon. From World Health, the Magazine of the World Health Organisation, May, 1979

The sub-heading reads "Out of the 12 million leprosy cases in the world, one quarter are in India. The Government is using the primary health care approach in trying to curb the spread of this ancient scourge." And the final paragraphs summarize the approach envisaged. . . .

> "The Government of India is using multipurpose and community health workers in the campaign. India launched its first integrated community development programme, including primary health, back in October 1952. Since then, several national health programmes were introduced at various times, and in 1973 the multipurpose workers' programme was started, providing primary health care services through an integrated approach. Hitherto large numbers of health workers with differing objectives might all be working in the same area. Now teams of health workers will deliver a package of primary health care to their assigned population.
>
> In October 1977, exactly 25 years after the launching of the community development programme, the Government began its rural health scheme, with the community health worker (CHW) at the village level as the base. There will be one CHW for every village or community with 1000 population, selected by the community and operating as an agent of social change. The emphasis is on community participation with its philosophy of placing 'people's health in people's hands'. As regards leprosy, the work of the CHW will be mainly educational, promotional

and social, and the multipurpose worker will be responsible for diagnosis and treatment since these require specialized training.

The Government entrusted anti-leprosy work to the multipurpose workers in 28 districts in June 1977 and in another 60 districts in November 1978. The remaining districts will be covered within the next five years. Success will largely depend on their proper training and motivation for this work.

There is every reason to hope that, by the next decade, the foundations will have been well and truly laid for gaining full control over leprosy, and India will be well on its way to eradicating this disease. What would bring this goal much nearer would be the hoped-for break-through by research scientists, who are already striving hard to develop an anti-leprosy vaccine."

Lepr. Rev. (1979) **50,** 307–313

Field Workers Forum

(Even at the risk of repetition, we continue to supply under this heading, information which may be of value to medical and para-medical field workers. Its general object is that it should, (1) help people to do their work more effectively and (2) enable them to analyse and report findings, chance observations — and difficulties — for the information of others working in leprosy. *Editor.*)

The Leprosy Mission, 50 Portland Place, London W1N 3DG. Books and Pamphlets available from TLM, June 1979.

Miss Jane Neville has very kindly supplied the following list and information. The letters shown on the left of each item in brackets have the following meaning —

(L)= Any literate person. (A)= Auxiliary. (P)= Trained nurse, programme manager or other professional. (D)= Doctor. (S)= Specialist.

(A) *A Guide to Leprosy for Field Staff*

W. F. ROSS (ALERT Addis Ababa); Publisher–African Medical and Research Foundation; 1977; Revised edition; 62 pages; many diagrams and illustrations.

This book is for the paramedical worker and is written in simple English.

(D, P) *The Diagnosis and Management of Early Leprosy*

S. G. BROWNE; Publisher– The Leprosy Mission, London; Revised edition 1979; 35 pages with illustrations.

(P, D) *Memorandum on Leprosy Control*

S. G. BROWNE; Publishers–jointly–Oxfam, LEPRA and The Leprosy Mission; 1976; 27 pages. Outlines in simple and mainly non-technical language the modern approach to leprosy control.

(A) *A Practical Guide to the Diagnosis and Treatment of Leprosy in the Basic Health Unit*

H. W. WHEATE & J. M. H. PEARSON (ALERT Addis Ababa); Publisher–German Leprosy Relief Association (DAHW); 1978; 26 pages; illustrated.

Written for health centre staff in Africa, and it aims to help any member of the team diagnose leprosy accurately and to initiate treatment.

(P, D) *Essentials of Leprosy*

Ed. J. M. H. PEARSON & H. W. WHEATE (ALERT Addis Ababa); Publisher–German Leprosy Relief Association (DAHW); 1979.

(P, A) *Physical Therapy in Leprosy for Paramedicals*

ELLEN DAVIS KELLY; Publisher–American Leprosy Missions Inc.; 1978; 235 pages; Bibliography; diagrams.

This manual covers everything a paramedical should know in order to give good physical therapy care to patients.

(A, P) *Anatomy and Physiology Prerequisites for Physical Therapy Technicians in Leprosy Service*

Ellen Davis Kelly; Publisher–American Leprosy Missions Inc.; 1976; 174 pages.

A self-instructional work book (programmed learning) on anatomy and physiology.

(L, A) *A Guide to Health Education in Leprosy*

P. J. NEVILLE (ALERT Addis Ababa); Publisher–German Leprosy Relief Association (DAHW); Revised edition 1979; 20 pages.

A handbook on patient education and self care.

(D, P) *The Care of the Nose in Leprosy*

R. P. E. BARTON; Publishers–jointly LEPRA and The Leprosy Mission; 12 page booklet.

(D, P) *Insensitive Feet*

P. W. BRAND; Publisher–The Leprosy Mission, London; 1977; 88 pages; illustrated.

A practical handbook on foot problems in leprosy; in particular discussing ways of recognizing early signs and so making it possible to prevent deformity.

(D, P, A) *A Footwear Manual for Leprosy Control Programmes*

P. J. NEVILLE (Editor) (ALERT Addis Ababa); Publisher–German Leprosy Relief Association (DAHW); 1977.

This manual is printed in two parts–

PART I contains information for Administrators of Footwear programmes and for the prescribers of footwear or simple appliances (doctors, supervisers).

PART II is for the workshop technician; contains many drawings for the manufacture of the shoes or appliances.

(D, P) *Leprosy Control Services as an Integral Part of Primary Health Care Programs in Developing Countries*

HORST BUCHMANN; Publisher–German Leprosy Relief Association (DAHW); 1978; 80 pages; Extensive bibliography.

This booklet represents a revised version of the author's thesis submitted for a degree in public health.

(D, P) *Drugs to Combat Dapsone Resistance*

ILEP Publication No. 1; Heathrow Report 1977. Printed by LEPRA; 20 pages.

Guidelines for the therapeutic selection of drugs to be used in large scale leprosy control programmes in view of the emergence of dapsone resistance.

(A, P, D) *Drug Resistance in Leprosy*
S. G. BROWNE; Publisher–The Leprosy Mission; 6 page pamphlet.
Concerns the recognition of sulphone resistant leprosy and practical recommendations as to how to deal with it.

(L) *Danger and Safety in Leprosy*
MASAYOSHI ITOH & PAUL W. BRAND; Publisher–The Leprosy Mission; 1965; 44 pages.
Cartoon pictures designed for the literate patient but which could also be used as a basis for designing posters.

(A) *Partners*
A magazine for paramedical workers in leprosy; Publisher–The Leprosy Mission; twice a year; 20 pages; illustrated.
NOTE–To receive PARTNERS in India, Nepal, Bhutan, Sri Lanka, Burma, write to The Leprosy Mission, Massey Hall, Jai Singh Road, New Delhi 110001.
A French edition is available from: La Mission Évangélique contre La Lépre, chemin de Rêchoz, 1027 Lonay/VD, Switzerland.

(D, P) *Handbook of Leprosy*
W. H. JOPLING; Publisher–Heinemann Medical Books Ltd., London; 1978; 139 pages; illustrations and bibliography; second edition. £3.75

(D, P) *Leprosy*
A. BRYCESON and R. E. PFALTZGRAFF; Publisher–Churchill Livingstone; 1979; second edition. £4.00

(S, P) *Reconstructive Surgery in Leprosy*
E. P. FRITSCHI; Publisher–John Wright & Sons Ltd., Bristol *but* available from The Christian Literature Society, Post Box 501, Madras 600 003. 1971; 225 pages; illustrations and bibliography.
Handbook for surgeons, but physiotherapists and occupational therapists in the reconstructive surgery or rehabilitation team will also find it useful.

(P, D) *WHO Expert Committee on Leprosy*
5th Report; WHO Technical Report Series No. 607, 1977 £1.68

(P, D) *Leprosy in Children*
WHO; 28 pages; excellent colour photographs

Publications may also be obtained direct from their publishers:

African Medical and Research Foundation,
P.O. Box 31025,
Nairobi, Kenya.

American Leprosy Missions Inc.,
1262 Broad Street,
Bloomfield, New Jersey 07003, U.S.A.

German Leprosy Relief Association (DAHW),
D 8700 Wurzburg,
Postfach 348, Germany.

Churchill Livingstone,
Longman Group Ltd.,
Ravelston Terrace,
Edinburgh, Scotland.

LEPRA,
Fairfax House,
Causton Road,
Colchester CO1 1PU,
Essex, England

World Health Organization,
Geneva,
Switzerland.

William Heinemann Medical Books Ltd.,
15 Queen Street,
London W.1.

Voluntary Health Association of India,
C-14 Community Centre,
Safdarjung Development Area,
New Delhi–110 016, India.

Films on Leprosy produced in October–November, 1978 by NSL
Nederlandse Stichting voor Leprabestrijding (NSL), Mauritskade 63,1092 AD Amsterdam

KARIBU (Be Welcome)
A film by: Manus van de Kamp
Camera: Garmt Koopmans
Time Length: 31 min./15 sec.
Sound; optical
Location: Kenya.

"Leprosy is neither a curse, nor a hereditary disease. Neither can one contract it from the eating of fish, nor of goat's flesh, nor even of cassava. Leprosy is a disease, that, just like so many other types of illness, is caused by a "Dudu" (an insect), a bacillus. Yet this type of illness can be cured, if one reports straight to the nearest health centre when spotting the very first signs of the disease, and if one will take without fail the "Dawa" (tablets), prescribed by the doctor.

In that case these horrible "Dudus" won't stand a chance to transmit the disease to other, still healthy people, and the disease won't be able to lead to paralysis or mutilation.

For this very reason, one can with all one's heart say: 'Karibu", Be Welcome, to a leprosy patient, who never fails to take his tablets, as a fully accepted member of our society."

KUSTA (Leprosy)
A film by: Manus van de Kamp
Camera: Garmt Koopmans
Time Length: 27 min./30 sec.
Sound: optical
Location: Indonesia (Tangerang near Jakarta, Surabaya and Sulawesi, formerly Celebes.

"More than 140 million inhabitants, scattered across the Indonesian archipelago, consisting of over 13,000 islands. This is but one of the problems the Indonesian Authorities are facing in their campaign against leprosy. In some of the islands the population is so dense, that the chances of the spreading of leprosy are higher, than in the less densely populated areas of the world. So there one not seldom shows a deeply rooted fear of the disease, that they call "Kusta" (a word taken from the Sanskrit), the mean disease,

mutilating people and bringing about intense human suffering. This film will try and give the audience a picture of to-day's efforts applied in Indonesia to establish an effective control system of the still widely endemic disease in this part of the world."

MORBUS HANSEN (Hansen's Disease)
A film by: Manus van de Kamp
Camera: Garmt Koopmans
Time length: 25 min.
Sound: optical
Location: Kenya and Indonesia

"History sometimes leads to the conclusion that for a long time the campaign in the fight against leprosy was aimed at the leprosy patient, rather than against the very cause, namely: the leprosy bacillus (the Mycobacterium Leprae), discovered by the Norwegian medical doctor Gerhard Henrik Armauer HANSEN in 1873. Yet this seemingly obvious conclusion appears on critical examination far from justified. For if ever the leprosy patient was discriminated against, and even banned from society in those days, it merely happened because of the fact that there was just no herbal cure for it.

This "herb" was discovered only after World War Two, when in 1948 DDS, diamino difenyl sulfon, was found to serve as an extremely effective chemo-therapeutic medicine (other chemo-therapeutic medicines, though far more costly, have meanwhile been developed).

This film wishes to confront the audience with some aspects of modern leprosy control, both in Indonesia and Kenya. For example the school (random) surveys play an important role in the continuous hunt for this disease in its most early stage."

Copies can be ordered through NSL, Amsterdam
Costs: HFL. 2.000,–per copy with English commentary, unaltered.
HFL. 2.00,–per copy with Dutch commentary, unaltered.
HFL. 2.000,–per copy with Swahili commentary, unaltered, of KARIBU.
HFL. 2.000,–per copy with Bahasa Indonesia commentary, unaltered, of KUSTA.
HFL. 5.500,–per copy with any other commentary.
HFL. 2.000,–per each extra copy of the same commentary.
Above quotes do not include shipping costs.

We reprint the following entry with grateful acknowledgement to the Journal of Tropical Medicine and Hygiene.

MEDDIA, INTERNATIONAL SLIDEBANK OF TROPICAL DISEASE

The Royal Tropical Institute of Amsterdam in association with the Council of European Schools of Tropical Medicine are producing a series of ten visual reading programmes on parasitic diseases.

The first on the market is one on Schistosomiasis. The issue consists of a microfiche handviewer, a sheet of 84 microfiche coloured photographs and a fifteen page explanatory booklet on the pictures. The booklet associated with the coloured photographs is excellent. The booklet starts with a brief account of the life history of schistosomiasis and then there are brief descriptions of all 84 photographs which cover the life history of the parasite and the clinical symptoms of the disease. The handviewer however is rather disappointing and focussing can be a problem but at a price of only $2 perfection can not be expected. Schistosomiasis is the only disease so far presented but leprosy, malaria, trypanosomiasis and basically all the tropical parasitic diseases will follow making up a total of ten issues. At $9 per disease with picture strip and instruction booklet this is a good production. At a total cost of $65 for all ten diseases including the viewer it is excellent. It can also be purchased as unmounted slides at $15 per disease or $130 the set.

The Royal Tropical Institute are to be congratulated on this production.

ROYAL TROPICAL INSTITUTE, AMSTERDAM

APPROPRIATE TECHNOLOGY FOR HEALTH DIRECTORY, December 1978, WHO, GENEVA

This is a 75-page, paperback, Directory, issued by WHO, compiled by the Appropriate Technology for Health Programme (ATH), giving information on 382 organisations, institutions and individuals in 75 countries. It is an extremely valuable document, covering a wide range of health and related disciplines, with a brief summary of the main activities and interests under each entry, and the address. The Introduction includes a plea that all those working in ATH should complete a questionnaire, so that their information may be included. Individuals and agencies working in leprosy should take note of this, since the subject is as yet by no means fully listed in this Directory.

WHO PUBLICATIONS; CATALOGUE 1947–1977

We have previously drawn attention to this complete list of WHO publications. The previously well known "Guide to Leprosy Control" (1966) is a reprint of WHO document PA/66.214. More recent publications on leprosy in this Catalogue include:—

*NOUSSITOU, F. M. ET AL. (1976)
Leprosy in Children
WHO publication, Geneva, 28 p. illus. Available in English, French, Spanish.

*SANSARRICQ, H. (1976)
La Lèpre. Epidémiologie–Principles de lutte
3ème Cours International en Langue Française de Surveillance Epidémiologique et de Lutte Contre les Maladies Transmissibles, Genêve, 5–9 avril 1976 WHO document code not indicated. Available in French only.

*WALTER, J. ET AL. (1976)
Formulation of a Leprosy Programme
WHO document LEP/WP/76.4. English only. Paper presented at the WHO Expert Committee on Leprosy, Geneva, 19–25 October 1976.

*GUILBERT, J. J. (1976)
How to Organize a Short Educational Workshop
WHO document HMD/76.1 addendum

*WHO Catalogue of Publications 1947--1973;
*Supplement to the WHO Catalogue of Publications, 1974–1976.

Health Centre Laboratory Manual for Tropical Countries by Monica Cheesbrough FIMLS Tech. RMS

We have previously drawn attention to this Manual which is available from Rural Communications, South Petherton, Somerset, U.K., TA13 5BS. Cost £1.50 plus 54 p. postage in U.K. and Europe; 95p and 43p postage in developing countries.

Not to be confused with this, is the preparation of a further "hospital laboratory manual for developing countries". We are indebted to the WHO Chronicle for the following entry:—

In preparation a hospital laboratory manual for developing countries

Miss M. Cheesbrough, a former WHO Temporary Adviser, is currently engaged in the preparation of a low-cost laboratory manual that can be used for both working and training purposes in district and regional hospitals in as many developing countries as possible.

Readers who have found it necessary to modify a laboratory method, to develop a new technique, or to design new equipment for the diagnosis of diseases prevalent in developing countries, and who would like to share this information with others, are requested to send full details, together with illustrations if appropriate, to Miss M. Cheesbrough, c/o Dr J. McArthur, Landbeach, Cambridge CB4 4ED, England, as soon as possible.

(Those with considerable experience in laboratory work in leprosy should remember that others may find it difficult to assess — and write — on subjects such as fluorescence in the detection of acid-fast bacilli in leprosy, nasal smears, the choice of sites for slit-skin smears, the best use of various fixatives, etc. Monica Cheesbrough would welcome correspondence.)

RURAL COMMUNICATION SERVICES, 17 St James' Street, South Petherton, Somerset, England

RCS have kindly written to remind us that amongst their many activities. they are the UK distributors for WHERE THERE IS NO DOCTOR, by David Werner. It costs £3.91, including postage (£2.40 to people in developing countries).

Lepr. Rev. (1979) **50**, 315–329

News and Notes

DR S. G. BROWNE RETIRES AS MEDICAL CONSULTANT OF THE LEPROSY MISSION

On 31 December 1978 Dr Stanley G. Browne, C.M.G., O.B.E., M.D., F.R.C.P., F.R.C.S., retired as Medical Consultant to The Leprosy Mission, a position he had held since his return to the United Kingdom in 1965, following a distinguished career as a missionary doctor in Zaire (then Belgian Congo) and later as Government leprologist in Nigeria.

As Medical Consultant Dr Browne contributed significantly to the development of progressive medical policies within and beyond The Leprosy Mission, serving on its Executive, and Planning and Development Committees, and continually advocating policies which combined the best of modern scientific thought and technology with a Christian concern for the needs of the individual.

As a travelling teacher Dr Browne's scholarship and enthusiasm has enlivened leprosy seminars organized by the Mission in many countries around the world, from Korea to Swaziland.

On 21 July, a lunch, was held in London to honour Stanley and Mali Browne, and a small presentation was made on behalf of the Mission.

Dr Browne is succeeded as Medical Consultant to the Mission by Dr M. F. R. Waters, O.B.E., F.R.C.P., M.R.C.Path.

A. D. ASKEW

THE THIRD NATIONAL CONGRESS OF THE INDONESIAN SOCIETY FOR DERMATO-VENEREOLOGY

This Congress will be held on 31 May–4 June, 1980, in Medan, North Sumatra, Indonesia. Purpose; to exchange knowledge and experience on current problems in dermatology, verereology and leprosy. For further information please contact:—

Dr Marwali Harahap, Department of Dermatology, School of Medicine, University of North Sumatra, Rumah Sakit Umum Pusat, Jln. Prof. H. M. Yamin SH 47, Medan, Indonesia.

INTERNATIONAL CALENDAR OF BIOMEDICAL CONFERENCES, WORKSHOPS AND SYMPOSIA,
issued bi-monthly by the Fogarty International Centre

The Fogarty International Center is conducting a 1-year feasibility study to determine if a useful list of biomedical research meetings can be developed and

distributed. Its success will depend largely upon the cooperation FIC receives from all persons concerned.

Some meetings listed here are confirmed, others still tentative. FIC cannot assume reponsibility for the accuracy of material submitted.

Information may be submitted to, or copies received from: Mrs Toby P. Levin, Conference and Seminar Program Branch, Fogarty International Center, National Institutes of Health, Building 31, Room 2C15, Bethesda, MD 20205, USA, (301) 496–2516.

THE TANZANIA HEALTH PROJECT
Overseas Development Administration/Technical Cooperation, The British Government, UK.

This Project between the ODA of the British Government and the Tanzanian Government is now begininning to take shape, after a certain amount of delay due to administrative difficulties in the southern areas concerned, which are basically the regions of Lindi, Rvuma and Mtwara. Three more have been added, Rukwa, Mbeya and Iringa, though it is not yet entirely clear if these will benefit from the full coverage of the project, or specifically from TB/Leprosy control only. The Project was conceived in 1977, with a British Commitment of 2 years, with the option of extension, and funding from the British Government of over £8 million pounds sterling. The plan is basically for primary health care, with an upgraded referral hospital at Mbeya. Tuberculosis and leprosy are to be tackled together, under the overall direction of Dr Nkinda in the Tanzanian Ministry of Health. Dr Richard de Soldenhoff (UK) has recently been appointed from UK to coordinate work in the project area. Great emphasis has been placed on the proper provision of suitable microscopes from England; 1000 standard instruments will be provided for routine laboratory use, together with a further 8 special units for fluorescence microscopy. A microscope maintenance and repair centre is seen as an essential element at the outset. We await further news of the development of this important and ambitious project with great interest.

NINE-BANDED ARMADILLOS (*Dasypus novemcinctus*, Linn.); breeding and conservation experiments in the Guernsey Zoo, The Channel Islands, UK, on armadillos bred in captivity, and imported from the USA.

In May this year, the *Guernsey Evening News and Star* reported a remarkable initiative on the part of Dr David Jamison (who previously worked with Professor A. G. M. Weddell in the Department of Human Anatomy, Oxford) and the Director of the Zoo, Mr James Thomas. On 9 March, 1979, they acquired two male, nine-banded armadillos bred in captivity and imported from the United States, quarantined for 6 months in the United Kingdom, and believed to be 18 months of age on arrival. Their intention is to study these animals with a view to obtaining scientific information which may lead to the breeding of armadillos in captivity. Both animals settled down well on a diet of

dog food, raw eggs, tinned milk and added vitamins, and after initial housing in a small quarantine room, they were moved to permanent quarters, constructed of 6-inch concrete blocks and asbestos roof, heated by 6 tubular heaters to a thermostatically controlled temperature of 70°F. Two weeks after this change, one of the animals unfortunately developed features suggesting intestinal empactation, which was relieved by forcible feeding of liquid paraffin and glucose, but this recurred 10 days later, with failure to feed, leading to death. Autopsy revealed the cause of death as empactation of the small intestine, probably associated with the ingestion of excessive amounts of peat, used in bedding; examination of the other organs was completely normal.

These researchers intend to import 2 females in September, 1979, and possibly to expand the facilities to accommodate more animals in the future. The breeding of nine-banded armadillos in captivity is a matter of the utmost concern to WHO's IMMLEP and THELEP programmes, and it has not so far been confirmed by researchers working with this animal in the United States or South America. We wish Dr Jamison and Mr Thomas every possible success in this potentially very important project. [If other units in Europe, or in areas outside the Americas, are conducting similar studies on any aspect of armadillo physiology, we would be grateful to receive information for publication. This applies particularly to any conceptions and births which occur *in* captivity, as opposed to the taking in of pregnant females. *Editor*]

ACWORTH LEPROSY HOSPITAL SOCIETY FOR RESEARCH, REHABILITATION AND EDUCATION IN LEPROSY, WADALA, BOMBAY–400 031

Proceedings of the Seventh "Workshop on Leprosy".

The Seventh "Workshop on Leprosy" was held on 7 March, 1979, under the auspices of this Society at the Acworth Leprosy Hospital, Wadala, Bombay–400 031. Dr N. H. Antia, Trustee of the Foundation for Medical Research was the chairman. The following reports were presented.

1. *Prevalence of Leprosy among In patients in General Hospitals— A Preliminary Survey in Bombay*
   R. Ganapati, C. R. Revankar, S. S. Pandya, and M. Y. Acharekar.

It is our experience that a significant proportion of the adult population is not available for examination during leprosy surveys. It is in this group that a high prevalence of leprosy and a high percentage of infectious cases are found. A screening programme of 11,505 adult patients in large general and TB hospitals was undertaken. This revealed 102 leprosy cases with a prevalence rate of 8.9 per 1000. Ten were smear positive (prevalence of smear positive cases was 0.9 per 1000). One of these (ESIS hospital) showed the highest prevalence rate of 26.5 per 1000. No grade III (WHO grading) deformity patients were detected. This study indicates that such surveys provide a quick and convenient method of screening adult populations for leprosy.

Dr Antia–How many cases were known to the hospital doctors?
What was their attitude?

Dr Ganapati – None of them. 78 cases out of 102 were untreated. An assessment of knowledge about leprosy of hospital staff was attempted; but it could not be carried out because of resistance from hospital administrators.
Mr Lahiri– Is it possible to examine the adults at their place of work?
Dr Ganapati – The existing employment rules prevent us from conducting such surveys in factories because a person found to have leprosy (particularly of the infectious type) is likely to lose his job.

2. *Leprosy in Preschool Age–A Preliminary Report*
C. R. Revankar, P. R. Dewarkar, Moolchand Singh and R. Ganapati.

In this report, figures from two urban field projects and from clinics were analysed to determine the clinical epidemiological features of leprosy among preschool age group (1–5 years).

The examination of 4235 preschool children in the slums revealed 20 with leprosy (prevalence of 4.7 per 1000), the overall prevalence rate in the population of these slums being 19 per 1000.

A separate analysis of 511 cases from various clinics revealed that 5 were smear positive cases. 19% cases belonged to N?L type (BT to BL type). One child was typed as having lepromatous leprosy. The remaining had indeterminate or tuberculoid types of disease.

232 (45%) children were derived from multiple case families; 126 (25%) had an infectious case in the family. It is highly probable therefore that intrafamilial infection is very important in preschool children in endemic areas.

3. *Leprosy case detection through health education.*
V. V. Dongre, R. Ganapati, C. R. Revankar and K. R. Bankar.

The "total" population surveys are never total since as indicated above, the male adult population is incompletely covered even after repeated visits. An attempt was therefore made to enlarge case detection rate by repeated health education programmes, in the area under study in two strata of society from high and low socio-economic groups. In the low socio-economic slum population of 20,000, repeated health education revealed 120 leprosy cases (prevalence rate 6 per 1000) with 13 smear positive cases.
Dr. Antia–Have you done any comparison regarding cost-effectiveness in health education programmes and total population surveys as was done in the Pogiri and Aska projects?
Dr Dongre–This study is in progress and total population survey is still to be carried out and thus cost effectiveness of this project is not yet analysed.

4. *Dapsone injection therapy:*
K. K. Koticha, P. S. Juwatkar, and M. H. Shah.

It is now common knowledge that only a small percentage of patients attending leprosy treatment centres regularly, actually consume their dapsone tablets with any degree of regularity. To ensure therapeutic dapsone concentration in the tissues, a parenteral dapsone preparation was used. Twenty-four

lepromatous cases who had not shown improvement even after 4 years of treatment were selected for this trial. The trial is continuing with 375 mg/5 ml/injection giving a level equivalent to 50 mg DDS/day/orally. This was repeated after 7th day. Urine was collected at zero hour and 7th day just before the next injection.

5. *Multiple drug therapy.*
K. K. Koticha *et al.*

Untreated (confirmed by urine examination for DDS) lepromatous patients from the Acworth Leprosy Hospital OPD were examined clinically and bacteriologically and divided into four groups for this trial. Skin biopsies were sent both for mouse foot pad inoculation and *in vitro* study of viability by uptake of labelled DOPA and thymidine.

Group I– Rifamycin 1500 mg daily in 3 divided doses for 2 days followed by injection DADDS every month.

Group II– Rifamycin 600 mg single dose for 15 days followed by injection DADDS monthly.

Group III–Injection DADDS monthly.

Group IV–Injection DADDS monthly and oral 50 mg daily.

Group V– Rifamycin 600 mg daily for one month and injection DDS every month.

6. *Correlative histological* in vitro *electro-physiological studies in leprosy and other acrodystrophic neuropathies.*
S. S. Pandya, R. G. Chulawala and D. K. Manghani.

Electrophysiological and histological findings in sural nerve biopsies in 6 patients with plantar ulcers of non-leprous etiology are compared and contrasted with those in different types of leprosy. In nerves from the former group, there were marked abnormalities in the mylinated fibres–large and small, which appear to be important in the etiopathogenesis of plantar ulceration. The unmyelinated fibre activity was relatively unimpaired. In the leprosy nerves, on the other hand, both myelinated and unmyelinated fibre potentials were commonly altered and these abnormalities were not specific for the type of disease.

7. *Serum lysozyme in leprosy–a preliminary report.*
S. S. Naik and S. Gurnani.

Lysozyme enzyme (muramidase) is of considerable interest for its antimicrobial activity.

Serum lysozyme has been found elevated in conditions characterized histologically by epithelioid cells e.g. tuberculosis and Crohn's disease. This preliminary report of 94 serum samples from leprosy patients showed that serum lysozyme values were elevated in the following order ENL/Lepromatous/Intermediate / Tuberculoid / untreated / treated with DDS, when compared with normal controls.

THE FIRST THREE YEARS, 1975–1978
THE FOUNDATION FOR MEDICAL RESEARCH, Bombay, 84A, R. G. Thadani Marg, Sea Face Corner, Worli, Bombay, 400 018, INDIA.

A report of 29 pages on the activities of this centre has been issued, giving a most interesting account of the scientific and other achievements during this brief period. One of the projects concerns work on the early detection of leprosy and its chemotherapy, and Mr N. H. Antia, FRCS, Trustee and Research Director, has very kindly supplied the following additional information —

"In regard to Early Detection of Leprosy, we have been studying consanguinous contacts of leprosy patients, since population studies have revealed an increase in the incidence of leprosy among family members. Early studies carried out by us had shown moderate nerve involvement even in patients with less than 6 months clinical history and whose nerves appeared to be normal on clinical testing. On the basis of these observations it was felt that screening of contacts for nerve involvement by using more refined methods would help in the detection of preclinical cases of leprosy.

In the initial study nerve conduction velocity of the index finger branch of the radial cutaneous nerve was carried out, followed by nerve biopsies of selected individuals which was further analysed qualitatively, quantitatively (fibre density and size distribution), ultrastructurally and by tease fibre studies. A total of 70 nerves from 35 contacts were studied for their nerve conduction velocity; 27 nerves showed delayed average nerve conduction velocity of which 10 were biopsied. In four nerves demyelination was observed ranging from 8%–13%. Five nerves with normal nerve conduction velocity were also biopsied and one showed demyelination.

On the basis of these observations, a second study was carried out to assess the alterations in the cell mediated immunity status of the contacts. The tests so far employed have been:

1. Enumeration of T (active) & T (total) lymphocytes by the 'E'–rossette technique.
2. Leucocyte migration inhibition test to lepromin and PHA.
3. Macrophage function as studied by level of protein synthesis.
4. *In vivo* lepromin skin test.

This study is still in progress and therefore definite conclusions cannot be reached. However, a consistent increase in T_1 cells and a normal response to lepromin in leucocyte migration inhibition test indicate that the first two parameters relate to the quality of exposure.

Macrophage function of only 2 lepromatous contacts was similar to LL patients i.e. in the presence of viable *M. leprae* a depression was observed in 3H-leucine uptake. Its implication as a possible measure of susceptibility to lepromatous leprosy will have to await further follow-up studies. This parameter does not seem to assist in the early detection and/or susceptibility to tuberculoid leprosy, for which the nerve studies (nerve conduction velocity) appear more indicative. Those contacts who have similar behaviour like established cases of lepromatous or

tuberculoid leprosy will then have to be followed as individuals who may in the future show clinical symptoms. Thus it is a long-drawn-out project with no quick answers. But continued study for 3 to 4 years may give some directions and hopefully indications towards utility of such an approach.

We have several preliminary observations which are very indicative but we still need clearer supporting data."

EXCERPTA MEDICA, 1979, Volume 1, issues 3 and 4, published for Leprosy Documentation Service, Royal Tropical Institute, Mauritskade 63, 1092 AD Amsterdam, the Netherlands

Although it is now almost inconceivable that any reader of this journal, or any member of ILEP, will not be aware of the production of *"Leprosy and related subjects"* from this international medical abstracting service, we continue to draw attention to what must surely now be the most up-to-date and comprehensive source of information on leprosy publications available anywhere. Furthermore, these issues contain so much on tuberculosis and other mycobacterial diseases, that they will soon become essential reading for workers in these subjects also. The extremely rapid production and publication of these issues, with their remarkably comprehensive cover, will inevitably raise doubts about the value of laboriously collecting and publishing abstracts in leprosy journals. A further point to consider would be the free air-mailing of *"Leprosy and related subjects"* to all bona-fide clinical and research workers outside Europe and the USA.

THE HEISER PROGRAM FOR RESEARCH IN LEPROSY, 450 East 63rd Street, New York, 10021, USA.

The latest information brochure issued from the above office carries the following introduction:—

Dr Heiser set up his fund in The New York Community Trust and stipulated that income generated be used not to treat patients but to try to find a cure or preventative for leprosy. The New York Community Trust, a public foundation designed to carry out the charitable purposes of donors, met with medical experts and scientists to determine the best approach. It was decided that the three most important objectives should be: to attract the brightest, most highly motivated young biomedical scientists to train in research fields related to leprosy; to support the training efforts of laboratories and senior investigators who are experienced in leprosy research; and to promote collaborative research studies of leprosy and encourage international sharing of scientific information.

The following awards were established and are available:

Heiser Program for Research in Leprosy

Beginning postdoctoral research fellowships, small research grants, visiting research awards available. Stipends range from $12,000 to $15,000. Applicants

should have M.D., Ph.D., or equivalent degree. Applications by February 1 for awards to be activated June–December, 1980. For information write: Heiser Program for Research in Leprosy, 450 East 63rd Street, New York, NY 10021, USA.

VOLUNTARY SERVICE OVERSEAS (VSO), 9 Belgrave Square, London SW1X8PW *"Health Care in the Third World; a new policy for VSO". April, 1979.*

This is a 9-page, A4 paperback, describing an interesting and in some ways fundamentally new approach for this organization. *The Guardian* Newspaper (UK) of April 23rd, 1979, has kindly granted permission for a reprinting of their article:—

> ECONOMIC and political awareness is as important as medical training for all health personnel recruited by Voluntary Service Overseas for the Third World. This is the conclusion of a policy paper* just issued by VSO, the British organization which has over 80 health personnel working in 18 countries.
>
> Diseases in Third World countries are rarely "tropical" in the accepted sense, claims the paper, but largely caused by poverty. They "would virtually disappear if people had access to land, employment, adequate housing, water supply, sanitation, and education."
>
> The most fatal illnesses in developed countries today — heart disease, strokes, and malignancies — cause very few deaths in the Third World, where the chief problems are malnutrition and communicable diseases.
>
> The paper points out that in fact the disease spectrum almost exactly mirrors that of nineteenth-century Europe which was dogged not only by epidemics of plague, cholera, and typhoid, but also by a high incidence of kwashiorkor and even malaria.
>
> As in Europe, where poor health was a symptom of poverty, "the health status of a Third World population will ultimately depend far more on the decision of the people in power than the provision of prevention and curative health institutions," says the paper.
>
> In most developing countries health care systems have been inherited wholesale from the West. But there is a growing awareness that these models are inequitable in their distribution of resources, perpetuating a system of dependency, and are inappropriate for the actual disease problems which occur.
>
> It has been estimated, for instance, that a well-trained primary health worker can adequately cope with up to 97 per cent of health problems encountered, leaving only 3 per cent to be referred onwards.
>
> This analysis has major implications for VSO, and its new policy paper states that it will now only support projects which are involved in the promotion of more equitable and appropriate systems of health care.
>
> "This means continuing the move to rural rather than urban projects, backing low-cost systems such as health centres rather than hospitals, and training village health workers rather than doctors or pharmacists. It

means participating in ongoing health education, public health, and immunisation programmes and sometimes supporting or working alongside the practice of traditional medicine."

The British doctors, nurses, and paramedical workers who can be involved in such schemes must have, in addition to the personal and professional qualities which VSO has always sought, an awareness of the political, social and economic factors affecting health in the Third World.

The skills most needed will be those of nurse midwives, nutritionists, and community physicians. Pharmacists, dentists, general medical laboratory technicians, remedial therapists, and certain other doctors will also be recruited to fill a small number of specific requests.

**Health Care in the Third World—a new policy for VSO. Voluntary Service Overseas, 9 Belgrave Square, London SW1.*

CONFERENCE ON LEPROSY TRAINING IN AFRICA

Africa Hall, Addis Ababa, March 1979. Report and Recommendations. ALERT, P.O. 165, Addis Ababa, Ethiopa

The objectives were as follows:—

1. To determine the views of delegates on the extent to which the International Training Centres (The Institut Marchoux, Bamako, The Institut de Leprologie Appliquée, Dakar and ALERT) had met the needs for appropriate training in leprosy of health personnel of all cadres in the countries represented.
2. To identify the difficulties and constraints faced by leprosy control programmes, in particular the problem of secondary Dapsone resistance and their effect on the content of training programmes.
3. To determine how best training in leprosy to an appropriate level of competence, can be incorporated in the teaching programme of all cadres of health personnel, including both medical students and primary health care workers, with particular reference to the requirements for such training implicit in a policy of integration.
4. To define the levels of training to be given by international, regional and national training centres in order to meet the needs for the various cadres of specialized personnel required, by an integrated health care programme.

In order to meet these objectives the assistance of WHO and of ILEP was requested and obtained, and delegates were invited from both the training centres and the Ministries of Health of a number of African countries.

And the recommendations:—

Recognizing the need for increased training in leprosy particularly in the light of the adoption of the policy of integration by many countries and the spectre of mycobacterial resistance to treatment with DDS, this Conference, meeting in plenary session, makes the following recommendations:—

1. That appropriate training in leprosy for all cadres be an integral part of the schools of public health, nursing and other paramedical staff including primary health care workers, and that postgraduate specialized training in leprosy, which will include public health training should be given for certain

cadres including supervisors and medical officers, and be recognized by the award of an appropriate diploma.

2. That leprosy training programmes be based on the work to be done by the trainees after completion of the course (principle of training by instructional objectives) and that existing programmes adapt their activities so as to give priority to assisting in the provision of cadres of trainers in leprosy for medical training centres generally.
3. That leprosy workers at all levels accept the principle of integration and participate in its application, as they have opportunity, so as to ensure that its potential benefits are realized and its dangers avoided.
4. That basic and general health workers accept their responsibility for leprosy patient care and leprosy control and involve themselves in this work.
5. That close co-ordination and co-operation between leprosy and tuberculosis work and workers should be encouraged.
6. That interchange of information and ideas between countries of Africa with similar problems and different public health and cultural systems should continue and be further developed.
7. That people with appropriate expertise should work together to develop and evaluate techniques for the diagnosis, management, recording and follow up of leprosy patients, suitable for use in integrated health care programmes.
8. That the assistance of WHO and other appropriate organizations be sought in the implementation of these recommendations especially by those engaged in: (a) the development of educational methods; (b) the development of simplified techniques; (c) the setting up of a means to continue inter-country consultation.
9. That a permanent working group be set up to foster the adoption of these recommendations.

ILEP: THIRTY-SECOND MEETING OF THE ILEP MEDICAL COMMISSION, MADRID, JUNE 1979

President: Dr K. F. Schaller; *Vice-president:* Dr A. Cap; *Vice-president* and *Rapporteur:* Dr A. C. McDougall

Amongst a long list of important topics raised at this Medical Commission (and later reported to the General Assembly by Dr K. F. Schaller) were the following—

1. An Atlas of Leprosy

Professor M. F. Lechat of the École de Santé Publique, Clos Chapelle aux Champs, 30, Bruxelles, Belgium, presented an atlas giving detailed information on the leprosy situation in 59 countries. In their introduction on behalf of the Damien Foundation (to whom we are indebted for this remarkable achievement), Mrs C. B. Mission and Miss Miriam Cap summarize the data recorded by the atlas under the following headings—

(a) *A prevalence map by region:*

The prevalence shows the ratio of *registered patients* against the population of the region.

The source of data is indicated on each map, as well as the year to which they apply. The information has been given either by the Ministry of Public Health or by a correspondent engaged in leprosy work in the country itself.

Considering the important variations of prevalence in the world, and the desire to get a more precise idea in each country, we have decided to use two different scales (indicated on each map).

(b) *A second map* shows the projects supported by ILEP-members. However this has been omitted when those projects cover the entire country through support to a national program. Some maps are incomplete for lack of information.

(c) *Statistical data:*

(a) the population by region,
(b) number of registered patients,
(c) the prevalence (registered patients/population),
(d) number of patients in the projects supported by ILEP-members. If the entire country is covered through a national program, only the total number of patients is indicated.

(d) For some countries, we have been able to show the number of estimated and treated patients.

This formidable work both complements and expands the information already compiled by WHO and should be of immense value not only to ILEP members, but to all those who have responsibility for allocating resources in leprosy control. A copy may be obtained on application to the Brussels address above.

2. ILEP Sample Survey Teams

Dr. D. L. Leiker of the Royal Tropical Institute, Mauritskade 57, Amsterdam, Netherlands, presented further practical points for the formation of these teams, which are envisaged to consist of a medical officer (as team leader), an administrative assistant and/or laboratory technician, and a statistician. It was thought that 2 rather than 3 areas might be covered per year in selected countries with endemic leprosy; that the base could be in Europe (possibly at ILEP headquarters), or in a regional centre such as ALERT in Africa, and that selection of personnel should be from Members of ILEP to the Medical Commission. A detailed job description would clearly be needed. WHO collaboration was invited, especially in the training of team members; Ujung Padang in Indonesia might be a possible centre for such training. The possibilities of combining such survey work with studies on drug intake (compliance), drug resistance and tuberculin testing were also discussed, but it was thought that these additional matters would have to be reviewed in the light of the work-load encountered during actual surveys.

3. Standard Information, Registration and Reporting System for Leprosy (OMSLEP)

Professor M. F. Lechat presented details of this system which is now fully developed and already distributed to a number of countries for field use. It is available in English, French and Spanish; a Portuguese translation is in preparation, and a full manuscript has already been submitted (June, 1979) for publication in the medical press. This is a collaborative project between WHO and the Department of Epidemiology in the Catholic University of Louvain. This operational research project is confidently expected to assist endemic countries in a better definition—and assessment—of their activities. All who are interested in this system, and in assessing its feasibility in the field, are encouraged to contact Professor Lechat's unit in the University of Louvain.

From the same unit in this University, there is also now available a *Central Register of Resource People,* established after extensive screening of the literature concerning all those involved in leprosy research over the past 6 years (from 1974). This has been completed with the help of the Institute for Scientific Information in Philadelphia, Pennsylvania, and the Damien Foundation. The Register prints out a list of over 1500 scientists, with their scope of research and address. Its key words were—Diamino diphenyl sulfone, leprosy, leper, *Mycobacterium leprae,* Hansen disease, Hansen's disease, lepromatous, *lepraemurium,* DDS and lepromin.

4. Combined Multiple Chemotherapy in Malta

Dr D. L. Leiker (Amsterdam) gave a preliminary account of the results of combined multiple drug therapy used in the treatment of patients of various classification in Malta, followed by stopping drug treatment altogether. Further details of this group of patients, which could clearly have a most profound influence on our approach to drug treatment, are not yet available, but some of Dr Leiker's views may be read, as a personal communication in *Leprosy Scientific Memoranda,* Memo L-1025, June, 1979.

(The next meeting of the Medical Commission is in Brussels, on Thursday, 13 December, 1979.)

WHO. Regional Office for the Western Pacific; Final Report on the First Regional Working Group on Leprosy, Manila, Philippines, 7–12 December, 1978. (The report is dated February, 1979)

This is a 57-page report, paper back, A4 size, of an important Regional Working Group, whose objectives were:—

(a) to review ongoing leprosy control activities, including (i) the magnitude of the problem and (ii) the programme management of leprosy control;

(b) to recommend to the Regional Director strategies for the programme management of leprosy control activities in the country in line with the proposed regional strategy, including manpower training for leprosy control;

(c) to review all chemotherapeutic regimens currently being used to determine the frequency of dapsone-resistant cases being encountered;
(d) to develop a system of monitoring the spread of dapsone-resistant leprosy and to propose effective countermeasures to minimize this resistance.

The whole subject of leprosy, as seen in this geographic area, was considered in detail under 16 headings and the Report ends with 4 pages of Recommendations. It is nowadays becoming increasingly clear that the most complex, and at times the most controversial areas covered by such meetings of experts have to do with the treatment of the bacillary infection, and with adverse reactions. It is therefore of interest to read (page 21) that "All suggested regimes for dapsone resistance recommended by the Workshop on Epidemiology and Control, including Field Therapy, at the XI International Leprosy Congress in Mexico City, November, 1978, are moderately priced or very expensive. Therefore possible "low-cost" regimens which could undergo clinical trials are:
(a) Rifampicin 1500 mg, single dose on the first day of treatment, plus clofazimine 100 mg daily for two months, then 100 mg three times weekly, indefinitely and ethionamide 375 mg daily for two months, then thiacetazone 150 mg daily, indefinitely.
(b) Rifampicin 600 mg daily for two weeks, then 600 mg on the first day of each month, indefinitely, plus ethionamide 375 mg daily for two months, then thiacetazone 150 mg daily indefinitely.
(c) Clofazimine 100 mg daily for two months, then 100 mg three times weekly, indefinitely, plus ethionamide 375 mg daily for two months, then thiacetazone 150 mg daily, indefinitely."

Under *Duration of therapy,* (page 22), the text reads . . .

"More research is needed on the duration of treatment in non-lepromatous leprosy. It is proposed here to give simple recommendations, based on the date of commencement of treatment, or of recommencement in the case of relapse through failure to take treatment, or of change to effective treatment in the case of relapse due to the emergence of dapsone resistance.

Type of leprosy	duration of chemotherapy	Period of intensive follow-up (because of threat of reaction, etc)
TT	3 years	0–3 months
BT	5 years	4 months
BB	10 years	0–6 months
BL	15 years	0–12 months
LL	at least 20 years (life preferred)	0–7 years (subsequently an annual complete check for relapse remains essential, indefinitely)

Indeterminate–treat for three years, and then lepromin-test.
(a) if lepromin positive, stop at three years;
(b) if lepromin negative, continue for another three years (i.e. total of 8 years)"

Under *"Suggested field treatment of regimens for reactions"* (page 25) that dealing with severe ENL includes the following recommendations:

"It is suggested that a short-term course of prednisolone should be first given:

prednisolone 10 mg three times a day for one week,
then prednisolone 10 mg twice daily for one week,
then prednisolone 10 mg daily for one week,
then prednisolone, 5 mg daily for one week.

If the patient's skin lesions immediately relapse, or if ENL iridocyclitis, orchitis, neuritis, arthritis or nephritis is not completely cured in a single course, then alternative drugs should be employed.

Possible courses are:

either thalidomide 200 mg twice daily for three days,
then thalidomide 100 mg mane, 200 mg nocte for four days,
then thalidomide 200 mg nocte for two weeks,
then thalidomide 200 mg nocte for eight weeks.
(Do not give prednisolone with thalidomide.)

Or clofazimine 100 mg three times a day for two months,
then clofazimine 100 mg twice daily for one month,
then clofazimine 100 mg daily indefinitely.
Plus prednisolone 10 mg twice daily for the first two weeks,
then prednisolone 10 mg once daily for the next two weeks,
then prednisolone 5 mg daily for the third two weeks (then stop prednisolone).

Patients should be reviewed around eight weeks by the control scheme leprosy specialist. At his discretion, patients may be discharged home on clofazimine, subject to review every three months. Out patient use of thalidomide, although by and large cheap, simple and very satisfactory, must be under direct control of the specialist, and subject to any regulations imposed by the national health authority. Regular checks are advisable to exclude thalidomide neuropathy."

Under *"Recommendations.'* (page 34) extracts from paragraphs (1) and (2) include the following—

(1) In the countries of the Western Pacific Region leprosy has been recognized as a major public health problem and anti-leprosy activities are being carried out.

Having analysed the overall results of leprosy control in the last 17 years during which WHO has been involved it appears that the number of registered cases represents only 42% (Table 1a) of the estimated total and this figure is well below target. Some 16% of registered cases are still institutionalized. Concerning treatment and in particular *regular* treatment, although data are difficult to obtain, it is obvious that regularity of attendance for treatment generally has not reached accepted standards.

(2) The problems in leprosy control are fully recognized—the relatively high proportion of multibacillary patients representing a potential reservoir for continued spread of the disease, e.g. in Fiji over 20 per cent of lepromatous cases are children and young adults."

[In view of the fact that only 42% of the estimated cases in this vast area have been registered, and the known deficiencies in trained staff who might be able to find and treat more cases, or supervize others in doing so, one wonders how the therapeutic advice in this interesting report will ever be applied in practice. In Annex 1, page 5, it is difficult to understand the arithmetic on the number of rifampicin capsules needed per year, with regard to the cost in brackets, Clofazimine is printed as 600 mg, which should surely be 100 mg, in the first column.]

A. C. McDOUGALL

Lepr. Rev. (1979) **50,** 331–332

Letters to the Editor

Interaction Between Rifampicin, Steroids and Oral Contraceptives

We would like to draw the attention of leprosy workers to recent reports of the action of rifampicin (rifampin) in reducing the pharmacological effects of steroids (corticosteroids) when then given concurrently to patients. Edwards *et al.* (1974) were the first to describe a reduction in the pharmacological half life of cortisol in a patient with tuberculous Addison's disease being treated with rifampicin and replacement cortisone. Buffington *et al.* (1976) reported impaired renal allograft function when short-term rifampicin was given with methylprednisolone, and in one patient receiving 32–40 mg/day of the steroid for more than $1\frac{1}{2}$ years with no toxicity. when long-term rifampicin was stopped, signs of steroid toxicity dramatically appeared. These authors recommend that double dosage of steroid should be given when rifampicin is given concurrently. More recently Hendrickse *et al.* (1979) have reported the case of a boy suffering from nephrotic syndrome who failed to respond to steroid due to drug interaction with rifampicin, and warn about the risks of giving these two drugs together when treating conditions such as tuberculous meningitis. Rifampicin stimulates the production of hepatic microsomal enzymes which, in turn, increase the metabolic degradation of steroids and thus reduce their pharmacological effectiveness. Therefore we wish to warn leprosy workers to expect a poor response to steroid therapy for severe type 2 lepra reaction (ENL reaction) if rifampicin is being given at the same time.

Rifampicin also impairs the effectiveness of oral contraceptives (Skolnick *et al.,* 1976), and this could lead to an undesired pregnancy in a lepromatous woman of child-bearing age; worse still, if the woman is given thalidomide to control a prolonged and severe lepra reaction on the strength that the contraceptive pill will prevent pregnancy, the consequences could be disastrous.

W. H. JOPLING

33 Crown Lane Gardens,
Crown Lane, London SW16 3HZ

J. H. S. PETTIT

Room 303, China Insurance Building,
174 Jalan Tuanku Abdul Rahman, Kuala Lumpur,
Malaysia.

References

Buffington, G. A., Dominguez, J. H., Piering, W. F., *et al.* (1976). Interaction of rifampicin and glucocorticoids. Adverse effect on renal allograft function. *J. Am. med. Ass.* **236,** 1958.

Edwards, O. M., Courtenay-Evans, R. J., Galley, J. M. and Hunter, J. (1974). Changes in cortisol metabolism following rifampicin therapy. *Lancet* **2,** 549.

Hendrickse, W., McKiernan, J., Pickup, M. and Lowe, J. (1979). Rifampicin-induced non-responsiveness to corticosteroid treatment in nephrotic syndrome. *Br. med. J.* **1,** 306.

Skolnick, J. L., Stoler, B. S., Katz, D. B. and Anderson, W. H. (1976). Rifampin, oral contraceptives, and pregnancy. *J. Am. med. Ass.* **236,** 1382.

Lepr. Rev. (1979) **50,** 333–336

Book Reviews

Two New Medical Journals: (1) The Journal of Immunopharmacology, (2) Parasite Immunology.

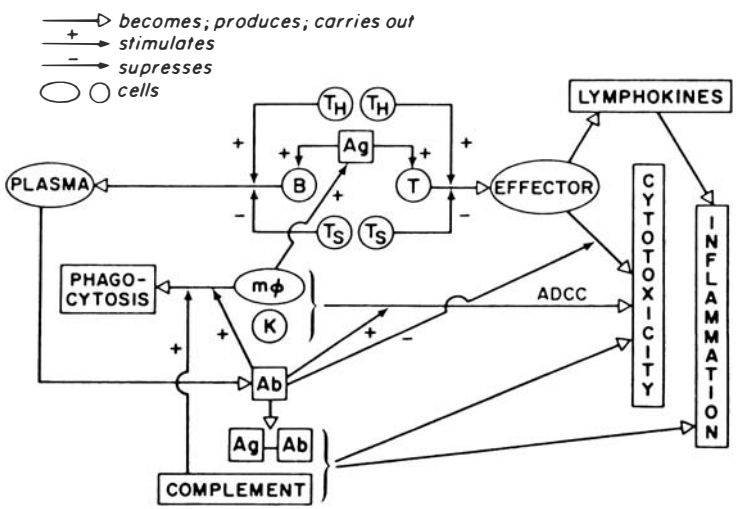
(1) The Journal of Immunopharmacology

The first number of Volume 1 is now available (1978–1979), published by Marcel Dekker, Inc., 270 Maddison Avenue, New York, 10016.

There is a discount for Volume 1, expiring 31 October 1979, as follows:
Institutional rate for Volume 1 of 4 issues: $36.00 (normally $40.00)
Individual rate for the same: $18.00 (Normally $20.00).

This journal presents a forum for publication of clinical studies and research results in the area of immunopharmacology. Immunopharmacology represents an interface between the disciplines of immunology and pharmacology and implies the use of drugs or other agents in modulation of the immune system. The scope of both these areas encompasses a wide variety of topics which are constantly changing. It is, consequently, difficult to define these disciplines without excluding some facets which may be pertinent. However, with currently understood definitions of immunology and pharmacology as a basis, the Journal will accept papers which are concerned with the meeting of these disciplines. Papers will be accepted in areas of both clinical and basic research. Categories for manuscript will include invited reviews, full papers, and brief communications.

In their editorial, the Executive and Associate Editors say that ". . . the principal impetus for the current interest in agents which modulate the immune system has been the extraordinary increase in understanding of the immune system, with the concomitant realization of its complexity." and they offer the figure below



as "an attempt" to summarize the principal reactions of the immune response, adding that "in addition to the control mechanisms already built into the system it is obvious that there are many reactions at which pharmacological control may be possible. The number of reactions presently controllable represent merely a beginning and in many cases the control is, unfortunately, relatively non-specific. There is no doubt that our ability to control these reactions will increase as we learn more about the systems involved. It is conceivable that it will, in the future, be possible to control all of the reactions indicated in the figure."

(Material from this journal, which has no fewer than 40 eminent names on its Editorial Board, should clearly be watched with care by those working on the immunology and drug treatment of leprosy and its reactions.)

(2) Parasite Immunology

Following a preliminary note in *Leprosy Review,* the first number of Volume 1 (Spring, 1979) is now available, with an editorial by R. J. Terry, School of Biological Sciences, Brunel University, Uxbridge, U.K. and A. C. Allison, Ilrad, Nairobi, Kenya. The last paragraphs of this read:—

> "The literature on the subject is currently scattered in many journals which deal at the same time with other aspects of parasitology, immunology and tropical medicine. We have no wish to see this practice discontinued, but we do feel that it is timely to provide a central forum where, through publication, ideas may be exchanged and new concepts rapidly disseminated. As Editors of *Parasite Immunology,* we welcome papers dealing with any parasite, relating to either fundamental or applied aspects of immunity. We shall, of course, require that they tell us something new, and that the investigations have been soundly conducted.
>
> We look forward to presenting the results of work in these related fields of investigation to the widest possible audience through the growth of this new venture—*Parasite Immunology*."

This new journal will be published quarterly at an annual subscription of £21.00 (U.K.), £26.00 (overseas) and $57.50 (U.S.A. and Canada). It is printed by Blackwells Scientific Publications, 8 John Street, London WC1N 2ES, and papers should be sent to the Editors at that address.

Leprosy, 2nd edit. By Anthony Bryceson and Roy E. Pfaltzgraff, 1979. Published by Churchill Livingstone, Edinburgh, London and New York. Price £4.00.

The first edition of this book, published in 1973 under the title "Leprosy for Students of Medicine", was, of course, extremely popular. It is a pleasure to see this second edition, which will undoubtedly be of the greatest value to doctors, medical students and para-medical workers at various levels. The subject matter has been expanded and brought up to date. There are 56 black and white plates, many of which are of absolutely superb quality; it is in fact doubtful if such excellence has ever before been achieved in a book of this kind, and they should stimulate those who are concerned with education in leprosy to obtain comparable prints for everyday use in the classroom or seminar.

[As the authors say in their preface, a number of mistakes in the first edition have now been remedied, but it is still slightly irritating to see that many authors' initials are incorrect, and that the following names (here spelt correctly) are mis-spelt in the references or text—Refsum, Ziehl-Neelsen, Wassermann, Møller-Christensen, Shepard, Kirchheimer, Skinsnes, Pettit, Narayanan, Dupuytren and *Culex fatigans.*]

This book, at only £4 is a treasure-house of information on the theory and practice of leprosy. Much of the authors' experience is from Africa, and one cannot help wondering if there is not a case for ensuring that a book of this kind should be distributed systematically, and without delay, to the appropriate teachers in all the universities of Africa with a medical school.

The Leprosy Foot Project, by George Clarkson. Printed privately. Obtainable as below

This is a loose-leaf paperback of 37 pages on the subject of deformity of the feet in leprosy and the provision of suitable shoes, under the following main headings:— (1) The Leprosy Foot Project, (2) Making Plastazote shoes, (3) Organizing the Project. The author has had a practical training in footwear construction and spent four years during the war in medical work.

His main interest in the subject developed in 1969, in the leprosarium of Ifakura in Tanzania. This booklet contains many excellent colour photographs illustrating what can be done, with patience and skill, for patients with advanced grades of disability in the leg and foot. It is full of practical advice: for instance (p. 35), "Don't tell Sisters how to treat leprosy".

Mr George Clarkson has very generously written to say that he would be happy to send a copy of this book free of all cost to leprosy field workers. For those who are in a position to pay, however, we feel it should be recorded that each copy costs £1.50 to produce. His address is 173 London Road, Clacton on Sea, Essex, U.K.

A. C. McDOUGALL

Footwear Manual for Leprosy Control Programs, Edited by P. J. Neville of ALERT

The All Africa Leprosy and Rehabilitation Training Centre in Addis Ababa, Ethiopia has some excellent publications to its credit. They have been pertinent, clear and readable. This new "Footwear Manual for Leprosy Control Programs", is outstanding. It has a clear objective and is aimed at specific personnel for a defined purpose. It is intended for use by the staff who produce footwear under supervision in rural areas. It is clearly based on experience and this experience has been obtained in Ethiopia. Herein lies both its strength and its weakness. Most of the patients in the clinics served by ALERT have been barefoot and have come from a background entirely without shoes. Thus, if they can accept the need for footwear they are willing to use the simplest variety. In a slightly more sophisticated society some of the footwear described in this manual might not be accepted. It would have been nice to have had a section on modification of regular shoes or sandals suitable for an urban population.

I would also have liked to have seen something on the clog principle, a rocker shoe or boot with a rigid sole. This would have been for the patient with a foot too bad for the Plastazote sandal, but not bad enough for the FAB walker.

Notwithstanding these limitations this is by far the best footwear manual for leprosy programs that I have seen. It starts with no assumption of previous knowledge. It tells what a hammer is and how to set up a bench. There are clear diagrams on how to utilize different grades of leather and parts of a motor tire. We learn how to take a plaster model of a foot and how to sew and glue materials together. There is information on how to set up a workshop and how to estimate the cost of footwear. There is an admirable section on the kneeling prosthesis and the kneeling device for healing ulcers. Both of these are geared to rural areas, but that is where the need is and that is where technology is lacking.

Not every shoe or prosthetic department in the world will want to produce exactly the types of shoe described here, but there must be few who would not learn a lot from the instructions and probably none who would not benefit from the philosophy which shines through the whole production. It is a philosophy which says that if a need exists—go ahead and meet it with whatever you have available and with appropriate technology applied by the people on the spot, no matter what their previous qualifications. To that I say AMEN!

PAUL BRAND

Physical Therapy in Leprosy for Paramedicals, by Ellen Davis Kelly, Ph.D.

This book is a training manual for paramedical workers in leprosy. It is a remarkable production and the author is to be congratulated for the patient work that has gone into its production and for the admirable clarity and discipline which characterizes it.

Dr Kelly has an impressive background for her authorship. She has been a teacher of health education and physical education for more than 40 years. She is in fact a teacher of teachers and is the author of a standard text "Adaptive and Corrective Physical Education", which is still used in the United States for teacher training. Since her retirement Dr. Kelly has worked as a volunteer in Ethiopia where she organized all the training programs at ALERT and did a lot of the teaching herself.

Lest the casual observer thinks this either too large a book or too advanced for health workers in leprosy, one has only to read the sections carefully to see that its size is used chiefly to make quite sure that each statement is understandable on the basis of earlier statements in the book. No pre-knowledge is taken for granted. The whole teaching and learning process flows in

an orderly sequence and is understandable step by step by anyone who can read and understand English. The manual is arranged in three levels. Level I is a summary of aspects of leprosy which are important to physical therapy, health education, and home health care. Level II covers physical therapy techniques for use in hospitals, clinics and in the field. Level III covers pre and post-operative physical therapy and the anatomy and physiology necessary to understand it.

Throughout the manual there is a parallel teaching of Knowledge and Skill. Each piece of knowledge is matched with the skill or application which grows out of it. The whole production is illustrated and clarified with diagrams from artist David White who has combined beauty and simplicity in his work.

In almost any manual for programmed education the subject is taught with a certain dogmatic assurance, as if we knew the answers and as if each question had just one right answer. This is justifiable because this is not a background for research but to put our existing knowledge to work where it is needed. Even so, some teachers may be annoyed to find instructions that they do not agree with. In the application of a plaster cast for example, some would want padding placed around the malleoli before the plaster casts are applied, others, like myself would want to go on moulding the first layer of plaster until it had set—to get a perfect inner layer before all the plaster slabs and strengthening foot plates are applied. I also would have wanted a warning about the need to remove the cast early (a) if the leg had been swollen before the cast was applied (b) if the cast became loose or cracked even a little, and (c) if the patient felt something was wrong inside. These individual differences of emphasis are inevitable and I would hope that nobody would allow any book to become a substitute for personal supervision and teaching; however, this should not make any teacher discard a teaching manual such as this simply because it does not accord with all of his or her own ideas. Most of us over-emphasize the details we have learned from our own experience and neglect the wealth of wisdom available from the experience of others. This manual has been carefully collated from many sources and will serve to ensure a broad solid background of knowledge and skill on the basis of which each of us may highlight our own special insights and unique experience.

PAUL BRAND

Lepr. Rev. (1979) **50,** 337–346

Abstracts

1. MICROBIOLOGY

98. KATO, L., MANKIEWICZ, E. & de THOKOLY, I. **An approach for the *in vitro* screening of drugs for activity against leprosy.** *Experientia,* 1978, 34/10.

After an introduction stressing the difficulties of assessing new drugs for their action against *M. leprae,* the authors indicate the disparity between the efficacy of a range of drugs against *M. leprae* as measured in mouse and man. Four drugs, streptomycin, isoniazid, P.A.S., and ethionomide, completely suppress multiplication in mice but have little or no effect in man. Two drugs, a thiosemicarbazone and cycloserine, partially suppress multiplication in the mouse and have little effect in man and ethambutol has no effect in either mouse or man. Only DDS and rifampicin have a similarly good effect in both animals. Against this background the authors assess the *in vitro* sensitivity of three strains of *M. scrofulaceum* isolated by Professor Skinsnes from leprosy patients and one strain isolated from a patient with pulmonary mycobacteriosis to the same range of drugs. All strains are sensitive or partially sensitive to 1μg/ml rifampicin, but only the strains from leprosy patients are sensitive to 25 μg/ml of DDS. None of the strains are sensitive to any of the other drugs.

This apparent similarity between the sensitivity of Skinsnes' strains *in vitro* and therapeutic efficacy in man is taken as the basis for the authors recommendation that *in vitro* sensitivity tests with these strains should be used for primary selection of new leprosy drugs.

Comment. The significance of the disparity between the *in vitro* results and those obtained in experimental *M. leprae* infection of mice is not discussed and the difference in dose of DDS effective in mouse and man and that effective in the *in vitro* studies is barely mentioned. To achieve the *in vitro* suppressive level of 25 μg/ml a 70 kilogram individual would require more than 1700 mg of DDS to be equally distributed over his entire volume. The selection of any one group of mycobacterial strains with very limited drug sensitivity as a primary screening method for the selection of new drugs seems a thoroughly bad recommendation. Nevertheless organisms of this kind should be amongst the battery of strains, thoroughly representative of the genus *Mycobacterium* that are used for screening procedures.

J. L. Stanford

99. BAPAT, C. V. & MODAK, M. S. **Growth of the ICRC bacilli in the footpad of mice.** *Lepr. India,* 1978, v.50, 144–155.

The work reported here is part of a comparative study of *Mycobacterium leprae* and the ICRC bacillus, which was originally isolated in tissue culture from human leprous nodules, and subsequently adapted to bacteriological culture media. The strain selected was C-44, isolated by S. R. Khanolkar, a slow-growing non-chromogenic acid fast bacillus with bacteriological characteristics similar to those of *M. intracellulare,* which was known to give "lepromin" reactions very similar to those of ordinary lepromin. Other strains had previously been shown by Dr K. Ranadive, Dr C. V. Bapat and their co-workers to produce foot-pad infections in mice similar to those due to *M. leprae,* and in some cases there were deformities suggestive of footdrop. The present object was to study multiplication and growth patterns.

In normal CBA mice the organism gave limited multiplication in the footpad, reaching a plateau after about 6 months, with a maximum of about 3×10^7 organisms. The bacilli were located principally in skeletal muscle or in macrophages adjacent to it. There was no nerve involvement. However, in thymectomized irradiated (T/900r) mice a few bacilli were observed in a local nerve twig and in the sciatic nerve, and there was a mild foot-drop. The generation time was estimated at 15 to 20 days.

The reported results are so similar to those associated with *M. leprae* that one immediately has to ask, why is this organism not *M. leprae* or an organism closely related to it which has become slightly modified through adaptation to culture media? Obviously there is more data needed, the biochemical and serological properties of the organism and its sensitivity to drugs. But the question is perplexing when one recollects that isolation of ICRC bacilli of this type has been going on from human leprosy lesions for almost 20 years, and the fact that the strains appear not to be identical does not simplify the problem. Surely there is a need for some other group of workers to repeat and confirm these findings.

D. S. Ridley

100. SEOK DON PARK. **Microbiological studies of plantar ulcers in leprosy patients.** *Korean Medical Abstracts,* 1979, v. 9, 27. (original in Korean).

From the leprosy patients hospitalized at the Korean National Leprosarium on Sorokdo Island, forty-five leprosy patients with plantar ulcers were selected randomly for microbiological studies.

A total of 84 strains of bacteria, with the most common being Neisseria sicca (25 strains: 29.8%), 34 strains (40.5%) were present as a pure growth and 50 strains (59.5%) were present in ulcers with multiple infection. Antibiotic susceptibility tests indicated that bacterial isolates were rather highly susceptible to gentamicin and kanamycin, but varying degree of isolates were resistant to 12 antibiotics including streptomycin, rifampicin, lincomycin, penicillin, terramycin, colimycin etc. From a total of 30 plantar ulcers, 17 ulcers produced 24 strains of fungi and 1 strain of Balantidium coli. They consisted of 17 strains of saprophytic fungi (70.8%) and 7 strains of yeast-like fungi (29.2%).

Of the culture media for Balantidium coli, Sabouraud's glucose medium is the most specific and selective that the author found.

The Abstracts which follow are reprinted from the Tropical Diseases Bulletin, June, 1978, *through the courtesy of the Director, Bureau of Hygiene and Tropical Diseases, London. They are classified according to subject.*

101. KIRCHHEIMER, W. F. **Experimental transmission of leprosy world-wide.** *Lepr. India,* 1978, v. 50, No. 3, 371–374.

This short article emphasizes the need in leprosy research for experimental animals which would present fewer problems than do the armadillo and the mouse. Reference is made to the European hedgehog, the slender loris (India), the Korean chipmunk, and the white-handed gibbon (Malaysia) in all of which some preliminary work has shown promise.

T. F. Davey

102. HASTINGS, R. C. **Growth of sulfone-resistant *M. leprae* in the foot pads of mice fed dapsone.** *Proc. Soc. Exp. Biol. Med.,* 1977, v. 156, No. 3, 544–545.

"One hundred and twenty-three viable isolates of *M. leprae* from skin biopsies of leprosy patients have been tested for sulfone resistance in the mouse foot pad since 1970. In 33 strains, growth occurred in animals fed 0.0001% (w/w) dapsone, but not at higher concentrations; in 22, growth occurred at 0.001 and 0.0001% (w/w) dapsone, but not at the higher concentration; and in 20 isolates, growth occurred at all three concentrations, 0.01, 0.001, and 0.0001% (w/w) dapsone. In each group, in animals fed the highest concentration of dapsone at which growth occurred, the number of bacilli harvested was significantly less than that in controls. Thus 75 strains of *M. leprae* had some degree of sulfone resistance, and with each degree of sulfone resistance, there was a threshold above which dapsone could still inhibit multiplication of the resistant strain in the mouse foot pad. This finding, in light of the probable mechanism of action of sulfones and mechanism of bacterial resistance to sulfones, strongly implies that maximal subtoxic dosages of dapsone are indicated in all leprosy patients with multibacillary disease treated with this drug."

2. IMMUNOLOGY, PATHOLOGY

103. GUPTA, S. C. *et al.* **Serum proteins and immunoglobulins in leprosy.** *Int. J. Lepr.,* 1978, v. 46, No. 1, 9–13.

"Serum proteins and immunoglobulins were studied in patients suffering from various types of leprosy. A significant increase in total protein and decrease in albumin was found in all types of leprosy except borderline-tuberculoid. Gamma globulin was found to be increased in all types. An increase of alpha-2-globulin in lepromatous, a decrease of beta globulin in borderline-lepromatous, and a decrease of alpha-2 and increase of beta globulin in borderline-tuberculoid were observed. These changes do not seem to be of diagnostic importance.

"A statistically significant increase of IgG in borderline-lepromatous and lepromatous, IgM in all types of leprosy and IgA only in lepromatous was found. The increase of different immunoglobulins in leprosy, especially the lepromatous type, suggests a humoral response which was found to be directly proportional to the severity of the lesion."

[See also *Trop. Dis. Bull.,* 1969, v. 66, abstr. 1039.]

104. HOGERZEIL, L. M. & PRABHUDASS, N. **Delayed hypersensitivity skin reactions to lepromins prepared from *M. leprae* and selected cultivable mycobacteria. Investigations at the Victoria hospital, Dichpalli.** *Lepr. India,* 1978, v. 50, No. 4, 560–565.

"Lepromins prepared from *M. leprae* and from selected cultivable mycobacteria were tested in 5 leprosy patients. Preparation M.W. showed the best correlation with true lepromin, especially in the group of TT patients."

105. COWDRY, E. V. **Cytological studies on globi in leprosy.** *Int. J. Lepr.,* 1978, v. 46, No. 2, 175–201.

It is valuable to have a reprinting of this little known classic, a study of globi made in 1939 which has not been bettered from some points of view, and deserves to be read in the original by those interested. The distribution of leprosy bacilli in various types of cell is described. The clumps of bacilli known as globi are classified as cigar packs, seed globi (more elongated structures) and giant globi, the latter being enveloped by a volume of "Schleim" (watery fluid and amorphous debris). These forms are regarded as specific for human leprosy, whereas rosettes are characteristic of rat leprosy, peripheral bodies of Johne's disease and large bundles embedded in much fat of water buffalo leprosy. Some space is devoted to the controversy of the period, that giant globi might be in lymphatics or other extra-cellular situations. This view is disposed of, though it is shown that in lymph nodes giant globi may communicate with sinuses. These globi are shown to be situated in, or derived from, giant cells. The author touches on a present day controversy when he remarks that granular forms of bacilli are not an expression of death because they occur in actively extending lesions.

[See *Trop. Dis. Bull.,* 1941, v. 38, 23.] *D. S. Ridley*

106. SENGUPTA, U., RAMU, G. & DESIKAN, K. V. **Assessment of Dharmendra antigen.** *Lepr. India,* 1978, v. 50, No. 4, 599–609.

"Dharmendra antigen has certain advantages over Mitsuda antigen and these have been enumerated. Consequently, a reappraisal of Dharmendra antigen has been done. A variation in the degree of lepromin reaction was noted when the tests were performed with different batches of Dharmendra antigen. This was found to be due to variation in the bacillary content which was further confirmed by dilution experiments. Standardization of the antigen by bacillary count has been found to give better results. Dharmendra antigen prepared with a concentration of 160 million bacilli per ml was found to give not only early lepromin reaction but also late reaction comparable to Mitsuda antigen. It was also found that with a concentration of 16 million bacilli per ml (one tenth the concentration of Mitsuda antigen), the results were consistent and reproducible."

107. REA, T. H. & LEVAN, N. E. **Lucio's phenomenon and diffuse non-nodular lepromatous leprosy.** *Arch. Derm.,* 1978, v. 114, No. 7, 1023–1028.

This is a retrospective study of 10 Mexican patients with diffuse non-nodular lepromatous leprosy who were admitted to hospital in Los Angeles because of the reactive phase known as Lucio's phenomenon. In 8 patients this occurred prior to the diagnosis and treatment of leprosy.

The authors describe the clinical, laboratory and histological findings, and stress the differentiation from erythema nodosum leprosum (ENL) reaction as shown by absence of fever and leucocytosis, no tenderness of reactive lesions, failure of response to thalidomide, and good response to anti-leprosy drugs such as dapsone and rifampicin. Similarities to ENL reaction include anaemia, raised erythrocyte sedimentation rate and immunoglobulins, good response to prednisone, and glomerulonephritis in 1 patient (although immune-complex deposition was not found on renal biopsy). Three patients were found to have lymphopenia and splenomegaly, and 4 developed typical ENL after the institution of dapsone therapy.

W. H. Jopling

108. MITTAL, M. M., MAHESHWARI, H. B., SAHA, K. & SHARMA, R. **Hepatic lesions in asymptomatic children of leprosy patients.** *Int. J. Lepr.,* 1978, v. 46, No. 1, 42–46.

Forty-two asymptomatic children of leprosy patients were studied for possible hepatic lesions, which were observed in 47%. In order of frequency, these were Kupffer cell hyperplasia, portal triaditis, focal necrosis and granuloma (4 cases). Acid-fast bacilli were found in 4 cases. There was no correlation between the hepatic lesions and skin test positivity to tuberculin or lepromin. The results provided considerable new evidence of bacillaemia in leprosy contacts.

[If confirmed the results would imply that the liver might be the site of a primary leprosy lesion, but a series of control patients would be needed. The photographs do not show any definite epithelioid cells, or group of cells sufficiently compact to be called a granuloma.]

D. S. Ridley

109. PATEL, P. J. & LEFFORD, M. J. **Specific and nonspecific resistance in mice immunized with irradiated *Mycobacterium leprae*.** *Infection & Immunity,* 1978, v. 20, No. 3, 692–697.

"Following subcutaneous inoculation of irradiated *Mycobacterium leprae* (I-ML) into the left hind footpad of mice, there was increased resistance to *Listeria monocytogenes,* indicative of macrophage activation, at the immunization site. In spite of the high level of localized macrophage activation which was proportioned to the immunizing dose of I-ML, no such activity could be demonstrated systematically in these mice, as evidenced by the absence of increased resistance to an intravenous challenge with *L. monocytogenes.* Under these conditions, I-ML-immunized mice were nonetheless resistant to intravenous infection with either *M. tuberculosis* or *M. bovis* BCG, and this immunity was transferred to normal recipients using spleen or lymph node cells. Neonatal thymectomy completely abolished the development of antimycobacterial immunity after vaccination with I-ML, but immunity was restored by an intraperitoneal infusion of synegeneic thymocytes. Systemic nonspecific resistance could be generated in I-ML-immunized mice by an intravenous injection of disrupted I-ML. This study reveals that, after subcutaneous vaccination with I-ML, there is local accumulation of activated macrophages at the inoculation site and a widespread distribution of lymphocytes which are sensitized to mycobacterial antigens. Nonspecific resistance is mediated by the former cells and specific antimycobacterial immunity by the latter."

110. PATEL, P. J. & LEFFORD, M. J. **Induction of cell-mediated immunity to *Mycobacterium leprae* in mice.** *Infection & Immunity,* 1978, v. 19, No. 1, 87–93.

"The immune response of mice to armadillo-derived, irradiation-killed *Mycobacterium leprae* (I-ML) was investigated. Following injection of 100 μg of I-ML into the left hind footpads of mice, a state of cell-mediated immunity (CMI) was engendered to antigens of *M. leprae.* The evidence for CMI was as follows: (i) development of delayed-type hypersensitivity to both human tuberculin purified protein derivative and soluble *M. leprae* antigens; (ii) T-lymphocyte-

dependent macrophage activation at the inoculation site; (iii) specific systemic resistance to the cross-reactive species *M. tuberculosis*; and (iv) immunopotentiation of the delayed-type hypersensitivity response to an unrelated antigen. The CMI induced by I-ML in aqueous suspension was greater than that obtained with the same antigen in water-in-oil emulsion, even though the latter generated a more severe reaction at the site of immunization. I-ML also induced a stronger CMI response than the corresponding dose of heat-killed BCG."

111. MASSOUD, A., NIKBIN, B., NAZARI, G. R., SYADAT, N. A. & ALA, F. **A study of cell-mediated immunity and histocompatibility antigens in leprosy patients in Iran.** *Int. J. Lepr.*, 1978, v. 46, No. 2, 149–153.

"Fifty-six male and 14 female leprosy patients, aged 11–62, were studied for cell-mediated immunity (CMI) and histocompatibility antigens. Healthy blood donors were used as normal controls. All patients were receiving anti-leprosy drugs. T and B cells were detected by E and EAC rosette formation technics, and the leukocyte migration test (LMT) was done in the presence of PHA. HLA antigens were defined by a modified N.I.H. lymphocytotoxicity test in order to type 48 patients and 100 controls.

"There was a significant difference ($P < 0.01$) in the number of T cells between tuberculoid and lepromatous forms of the disease as compared to normal controls. We did not observe any differences in EAC rosette cells. It should be noted that the migration index is significantly higher in controls than in leprosy patients for PHA.

"There are no significant differences in the distribution of the A locus antigens between leprosy patients and controls, although a higher percentage of A-11 was obtained in leprosy patients. A slight elevation of B5 antigen was observed but these results are preliminary and our information regarding the B locus is incomplete. Thus, it is difficult to establish any precise relationship between HLA antigen and leprosy at this stage."

112. BJUNE, G., DUNCAN, E., BARNETSON, R. STC. & MELSOM, R. ***In vitro* modulation of lymphocyte resonses to phytohaemagglutin by plasma in mother and baby at the time of birth. Increased lymphocyte responses in babies of mothers with lepromatous leprosy.** *Clin. Exp. Immunol.*, 1978, v. 32, No. 3, 517–522.

"Peripheral blood lymphocytes from nineteen healthy mothers, sixteen mothers with borderline tuberculoid leprosy and fourteen mothers with borderline or polar lepromatous leprosy, and their newborn babies, were stimulated *in vitro* with phytohaemagglutinin (PHA). The responses in medium supplemented by serum from a pool of healthy non-pregnant individuals were compared with responses in medium supplemented by plasma from the mothers or from their babies, to assay for the presence of non-specific effects on T-cell responses. It was found that plasma from the mothers at the time of labour profoundly suppressed their own lymphocyte responses to PHA. However, the lymphocyte responses of healthy mothers were not significantly suppressed when cultivated in the presence of plasma from the babies, indicating that the suppressive factor(s) of normal pregnancy did not pass the placental barrier. Plasma from mothers with leprosy had a greater inhibitory effect on their babies' lymphocytes than plasma from healthy mothers. This raises the possibility that plasma from leprosy patients contains suppressive factors other than those associated with pregnancy. Babies of lepromatous leprosy mothers, who might have been exposed to mycobacterial antigens *in utero*, had higher PHA responses than the other babies, possibly due to a compensatory reaction to early stresses in the immune system."

The immunological interaction(s) between pregnant lepromatous patients and their offspring raises important concepts and this paper will repay reading of the full text.

M. F. R. Waters

113. BJORVATN, B., NAAFS, B. & KRONVALL, G. **Stability of individual anti-mycobacterial precipitation patterns during treatment for lepromatous leprosy.** *Int. J. Lepr.*, 1978, v. 46, No. 2, 144–148.

"Sixty serum specimens obtained from 16 lepromatous patients at intervals during the first year of DDS treatment were studied in crossed immuno-electrophoresis against an *M. leprae* sonicate

for possible variations of specificities and titers of antimycobacterial antibodies. All sera tested showed antibody activity against *M. leprae,* the number of precipitation lines produced varying between two and seven. In individual patients the numbers and positions of the precipitation lines remained remarkably constant throughout the period of study."

3. CLINICAL

114. CARAYON, A.; COURBIL, J. L.; BRUN, M.; ROFFI, J.; MARTINE, J. Bilan de recherches physiopathologiques sur la névrite lépreuse. I. Rôle de la température, des microtraumatismes par élongation ou subluxation nerveuse et de la striction canalaire. [**A review of pathophysiological studies on leprous neuritis. I. Role of temperature, microtraumatisms by elongation or subluxation and canalar stricture.**] [CARYAYON.] *Méd. Trop.,* 1977, v. 37, No. 6, 637–654. II. Modifications de l'hémodynamique dans les troncs névritiques hanséniens (hypertension-ischémie fasciculaire. Part de la compression canalaire). [**II. Haemodynamic changes in the neuritic trunks in leprosy (fascicular hypertension and ischaemia. Role of canalar compression).**] [CARAYON, COURBIL & BRUN.] *Ibid.,* 655–678. III Dérèglements métaboliques dan la névrite lépreuse (action potentialisatrice bactério-immunologique). [**III. Metabolic disorders in neuritis (the potentiating effect of the bacterio-immunological processes).**] [CARAYON, ROFFI, MARTINE & BRUN.] *Ibid.,* 679–687. IV. Répercussions de la névrite lépreuse sur la conduction et la douleur nerveuses. [**IV. Nervous conduction and pain in neuritis in leprosy.**] [CARAYON.] *Ibid.,* 689–697. English summaries.

115. KAUR, S., MEHTA, S. K., KUMAR, B., CHAKRAVARTY, R. N. & SIDHU, H. K. **Involvement of the gastrointestinal tract in leprosy.** *Int. J. Lepr.,* 1978, v. 46, No. 1, 35–41.

"The published information about involvement of the gastrointestinal tract in leprosy is scanty and conflicting. Twenty-five patients having leprosy (L-15, B-5, T-5) were subjected to investigations pertaining to the gastrointestinal tract. . . .

"Correlation was not found between type of leprosy, malabsorption and jejunal histology. A sizeable population in the tropics, even normally, has disturbances of absorption tests and jejunal mucosa. The percentages of abnormalities detected in the stomach and small intestine were not significant. It can thus be concluded that the gastrointestinal tract remains unaffected in leprosy."

116. NAAFS, B. & VAN DROOGENBROECK, J. B. A. Intérêt en léprologie d'un indice névritique de gravité et d'évolutivité établi d'après la vitesse de conduction motrice dans les nerfs cubitaux et médians. [**Advantage in leprology of a neuritis index based on motor nerve velocity to appreciate the severity and the evolution of disorders in the ulnar and median nerves.**] *Méd. Trop.,* 1977, v. 37, No. 6, 757–762. English summary.

4. THERAPY

117. VAN DROOGENBROECK, J. B. A. & NAAFS, B. Neurolyse et artériolyse du nerf tibial postérieur dans la lèpre: étude comparative de leur action dans les ulcères plantaires atones. [**Tibial posterior nerve release and arteriolysis in leprosy: a comparative study of their action in atonic chronic ulcers.**] *Méd. Trop.,* 1977, v. 37, No. 6, 777–779.

"In an approach of neuritis treatment in leprosy, more than 130 nerve releases were performed with 26 concerning the posterior tibial nerve, and completed with arteriolysis.

"From these 26 releases 12 were performed for neuropathic disorders, and 14 for chronic ulcers.

"Eleven patients remained ulcer free after one year (75%), while in a control group this proportion was only about 30%. The difference is significant."

118. NAAFS, B. & VAN DROOGENBROECK, J. B. A. Décompression des névrites réactionnelles dans la lèpre: justification physiopathologique et méthodes objectives pour en apprécier les résultats. [**Nerve decompression in reversal reaction and ENL in leprosy: a pathological approach and objective method for evaluation of the results.**] *Méd. Trop.,* 1977, v. 37, No. 6, 763–770.

"... In this paper a pathophysiological model is presented, which may explain nerve damage during reversal reaction and ENL. The influe f nerve decompression and prednisolone is discussed. The authors are of the opinion that nerve surgery always should be done under prednisolone cover. An arbitrary numerical system—nerve index—is presented which makes it possible to control follow-up studies of nerve surgery in order to evaluate objectively its value. The different parameters used are discussed and shown in relationship with each other."

119. VAN DROOGENBROECK, J. B. A. & NAAFS, B. Étude comparative d'une série de nerfs lépreux décomprimés chirurgicalement par rapport aux nerfs controlatéraux non opérés. [**Surgical nerve release in leprosy: a study with comparison with non-operated opposite nerves.**] *Méd. Trop.,* 1977, v. 37, No. 6, 771–776. English summary.

120. GIRDHAR, B. K., RAMU, G., SREEVATSA, & DESIKAN, K. V. **Introductory rifampicin therapy in lepromatous leprosy: a six month follow-up study.** *Lepr. India,* 1978, v. 50, No. 3, 363–370.

This is a report from the Central Jalma Institute for Leprosy, Agra, comparing the effects of 300 mg rifampicin daily with 50 mg dapsone (DDS) daily for 3 months in the treatment of 24 new (untreated) cases of lepromatous leprosy. All patients were observed for a further 3 months on DDS. There was clinical improvement in both groups, with rifampicin producing speedier healing of nasal ulceration, and 2 patients in each group developed erythema nodosum leprosum during the first 3 months. Fall in Morphological Index as judged by skin smears, and killing of bacilli as judged by mouse footpad tests, were much more rapid in the rifampicin group, and the authors plan another trial to see if a shorter course of therapy will produce equally good results.

[It is to be hoped that the authors will carry out nasal scrapings as well as skin smears in their next trial.]

W. H. Jopling

121. NAIK, S. S. **Irregularity of dapsone intake in infectious leprosy patients attending an urban treatment centre—its magnitude and causes.** *Lepr. India,* 1978, v. 50, No. 1, 45–53.

This article does more than provide evidence that the irregularity of dapsone intake among leprosy out-patients found in other countries is also applicable to Bombay, where 48.7% of patients were involved. Useful data are presented regarding the educational, residential and occupational status of 322 infectious patients who were irregular in attendance and treatment. The results are not quite what might have been expected and invite further sociological study. The groups most involved were poorly educated factory workers and unemployed people living in cramped accommodation. The reasons for irregularity of attendance and treatment given by this group and an additional 110 non-Bombay residents indicate the complexity of the problems involved.

T. F. Davey

122. CASTRO-COTO, A. Clofazimina. G 30320–B 663–Lamprén. [**Clofazimine in leprosy.**] *Dermatologia,* 1977, v. 21, No. 1, 49–56.

This is a dissertation on clofazimine comprising a review of its history, chemistry, pharmacology, absorption, metabolism, mode of action and toxicology. Activity against various species of *Mycobacterium,* including *M. tuberculosis* and *M. leprae,* is reviewed, together with therapeutic results in the treatment of leprosy and the principal side-effects.

After discussing other uses of the drug the author concludes by summarizing the indications for the employment of clofazimine in the treatment of leprosy cases.

[Although various authorities are cited in the text there is no list of references.]

J. M. Watson

123. CHAUDHURI, S., GHOSH, S., CHAKRABORTY, T., KUNDU, S. & HAZRA, S. K. **Use of a common Indian herb "mandukaparni" in the treatment of leprosy.** *J. Indian Med. Ass.*, 1978, v. 70, No. 8, 177–180.

Mandukaparni (*Centella asiatica*) is a common Indian plant growing in marshy places. It contains the glucoside asiaticoside. Following favourable reports on its use in leprosy in the 1950s the authors describe a trial in which 15 untreated lepromatous patients were given pills made from the crushed whole plant administered daily for 12 months. Twelve completed the course. Their progress is compared with that of 10 lepromatous patients (? untreated) on standard dapsone therapy. The clinical and bacteriological progress of the trial group over the 1-year period compared favourably with the controls, with no reactions or toxic effects. The authors suggest that asiaticoside may have a bacteriostatic action by depressing the biosynthesis of hyaluronic acid.

T. F. Davey

124. SAINT-ANDRÉ, P., LOUVET, M., GIRAUDEAU, P. & DISCAMPS, G. Essai de différents protocoles thérapeutiques antilépreux avec rifampicine initiale suivie d'associations de sulfones et d'immunostimulants. [**Testing of several therapeutic anti-leprosy regimens with rifampicin as a starter followed by sulphones combined with immunostimulants.** *Méd. Trop.*, 1977, v. 37, No. 6, 721–729. English summary.

5. EPIDEMIOLOGY

125. WKLY EPIDEM. REC., 1979, v. 54, No. 3, 17–23. **Leprosy.**

The world-wide distribution of leprosy is given for the year 1975, seven years after the previous evaluations in 1968. In 154 countries, 3,599,949 patients were registered, an increase of 710,000 (25%) over 1968, but as the countries reporting are not identical, it should be noted that the populations from which these figures are derived have increased by 19% in the period. Taking this increase of population into account, leprosy registration has increased.

A true comparison over 1968–1975 is possible for 110 countries, and shows an increase in registered cases of 17%, a total of 835,000. Africa (with the least satisfactory comparison with 1968) shows only 5% increase, but Burma reveals 25%, India 56% and Indonesia 86%. The proportion of lepromatous cases in Africa is 10–15%, but in Asia it is greater (34% in Indonesia, 40% in Thailand). In the Americas it is frequently over 50% and in Brazil 55%.

Those receiving regular treatment (i.e. 75% of the prescribed doses) are still very low (Africa 41%, Eastern Mediterranean 53%, South East Asia 47% and Western Pacific 74%).

The tables provided detail the estimated number of cases, numbers registered, proportions of lepromatous, tuberculoid and indeterminate, numbers treated and numbers released from control for each country.

Less than a third of the countries provide estimates of the total cases, and this is to be regretted since the figures which are available suggest that only a third of the total world cases are as yet detected. But it is probable that the total number of cases in 1975 is not substantially different from that of 1968.

R. Schram

126. BELDA, W. Aspectos da "incidência" da hanseníase no Estado de São Paulo em 1976. [**Leprosy in São Paulo State in 1976.**] *Hansenologia Int.*, 1977, v. 2, No. 1, 73–88. English summary.

The 1853 cases registered during 1975 are analysed according to clinical form and regional distribution within the State, duration of the disease and the method of its detection. The countries of origin of immigrant patients are noted.

Ann Grant

127. MATHUR, N. K., KANWAR, A. J., KALLA, G. & UJWAL, J. S. **Leprosy in Jodhpur (Rajasthan). Clinical and epidemiological study.** *Lepr. India,* 1978, v. 50, No. 2, 204–209.

This is an analysis of leprosy cases attending the out-patient department of S.N. Medical College, Jodhpur between March 1975 and June 1977. In an area where leprosy is not believed to be endemic, 232 patients with leprosy were registered, 164 of them lepromatous in type. It is suggested that improved medical and health-care facilities may be causing an increased awareness of the disease encouraging early detection.

T. F. Davey

6. MISCELLANEOUS

128. BROWNE, S. G. **India's role in the fight against leprosy.** *Lepr. India,* 1978, v. 50, No. 2, 231–239.

Dr Stanley Browne gave this address on 30 January 1978 in New Delhi. At the same time the Silver Jubilee Commemorative Volume of The Gandhi Memorial Leprosy Foundation, entitled *A window on leprosy,* was launched. The lecture was given on a historic occasion to a galaxy of distinguished guests, and there can be few other men, if any, capable of presenting the theme in a more attractive and thought-provoking way.

In it he has much to say of the origins of leprosy relief and control in India, as well as pointers to India's role in the future. In doing so he provides a brief description of several Christian men, medical and non-medical, of importance to the story, William Carey of Serampore, Wellesley Bailey (founder of the Leprosy Mission), Sir Leonard Rogers, Dr Donald Miller and Dr Robert Cochrane. But also woven into the story is the great contribution of Mahatma Gandhi, his attitudes, foresight and loving persuasion of all to be deeply concerned for the leprosy sufferer.

The author also paints the picture of the growth of societies such as BELRA, later to become LEPRA, and the effect of aid programmes in the prevention and control of the disease and the rehabilitation of its sufferers. Looking to the future, he speaks of the great need for further research, greater commitment to the task by the medical profession and by health workers, a real attack on social discrimination against sufferers, and an increase in the conferring and sharing of knowledge by all leprosy control workers. These points he brings out by reference to seven of the Gandhiji's emphases. (The lecture was given at the time of the 30th anniversary of his martyrdom. It was also the 54th anniversary of the foundation of the Hind Kusht Nivaran Singh, and coincided with the 25th World Leprosy day.)

India's export of trained workers in leprosy and their contribution to the world-wide problem are described, instancing Robert Cochrane and Paul Brand from Vellore, John Lowe and Ernest Muir from Calcutta, and James Ross Innes from Cawnpore. Modern workers of renown, Dharmendra, Chatterji, Kanolkhar and Job and the Indian government's initiatives are next mentioned, and the lecture ends with a challenge in Gandhi's own words:

"Leprosy work is not merely medical relief; it is transforming the frustration in life into the joy of dedication, personal ambition into selfless service. If you can transform the life of a patient or change his values of life, you can change the village and country."

All concerned with leprosy work, and those who should be, should read this lecture.

R. Schram

129. KULKARNI, A. **Sponsorship of children of leprosy parents.** *Lepr. India,* 1978, v. 50, No. 2, 173–180.

This is an interesting initial report of the Community Aid and Sponsorship Programme (CASP), an India-based child care organization inspired by Gandhiji's deep involvement with leprosy

patients. The programme, created by the coming together of 3 related charitable organizations, aims to offer sponsorship for all physically handicapped children as well as the children of leprosy patients. The primary intention is to give economic and educational assistance to the families of such children, hoping both to preserve the family relationship as far as possible and give such children the best possible chance in life.

Beginning in Greater Bombay, 15 children were sponsored in June 1975. By April 1978 the number had increased to 600, of whom about 200 are the children of leprosy patients. The service is expanding rapidly but there are over 400 children on the waiting list. This type of work abounds in problems, some of which are illustrated. It clearly calls for well-identified objectives and devoted helpers with great patience and persistence.

T. F. Davey

130. McDOUGALL, A. C. & ROSE, P. **Integrated leprosy control in Guyana.** *Bull. Pan Am. Hlth Org.,* 1978, v. 12, No. 1, 11–16.

"Guyana instituted a 'find and treat' leprosy program in 1971 that made use of existing outpatient facilities and staff. The program based on an integrated domiciliary approach to diagnosis, treatment, and examination of contracts, has proved successful. This article describes development of the program and discusses the prospects for control and eventual eradication of leprosy in Guyana."

INSTRUCTIONS TO AUTHORS

"Uniform Requirements for Manuscripts Submitted to Biomedical Journals"; International Steering Committee of Medical Editors; adoption of the "Vancouver style" by LEPROSY REVIEW, *from Number 1,* 51, *1980*

Following an approach from the Editor of the *British Medical Journal* in April 1979, the Editorial Board of *Leprosy Review* gave detailed consideration to the possibility of changing to the 'Vancouver style' of printing, as first developed in 1978 by a group of editors of internationally famous journals, and published as a discussion document in February 1979. In brief, the International Steering Committee of Medical Editors proposed a uniform style for submitted manuscripts, full details of which were published in the *British Medical Journal* of 24th February, 1979, pages 532–535. This article is also available as a small booklet (50p, from the Editor of the British Medical Journal, BMA House, Tavistock Square, London WC1H 9JR), but the necessary format can be seen in any number of the *British Medical Journal* or the *Lancet.* The original group of editors included those of the *British Medical Journal,* the *Lancet,* the *American Review of Respiratory Diseases, Annals of Internal Medicine, Canadian Medical Association Journal, Journal of the American Medical Association,* and *New England Journal of Medicine.* A full list of the many journals who have already agreed to the style will be available later, but amongst those already participating in the UK are the following:

Anaesthesia
Annals of the Royal College of Surgeons
British Dental Journal
British Journal of Haematology
British Journal of Ophthalmology
British Journal of Venereal Diseases
Cardiovascular Research;
Journal of Clinical Pathology
Journal of Medical Genetics
Lancet
International Rehabilitation Medicine
Annals of the Rheumatic Diseases
Archives of Disease in Childhood
British Heart Journal
British Journal of Industrial Medicine
British Journal of Surgery
British Medical Journal
Gut
Journal of Epidemiology and Community Health
Journal of Neurology, Neurosurgery and Psychiatry.
Thorax

As soon as printing arrangements permit, the requirements will be included on the cover of *Leprosy Review,* but in case this should not be possible in the last Number of *50* (1979), we take this opportunity of including the following essential information on references, which must be followed for all submissions from 1st January, 1980.

REFERENCES

Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legends by arabic numerals (in parentheses). References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration.

Use the form of references adopted by the US National Library of Medicine and used in *Index Medicus*. Use the style of the examples cited at the end of this section, which have been approved by the National Library of Medicine.

The titles of journals should be abbreviated according to the style used in *Index Medicus*. A list of abbreviated names of frequently cited journals is given in Appendix 2; for others, consult the "List of Journals Indexed," printed annually in the January issue of *Index Medicus*.

Try to avoid using abstracts as references; "unpublished observations" and "personal communications" may not be used as references, although references to written, not verbal, communications may be inserted (in parentheses) in the text. Include among the references manuscripts accepted but not yet published; designate the journal followed by "in press" (in parentheses). Information from manuscripts submitted but not yet accepted should be cited in the text as "unpublished observations" (in parentheses).

The references must be verified by the author(s) against the original documents.

Examples of correct forms of references are given below.

Journal

(1) *Standard journal article*—(List all authors when six or less; when seven or more, list only first three and add *et al.*)

Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. N Engl J Med 1976; 294: 687–90.

(2) *Corporate author*

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. Scand J Clin Lab Invest 1976; 36: 119–25.

Anonymous. Epidemiology for primary health care. Int J Epidemiol 1976; 5: 224–5.

Books and other monographs

(3) *Personal author(s)*

Osler AG. Complement: mechanisms and functions. Englewood Cliffs: Prentice-Hall, 1976.

(4) *Corporate author*

American Medical Association Department of Drugs. AMA drug evaluations. 3rd ed. Littleton: Publishing Sciences Group, 1977.

(5) *Editor, compiler, chairman as author*

Rhodes AJ, Van Rooyen CE, comps. Textbook of virology: for students and practitioners of medicine and the other health sciences. 5th ed. Baltimore: Williams & Wilkins, 1968.

(6) *Chapter in book*

Weinstein L, Swartz MN. Pathogenic properties of invading microorganisms. In: Sodeman WA Jr, Sodeman WA, Eds. Pathologic physiology: mechanisms of disease. Philadelphia: WB Saunders, 1974: 357–72.

(7) *Agency publication*

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States July 1968–June 1969. Rockville, Md.: National Center for Health Statistics, 1972. (Vital and health statistics. Series 10: Data from the National Health Survey, No 69) (DHEW publication No (HSM)72–1036).

Other articles

(8) *Newspaper article*

Shaffer RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help cure alcoholism and insomnia, explain mental illness. How the messengers work. Wall Street Journal 1977 Aug 12: 1(col 1), 10(col 1).

(9) *Magazine article*

Roueché B. Annals of medicine: the Santa Claus culture. The New Yorker 1971 Sep 4: 66–81.

Index

VOLUME 50

A

B

C

D

E

F

G

H

I

J

K

L

M

N

O

P

R

S

T

V

W

Y

®Lamprene Geigy

Antileprosy drug with anti-inflammatory[1] properties

effective in the prevention[2] and treatment[3] of lepra (ENL) reactions

indicated as a part of combined therapy for the prevention and treatment of dapsone resistance in lepromatous and borderline leprosy[4].

1. Browne, S.G.: Lepr. Rev. *37*, 141 (1966)
2. Azulay et al.: Lepr. Rev. *46* (Suppl.) 99 (1975)
3. Schulz, E.J.: Lepr. Rev. *42*, 178 (1972)
4. Yawalkar, S.J., & Vischer, W.A.: Lepr. Rev. *50*, 135 (1979)

Instructions to Authors

Papers submitted for publication in *Leprosy Review* should be sent to the Chairman of the Editorial Board. The name(s) of the author(s), principal appointments held and the place where the work was done should be clearly indicated below the title of the paper. Degrees and diplomas are not to be included.

It is understood that the paper is offered to *Leprosy Review* alone, that it will be subject to editorial revision, and that its copyright becomes the property of the British Leprosy Relief Association. Papers should typewritten, in double spacing, on one side of (preferably) quarto paper, with wide margins (4 cm left, and 2 cm right). The top copy and a carbon copy of all papers should be sent.

Tables should be typed on separate sheets and numbered in sequence, in arabic numerals; captions should be typed in double spacing.

Graphs and line drawings should be in Indian ink on tracing linen (if possible) or plain white board or paper, about twice as large as the probable size of the finished block. They should be numbered in sequence, in arabic numerals. Indicate in the margin of the text where tables and graphs should be inserted.

Photographs. A reasonable number of black and white plates will be reproduced. Glossy original photographs (positive prints) should be supplied, and clear indications (number, caption, top side) should be given. Any writing on the back of the photograph should be lightly done in pencil.

References. In the text, references are made thus: "Jones (1968) has shown..."; or "It has been shown (Smith, 1967; Jones, 1968) that...". If more than 2 authors: "Smith *et al.*" If the same author is cited more than once in a year, then the references should be consecutively indicated thus: "Jones, (1968*a*)".

In the final list, surnames of authors should be given in alphabetical order, followed by initials, year in parentheses, full title of article, accepted abbreviated name of journal (if in doubt, write the name of the journal in full), volume (underlined), and first page of the article.

Numbers. All numbers are to be given in arabic numerals.

Summary. A brief summary should be given before the body of the paper.

Contractions. All weights, measures, temperatures, etc., should be given in metric units, suitably contracted. Authors may refer to "Symbols, Signs and Abbreviations Recommended for British Scientific Publications", published By The Royal Society. British (Imperial) equivalents may be added within parentheses. In the case of (body) temperatures, the Fahrenheit equivalents of Celsius (Centigrade) figures should be given within parentheses.

Proofs are submitted to authors for immediate return by air.

Copyright/Offprints. Authors submitting a manuscript do so on the understanding that if it is accepted for publication, copyright in the paper for the United States of America shall be assigned to the Association. In consideration for the assignment of copyright, the Association will supply 50 offprints of each paper. Further offprints may be ordered at extra cost and a price list/order form is sent to authors on acceptance of their typescript. The Association will not put any limitation on the personal freedom of the author to use material contained in the paper in other works which may be published in North America.

CONTENTS

Printed in Great Britain by The Whitefriars Press Ltd., London and Tonbridge