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British Leprosy Relief Association
Registered Offices: 50 Fitzroy Street, London, WIP 6AL

Editorial

HOW INFECTIOUS IS LEPROSY?

As Socrates knew, and as his pupils soon became aware, a question may be deceptive in its simplicity and conceal unsuspected snares and pitfalls. But the very actions of formulating a question and of fearlessly pursuing its answer are both stimulating and rewarding.

The question, "How infectious is leprosy?" is being asked today by clinicians and epidemiologists, by microbiologists and immunopathologists, by interested laymen and astute politicians, and it is being asked with increasing awareness of the human problems involved in a world in which leprosy is still not controlled. On the informed reply to the question depend such very practical issues as the type of control measures adopted, the perpetuation of ancient attitudes towards the segregation of leprosy sufferers, the proportion of the health budget that will be devoted to the leprosy programme, and the degree of urgency with which the whole problem of the leprosy endemic is regarded. If leprosy is very contagious, then institutional segregation as for smallpox will be advocated, and apparent success will follow such measures as in Norway and Japan. On the other hand, if leprosy is but slightly contagious, and if that small degree of contagiousness can be reduced to zero within months by the administration of bacteriostatic drugs, or within weeks by high-dose oral rifampicin, then quite different measures will be adopted. Very rarely do workers in leprosy institutions contract leprosy, although there are certain indications that non-medical workers contract the disease more frequently than doctors or nurses. If leprosy were highly contagious, then it would be expected that expatriate staff, especially those of Caucasian origin, would contract leprosy much more frequently than they do.

The question, of course, is no new one: it has been raised, and answered, in succeeding centuries. With naïve illogicality, and an apparent unawareness of the mutual exclusiveness of the propositions, leprosy was at times held to be both an hereditary and a highly contagious disease. Sometimes one or other concept seemed to predominate. Within a few short years of the appearance of the *Report of the (London) Royal College of Physicians,* which came down boldly on the side of the hereditary theory, complacency was shattered by the dual arguments, reciprocally reinforcing each other, of a Father Damien somehow contracting leprosy after exposure to the disease in Hawaii, and Armauer Hansen identifying the suspected causative organism of leprosy. When the full implications of this revolutionary concept were realized, governments of many countries were stampeded to enact legislation requiring the compulsory segregation of leprosy sufferers for the protection of society.

A more humane and enlightened attitude may now prevail in most countries, but nagging doubts concerning the infectiousness of leprosy persist in the minds of many, and these doubts have not been dispelled by any very obvious reduction in the incidence of leprosy on a wide scale. So far, the most effective and

practical measure for reducing rates appears to be the reduction in the *réservoir de virus* by vigorous and regular treatment of all patients with multibacillary disease—"secondary prevention". In the continued and regrettable absence of a specific vaccine, and the logistically impossible large-scale prophylactic medication, such measures have given good results in just those countries where the leprosy prevalence rates, though high, are largely accounted for by patients with paucibacillary disease. So far, generally applicable and reliable methods of "primary prevention" of leprosy, and accurate techniques of identifying individuals at greatest risk after exposure to leprosy challenge, elude us.

Asking the question, "How infectious is leprosy?" thus leads to the raising of a whole series of related questions, which must become more precisely worded as knowledge advances in the realms of the microbiology of *Myco. leprae*, the immunological receptivity of refractoriness of the exposed individual, and all the intervening circumstances of environmental importance. Time was when "consumption" was equated with poverty and undernourishment, with a blighted romance or a broken heart. The heroine, with a hectic flush on her wan cheeks, "went into a decline" and wasted away, succumbing at length after a frightening gush of blood from the lungs. Leprosy is at length emerging from this pre-scientific setting, but many and serious gaps in our knowledge remain. The "infectiousness of leprosy" is related to, but not wholly dependent upon, the transmission of the bacilli. Transepithelial implantation of viable organisms—by droplet infection, by inhalation from contaminated fomites, by the gastro-intestinal route, or otherwise—may or may not be followed by overt and recognizable clinical disease, though evidence is mounting that tell-tale changes in the lymphocytes may indicate challenge by *Myco. leprae* some time in the past.

Nor are all patients with leprosy equally contagious—a fact long appreciated. Some doubt still lingers in some minds concerning the demonstration of non-viability by means of the mouse footpad inoculation technique: an optimum micro-environment—which may include the presence of adjuvant biochemical moieties, intact macrophage cell-walls, or symbiotic organisms—might favour the growth of certain puzzling possibilities such as L-forms, aberrant forms, highly refractile spores, non-stainable granules and the like. Mycoplasma-like bodies, diphtheroids, and non-acid-fast rods may prove to be important in the life-history of the taxonomical chameleon that is *Myco. leprae*.

The size and repetition of the invasive challenge must also be an important factor, especially in relation to the presence of a changing degree of immunological refractoriness dependent on heredity, exposure to related mycobacteria, urban residence, age, and other factors.

Many puzzling questions remain unanswered. To judge by the nasal secretion, the presence of viable *Myco. leprae* in the lumina of sweat glands and of pilo-sebaceous glands, and in hair follicles, as well as by the enormous parasitization of the dermis and submucosa of the upper respiratory tract, lepromatous and near-lepromatous leprosy should be many thousands of times as infectious as tuberculoid leprosy. But it is not. Epidemiological surveys would indicate that at certain stages, patients with tuberculoid leprosy may apparently be the source of household infection to an extent quite out of proportion to the extremely scanty (and non-viable) bacillary infection of the dermal nerve fibrils. The family "clustering" of leprosy, too, needs further investigation, as does the pattern of sib infection in households.

The source of infection may frequently remain unrecognized for years: perhaps

it is a patient with barely visible macular areas of very slight hypopigmentation—teeming with organisms; or a patient with early damage to the nasal mucosa. Sometimes it is an old person with wrinkled, corrugated skin, who may be shedding *Myco. leprae* by the thousand every day.

On the other hand, many persons suffering from the late results of neglected neuropathy, and with discharging ulcerations of the extremities, or with progressive deformities, are frequently regarded by laymen as highly contagious. Much public education will be required before such persons are regarded as no longer posing a threat to the community, before ordinary folk are as convinced as are medical men that the exudate from sphacelous ulcers contains no viable leprosy organisms.

The occurrence of carriers, of potentially contagious subjects suffering from no discernible clinical manifestations of leprosy, opens up fascinating and disturbing vistas of epidemiological importance. "Leprosy houses" are part of the folk-lore in many countries: will they eventually prove to be part of the scientifically established pattern of transmission of the disease?

Vectors, also, have from time to time been incriminated, and recent published work indicates a revival of interest in this possibility of transcutaneous implantation of the viable organism. This mode is potentially far more important than tattooing, vaccination or injection as a widespread phenomenon by which the epidermis is penetrated by a pointed "instrument".

We have come a long way in trying to answer the question "How infectious is leprosy?" but if the areas of ignorance are thereby exposed and precise derivative questions are formulated, then, in the process of asking and answering, the frontiers of knowledge and the effectiveness of leprosy programmes will be advanced.

Lepr. Rev. (1973) **44**, 102-111

News and Notes

LEPROSY WORKERS HONOURED

In the Birthday Honours List, Her Majesty Queen Elizabeth has admitted two distinguished leprosy workers to the Order of the British Empire. Dr B. David Molesworth, now the Director of LEPRA's Control Scheme in Malawi, and Dr Harold Wheate, formerly Leprosy Adviser to the Government of Tanzania and now on the staff of A L E R T (Addis Ababa), both become Officers of the Order (O.B.E.). *Leprosy Review* extends its warm congratualtions to both Dr Molesworth and Dr Wheate.

LEPROSY IN THE WORLD

The figures given in the *Weekly Epidemiological Record,* published by the World Health Organization (*Wkly epidem. Rec.*, 1973, **48**, 49-53), are based mainly on replies received to a questionnaire circulated to governments.

The total number of registered cases of leprosy in 124 countries is 2,887,481, which represents an increase of about half-a-million over the figures from the same countries in 1965. It is encouraging to note that in some of the few areas where effective long-term programmes for leprosy treatment/control are in operation, the incidence of new cases appears to be declining slightly or at least is remaining constant.

As is the case in most European countries, the proportion of patients with lepromatous leprosy (the L/T ratio) is high in those European countries with an endemic leprosy problem–30% in Greece, 60% in Spain, and 72% in Portugal. Lack of uniformity in classification and inadequate case-finding, however, make comparisons in the L/T ratio between different countries invalid and misleading.

The numbers of "inactive cases" (544,719) and those "released from control" (368,789) show an encouraging increase that reflects the effectiveness of the measures adopted, but the numbers of known sufferers from leprosy who fail to continue with regular treatment, or who are "lost from control", are disturbingly high, even in countries with good leprosy programmes. Statistics concerning the presence and degree of disability are difficult to evaluate. Where the proportion of disabled patients is high, case-finding may be poor or facilities for treatment rudimentary.

Whereas in villages or small foci prevalence rates of 82 per 1000 have been reported, the maximum rates for larger foci (such as communes and districts) do not exceed 50 per 1000–a conclusion that will come as a surprise to those who have done regular whole-population surveys in areas in Tamil Nadu, West Bengal, Zaïre, Northern Nigeria and elsewhere.

The total number of cases of leprosy in the world, notwithstanding the increase in population, has probably not greatly changed in the years between 1965 and 1970.

THE WORK OF THE WORLD HEALTH ORGANIZATION IN 1972

The Annual Report of the Director-General of the World Health Organization for 1972 (Official Records No. 205) includes a very adequate summary (pp. 23-27) of the leprosy projects assisted or sponsored by WHO in various countries; and of the leprosy treatment/control programmes where the WHO contribution in technical guidance and advice, as well as in staff, drugs and transport, is proving of critical value.

Mention is made of the gradual integration of leprosy-control series into the basic health services in some countries, and the much-appreciated financial contribution of certain voluntary agencies to the Special Account for the Leprosy Programme. Co-operation between WHO and ELEP is reported to have been strengthened during the year.

In Central America (p. 24), the accent has been on the prevention of disabilities due to leprosy. In South-East Asia, WHO had assisted the leprosy campaign in such countries as Burma, Nepal, Sri Lanka and Thailand by providing the services of expert advisers, who have assisted in the gradual integration of leprosy into the general health services. Much still remains to be done in Ethiopia and the Sudan.

UNICEF continues to supply drugs to projects in a number of countries.

Epidemiological research in the field (p. 25)—microbiological research in the laboratory using modern technical resources and epidemiometric models, and animal inoculation (the mouse footpads, the armadillo) and the investigation of such problems as drug-resistance, growth requirements of *Myco. leprae* and its culture on soft agar and other media, and experimental transmission—are all being actively encouraged by WHO. Evidence is becoming available to suggest that the well-known form of *Myco. leprae* may be but a phase in the life-cycle of the organism.

The work on infusions of normal allogenic leucocytes from healthy donors into patients with lepromatous leprosy is referred to (p. 26), and the dramatic remissions observed in all patients so treated. Studies in the antigenic structure of *Myco. leprae* and attempts to develop a polyvalent vaccine come in for brief review.

The report provides encouraging evidence of a widespread interest in leprosy research and of fruitful co-operation between experts in various fields. In the course of the year 1972, no fewer than 41 institutes in 23 countries participated in 56 different research projects under the aegis of WHO.

It is stated (p. 40), that the risk of ocular complications in leprosy has been diminished by better methods of treatment. In Africa (p. 183), the function of WHO is mainly advisory, since leprosy control is in general carried out with assistance from other sources. The ambulatory treatment of leprosy patients is being emphasized in the Americas (p. 187) with the hope of avoiding unnecessary institutionalization. In the Western Pacific Region (p. 205), scarce funds are still being directed to maintaining patients in outmoded leprosaria.

The very useful meeting of investigators on immunological problems in leprosy research at New Delhi in December, 1972, is mentioned (p. 92). The meeting recommended the organization of a trial to determine the usefulness of transfer factor in increasing cellular immunity in lepromatous leprosy, and suggested promising areas of research into the immunology of leprosy and various collaborative investigations.

The detailed list of recommended research projects makes impressive and

imaginative reading: Burma (p. 245), Colombia (p. 226), Ecuador (p. 229), India (p. 246), Nepal (p. 249), Korea (p. 280), Sri Lanka (p. 250), and Sudan (p. 271), with special reference to the BCG trial in Burma (p. 285).

Altogether, a very useful document.

WORLD HEALTH ORGANIZATION–REPORT OF THE 25TH ASSEMBLY, 1972

This bulky volume of 635 quarto pages contains the reports of proceedings at the 25th World Health Assembly, held in Geneva from 9 to 26 May, 1972. The items of particular interest to readers of *Leprosy Review*, occurring in speeches of delegates, are summarized below.

Sierra Leone (p. 64). "Leprosy is well under control".

Nepal (p. 80). Pilot projects for the control of leprosy and tuberculosis will be improved on the basis of recommendations made by experts provided by WHO.

Mali (p. 97) confessed that the battle against leprosy was not yet won.

Chad (p. 104) optimistically proclaimed that leprosy control was undoubtedly well under way: the number of patients under treatment had declined from 50,175 to 27,791 in 10 years, and 21,975 had been discharged, "disease arrested". Much-appreciated help had been received from UNICEF.

The Republic of Congo (p. 105) had to report that the number of leprosy sufferers was still very large and that communicable diseases in general were still rife.

In Korea (p. 107), measures will be taken to decrease the incidence of leprosy, with mitigation of its economic consequences.

Peru (p. 120) promises an intensification of the programme for the control of endemic diseases, including leprosy, as does the Cameroon Republic (p. 123).

Malta (p. 129) acknowledges the help received from the Order of Malta in the control and eradication of the remaining foci of leprosy in the island.

Gabon (p. 134) hopes that the day is not far distant when a means will be found, perhaps a vaccine, of eradicating leprosy.

Niger (p. 138) reports success in its leprosy campaign. Half of the registered 18,000 cases have been treated, of whom 3000 have been placed on observation after adequate treatment.

Sri Lanka (p. 142) reported no change in the incidence rate of leprosy, which stands at 0.5 per 1000.

In Malaysia (p. 168) the leprosy control programme is being integrated with the existing health services.

Guinea (p. 170) confessed to a continuing concern about the leprosy problem. There are 69,794 known sufferers in the country.

In Paraguay (p. 177), the prevalence of leprosy is 2 per 1000, and the incidence 11.4 per 100,000. Help has been received from the German Leprosy Relief Association, and also from the Government of Japan.

The Regional Director of WHO for Africa admitted (p. 394) that leprosy programmes in some countries had not received priority in WHO assistance because sources "outside the Organization" (i.e. voluntary agencies) were already providing funds for leprosy. In order to avoid overlapping, and in the interests of the proper deployment of the limited resources available to WHO, a certain selection had to be made.

In view of its importance, and its relevance to the leprosy situation in many countries, which must be viewed in the context of the general health services, the following release from the World Health Organization is published *in extenso*.

TWENTY-SIXTH WORLD HEALTH ASSEMBLY– WIDESPREAD DISSATISFACTION ABOUT HEALTH SERVICES

Health services in many countries reveal a situation which should be of real concern. There appears to be widespread dissatisfaction of populations about their health services in many countries, rich and poor. This alarm is sounded in an organizational study of WHO's Executive Board on methods of promoting the development of basic health services. The study, which is before the World Health Assembly, states "in many countries the health services are not keeping pace with the changing populations either in quantity or in quality. It is likely that they are getting worse". Even if it is said that the health services are improving, the study considers that "a major crisis is on the point of developing and that it must be faced at once, as it could result in a reaction that could be both destructive and costly".

After considering the WHO study, the World Health Assembly in Committee stressed that: "Every Member State should develop a health service that is both accessible and acceptable to the total population, suited to its needs, and to the socio-economic conditions of the country." In certain countries there hardly exist any basic health services, but even in rich countries with developed services these are often not accessible to large sections of the public. Other causes of dissatisfaction can be summarized as follows: (a) failure to meet the expectations of the population; (b) inability of the health services to deliver a level of national coverage adequate to meet the stated demands and changing needs; (c) a wide gap (which is not closing) in health status between countries, and between different groups within countries; (d) rapidly rising costs without a visible and meaningful improvement in service; (e) a feeling of helplessness on the part of the consumer, who feels (rightly or wrongly) that the health services and personnel within them are progressing along an uncontrollable path of their own which may be satisfying to the health professions but which is not what is most wanted by the consumer.

The study goes on to list likely reasons for some of these occurrences: (a) there are insufficient health service funds in many countries, although the proportion of the national income spent on health services may often be similar in the wealthy and in the less wealthy countries; (b) many countries have an inadequate coverage of the population by state-supported health services; (c) people should be able to afford to use the services, and the services should provide a level of health care which people consider proper to use. A pattern is emerging of less or least utilization of health services in areas that have the least sufficient services; (d) there is a shortage of trained staff at all levels; but countries that have insufficient staff show the greatest maldistribution within the country, and appear to have the highest professional emigration rate.

Most of these factors are correctable and all deserve detailed attention. When applied to health services, existing techniques of planning, operational research and management may help decision making, but health service questions should be expressions of the national will, rather than of abstract mathematical considerations.

The Assembly Committee recommended that WHO should: (1) concentrate upon specific programmes that will assist countries in developing their health-care systems for their entire populations, special emphasis being placed on meeting the needs of those populations which have clearly insufficient health services; (2) so design its programmes as to encourage Member States to develop a strong national will to undertake intensive action, WHO resources being made available especially to such Member States as have this will; and (3) further develop management methods suited to health service needs and assist countries in developing a national capability of applying these methods.

The study was discussed in Committee B of the Assembly whose Chairman is Dr A. W. Al-Mufti (Iraq), the Vice-Chairman Dr jur. J. de Coninck (Belgium), and the Rapporteur Dr P. Mikem (Togo).

LEPRA ESSAY COMPETITION

To encourage the study of leprosy by Oxford medical students, the British Leprosy Relief Association (LEPRA) inaugurated an Essay Competition in 1972, offering a prize of £100 to the successful entrant. The subject, "The pathogenesis of human leprosy", attracted 7 entries.

This year, 9 scripts were submitted on the subject "The transmission of human leprosy". The general standard was very high, but one entry was outstandingly good. At the Annual General Meeting of LEPRA held in London on 7 June, 1973, Lord Boyd (the President of LEPRA) presented to Miss Celia Moss of St Anne's College, Oxford, a cheque for £100. In 1972, Miss Moss had had the advantage of spending some weeks at LEPRA's project in Malawi.

Leprosy Review offers its congratulations to Miss Moss, and thanks the other entrants for their interest in leprosy.

A L E R T, 1972

The Annual Report for 1972 of the All-Africa Leprosy and Rehabilitation Training Centre records a year of increasing activity and steady progress, despite staff shortages. During the year 80 trainees from outside Ethiopia and 111 Ethiopians followed full-time courses. The postgraduate course in Clinical Leprology was much appreciated by the 24 doctors who attended, most of whom had had little previous experience of leprosy. A 4-months' course for rural area supervisors was organized for 31 students. A highly successful joint seminar on Cellular Immunity and Resistance to Leishmaniasis, Leprosy and Tuberculosis in the Tropics was organized in association with the Armauer Hansen Research Institute. No fewer than 52 participants came for the 1-week seminar. An internationally renowned panel conducted the sessions and gave lectures.

A gratifying feature of the year's work was the liaison established with Professor General J. Languillon of the Institut de Léprologie Appliquée in Dakar. The General shares in the postgraduate course for doctors, and plans to visit Addis Ababa again for the same purpose in 1974.

The pattern of training and service is now becoming established, and the Board of Directors, aided by substantial financial help from a variety of sponsoring agencies and full co-operation from the Imperial Ethiopian Government, can now plan for the tasks ahead.

PROGRESS AT A L E R T

The 7th Annual General Meeting of Members of A L E R T this year was preceded on 8 March by a Workshop on Rehabilitation, chaired by Professor Paul Brand. It was generally agreed—after a discussion opened by Dr Ernest Fritschi in which many Board Members and staff joined—that A L E R T has assumed responsibility for leprosy patients, which includes concern for their rehabilitation and employment as well as their medical care. In the future, A L E R T should undertake the training of suitable candidates in the field of rehabilitation so that, in the context of African countries, the problems presented by disabled and unemployed patients whose disability is attributable to leprosy and other deforming conditions might be realistically and energetically tackled.

The provision of sheltered workshops, industrial projects, resettlement farms, and the organization of training units were huge problems, largely unmet up till now. Such costly projects could not be undertaken by A L E R T itself, whose rôle would probably be to train supervisory staff for various African countries, but pilot projects might well be developed to explore possible solutions. It was suggested that some form of Rehabilitation Agency might contribute to the integration of the efforts that may tend to be haphazard and fragmentary and hence less than optimally effectual.

Courses for Rural Area Supervisors, Rehabilitation Technicians and Nurses have attracted many participants, and in-service facilities for doctors and others with different interests have been provided.

Dr John Pearson, Dr Harold Wheate and Miss Ellen Kelly have been welcomed as new members of the staff. They will be devoting much of their time to teaching African nationals, who will in their turn, it is hoped, commit themselves to teaching their fellow-countrymen on their return home.

THE CHANGING PICTURE AT VALBONNE, FRANCE

Because of the decrease in the number of leprosy patients needing in-patient care for long periods, the population of this residential leprosarium in the south of France is declining. The authorities have guaranteed that any leprosy sufferer now in residence and needing in-patient treatment will be able to have it at Valbonne, and for as long as he needs it.

In order to do this and to ensure the necessary financing, it is proposed to open at Valbonne a service for the social rehabilitation of psychiatric patients. This new departure will fulfil a need and ensure utilization of the physical facilities available, as well as helping Valbonne financially. Such patients, numbering 25 at first and eventually rising to 80 or even 100, will stay for at least a year, and will be encouraged to participate in the activities of the Centre—agricultural and horticultural, building and construction, carpentry, etc. The ample area of 125 acres (50 ha) at present under cultivation will afford opportunities for the rehabilitation of another class of patients who have for long suffered from the social stigma and prejudice of society. Some new construction and much adaptation of old buildings will be needed before the plan is fully operative.

Metropolitan France is well served with facilities for the care of leprosy sufferers, and in Paris, Marseilles and Bordeaux, medical treatment and reconstructive surgery are available, and pathological investigations are proceeding.

The *Association de Léprologues de Langue Française* is actively concerned as a body and through its members with the problems of leprosy, both in France itself and in the French-speaking countries of the world.

PROGRESS IN DAKAR

The Second Meeting of the Scientific Advisory Board of the *Institut de Léprologie Appliquée* met at the offices of the Institute in Dakar on 13 April, 1973. Several representative personalities from Europe managed to be present despite the claims of the *Journées Médicales de Dakar*.

The Institute, under its dynamic Director, General J. Languillon, has made a good start, concentrating on exploratory surveys, evaluation of the existing leprosy control programme, and training of auxiliaries and medical students. Tentative proposals were announced for a series of lecture-demonstrations (in French) for doctors, similar to the courses given mainly in English at A L E R T, Addis Ababa.

The existing 26 beds in the clinic will shortly be augmented by another 24, intended for patients requiring reconstructive surgery for deformities and surgical treatment of the acute neurological complications of leprosy.

INDIA—BACKGROUND TO LEPROSY

The Union Ministry of Health of the Government of India is making far-reaching proposals for redressing the imbalance between towns and rural areas in the matter of availability of medical services. Eighty-two per cent of the population in the villages have access to only one-third of the qualified doctors. Since 1952, an integrated comprehensive scheme for the establishment of a Primary Health Centre in each community block (now containing between 125,000 and 250,000 people) has been slowly implemented, but the rapid growth of population has outstripped the original plans. Long distances, difficult terrain and lack of public transport have increased the disadvantages experienced by people living away from the Health Centres. Some 5131 Primary Health Centres had been established by the end of 1971—a figure not much below the target—but a rudimentary medical service is available to only about one-third of the rural population.

The Central Government, conscious of the growing demand and the growing need, and impressed by the success of the "feldsher" programme in the U.S.S.R. and the "bare-foot doctors" in the People's Republic of China, proposes to recruit enormous numbers of "Rural Medical Practitioners", giving them 16 weeks of training in Indian medicine and Homoeopathy before sending them out to the villages to engage in "programmes relating to health, hygiene, nutrition and also sanitation". Each such practitioner would serve a rural population of about 2000 persons living in 3 or 4 villages. Pilot projects are proposed before nationwide coverage is attempted.

The proposals have encountered the determined opposition of the Indian Medical Association, which has made a detailed and informed criticism of the fundamental assumptions of the plan to utilize the services of partly-trained auxiliaries who would have to combine loyalty to traditional healing with the practice of scientific medicine.

Leprosy workers engaged in the Survey-Education-Treatment programme in India, and those working in rural areas in other countries, will watch these moves in India with much interest. It remains to be seen whether the leprosy patient will receive a better deal from the proposed Rural Medical Practitioner than he is at present getting from an admittedly inadequate conventional medical service.

The first State to consider a Bill for registering these practitioners is Kerala.

The Bill has been referred to a select Committee of the State Legislature. It is expected that following the definite directive of the Central Government, other States will shortly follow suit.

MADAGASCAR

For some years the leprosy situation in Madagascar has been a matter of concern to voluntary agencies and to the government. Despite the expenditure of considerable sums of money and the efforts of many devoted workers, little lasting impression has been made on the total prevalence of leprosy.

In June, 1972, the Medical Commission of ELEP recommended that a small team should investigate the leprosy situation and advise. Two distinguished Frenchmen—Monsieur J. Masselot (the former Inspector-General of Overseas Territories) and Monsieur P. Ricolfi (an experienced civil engineer)—have recently published their report on an exhaustive and detailed examination of the leprosy programme in Madagascar. The prospects are not very reassuring.

In a population of some 7 million, the number suffering from leprosy would probably reach 70,000. Since the total population is increasing at the rate of 2½% per year (i.e. doubling in less than 30 years), case-finding at the present rate will not result in total coverage for several decades.

Meanwhile, the number of patients newly recorded for treatment each year represents a diminishing proportion of those diagnosed as suffering from leprosy and needing treatment. Futhermore, the number of patients who have attained clinical quiescence as a result of treatment also shows a progressive diminution year by year, and the proportion of patients under treatment who attend regularly is slowly falling and is now about 70%. The percentage of lepromatous (or "multibacillary") leprosy, according to the official statistics, would be from 25 to 30%.

The authors of the report give a very full appraisal of their visits to all the centres organized by the voluntary agencies concerned—*Emmaus Suisse, Les Amis du Père Damien, l'Ordre de Malte, DAHW*—and make firm recommendations regarding the re-orientation of the work in conjunction with the government policy and plans.

GANDHI MEMORIAL LEPROSY FOUNDATION—ANNUAL REPORT, 1971-72

The Foundation's 22nd Annual Report provides an interesting survey of its activities. After more than 10 years of investigation of the use of dapsone in different parts of India, the Foundation became convinced in 1955 that dapsone could "control leprosy". It therefore embarked upon the application of control measures in 4 areas. To date, 4326 patients have received treatment for leprosy, of whom 114 were diagnosed in 1971-72. As the result of different methods of attack adopted in different areas, it is concluded that there is no effective replacement for the time-honoured "survey-education-treatment" programme officially recognized by the Indian Government.

More recently, the Foundation has added health education to its activities, concentrating initially on doctors and teachers and then extending its work to schools and villages. In 1971-72, some 1946 doctors were among the 4343 community leaders who were brought into contact with the health education units, and 335 doctors in 10 batches followed some course of instruction in

leprosy. Since there are over 80,000 doctors working in Indian States where endemic leprosy is a problem, the Foundation arranged an orientation programme for Professors of Medical Colleges, and hopes that State Governments will co-operate in releasing these influential teachers for 3-day orientation courses in leprosy.

ELEP AND LEPROSY RESEARCH

In the year 1972 Members of the Federation of European Leprosy Associations (ELEP) contributed from their general funds about 440,000 dollars (U.S.) for leprosy research. This very respectable sum was mostly devoted to projects approved by the Medical Commission of ELEP or a Member Organization, but a proportion was used by the World Health Organization for its progamme on the culture of *Myco. leprae*, or through its special leprosy fund.

When the research activities of other voluntary agencies throughout the world are taken into account, together with those of governments and foundations, and also the tremendous up-surge in interest in departments not hitherto concerned with leprosy, it will be concluded that the volume of research in leprosy is truly impressive.

ELEP IN ROME

During the meetings of the Medical Commission and the General Assembly of ELEP held in Rome from 6 to 8 April, 1973, participants were invited to 2 functions that took them away from their deliberations on world-wide problems of leprosy.

The first was on Friday, 6 April, when His Holiness the Pope gave an audience to representatives of Member Organizations and their ladies. After His Holiness had welcomed them in a warm tribute to those engaged in one way or another in the struggle against leprosy in the world, His Excellency the Ambassador Béat de Fischer, President of ELEP for the year, replied suitably before presenting 5 representatives, including 2 members of the Medical Commission, Doctors L. P. Aujoulat and S. G. Browne.

The second occasion was a Reception given the following day by His Most Eminent Highness, the Prince and Grand Master of the Order of Malta, in the Palace of the Knights of Malta, historic headquarters of the Order in the centre of Rome. At this ceremony, Dr S. G. Browne, President of ELEP's Medical Commission, received the Cross of Commander *"pro merito melitensi"* for his services to the cause of leprosy.

During the year 1972, the Member Associations of ELEP were responsible for collecting over 7,700,000 dollars (U.S.), which was used to help 586 centres treating over 900,000 leprosy patients.

THE ARMADILLO

Dr Eleanor Storrs and her colleagues at the Gulf South Research Institute, Louisiana, are vigorously pursuing several promising research projects using the armadillo.

Reports of the susceptibility of this animal to infection with *Mycobacterium ulcerans* are now confirmed. The organism grows slowly on artificial myco-

bacterial media, and apparently grows best at a temperature of 32°-33° C. The successful inoculation of 2 armadillos (out of 4) with *Myco. ulcerans* opens the way to investigations that should not only identify the substances that cause the severe tissue damage seen in Buruli ulcer, but should indicate the direction to be pursued in chemotherapeutic studies.

Reports of the discovery of *Myco. leprae* in the central nervous system (cerebrum, cerebellum, spinal cord and meninges) of armadillos inoculated intravenously with a suspension of the organisms, suggest that the choroid plexus barrier may be traversed in an animal more susceptible than man to leprosy infection. Recent isolated findings in the experimental mouse infected through its footpads points the way to a more widespread infection in the armadillo. Perhaps the histopathologists will now stain and painstakingly examine serial sections of brain tissue from human patients dying after long-standing lepromatous leprosy.

The German Leprosy Relief Association (Deutsches Aussätzigen-Hilfswerk E. V.) has recently made a welcome grant of 3000 U.S. dollars to support the work at Indian Camp, Louisiana.

Lepr. Rev. (1973) **44**, 112-119

Dopa Metabolism by *Mycobacterium leprae:* Its Implications in Culture of the Bacillus and Chemotherapy of Leprosy*

K. PRABHAKARAN

U.S. Public Health Service Hospital, Carville, Louisiana 70721, U.S.A.

An integrated review is made of the investigations on a new type of tyrosinase (*o*-diphenoloxidase) detected in *Mycobacterium leprae*. The enzyme was different in several respects from tyrosinase obtained from plant or mammalian sources. Inhibitors of *o*-diphenoloxidase suppressed multiplication of leprosy bacteria in mouse footpads, indicating that the enzyme might have a key metabolic rôle in the growth of *Myco. leprae*. Suspensions of the organisms exposed *in vitro* to one of these inhibitors (diethyldithiocarbamate) completely lost their viability. The host tissues preferentially invaded by the bacilli (i.e. the skin and the peripheral nerves) are of ectodermal origin where metabolism of DOPA or its derivatives is important. Our results show that DOPA and other phenolic substrates are rapidly utilized *in vitro* by *Myco. leprae*. These observations suggest that, besides other factors, small amounts of DOPA continually generated by living cells may be essential for the survival and proliferation of the leprosy bacteria.

Introduction

Ever since the discovery of *Mycobacterium leprae* was reported in 1874, innumerable attempts have been made to cultivate the organism in bacteriological media; however, no established procedure is available as yet for culture of the bacillus. Similarly, little success had been achieved until recently to transmit the systemic (lepromatous) form of the disease to normal (immunologically intact) experimental animals. Now it has been found that some 9-banded armadillos (*Dasypus novemcinctus* L.) develop the systemic type of the infection on inoculation with *Myco. leprae* (Kirchheimer and Storrs, 1971). Previously it had been shown that a limited multiplication of the bacilli takes place in the footpads of mice (Shepard, 1960).

The sulphone drugs which are generally used at present in leprosy have to be administered for prolonged periods and many patients develop adverse reactions in the course of the treatment. Moreover the emergence of sulphone-resistant *Myco. leprae* is becoming increasingly evident (Browne, 1969; Jacobson and Trautman, 1971). The antibiotic, Rifampin (rifampicin), recently introduced in the treatment of leprosy has shown a profound bactericidal effect on the organisms (Rees, Pearson and Waters, 1970). However, it is known that resistance to Rifampin occurs not uncommonly in several other species of bacteria (Riva and Silvestri, 1972).

An understanding of the metabolic properties of the leprosy bacillus might be of use in developing more effective chemotherapeutic procedures and in attempts

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at cultivation of the organism. When we started our studies, almost nothing was known about the metabolism of *Myco. leprae*. In human leprosy the causative organism preferentially invades the skin and the peripheral nerve tissues. This may indicate the requirement of a common metabolite present in both these tissues for the survival and proliferation of *Myco. leprae*. The multiplication of brucellae in specific tissues of certain animals has been shown to be due to the presence of erythritol at these sites (Smith, 1968). There are reports that the body temperature in areas of the human body invaded by the leprosy bacilli is lower than normal (Binford, 1956; Brand, 1959; Hastings *et al.*, 1968). It may be pointed out, however, that the skin and the nerve tissues are of ectodermal origin and that the metabolism of 3,4-dihydroxyphenylalanine (DOPA) or its derivatives is important at these sites.

Source of Bacilli

Since no culture of *Myco. leprae* is available, the organisms used in our investigations are obtained from leprous human tissues or from the tissues of armadillos which developed massive infection after inoculation with the bacilli. The bacteria have to be prepared so as to be essentially free of host tissue material and in a metabolically active state. For this purpose solvents which might denature proteins and inactivate enzymes cannot be employed. We homogenize the infected tissues and separate the bacilli by differential and density gradient centrifugations in inert solutions such as those of sucrose and KCl. The preparations obtained by this method (on staining by the Ziehl-Neelsen procedure) proved to be concentrates of mycobacteria free of any visible tissue debris (Prabhakaran, Harris and Kirchheimer, 1969, 1971). The organisms are used in the intact state or are disrupted by ultrasonic oscillation. To remove any substances adsorbed from host tissue, the bacilli are treated with trypsin, acetone, and ether, or repeatedly washed with saline and water.

Phenoloxidase

Measurement of oxygen uptake by the Warburg manometric technique showed that *Myco. leprae* rapidly oxidizes DOPA (Prabhakaran, 1967*b*). But this method requires large amounts of material which are not readily available, and therefore more sensitive techniques had to be adopted to assay the DOPA oxidase activity of the bacilli. The enzyme involved in the conversion of tyrosine or DOPA to pigmented products is referred to as tyrosinase, phenolase, or *o*-diphenoloxidase. Tyrosinase is not restricted to vertebrate melanocytes; it occurs in invertebrates and is widely distributed in the plant kingdom. Fungi are rich sources of the enzyme; lyophilized mushroom tyrosinase is commercially available. Extracts of mouse melanomas are used in our studies as sources of mammalian *o*-diphenol-oxidase. Several species of mycobacteria tested, including *Myco. lepraemurium*, *Myco. tuberculosis* and some so-called *Myco. leprae* cultures showed no phenolase activity. Oxidation of DOPA has been proposed as an identification test of the leprosy bacilli (Prabhakaran and Kirchheimer, 1966, Kirchheimer and Prabhakaran, 1968). *Myco. leprae* did not oxidize tyrosine to quinone.

Two quinone intermediates in the oxidation of tyrosine or DOPA to melanin are chromophoric and have been identified by their characteristic absorption spectra (Mason, 1955). *o*-Diphenoloxidase from mammalian or plant sources gives

rise to the quinone dopachrome, which has an absorption maximum around 280 nm. Indoles-5,6-quinone, which is believed to polymerize to melanin shows a peak at 540 nm in the spectrum. The spectrophotometric method, being more sensitive than the manometric technique, was used in most of our experiments.

When the spectrum of the reaction intermediates was measured it was found that *Myco. leprae* obtained from leprous human tissues gives rise to indole-5,6-quinone from DOPA, whereas mammalian and plant tyrosinases produce dopachrome. The formation of indole-5,6-quinone involves a decarboxylation step. The results suggest that an active decarboxylase is associated with the *o*-diphenoloxidase of the leprosy bacilli separated from infected human tissues (Prabhakaran, 1968).

At present we are using the liquid scintillation-counting procedure, in which oxidation of tritiated DOPA by the bacilli is measured. By the radio-isotope tracer technique, oxidation of labelled DOPA has been demonstrated in organisms recovered from leprous human tissues as well as from tissues of experimentally infected armadillos (Prabhakaran, Harris and Kirchheimer, 1973).

It is known that the substrate specificity of *o*-diphenoloxidase becomes restricted with a rise in the phylogenetic scale (Mason, 1955). The enzyme from plants and microorganisms oxidizes several phenolic substrates, whereas tyrosinase from vertebrate melanocytes is relatively specific for L-tyrosine and L-DOPA. Because *Myco. leprae* is a micro-organism obtained from human tissues, it was of interest to study the substrate specificity of the enzyme in the bacilli. Our studies showed that *Myco. leprae* oxidizes D-DOPA at the same rate as L-DOPA and oxidizes also a variety of phenolic compounds *in vitro*, indicating that the enzyme has a wide substrate specificity. Mammalian tyrosinase obtained from melanomas rapidly converted L-DOPA to dopachrome; it showed very little activity towards D-DOPA and was completely inactive towards the other phenolic substrates (Prabhakaran, Harris and Kirchheimer, 1972).

Certain enzymes like acetylcholinesterase are inhibited by increasing substrate concentration (Davies and Green, 1959). In the oxidation of L-DOPA by mammalian tyrosinase a distinct inhibitory effect was observed when the substrate concentration was increased. In *Myco. leprae*, high substrate levels produced no inhibition of *o*-diphenoloxidase (Prabhakaran, Harris and Kirchheimer, 1972).

Besides *o*-diphenoloxidase, a few other enzymes and copper proteins oxidize phenolic substrates to pigmented products. Diphenols like DOPA are oxidized by peroxidase. It has been reported that along with tyrosinase, peroxidase is involved in the formation of melanin pigment in the human skin (Patel *et al.*, 1971). In our experiments peroxidase, as well as catalase oxidized DOPA in the presence of hydrogen peroxide. Without peroxide, these enzymes showed no activity towards DOPA. Phenolase of *Myco. leprae* and tyrosinase of plant or mammalian origin oxidized DOPA without added hydrogen peroxide and also did so when catalase was added to destroy any endogenous peroxide (Prabhakaran, Harris and Kirchheimer, 1972). Previous results showed that *Myco. leprae* contains both catalase and peroxidase (Prabhakaran, 1967*a*).

All the evidence led to the conclusion that the phenolase of the leprosy organisms is probably a true *o*-diphenoloxidase, and that other copper proteins and catalase or peroxidase are not involved in the enzyme activity observed (Prabhakaran, Harris and Kirchheimer, 1972). Presence of phenolase in *Myco leprae* has been corroborated by other workers (Beaman and Barksdale, 1970).

Reducing Agents

In the formation of melanin pigment by skin melanocytes, substances like reduced glutathione are known to have a regulatory function. Decrease of reduced glutathione caused by ultraviolet rays results in greater pigment production. In our *in vitro* studies, using mammalian and plant phenolase, no quinone formation from DOPA was observed in the presence of reducing agents (ascorbic acid, reduced glutathione or cysteine). When these substances were added after the quinone was formed, it was rapidly decolorized, indicating that the quinone is reduced back to diphenol. However, in the case of *Myco. leprae*, reducing agents had no effect on the formation of quinone from DOPA. The reducing substances prevented further oxidation and polymerization of the quinone to melanin; but they did not reduce the quinone back to diphenol (Prabhakaran, 1971).

Detergent Treatment

The phenoloxidase of *Myco. leprae* was found to be firmly attached to particulate elements in the bacterial cell, unlike plant tyrosinase which is a soluble enzyme. Recently we have been able to release the phenolase of the bacilli from the particles by detergent-treatment. The anionic detergent, sodium dodecyl sulphate, liberated at least two-thirds of the enzyme activity of the disrupted bacteria into the soluble fraction. Deoxycholate was the most effective detergent for releasing mammalian tyrosinase from particles; this detergent, however, was ineffective in *Myco. leprae* (Prabhakaran, Harris and Kirchheimer, 1973).

Inhibitors of Phenolase

If phenoloxidase has a biological rôle in the leprosy bacilli, inhibitors of the enzyme might be of value in developing a rational chemotherapy of leprosy. Several inhibitors were tested *in vitro* on *o*-diphenoloxidase from *Myco. leprae* and from mammalian and plant sources. Copper chelators proved to be more effective than substrate analogues. Diethyldithiocarbamate (DDC) was found to be the most potent inhibitor (Prabhakaran, Harris and Kirchheimer, 1969). This compound produced total inhibition of the phenolase of *Myco. leprae* even at low concentrations. The molecular model showed that DDC has 2 ethyl groups (lipid-soluble, non-polar masses), which shadow the 2 sulphurs (the polar region). As such DDC could easily pass through lipid-predominant pores or membranes.

Chemotherapeutic Implications

To ascertain whether phenolase activity is important in the survival and proliferation of *Myco. leprae*, the effect of several inhibitors of phenoloxidase was tested on the multiplication of this organism in the mouse footpad (Prabhakaran, Harris and Kirchheimer, 1972). After inoculation of the mice with *Myco. leprae*, 30 μg of the drug in 0.03 ml of saline was injected once daily into the footpads, on 5 days a week for 6 months. Untreated mice and mice treated with saline (after inoculation with *Myco. leprae*) served as controls. Enumeration of the bacilli in the footpads showed that no multiplication of *Myco. leprae* occurred in

mice treated with phenolase inhibitors. Inoculation with normal saline had no effect. Penicillamine and mimosine are inhibitors of tyrosinase from mammalian and plant sources, but they do not inhibit the enzyme in *Myco. leprae*, either intact or disrupted. These compounds also did not suppress multiplication of the bacilli in the mice (Prabhakaran, Harris and Kirchheimer, 1972).

The above results do not indicate whether inhibitors or phenolase will have any effect on established infections of the bacilli in mouse footpads. Further studies, in which treatment was started 3 months after inoculation of the mice with *Myco. leprae*, showed that diethyldithiocarbamate (DDC) was the most effective phenolase inhibitor which prevented proliferation of *Myco leprae*. DDC penetrated intact bacilli and produced complete inhibition of phenoloxidase, whereas the other compounds partially inhibited the enzyme in disrupted bacilli. One of these inhibitors, thioadenine sulphate, was tested in the mice and it did not suppress multiplication of *Myco. leprae*, once the infection had established itself in the footpads (as revealed by histological examination of the footpads in untreated mice) (Prabhakaran, Harris and Kirchheimer, 1972).

In another series of experiments, the mice were treated with DDC, sulphoxone sodium or Rifampin 6 months after inoculation of the footpads with *Myco. leprae*. Before treatment, bacterial counts in control mice showed that the bacilli had multiplied. After 6 months' treatment, no significant reduction in the number of organisms was found in the footpads. The bacilli recovered from the control and the treated mice were reinoculated into new groups of mice. Six months later the organisms from untreated mice had multiplied normally, but only a slight increase in number was noted in the case of organisms obtained from mice treated with sulphoxone sodium. On the other hand, bacilli from animals treated with DDC or Rifampin showed no multiplication at all (Prabhakaran, Harris and Kirchheimer, 1972). These results indicate that the drugs probably had a bactericidal effect on *Myco. leprae*.

DDC is a potent copper chelator and phenolase is known to be a copper enzyme. DDC has been successfully used in a patient with Wilson's disease (hepatolenticular degeneration), and in toxicity tests on animals the drug was found to be 5 times less toxic than penicillamine, which is generally used in the treatment of Wilson's disease (Sunderman, Jr, *et al.*, 1963). Diethyldithiocarbamate most likely inhibits tyrosinase by binding the copper moiety of the enzyme. As such, this compound promises to have two definite advantages over other drugs, especially in cases of leprosy where drug-resistance is encountered. (1) Rifampin-resistance in bacteria is reported to be mediated by a single-step mutation involving one amino-acid in the RNA polymerase enzyme, which is normally bound by the drug (Wehrli and Staehelin, 1971). Because DDC forms a complex with the copper moiety of phenolase and not the enzyme protein itself, any mutation involving amino-acid substitutions in the enzyme is not likely to influence its effectiveness. (2) Many bacteria become resistant to certain drugs because the bacterial cell membranes develop a permeability barrier. The molecular structure of DDC is such that it can easily penetrate lipid-predominant pores of membranes. These considerations show that DDC might be useful in cases where the bacilli have developed resistance to sulphones and other drugs employed in the treatment of leprosy. However, several problems regarding use of DDC in patients remain to be worked out. It has to be mentioned that DDC is unstable under acid conditions and has to be buffered before administration; moreover, it might produce copper depletion.

Physiological Rôle of *o*-Diphenoloxidase

The results reviewed here show that *o*-diphenoloxidase activity of *Myco. leprae* is probably essential for its multiplication. However, the exact physiological rôle of this enzyme is not clear. In plants, the quinones formed from DOPA have been reported to serve as electron carriers, undergoing reversible oxidation-reduction (Robinson and Nelson, 1944). In the presence of tyrosinase, reducing substrates interact with quinone and are oxidized; the quinoné which is reduced back to diphenol in the process is regenerated by the enzyme. *o*-Diphenoloxidase thus might serve as an alternative respiratory pathway. This would be important in organisms in which the cytochrome and flavoprotein systems are not fully active, as is probably the case in the leprosy bacillus (Prabhakaran, 1967*a*).

As mentioned earlier, *Myco. leprae* has a predilection for the skin and the peripheral nerve tissues where DOPA metabolism is important. In advanced cases of leprosy, the eyes are very often involved, the ciliary body and the iris being frequently invaded by the bacilli. Surprisingly, free DOPA has been demonstrated at these sites in the mammalian eye (Pirie, 1968). The testis is known to be a site where the leprosy bacilli proliferate; it has been found that human spermatozoa possess a characteristic enzyme which oxidizes DOPA (Ackerman, 1970). *Myco. leprae* also multiplies in the Schwann cells, the dorsal root ganglia of spinal nerves, and in the adrenal medulla. It may be significant that all these tissues have a common origin in the neural crest during embryonic development (Rawles, 1948). The melanocytes originate from the neural crest and are distributed in areas such as the skin and the mucosal membranes which are invaded by the leprosy bacilli. In the armadillo, in which systemic infection with *Myco. leprae* has been reported (Kirchheimer and Storrs, 1971), besides the special features mentioned by the authors, it may be noted that the skin of this primitive mammal has only a sparse coating of hair. As such, free melanocytes (not associated with the hair bulb) might be distributed in the skin, so differing from rodents and other mammals covered with hair. In animals like the mouse, *Myco. leprae* multiplies preferentially in areas such as the footpads and the ear lobes, which are free of hair.

When viable suspensions of *Myco. leprae* (which subsequently multiplied in mouse footpads) were added to cultures of melanocyte cells, the formation of melanin pigment was suppressed; non-viable bacteria (heat-killed organisms or those obtained from autopsies) failed to do so. It is likely that the utilization of DOPA by the bacilli produces this effect (Prabhakaran, Harris and Kirchheimer, 1971). Our studies *in vitro* demonstrate that the leprosy bacilli actively metabolize DOPA and its derivatives. These observations, and the predilection of the organisms for those specific sites in the human body derived from the neural crest, indicate that DOPA might be an essential metabolite in the growth of *Myco. leprae*. However, it is an unstable compound, which will undergo auto-oxidation if added to culture media. Probably a continual supply of small amounts of DOPA generated *in vivo* by the host tissue favours the multiplication of the leprosy bacteria, and an experimental system in which such conditions could be replicated *in vitro* has to be devised for the culture of *Myco. leprae*.

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"Mobile" Leprosy Control in the Luapula Province of Zambia*

B. JOGAN

Leprosy Specialist, Ministry of Health, Lusaka, Zambia

and

I. ROGERS

Leprosy Control Officer, British Leprosy Relief Association (LEPRA)

This is a brief report on the progress of a LEPRA Project in the Luapula Province of Zambia. The period from the start of the project in September, 1970, until the end of 1972 is reviewed. The operational methods employed are described and the results of the projects so far are reported, with pertinent statistics and comments.

Introduction

The first leprosy mobile treatment compaign in Zambia was introduced in the Eastern Province in 1968 as a joint venture of the Zambian Ministry of Health and the British Leprosy Relief Association. The Association provided an experienced Leprosy Control Officer, Mr A. H. Drake, and 2 Land Rovers. The Ministry provided 2 Medical Assistants, a Tuberculosis-Leprosy Preventive Assistant, and their accommodation, as well as funds for the running and maintenance of the vehicles. The results of the scheme were published in *Leprosy Review* (1970) 41, 115-120.

As the mobile treatment scheme in the Eastern Province of Zambia proved to be very successful, it was therefore decided to start a similar venture in the Luapula Province. This Province covers an area of 19,524 sq. miles with an estimated population of some 360,000 in mid-1972; it has pretty good lines of communication, and a reasonable number of Medical Centres in the most thickly populated parts of the Province.

Operational Methods

In August, 1970, LEPRA provided 2 Land Rovers and the services of Mr I. Rogers, an experienced Leprosy Control Officer, who was transferred from the LEPRA project in Malawi. The Zambian Government provided 2 Medical Assistants, in addition to funds for the running and maintenance of the vehicles.

For practical reasons, the Province was divided into 2 regions and 1 vehicle was based on Mansa, the provincial capital, while the other was based at Kabalenge Leprosy Settlement to provide the services for the northern part of the province. A Medical Assistant was placed in charge of each of these regions, with Mr Rogers

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in overall charge of the running and extension of the scheme for the whole province.

At the start of the project, it was decided to make some modifications in respect of the project in the Eastern Province where the entire leprosy out-patient treatment was undertaken by the mobile teams. The staff of the Rural Health Centres in Luapula Province remained responsible for the treatment of leprosy patients in their respective clinics, but under the strict supervision of the LEPRA teams. It was envisaged that with the new approach, the local staff would acquire an adequate knowledge of the problems of leprosy and would show more interest in the treatment of the disease. At the same time, such a decision was in line with the general policy of an integrated health service in Zambia.

Once the Project was well under way, mobile treatment runs would be established in those areas of the province having scarce medical facilities in order to bring treatment centres closer to the patients' homes.

Treatment

It was decided at the beginning of the project that mobile treatment would be dispensed to the patients by intramuscular dapsone injections at 4-week intervals, using disposable syringes. During the period under review not a single case of abscess formation was reported.

Preliminary Work

During the early stages of the project, the 2 teams visited Rural Health Centres in the province in an attempt to obtain a true picture of the leprosy situation then prevailing. It was very soon discovered that the available figures covering the leprosy situation could not be relied upon. (a) The leprosy registers were in complete disorder, many patients being listed who had not attended for treatment for many years. (b) Owing to the unreliability of the recording system, it was impossible to assess the percentage of attendance for treatment, but we would estimate it to be below 50%. (c) Many patients listed in the leprosy registers were without any personal records, and therefore, no data were available about the various types of leprosy or when patients had started treatment. (d) At many Rural Health Centres the treatment of leprosy patients was left to orderlies and dressers, who were not qualified to decide the best treatment. (e) The classification of leprosy was frequently left to staff with an inadequate knowledge of the disease. (f) A very high percentage of patients, though listed as "on parole", had not taken treatment for many years, but their names appeared on the register. There were 377 of these patients "on parole".

Case Finding Campaigns

1. SCHOOL SURVEYS

From the early stages of the project it had been decided to start an intensive school survey, and plans were set up accordingly. This was a priority objective for the following reasons: (a) There are no difficulties in the way of schools' medical examinations. (b) From experience gained in previous school surveys in the Eastern Province and elsewhere in Zambia, it was known that school authorities were very cooperative and helpful in carrying out surveys, and attendence for

TABLE 1

Out-patients on treatment at 31 December, 1970 (start of LEPRA project)

Classification	Male	Female	Children 0-14 yr	Total	Distribution (%)
Lepromatous	186	99	2	287	17.4
Borderline	249	271	12	532	32.2
Tuberculoid	291	394	37	722	43.7
Indeterminate and unclassified	23	51	37	111	6.7
Totals	749	815	88	1652	
Distribution by age and by sex for adults	45.3%	49.3%	5.3%	100%	

N.B. 377 patients were out on parole and are not included in the above figures.

TABLE 2

Out-patients on treatment at 31 December, 1972

Classification	Male	Female	Children 0-14 yr	Total	Distribution (%)
Lepromatous	241	109	1	351	14.3
Borderline	301	283	35	619	25.0
Tuberculoid	397	590	270	1257	51.3
Indeterminate and unclassified	39	61	123	223	9.1
Totals	978	1043	429	2450	
Distribution by age and by sex for adults	40%	42.5%	17.5%		

N.B. 164 patients on parole are included in the above figures.

examination was always very high. (c) With this type of survey it is comparatively easy to assess a valuable and reliable prevalence rate of leprosy in the chosen group.

2. VILLAGE SURVEYS

It is well known to leprosy workers that intensive village surveys are a time-consuming exercise, very costly, and require good planning, for the following reasons: (a) It is difficult to obtain correct census figures for areas chosen for the survey. (b) Contacts with local authorities and traditional Chiefs do not always stimulate the hoped-for enthusiasm and cooperation on their part. (c) Prejudices deeply entrenched in the local population play an adverse rôle against a successful response. (Similar difficulties were encountered during village surveys in the Luapula Province.)

Table 4 shows the statistics for village surveys.

Leprosaria

With the LEPRA project well established in the province, many leprosy patients, who were previously admitted to hospital because they lived far from

TABLE 3

Rate in schoolchildren

Schools visited	No. of children examined	Positive cases	Rate	Doubtful cases[a]	Rate
249	65,439	418	6.39 per 1000	555	8.48 per 1000

[a] Under "doubtful cases" are listed children with undefined skin lesions; these children will be followed up in future and some of them may develop clear signs of leprosy.

TABLE 4

Age distribution

0-15 years	15+ years	Total	No. of cases detected	Rate
2256	3140	5396	13	2.41 per 1000

TABLE 5

In-patient position on 31 December, 1970

Classification	Under 14 years	Over 14 years	Total	Distribution (%)
Lepromatous	–	88	88	56.4
Borderline	1	45	46	29.4
Tuberculoid	3	18	21	13.4
Unclassified	–	1	1	0.6
Totals	4	152	156	
Distribution by age	2.56%	97.43%		

TABLE 6

In-patient position on 31 December, 1972

Classification	Under 14 years	Over 14 years	Total	Distribution (%)
Lepromatous	–	57	57	52.7
Borderline	1	26	27	25.0
Tuberculoid	2	19	21	19.4
Unclassified	–	3	3	2.7
Totals	3	105	108	
Distribution by age	2.77%	97.22%		

the nearest treatment point, could be discharged from the Leprosaria to out-patients treatment. It soon became very clear that with the progress of the out-patients treatment programme, one leprosarium in the province was sufficient to provide any necessary hospital accommodation for all in-patients from the entire province. One of the two Leprosy Settlements in the province was, therefore, closed at the end of 1971. (See Tables 5 and 6.)

Observations

Comparing the figures in Tables 1 and 2, the following conclusions may be drawn.

(1) In the 2-year period of the LEPRA project the number of leprosy patients in the Province has increased from 2195 to 2450, but the actual number of patients on active treatment has increased from 1652 to 2286.

(2) During the same period, 370 patients were released from control, which means that the number of patients on active treatment has increased by 1004 new cases.

(3) Of the total number of patients in the province at the end of 1972, 39.3% are suffering from the infectious type of leprosy, and 60.4% from the non-infectious type.

(4) Comparing the percentage of the various types of leprosy in the 2 above-mentioned tables, it is easy to see that the number of cases of tuberculoid leprosy has increased in the 2 years under consideration. This is due to the following facts: (i) the adoption of the WHO classification; (ii) to improved recording; and (iii) a higher number of schoolchildren brought under treatment.

(5) There were no base-line data available showing the attendance for treatment before the start of the new project, so that no comparable figures are available Nevertheless, in the 2 mobile runs, where 227 patients are taking treatment, the attendance varies from 75% to 100%, compared with the attendance rate of 60% at the static clinics.

Economic Considerations: Cost per Patient

The current expenditure for the leprosy control programme in Zambia is included in the General Health Budget, and therefore no definite data are available. Nevertheless, an attempt was made a few years ago to ascertain the approximate cost per leprosy patient in the leprosaria and in the out-patient treatment programme.

The average annual cost per patient was as follows:

(1) Liteta Government Leprosy Hospital	*K460.00
(2) Chikankata Mission Leprosy Settlement	K130.00
(3) LEPRA Project–Eastern Province	K19.00
(4) LEPRA Project–Luapula Province	K5.43

Calculating the average cost per patient, we took into consideration the purchase cost of the Land Rovers, the cost for the running and maintenance of these vehicles (at the rate of 15n per mile), and staff salaries. The cost of drugs was not included, but this is not of great relevance to the final cost.

The higher average cost per patient in the Eastern Province is due mainly to the mobile treatment introduced throughout the entire province, the greater distances to reach the mobile clinics, and to the smaller number of cases on treatment, whereas in the Luapula Province much of the out-patient treatment was undertaken by the established Rural Health Centre staff, but under the supervision of the LEPRA teams.

It has been proved once again that out-patient treatment is the cheapest way of approach to the treatment of leprosy.

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* One Kwacha is equal to 80p.

It is too early to reach a conclusive judgement about the success or failure of the LEPRA project after 27 months of its operation, but nevertheless, the following are its main achievements so far: (1) We have now reliable statistical data about the prevalence rate of known leprosy patients in the Province. (2) Accurate figures for the prevalence rate of leprosy among schoolchildren in the Province are now available. (3) The attendance for treatment has greatly improved, but we are unable to say exactly by how much owing to the lack of base-line comparable data. In the mobile runs, which care for 227 patients, the attendance is now above 75%. (4) The LEPRA project in the province has proved to be the most economical approach to a successful leprosy control programme. (5) Under the regular supervision of the LEPRA staff, the para-medical staff in the Rural Health Centres have acquired a better knowledge of leprosy and they are now showing more interest in the treatment of leprosy. (6) The patients are aware that a greater interest is being shown in their welfare.

A lot of ground remains to be covered in our fight for the control of leprosy in the Province, but the LEPRA project has shown us the right direction towards achieving this goal. In the next stage of the Project we shall be concentrating on improving the attendance-rate for treatment, the examination of contacts of open cases of leprosy, extending the case-finding campaign in surveys of villages, and the establishment of more mobile-treatment runs in areas with as yet scarce or non-existent facilities.

Comments on Tables 1, 2, 5 and 6 relating to prevalence rates and leprosy indices:

(1) Prevalence rate of known leprosy cases in the Province. Estimated population for mid-year 1970, 349,300; rate, 6.4 per 1000. Estimated population for mid-year 1972, 360,000; rate, 7.1 per 1000.

(2) The case-type rate, i.e. the number of "open cases" per 100 cases of leprosy, for 1970 was 49.6% (819 out of a total of 1652 cases), and for 1972 it was 39.3% (970 out of a total of 2450 cases).

(3) Sex and childhood rate of the total number of cases:

Distribution in 1970 *viz*:

Adults (Male)	Adults (Female)	Children	Total (100%)
45.3%	49.3%	5.3%	1652 cases

The distribution in 1972 was:

Adults (Male)	Adults (Female)	Children	Total (100%)
40%	42.5%	17.5%	2450 cases

(4) The distribution by types of leprosy, sex, and age shown in Tables 5 and 6 is very similar, except for a higher in-patient and out-patient ratio. It is a general trend in leprosy control programmes that, with the expansion of out-patient treatment, the number of in-patients is diminishing. The ratio of in-patients to out-patients in 1970 was 1 in 13, but in 1972 it was 1 in 22.

(5) A sharp increase is noted in the childhood rate between 1970 and 1972. This is due to intensive surveys undertaken in the schools. For similar reasons, there is a sharp increase in the number of cases of the tuberculoid type of leprosy. This last should be attributed to the greater number of children brought under treatment in the period under review, and also in part to the World Health Organization classification which was adopted by the LEPRA teams.

Acknowledgements

We are indebted to the Permanent Secretary of the Zambian Ministry of Health, Lusaka, and to the British Leprosy Relief Association (LEPRA), London, for permission to publish this article.

We also thank Mr S. T. Mkandawire and Mr W. S. Chanda, the two Senior Medical Assistants, for their enthusiastic cooperation in the work described.

Lepr. Rev. (1973) 44, 127-130

The Treatment of Corticosteroid-dependent Lepromatous Patients in Persistent *Erythema Nodosum Leprosum* with Clofazimine*

F. M. J. H. IMKAMP†

Medical Superintendent, Liteta Leprosarium, Zambia

The trial of Lamprene (clofazimine), begun in 1966 and which has been the subject of a preliminary communication (Imkamp, 1968), has now terminated. The results of a follow-up study after 5 years are summarized in the accompanying table, the serial numbers of the patients being the same as in the paper cited above. All the patients had been suffering from lepromatous leprosy (LL) and all had been dependent on corticosteroids, given for persistent *erythema nodosum leprosum* (ENL).

Assessment

The smears were read by the same laboratory technician throughout. Biopsy specimens were taken every 6 months and reported upon by the same technician.

One male patient (No. 6) did not come for re-examination: according to the local Leprosy Control Officer, he is progressing well.

One female patient (No. 17) could not be traced. Another female patient (No. 13) was re-admitted with ENL. She was pregnant and very anaemic, the anaemia being due to malaria. She was delivered of a still-born baby. She was given Lamprene, which controlled the ENL. On discharge from the leprosarium she continued taking Lamprene at a dose of 300 mg weekly. She became pregnant again, and continues taking Lamprene at the same dose.

The trial has been most successful in that all patients have been weaned from corticosteroids and all have returned to normal life. All except one (No. 13) have resumed dapsone treatment. The length of time the individual patients had to take Lamprene varied within wide limits. Male patient No. 9 continued for 56 months, and the dosage had to be varied according to his clinical state.

The patients have been most cooperative, and except for one female patient (No. 17) and one male patient (No. 6), all came at the requested time for re-examination and assessment.

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* Received for publication May, 1973.

† Present address: Westfort Institution, Private Bag, Pretoria, South Africa.

TABLE 1

Serial number	Duration of treatment with Lamprene (months)	Bacterial status when Lamprene was replaced by dapsone B.I.	M.I.%	Recurrence of ENL	Duration of treatment with dapsone (until February 1971) (months)	Latest smear results B.I.	M.I.%	Summary of biopsy report	Comment
1 Male	19	2.1	0	None	35	0	0	No bacilli seen, almost complete clearance of infiltrate (Aug. 1970)	Discharged to out-patient clinic (Oct. 1969). In full-time employment
2 Male	29	3.1	0	None	25	1.2	0	Bacillary debris only (Jan. 1970)	Discharged to out-patient clinic (June 1969)
3 Male	19	4.2	0	Recurrence after 14 months of dapsone	3	3.2	0	No viable bacilli seen. No evidence of ENL (Nov. 1970)	Patient resumed treatment with Lamprene for further 18 months. Admitted as in-patient. Still taking dapsone
4 Male	25	4.0	0	None	35	2.2	0	No viable bacilli seen (Aug. 1970)	Discharged to out-patient clinic (Aug. 1968)
5 Male	20	0.4	0	None	25	0.2	0	No bacilli seen (Oct. 1970)	Employed as bricklayer
6 Male	18	1.0	0	None reported	35			Not available	Discharged to out-patient clinic (Dec. 1968)
7 Male	22	3.7	0.4	None	32	0.5	0	No viable bacilli seen (Feb. 1971)	Employed at Leprosarium
8 Male	19	2.0	0.1	None	35	0.2	0	No bacilli seen (Apr. 1970)	Discharged to a Mission (April 1969)
9 Male	56	3.0	0.2	Recurrence while still taking Lamprene[a]	3	1.1	0	No viable bacilli seen (Aug. 1970)	In-patient

10 Male	39	2.5	0	None	16	0.7	0	No viable bacilli seen (Nov. 1970)	Employed at Leprosarium
11 Female	24	2.8	0	None reported	32	1.7	0	No viable bacilli seen (Feb. 1971)	Discharged to a Mission (Aug. 1968)
12 Female	21	3.7	0.4	None reported	32	1.5	0	No biopsy report available	Discharged to out-patient clinic (Sept. 1968)
13 Female	22	3.2	0	Recurrence September 1970	26 till September 1970	1.5	0	No viable bacilli seen. Some ENL (Sept. 1970)	Discharged to out-patient clinic (March 1969). Returned (Sept. 1970) pregnant. Resumed Lamprene treatment. ENL controlled
14 Female	23	3.8	0	None reported	32	1.2	0	No viable bacilli seen (Jan. 1971)	Discharged to out-patient clinic (June 1969)
15 Female	21	4.5	0.4	None	32	1.7	0	No viable bacilli seen (Apr. 1970)	Discharged to a Mission (Apr. 1969)
16 Female	21	1.0	0	None	34	0	0	No viable bacilli seen (Sep. 1969)	Discharged to out-patient clinic (Sept. 1968)
17 Female	25	0.1	0	None reported				No biopsy report available	Patient lost to follow-up
18 Female	38	2.4	0	None	16	1.0	0	No viable bacilli seen (Apr. 1970)	Discharged to out-patient clinic (Nov. 1970)

B.I. = Bacterial Index; M.I. = Morphological Index.

[a] After 44 months of Lamprene, sudden ENL. X-ray showed a very slight infiltration (R) and a follow-up X-ray 2 months later showed a definite perihilar infiltrate with suspected cavity (?abscess) (R), reported by Radiologist, Kabwe Hospital. Bronchoscopy was advised as carcinoma could not be excluded. Patient was reluctant for bronchoscopy as he suffered for many years from severe ENL. He was therefore treated with thiazine 150/300 mg daily to cover possible pulmonary tuberculosis infection and there was no response to penicillin. Transparencies show the improvement and though we were unable to prove that the infiltrate was of tuberculous origin, the patient responded to the anti-tuberculous treatment. No more ENL occurred and on 16 November, 1970, dapsone treatment was started with low dosages, and the patient is in good health and ambulant.

Acknowledgements

I wish to thank Dr M. M. Nalumango, Permanent Secretary for Health, Zambia, for his permission to publish.

My sincere thanks also to Mrs J. Corbridge laboratory technician, who read the smears, reported on the follow-up biopsy findings, collected the data, and assisted me in every way during the drug trial.

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Lepr. Rev. (1973) 44, 131-138

Radiographic Examination of the Feet

A. GRACE WARREN

Hay Ling Chau Leprosarium, Hong Kong

The standardization of radiographic techniques assists in the demonstration of bony abnormalities. This paper describes simple devices which provide easy methods of obtaining comparable radiographs of the feet that will aid in the early diagnosis of lesions and in the planning of effective treatment.

Chronic ulceration of the anaesthetic foot is one of the greatest hindrances to the rehabilitation of leprosy patients. The scarred foot is ulcer-prone because scar tissue is less able to withstand the forces that act upon it in walking than is normal healthy skin.

The recurrence of ulceration may also be due to internal trauma caused by periosteal and bony irregularities. The latter may have resulted from infection and damage to the bones themselves, or may be caused by the laxity of ligaments and tendons associated with paralysis and paresis, or with increased mobility of joints after peri-articular bone damage.

In gross deformities, the roughness and irregularities of the bone may be felt by a sensitive palpating finger. In less obvious lesions, unsuspected roughness may sometimes be visible on a suitable radiograph. When the bone is examined at surgical operation, the actual damage may be found to be worse than the radiograph had suggested.

For adequate assessment of bone lesions of the feet, at least 2 radiographic positions are necessary. The view commonly ordered—the anterior-posterior (A.P.) (Kleiger, 1963)—is often taken in such a way as to show only the distal portion of the foot anterior to the cuneiform bones. This view can include the toes and the talus head, if carefully placed; both feet can be fitted on one 8 x 10 in (20 x 25 cm) radiographic film. However, in this view the small tarsal bones tend to overlap one another and so cannot always be clearly defined. To eliminate this problem, the anterior-posterior-oblique (A.P.O.) view is preferred. In this view, the radiographic beam is at right angles to the skin of the dorsum of the foot so that it strikes the film at an angle of 15° in both planes (Clark, 1956). The difference in the clarity of the tarsal bones as seen in these 2 views is shown in Figs 1 and 2.

A simple holder has been devized to provide the required constant angle so that the radiographic beam could be set vertically to give comparable pictures (Fig. 3). This holder has a rhomboid base, and a sloping square top (Fig. 4) on which the cassette rests. The construction of this device should present no difficulty to a competent carpenter. It has been found easier to cut out the base first. The rhomboid shape can be made by marking out the diagonal C-D (Fig. 5) 17 in (43 cm) long, and fixing the other angles at the intersecting point of arcs made

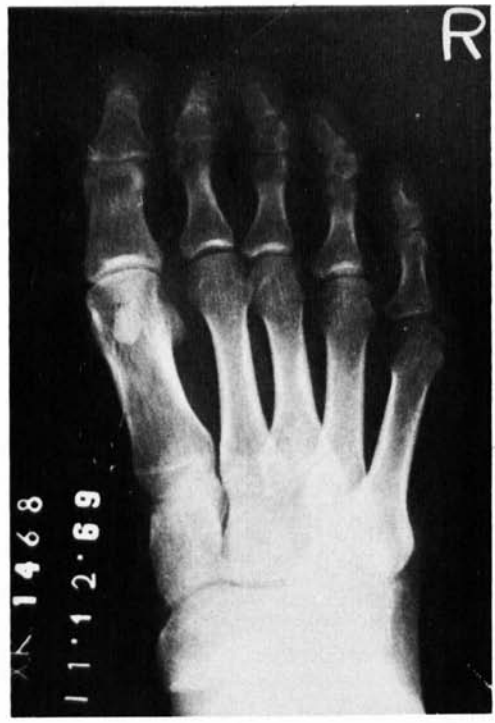

Fig. 1. Tarsal bones as seen in AP view.

with a compass at a radius of 11.6 in (29 cm) centred on the points C and D. The 4 sides are then cut: 2 of them are mirror images, as in Fig. 6, and 2 as in Fig. 7. These sides are mirror images and not identical because the corners have to be bevelled. Since the base is a rhomboid and not a square, the angle of bevel will vary. The bevels at point C and D will be at an angle of 43°, and those at A and B of 47° (Fig. 8). It should not be necessary to use a protractor to obtain these angles, provided it is remembered that the outer length of the sides is 11.6 in (29 cm, i.e. the same as the base) and that the sides must be exactly vertical to the base. When the sides are all attached to the base, it will be found that they will support the top, which should be a 12 in (30 cm) square, whose diagonal of 17 in (43 cm) is the same as the original diameter (CD) of the base, and whose sides are inclined at an angle of 15°. Projecting lips have now to be added to the lowest corners to prevent the cassette slipping off this inclined plane.

With this device, the patient sits on a stool with the foot to be examined resting on the top half of the cassette, the lower half of which is protected by lead sheeting. For the second foot, the cassette is rotated through 90°, as shown by the footprints superimposed on Fig. 4. For routine examination a K.V. is selected which will slightly under-expose the talus and slightly over-expose the toes, but with experience both can be adequately seen.

The second view is the lateral view of the tarsals. This view does not show the phalanges, but reveals many of the tarsal-bone lesions which are not shown in an

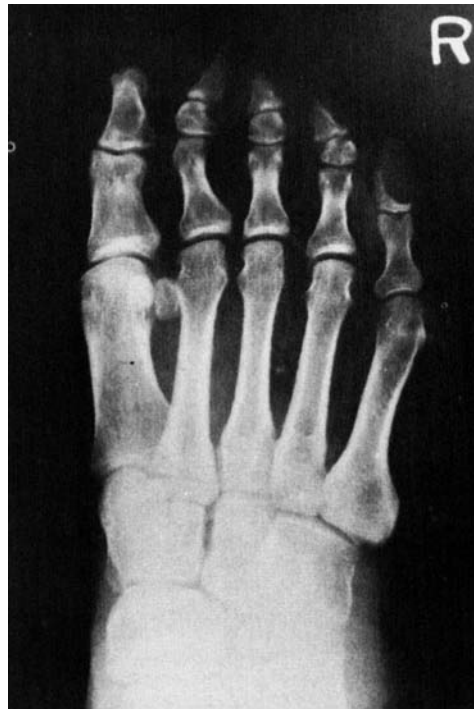

Fig. 2. Tarsal bones as seen in APO view.

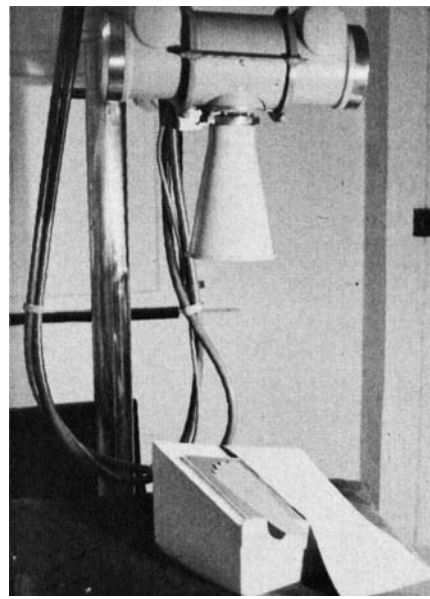

Fig. 3. Device for APO view showing head of radiographic machine, position of cassette and lead cover.

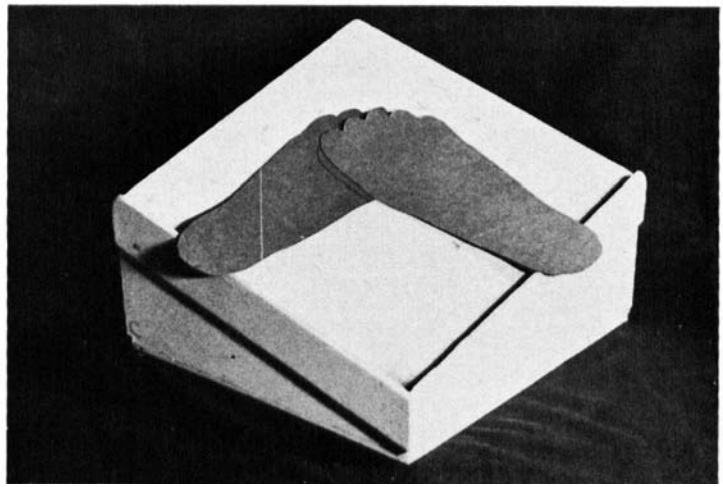

Fig. 4. Device for APO view.

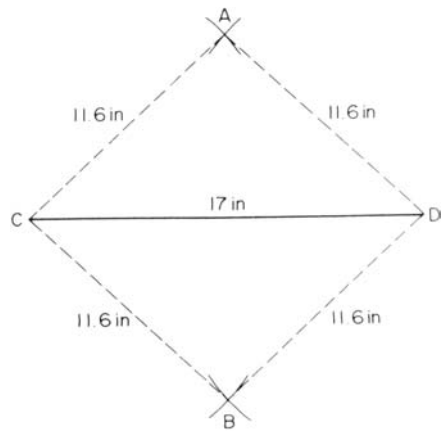

Fig. 5. Diagram for construction of the base.

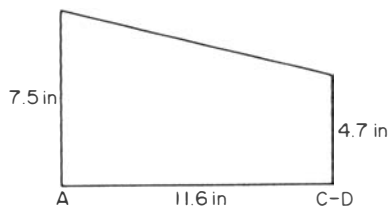

Fig. 6. Diagram for construction of sides A-C and A-D.

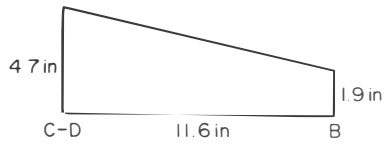

Fig. 7. Diagram for construction of sides B-C and B-D.

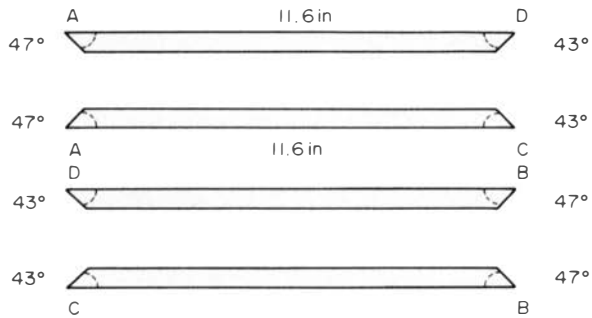

Fig. 8. Diagram to show the bevels of the sides so that they will form a rhomboid.

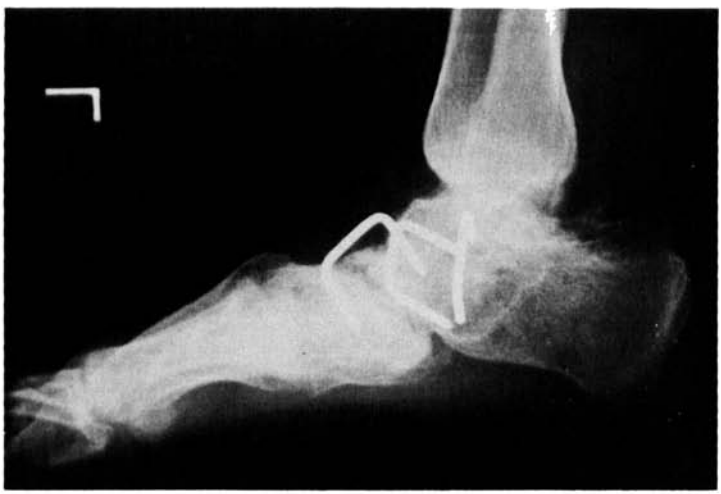

Fig. 9. Appearance of tarsal bones as seen in sitting lateral view.

AP or APO view. It is also of great value in indicating roughness of the bones of the foot that may cause ulceration due to trauma within the foot itself. Standard descriptions are for the lateral view to be taken in the sitting position, but this frequently results in a degree of obliqueness, so that the ankle-joint and the sole of the foot are not accurately visualized. It may also result in consecutive films that are not really or strictly comparable because of a difference in position.

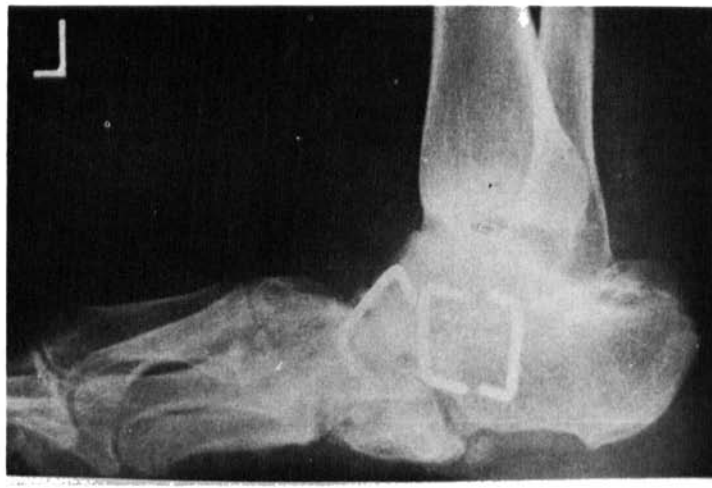

Fig. 10. Appearance of the same foot in standing lateral view. N.B. cuboid pressure.

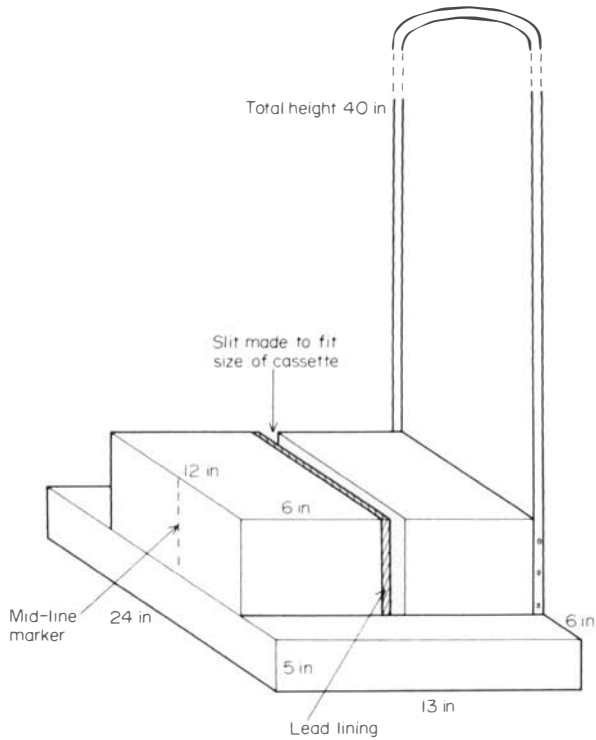

Fig. 11. Construction diagram for holder for standing lateral view.

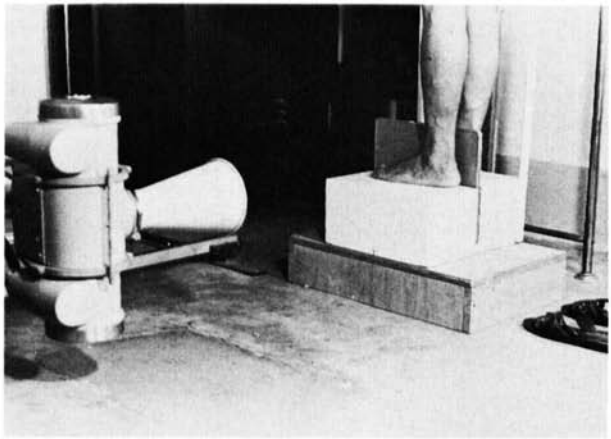

Fig. 12. Holder and cassette in use for standing lateral view.

Ideally, this radiograph should be taken in the weight-bearing position, which in the normal foot provides a true lateral view. A standing lateral position also reveals any irregularities of the weight-bearing surface, as well as any deformity that may occur during weight-bearing that is due to laxity of joints or ligaments. This is seen in Figs 9 and 10, in which a chronic ulcer was present over the mobile cuboid bone, which, however, appeared in a normal position in the sitting view.

To achieve a uniform lateral view with minimal inconvenience, a simple wooden holder (Fig. 11) was made to hold the cassette vertically (Fig. 12). The lower half of the cassette was shielded from exposure by a lead sheet incorporated into the holder, so that first one foot could be radiographed, and then the patient and the cassette turned round and a radiograph of the other foot taken. In this way the 2 feet can be fitted, sole to sole for ease of comparison, on to one 8 x 10 in (20 x 25 cm) film, or an APO and a standing lateral view of the same foot can be fitted on to one film.

In grossly deformed feet it may not be possible to take a standing lateral view, but the provision of a hand-rail makes it possible to take the same view without actually involving weight-bearing in patients in whom this is not desirable. In these feet, however, it will be necessary to order specific views required for each different stage or correction.

The standing lateral view also provides a free view of the anterior and posterior portions of the tibia and talus, as well as the best view of the posterior tarsal bones.

Ideally, for each patient control radiographs of both feet, in both views, should be available at diagnosis for the early detection and treatment of bone lesions, since many of these lesions develop insidiously (Warren, 1971). However, where films and funds are in short supply, 2 views of an affected foot can be fitted on to one film 8 x 10 in (20 x 25 cm). Although the diagnosis of minor lesions is easier when the radiographs of both feet are available for comparison, even these lesions can, with a little practice, be detected from one radiograph so that early and efficient treatment can prevent or minimize future disability.

Acknowledgements

The devices described here were designed and made by members of the staff at Hay Ling Chau; I wish to acknowledge their assistance at all stages in the making of these aids and in the production of this paper.

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Lepr. Rev. (1973) **44**, 139-141

Letters to the Editor

Professor Pattyn's paper, "Comments on the Chemotherapy of Leprosy as Influenced by Present Knowledge of *Mycobacterium leprae*" (*Leprosy Review* (1972) **43**, 126) is an excellent summary of our present knowledge of the treatment of leprosy, and in no sense do I mean to underrate the excellence of his presentation. However, one comment needs to be made on the subject of the treatment of leprosy. Dr Pattyn deals with the treatment of the *disease,* but I suggest we need to consider primarily the treatment of the *patient.* Our ultimate aim is to induce a state of health and well-being in the *patient,* and it is only for that reason that we attempt to kill and eradicate *Myco. leprae.*

Dr Pattyn discusses the host–parasite relation where the host response is poor, e.g. lepromatous leprosy; however, the majority of leprosy patients do not have this form of leprosy: they have at least a partial cell-mediated immunity (CMI). Nor does he take into consideration the very important fact that wherever significant disease exists, damage to nerves is always present. He states that "there is no need to change the existing dosage of 600 mg of dapsone per week for mass campaigns", although in tuberculoid leprosy "lower doses of dapsone ($\frac{1}{10}$ of the standard dose) could be adequate". And he does not take into consideration the stimulation of CMI that occurs during treatment, especially in patients suffering from BB or BT leprosy. This response may be reduced by smaller doses of dapsone than those usually recommended; it can be reduced even more by the use of other drugs.

By all means, the best chemotheraphy regime must be found and followed, but the actual need of the patients is the first and overriding consideration: elimination of disease should not leave the patient with a permanent iatrogenic nerve deficit.

The best result is attained by the suppression of CMI with corticosteroids while treating the leprosy with clofazimine. The individual response to this therapy is often quite unpredictable; both the duration of treatment and size of dosage needed therefore vary tremendously. In early nerve damage, adequate doses of corticosteroid should be used to control nerve pain and infiltration. Clofazimine should be initially used in doses of 400 to 600 mg daily, and reduced gradually as the activity of the disease diminishes. Eventually, after 6 months to 2 years, dapsone can be introduced.

Dramatic reversal of paralysis and anaesthesia may be attained whenever the disease is active; but if lesions are no longer infiltrated and there is no clinical evidence of activity in nerves, the prognosis for recovery of nerve function is poor. In the majority of patients, clinical activity is determined easily, but one group of patients with BT near BB leprosy have large, slightly infiltrated and markedly hypopigmented skin lesions, with little nerve pain or infiltration, yet actual nerve damage may be extensive and still active. In this group response to this kind of management will be striking.

The threat of disability following permanent anaesthesia and paralysis in

borderline leprosy is so important that this treatment is worth trying in any patient who appears to have even doubtfully active nerve involvement. Surely the retention or restoration of some nerve function is better than a lifetime of disability.

Our preliminary evaluation of this regime indicates that when the process in the nerves is active, at least 50% of distal sensory and motor deficit is reversible. It is urgent that our scientific efforts be mounted to aid this most important group of patients with borderline leprosy so as to establish without question the best treatment and management.

In treating the *disease*, let us not forget the *patient*.

Nigeria ROY E. PFALTZGRAFF

Dr Pfaltzgraff's letter was shown to Professor S. R. Pattyn, who replies as follows:

The main purpose of my paper was to show that techniques are now available that permit the rational interpretation of the antibacterial therapy of leprosy. The most urgent need now is, on the basis of laboratory evidence (experimental chemotherapy), to determine what are the best treatment schemes that necessarily take into account all relevant factors, such as the cost of different drugs and their administration, the possibility of controlling treatment, the reactions of the patients in terms of toxicity or other complications, etc., what I would like to call the "over-all acceptability". All these can be scientifically measured only in controlled clinical trials.

From a microbiological point of view, patients with multi-bacillary leprosy constitute a different challenge to antimicrobial therapy from those with paucibacillary forms of the disease. Independent studies will therefore have to be conducted on different types of leprosy.

In the meantime, while it is possible that individual patients may benefit from treatment with very high doses of clofazimine associated with corticosteroids, as proposed by Dr Pfaltzgraff, it is very doubtful if such a treatment, because of its high cost, can be applied on any large scale at present.

Antwerp, Belgium S. R. PATTYN

I am very pleased to announce that vacancies will exist from 1 September for 6-months' residency appointments at A L E R T, in the following departments:

(1) Clinical Leprology.
(2) Reconstructive Surgery of Leprosy.
(3) Leprosy Control.

You will appreciate that these appointments offer a very good opportunity indeed for young men wishing to work overseas to obtain an introduction to Africa, as well as to leprosy. In addition, it will provide A L E R T with staff to undertake basic medical care to our patients and free the senior personnel for teaching.

These appointments are renewable for up to one year. Accommodation will be provided on the A L E R T compound. Ordinarily, accommodation will consist of rent-free bachelor quarters, and the successful applicant will be expected to make his own arrangements for catering. If no bachelor quarters are available, residents will be accommodated in the students' hostel, and will be

charged 5 Ethiopian dollars per day for board. Apartments may be available for married couples at Eth. $100 per month. A salary of Eth. $500 per month will be paid.

Applications, giving *curriculum vitae* and the names and addresses of three referees, should be sent as soon as possible to Dr W. Felton Ross, Director of Training, A L E R T, P.O. Box 165, Addis Ababa, Ethiopia.

All-Africa Leprosy and Rehabilitation Training Centre, FELTON ROSS
P.O. Box 165,
Addis Ababa,
Ethiopia.

Lepr. Rev. (1973) **44**, 142

Book Review

A Leprosy Manual for Papua and New Guinea, by Audrey Davey, M.C.S.P., 112 pp. Government Printer, Port Moresby. $1.00 (Australian). Paper covers.

This polycopied brochure is really a practical manual for physiotherapist auxiliaries working in leprosy, and as such admirably fulfils its purpose. Its approach ranges from the very simple to the rather sophisticated, but with the help of line diagrams of muscles and bones and nerve supply, the text should be clear to those for whom it was written. The sections on physical examination and assessment of muscle damage will prove as helpful as those on the various forms of physiotherapeutic treatment that should be available at the centre of a leprosy control programme.

Miss Davey writes from 6 years of experience in a hospital in Papua, New Guinea, that has played a real part in demonstrating the practicability of the procedures advocated.

A limited number of this little manual is available at the price of $1.00 (Australian) from: The Department of Public Health, P.O. Box 2084, Konedobu, Papua, New Guinea.

S. G. BROWNE

Lepr. Rev. (1973) **44**, 143-148

Abstracts

1. **Zinc deficiency with altered adrenocortical function and its relation to delayed healing**, by A. FLYNN, W. H. STRAIN, W. J. PORIES and O. A. HILL, Jr. *Lancet* 1973, **i**, 789.

The importance of zinc in wound healing receives confirmation in this report of delayed wound healing in conditions associated with interference with adrenocortical function, that is, in patients whose adrenal glands had been surgically removed and in others who had been taking corticosteroid drugs for long periods. It is apparent that adequate levels of zinc in the serum and tissues are necessary for the normal rate of wound healing and that factors tending to depress these levels are associated with delay in healing.

S. G. Browne

2. **Leprosy: fifty years of progess**, by MERLIN L. BRUBAKER. *Bol. Ofic. Sanit. panamer. (English edition)* 1972, **6**, 1-14.

The author reviews the changes that have taken place in our knowledge of leprosy, treatment of the disease, and social attitudes during the 50 years that have elapsed since the publication of the first technical issue of the *Boletin*—which, incidentally, was devoted to leprosy. He summarizes the disease as seen in the Americas of 1922, and provides some interesting comments on the historical introduction of leprosy into the New World, first by Europeans and subsequently by Africans.

The Portuguese brought leprosy to Brazil and the Spanish to the rest of South America and the Southern States of what are now the USA. Subsequently, Chinese labourers brought leprosy with them to the West Cost of the USA, and Scandinavians settled in Missouri and Minnesota, with their leprosy. German and Czech immigrants and small French communities were responsible for persistent foci in various countries, notably the USA, Venezuela and Argentina.

The main milestones of recent leprosy research are then noted—the successful inoculation of *Myco. leprae* into the mouse footpad and the armadillo, immunology, and the treatment with the newer drugs.

The author concludes by emphasizing that the application of recognized methods of leprosy control will depend on the cooperation of leprosy sufferers and the "commitment of those responsible". The trend away from the institution and towards ambulatory care of patients is helping to remove the stigma of leprosy, and the volume of research being prosecuted at the present time augurs well for the future, as one by one the intractable problems posed by this disease are solved.

S. G. Browne

3. **Crowding as related to leprosy prevalence**, by H. V. HAGSTAD. *J. Christian med. Ass. India* 1973, **48**, 101-103.

A useful retrospective study is reported in which the author analyzed the leprosy situation in 20,808 families in a district in Andra Pradesh, India, in an attempt to discover if family size had any influence on the numbers of persons suffering from leprosy. With due attention to the possibility that he would be studying the results of the disease rather than its aetiologically

important environmental "causes", he found that there was no difference in family size between families in which a parent had leprosy and those in which a child was affected.

The author found a positive correlation between family size and prevalence rates, varying from 89 patients per 1000 families where the family size was 1 to 5 persons, to 240 per 1000 families where the family size was 11 persons or over. Numerous other environmental factors must also be considered.

S. G. Browne

4. **The histoid variety of lepromatous leprosy**, by J. H. KROLL and L. SHAPIRO. *Int. J. Derm.* 1973, **12**, 74-78.

The authors describe a single case of histoid leprosy in a 16-year-old Dominican girl seen in New York. The clinical presentation is well described, and the accompanying microphotographs are convincing.

The patient was not known to be suffering from leprosy and had received no treatment. Apart from nasal stuffiness, she complained of no symptoms. No skin rash was seen. The response to dapsone was good. It is noteworthy that, despite the absence of treatment, the Morphological Index of the numerous bacilli in the lesions was only 1 to 3%, and that clinically normal skin near the nodules contained small foci of cellular tissue typical of lepromatous leprosy.

S. G. Browne

5. **Renal transplantation in leprosy**, by D. ADU, D. B. EVANS, P. R. MILLARD, R. Y. CLANE, TIN SHWE and W. H. JOPLING. *Br. med. J.* 1973, **ii**, ~~200-231~~. 280-281

The authors give a detailed clinical and necropsy report on an Anglo-Indian male patient who received in 1966 (when he was 27 years old) a cadaveric kidney transplant because of end-stage chronic renal failure. He did not disclose until later that he had suffered from lepromatous leprosy, for which he had received treatment.

Two years after the operation he experienced a recrudescence of leprosy, coinciding with a reduction in the dosage of immuno-suppressive drugs. For a time, he responded well to clofazimine, but succumbed to a pulmonary infection with *Klebsiella aerogens*. At autopsy, many organs showed degenerative changes. No deposits of IgG, IgM or C3 component of complement were found by immuno-fluorescent studies. The grafted kidney had apparently been functioning well, but numerous ante-mortem thrombi were found in the intrarenal veins.

The well-known prolonged survival of allogenic skin grafts in patients with lepromatous leprosy (deficient in cell-mediated immune response) is discussed in the light of the renal transplant in this patient.

S. G. Browne

6. **Clofazimine ointment in the treatment of trophic ulcers**, by B. P. B. ELLIS and E. TAUBE. *South Afr. med. J.* 1973, **47**, 378-379.

The reported activity of clofazimine (Lamprene, Geigy) against some organisms responsible for infections of the human skin led the authors to try this drug (incorporated at 1% concentration in a bland ointment base) for the topical treatment of patients suffering from ulcerations of diverse causation. The dressing was left undisturbed for 4 days.

An interesting feature of the adequate laboratory investigations was that, despite the continued presence of viable pathogens in the exudate from the ulcers, healing proceeded rapidly and with good cicatrization. Further investigation is recommended.

S. G. Browne

The following abstracts are reprinted, with permission, from *Trop. Dis. Bull.* 1973, **70**.

7. **Incidence of leprosy in Gudiyatham taluk, S. India**, by P. S. S. RAO, A. B. A. KARAT, V. G. KALIAPERUMAL and S. KARAT. *Ind. J. med. Res.* 1972, **60**(1), 97-105.

The annual incidence of leprosy in the Gudiyatham taluk in Tamil Nadu, S. India, in the years 1967-69 was between 1.1 and 1.5 per 100 in a population of nearly 400,000. Twelve per cent of registered new cases had lepromatous leprosy, and 58% had the tuberculoid form. About a quarter were under the age of 10 years at the time of diagnosis, and the age-specific incidence rate was highest for the age-group 10-14 years. The overall prevalence rate in the taluk is 25.8 per 1000. No differences in rates between the sexes were noted in those reporting with signs of leprosy of less than one year's duration.

S. G. Browne

8. **Sur la lèpre en Guadeloupe (Leprosy in Guadeloupe)**, by H. A. FLOCH. *Bull. Soc. Path. Exot.* 1972, **65**, 35-46. English summary.

Despite an admittedly incomplete case-finding programme, the prevalence of leprosy in Guadeloupe has fallen from about 50 per 1000 in 1938 to 7 per 1000 in 1971. There are 2261 registered patients in a population of 330,000; 33% have lepromatous leprosy and 5% borderline. The author considers that the high proportion of patients with bacilliferous leprosy would be smaller if more and better surveys were carried out. In 1970, 61 new cases of leprosy were found among 18,765 schoolchildren examined.

The author advocates more extensive case-finding surveys, the systematic treatment of everybody found to be suffering from active leprosy, and BCG vaccination of all infants soon after birth. He considers that patients suffering from the self-healing types of leprosy should be treated, in order to prevent nerve damage and possible bacilliferous exacerbation. He is not convinced of the non-contagiousness of patients in whose skin only morphologically abnormal bacilli are present, nor does he find that long-acting sulphonamides are superior to dapsone.

S. G. Browne

9. **Topics in human genetics. Vol. I. A twin study of leprosy.** (M. R. CHAKRAVARTTI and F. VOGEL) pp. ix + 124, illustrated. 1973. Georg Thieme Verlag, Stuttgart, Germany. (Paperbound DM 54.) P. E. BECKER, W. LENZ, F. VOGEL and G. G. WENDT.

This is the report of a study in 3 areas of India, West Bengal, some areas of Andhra Pradesh, and the area around the Chingleput leprosy centre in Madras. After a brief survey of the literature on genetic aspects of leprosy, the methods and results are presented in 24 pages and then, in an appendix of 90 pages, the details of each twin studied are given. "Several thousand" leprosy patients were questioned as to whether they were one of twins, and 62 male-pairs, 28 female-pairs, and 12 male-female pairs were found. There were 62 monozygotic (MZ) pairs and in 37 each twin had leprosy; in 32 of these the leprosy was of the same type. In the 5 MZ pairs when the twins had a different type of leprosy, 3 of the pairs had probably been infected from the same source. In 25 MZ pairs only one twin had leprosy, and the authors attribute the disease to the fact that the diseased twin had "more close contact with open cases". (It is difficult to correlate the numbers mentioned in the text.) There were 40 dizygotic (DZ) pairs and in 8 each twin had leprosy, in 6 of these each having the same type of the disease. There were 32 DZ pairs in which only 1 twin had leprosy. The relative number of patients with leprosy among the siblings of the twins was "about the same in families of concordant and discordant monozygotic pairs. Besides, an interfamilial correlation of leprosy type was

observed. The combined results of this study show a definite genetic variability in susceptibility to the leprosy infection in the population investigated."

C. S. Goodwin

10. **The continuous bacteremia of lepromatous leprosy**, by D. J. DRUTZ, T. S. N. CHEN and W. H. LU. *New Engl. J. Med.* 1972, **287**(4), 159-164.

Venous blood was taken from 32 patients with leprosy. The first 5 ml was discarded and then 3 ml was obtained in a fresh syringe containing heparin. After centrifuging, smears of the leucocyte layer (buffy-coat) were prepared and stained by the Ziehl-Neelsen method. "The entire buffy-coat from 3 ml of blood was examined." When extracellular acid-fast bacilli (AFB) were seen in the buffy-coat "negligible numbers" of AFB were seen in the erythrocyte and plasma fractions. Two tables and 3 figures delineate the results. Of 5 lepromatous (LL) patients (Ridley classification) who had been treated with dapsone for more than 5 years, 2 had AFB in the blood; of 3 borderline patients, 2 had AFB in the blood and of 7 borderline tuberculoid patients, 4 had AFB in the blood. All of the 11 untreated LL or borderline lepromatous patients had AFB in the blood, as had all of the 6 LL patients who had been treated for up to 4 years. The "intensity of the bacteremia" was greatest in untreated LL patients, and became markedly less in patients after 4 months' treatment with dapsone. (No mention is made of the morphology of the bacilli.)

C. S. Goodwin

11. **Aspects de la lèpre en Polynésie française (Aspects of leprosy in French Polynesia)**, by J. SAUGRAIN and A. STRANGHELLINI. *Méd. trop* 1972, **32**(6), 735-741. English summary.

Leprosy was probably imported into French Polynesia by immigrant workers from China in the second half of the 19th century, although tuberculoid leprosy may have been present among the indigenous population.

In Tahiti itself, out of a total of 168 patients (of whom 40% had lepromatous leprosy), 72 were segregated in 1914. In 1958, the prevalence increased to 277, and to 329 in 1971—in a population numbering just under 100,000. Three hundred and seventeen of these are Polynesians and only 11 of Chinese extraction; at least 127 are considered to be suffering from the lepromatous form, as are about half of all cases diagnosed since 1965. Severe peripheral neuropathies are common and about one-third of all patients have some form of eye complication. No fewer than 11 patients have tuberculosis as well as leprosy. Relapses and severe reactional episodes are frequently encountered. The patients are said to tolerate sulphones and sulphonamides badly.

S. G. Browne

12. **The identification of leprosy among epithelioid cell granulomas of the skin**, by J. P. WIERSEMA and C. H. BINFORD. *Int. J. Lepr.* 1972, **40**(1), 10-32.

Skin biopsy is still the only, or the best, method for the laboratory diagnosis of some forms of leprosy. The present study on the differential diagnosis of leprosy from other causes of epithelioid cell granulomata is based on material referred to the Armed Forces Institute of Pathology in Washington. It is recommended that the biopsy should be taken from the periphery of the most active looking lesion, and should extend down to the subcutaneous fat. Up to 10 sections stained for acid-fast bacilli (Fite-Faraco method—see Fite *et al.*, *Trop. Dis. Bull.* 1947, **44**, 1008) were examined from each biopsy in addition to haematoxylin-eosin sections. The latter were used for making a profile of the nerves in relation to the dermal

infiltrate. The search for bacilli was limited to nerves, foci of necrosis and the centres of large granulomata, which are possible sites of destruction of nerves, and to any clear areas of the sub-epidermal zone. Eleven cases are analyzed and discussed. Whenever acid-fast bacilli are found in any of the situations listed, and there is associated nerve damage, it is a reasonably safe assumption that the diagnosis is leprosy, although the authors warn against the possibility of secondary nerve damage in other mycobacterial infections leading to a mistaken diagnosis of leprosy. Two histological patterns were observed in tuberculoid leprosy. In one, the distribution of the infiltrate followed the dermal nerves, which were usually severely damaged, and bacilli, if present, were found in the neural remnants. In the second type, the infiltrate was prominent in the superficial dermis and bacilli were usually seen in the sub-epidermal zone or in nerves that were not involved in the infiltrate. The differentiation of tuberculoid from borderline leprosy is usually not a difficult problem.

The legal and social dangers of misdiagnosing leprosy are emphasized. The paper is illustrated with numerous photomicrographs.

D. S. Ridley

13. **Acedapsone in leprosy chemoprophylaxis: field trial in three high-prevalence villages in Micronesia,** by N. R. SLOAN, R. M WORTH, B. JANO, P. FASAL and C. C. SHEPARD. *Int. J. Lepr.* 1972, **40**(1), 40-47.

Approximately 1500 highly inbred people, originating from Pingelap atoll in the Ponape District in Micronesia, are now living in 3 small villages in the district and have a high incidence of leprosy. A complete examination of that population in 1967 identified 99 cases of leprosy, a prevalence of 66 per 1000, and, judging by previous experience, it was expected that about 11 new cases would appear each year. The entire population (including all leprosy patients) was placed on the repository sulphone acedapsone (DADDS; Hansolar) given at 75-day intervals, those over the age of 6 years receiving 225 mg at each injection and those between 6 months and 6 years receiving 150 mg. All were re-examined in 1968, 1969, and 1970. Six new cases appeared during 1968 but none thereafter. Treatment of "non-cases" was stopped in 1970 and the population will remain under surveillance for at least 10 more years. No toxic effects of treatment were encountered.

W. H. Jopling

14. **Acedapsone in leprosy treatment: trial in 68 active cases in Micronesia,** by N. R. SLOAN, R. M. WORTH, B. JANO, P. FASAL and C. C. SHEPARD. *Int. J. Lepr.* 1972, **40**(1), 48-52.

This paper takes the trial (see abstr. 13 above) one stage further by describing the effect of treatment with acedapsone of 62 patients with active leprosy of various types between 1967 and 1970, together with 6 new cases discovered in 1968. Intramuscular injections were given every 75 days and all patients were re-examined annually. Apart from one patient with lepromatous leprosy, who had previously not improved on oral dapsone (DDS), and one patient whose indeterminate leprosy shifted to tuberculoid during the trial, all the remainder responded well and there were no toxic effects.

W. H. Jopling

15. **Studies in the viability of *Mycobacterium leprae* in human liver and bone marrow, using thymectomized mouse footpad technique,** by A. B. A. KARAT, H. HARMER, A. S. KUMAR and J. R. ALBERT. *Int. J. Lepr.* 1972, **40**(1), 1-3.

Bone marrow aspirates and skin and liver biopsy specimens were obtained from patients with lepromatous leprosy (possibly 4 patients), the material homogenized, and 5000 *Mycobacterium*

leprae used as inoculum in the footpads of thymectomized mice. The counts of bacilli from the skin specimens ranged from 1.9×10^7 to 3.3×10^8 per ml, from the bone marrow from 4.4×10^5 to 7.0×10^6 per ml, and from the liver 5.3×10^6 to 3.0×10^7 per ml. The percentage of evenly stained bacilli (MI) from the skin was 1 to 8%, from the bone marrow it was 0 to 16%, and from the liver it was 0 to 6%. All the inocula multiplied (which is surprising if the MI was 0%) reaching counts of 10^5 to 10^7 bacilli, and the MI ranged from 0 to 14%. The authors conclude that the bacilli were viable "despite the higher temperature in human bone marrow and the liver", and that these bacilli could be "reservoirs of viable lepra bacilli".

C. S. Goodwin

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 be 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.

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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.

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CONTENTS

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