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Editorial

WALKING ON AIR

We have known for a long time what we were looking for. Now at last the plastics industry seems to have come up with a material to meet our need. To prevent trophic ulcers the pressure forces of walking must be softened and spread over as wide a surface of the foot as possible. To do this we have needed either a soft material, to cushion each step, or a material that could be moulded and shaped to the foot so that every part of it shared the weight of the body. Best of all would be a material that would be both soft and easy to mould. For world-wide use it has to be inexpensive as well.

Foam rubber, sponge rubber, and foam plastic such as polyurethane foam, are all soft materials whose softness depends on the fact that they are full of air. But such material is a mass of air-bubbles which connect with each other, so that when the foam is squeezed the air escapes and the material is compressed or flattened. The result is that when thus flattened it is no longer soft.

A great advance on the foam or sponge is the closed-cell system of tiny bubbles of air or nitrogen which are formed in rubber by a chemical reaction. Because these air-cells do not connect with each other, the air cannot escape when the rubber is squeezed. Thus, when a foot presses down on a sheet of microcellular rubber, the material is not flattened and the foot floats on the compressed air in the tiny air-cells. Microcellular rubber is a great advance on earlier materials and is still to be recommended for routine use as an insole for the protection of insensitive feet.

When a patient's feet are deformed as well as insensitive, there are often points of high pressure which may become ulcerated in spite of the soft insole. For such feet it is necessary to have a moulded insole which is shaped to all the irregularities of the foot and allows equal pressure everywhere. If microcellular rubber is to be used for this, it has to be carved or shaped with great skill and any mistakes may result in unequal pressure, for this material cannot be moulded directly on to the foot. There are materials that can be moulded directly on to the sole of the foot, such as mixtures of cork-dust and rubber latex, and these are quite good, but they are not soft. Polyethylene is a plastic material which softens with heat and which can be moulded directly on to the foot while soft and which gives a perfectly moulded insole. This material was tried in Kano, Nigeria, 12 years ago, but it has two disadvantages—first, the heat required to soften the plastic may burn the foot, so that direct moulding presents problems; second, when the moulded insole sets it becomes hard.

Now industrial chemists have discovered how to produce a system of bubbles in polyethylene plastic. This is a closed-cell system like that of microcellular rubber so that the air cannot escape. This product is better than rubber, however, because it can be heat-moulded directly to the foot, and it does not burn the foot because the air-cells do not conduct heat well. As a final advantage, this material is cheap and easy to work. In a rather coarse large-celled form it has beeen used for some years for making life-belts and flotation equipment. Now it is produced in fine-celled sheets, made by Expanded Rubber and Plastics Limited, and has been placed on the market for medical use by Smith and Nephew Ltd., under the trade name of Plastazote.

Used as a flat insole, Plastazote probably has no advantages over microcellular rubber. Its value is as a moulded insole suitable for the deformed foot or the foot which has re-ulcerated even when using a regular soft sandal. Thus, Plastazote must always be moulded and it is therefore essential to have an oven in the workshop. A small home-made oven heated by a primus stove or a gas burner is suitable so long as baffle plates divert direct heat from the flame.

The temperature must be kept between 140° and 150° Centigrade, but a thermostat is not needed. A projecting thermometer allows the shoemaker to do his own regulating.

Unfortunately, some of the instructions that accompanied early samples of Plastazote suggested that patients should stand on the warmed material to make the mould. While this certainly shapes the material to the foot, at the same time it flattens the air-cells under the prominent parts of the foot and thus takes away the softness and the resilience where it is most needed. The proper way to use Plastazote is to have the patient seated in front of a large block of really soft rubber foam or polyurethane foam at least 6 in. (15 cm) thick. A sheet of Plastazote, ½ in. (1.25 cm) thick, is cut to shape a little larger than the foot and put into the oven for 5 minutes. It is then placed on the block of soft foam and the patient's foot placed on it. The shoemaker tells the patient to press his foot down into the foam without flexing his toes. The foam will bulge around the foot and shape the Plastazote so that it cups the heel and follows all the contours of the foot. A small card may be placed under the toes to prevent the Plastazote curving up around the ends of the toes and restricting their movement in the shoe. In 3 minutes the insole will be set and will be of even thickness everywhere. The only remaining problem is to support the shape from below, because the material is not strong enough to maintain its shape under heavy weights. A paste of sawdust or cork dust and rubber latex may be used to fill in the hollows between the insole and the undersole and to support the edges of the insole where they form a rim to cup the foot. A problem with any cupped insole is that dust and small stones may lodge in the hollow, whereas they might not stay on a flat insole. Patients should be warned about this.

The question is bound to be asked: "Can moulded Plastazote insoles be used to heal trophic ulcers as well as to prevent them?" The answer is that nobody should be allowed to walk on a trophic ulcer unless the foot is fully splinted, as in a plaster cast. However, when plaster casts cannot be used, or are refused, a moulded Plastazote insole on a rigid undersole or clog may allow a well localized ulcer to heal even though the patient continues to walk. The fact that Plastazote is washable is an added advantage in this type of case.

While further experience will certainly define further problems, and suggest improvements, there is no doubt that a new advance has been made in the war against trophic ulceration. So with thankfulness we move forward, walking on air.

Paul W. Brand.

Fontilles VIII International Course

The Fontilles VIII International Course in Leprosy for missionaries and auxiliary health workers is being organized to take place from 22 September to 18 October, 1969, under the direction of the Director of the Fontilles Leprosarium, Dr. José Terencio de las Aguas. The course is sponsored by the Sovereign Order of Malta, 3 Place Claparède, Geneva, Switzerland, and the lecturers include visiting professors as well as the Fontilles staff.

Zambia

A happy example of co-operation is provided by the news that the second LEPRA Land Rover covering the Eastern Province of Zambia has already travelled 10,000 miles in 5 months. So far, 1003 leprosy patients have been registered. In this Project, LEPRA works with the government, and the Zambian Land Rover teams were trained at ALERT in Addis Ababa. The administrative collaboration between official and voluntary agency personnel is paralleled by the combined attack on tuberculosis and leprosy. We await with interest further news of this scheme, and particularly its cost/benefit analysis.

Pakistan

The Pakistan Leprosy Relief Association proposes a scheme for a Rehabilitation Centre and Workshop for leprosy patients, to be built near Manghopir Leprosy Hospital. The Association's high aims are frustrated by lack of funds, but it is seeking and hoping for increased co-operation from the public as it publicizes more widely the needs of leprosy sufferers.

Polambakkam

A Souvenir Report, released on the happy occasion of the opening of a new ward at Polambakkam, Tamil Nadu (S. India), on 9 March, 1969, provides much informative and interesting material on the history of this Leprosy Control Project and the results so far achieved. Tribute was paid to the vision of the then young Dr. Robert Cochrane who inaugurated his "Night Segregation Centre" there as far back as 1936. It was in 1955 that the Belgian Foundation for Leprosy began its activities at Polambakkam under the stimulating direction of Dr. Fr. Hemerijckx.

Since that time 26,452 leprosy patients have been registered, and of these no fewer than 10,723 have been discharged "disease arrested". The prevalence rate in the control area is 4.1%, the lepromatous rate about 12%, and the population over 650,000.

Polambakkam represents one of the most successful and complete leprosy control projects in India. The reasons adduced indicate that inspiring leadership, continual co-operation at all levels—between Central and State governments and an expatriate agency, between professionals and auxiliary workers—are still the main ingredients of success. The well-known district control principles are here applied with enthusiasm: careful survey work, multiple mobile clinics "under the trees", standardized treatment mediated by trained paramedical workers, adequate supervision of and frequent refresher courses for these latter, a simple central organization providing in-patient care where necessary, laboratory facilities, reconstructive surgery, physiotherapy, occupational therapy, and simple protective footwear.

A worthy tribute was paid by Professor T. N. Jagadisan (Honorary Secretary and Treasurer of the Hind Kusht Nivaran Sangh) to Dr. Fr. Hemerijckx for his leadership, vision, and sheer hard work in bringing Polambakkam to the pitch of efficiency and evident success it now enjoys. Under the present Medical Officer-in-Charge, Dr. (Miss) Claire Vellut, and in continuing co-operation with the provincial authorities, Polambakkam faces the future with hope and confidence.

Honours and Awards

THE DAMIEN-DUTTON AWARD FOR 1969

At the 25th Anniversary of the Damien–Dutton Society which was commemorated on 19 April, 1969, in New Brunswick, New Jersey, U.S.A., the Award for 1969 was presented to the venerable leprologist, Dr. Victor G. Heiser. The announcement of the Award was actually made on 5 February, coinciding with Dr. Heiser's 96th birthday.

Dr. Heiser was the first President of the International Leprosy Association, serving from 1931 till 1938, and for many years was a member of the Medical Board of the Leonard Wood Memorial for the Eradication of Leprosy. It was while Dr. Heiser was Director of Health for the Philippines, from 1903 to 1915, that his life-long interest in leprosy was aroused. He saw leprosy in its familiar setting of rural environmental hygiene in the tropics and subtropics, and brought to bear on its epidemiology and control

a rich and very wide experience of tropical medicine. From 1915 to 1933, he served under the International Health Board of the Rockefeller Foundation.

We congratulate Dr. Heiser most heartily on this recognition of his significant contributions to leprosy and the world-wide campaign against the disease.

ROYAL AFRICA SOCIETY MEDAL

Congratulations to Mr. Frank Mead, formerly LEPRA Control Officer in the Gambia and now working in a similar capacity in Sierra Leone, on the award of a Royal Africa Society Medal in recognition of his dedicated service to Africa. He is made an honorary Life Member of the Society.

DR. OLIVER W. HASSELBLAD

Congratulations to Dr. Oliver W. Hasselblad, President of American Leprosy Missions Inc., who on 18 April, 1969, was honoured by the patients and staff of the United States Public Health Service Hospital at Carville, Louisiana, for his outstanding contributions to world leprosy control. At a ceremony attended by the participants in the 10th annual seminar for overseas workers, a silver plaque was presented to Dr. Hasselblad by Dr. John Trautman, director of the hospital, and Mr. Alfredo Yzaguirre, President of the Patients' Federation

The Work of WHO, 1968

The Annual Report of the Director General to the World Health Assembly and to the United Nations

This valuable compendium should be consulted in the original. From Chapter 2 (Communicable Diseases), we take the following extracts from the section on Leprosy (pp. 26-28).

PRIORITIES AND PLANNING

"The recommendations made in 1965 by the Expert Committee on Leprosy with regard to priorities and the planning of leprosy control programmes were reflected in the emphasis placed on the treatment of infectious cases and surveillance of their contacts. and on releasing from control those tuberculoid and indeterminate patients who had already completed the required period of disease inactivity and treatment.'

ASSISTANCE TO RESEARCH

"The Organization's assistance to research included a 'double-blind' trial, in Venezuela, which showed the action of thalidomide on the acute lepra reaction. In a further study the first results were confirmed, and the drug is considered effective in suppressing acute lepra reaction. Cases of acute polyneuritis incidental to lepra reaction were also controlled rapidly and completely with thalidomide. 'Double-blind' co-ordinated trials of this drug were also carried out in India, Mali, Somalia and Spain, using a uniform methodology studied by the Organization. Preliminary appraisal of the reports so far received—on 87 cases—also seem to show favourable results."

CHEMOPROPHYLAXIS WITH DAPSONE

"In the long-term chemoprophylaxis trial with DDS in India, after 5 years' observation 48 leprosy cases had been detected among 360 contacts in the control group and 22 among 358 contacts in the 'prophylaxis' group. The degree of protection was estimated to be 54.5% for the 'prophylaxis' group, but seemed significant only for children below 10 years of age, and was much higher for males. A chemoprophylaxis trial with DDS started in the Philippines in 1966 was continued. At the end of the first year, 12 cases had been detected in the control group of 275 child contacts and 3 in the 'prophylaxis' group (numbering 274); in the second year the number of cases was 11 and 10 respectively."

MICROBIOLOGY

"Studies were made on the growth of *Mycobacterium leprae* by employing macrophages harvested from animals.

In studies in India, further attempts were made to cultivate *M. leprae* in fresh fibroblastic cultures derived from human foetal spinal ganglia."

LEPROMIN

"In a WHO-assisted comparative study in Brazil on 'standard' lepromin (160 million bacilli/ml) and diluted antigens containing 80, 40 and 10 million bacilli/ml, the lepromin containing 40 million bacilli/ml seemed to be completely satisfactory for the Mitsuda reaction.

It was concluded that lepromin can be preserved in a refrigerator for 3 years but that freeze-drying should be recommended for storage over longer periods."

SEROLOGY

"A study of serum protein alterations was made in about 300 sera from patients with different forms of leprosy. The levels of the different immunoglobulins (IgG, IgA and IgM) were estimated by immunological methods. During the course of this investigation, the occurrence of hypergammaglobulinaemia and macroglobulinaemia in lepromatous leprosy was noted."

BCG VACCINATION

"In Burma the WHO leprosy/BCG team continued the trial started in 1964 to ascertain the value of BCG vaccination in the prevention of leprosy in children. General surveys of the population in the operational area and intake of children into the trial groups were completed during 1968. Of a population of over 75,000, 68,865 were examined, including 33,124 children (97.1% of all children); 26,858 children were included in the trial. Preliminary results were reported at the Ninth International Leprosy Congress, held in London in September 1968. By November, 138 cases had been detected in the control group and 121 in the prophylaxis group. There is thus no evidence that BCG vaccination confers significant protection, whatever the status of tuberculin allergy prior to vaccination, either in household contacts (who might reasonably be assumed to be at greater risk of infection prior to vaccination) or in children who are not exposed to *M. leprae* at home but might be so exposed elsewhere. There is no evidence so far that natural tuberculosis infection or infections with acid-fast organisms antigenically related to *M. tuberculosis* confer protection against leprosy."

Tuberculosis in Africa

The recent WHO seminar, held in Brazzaville, on the problems confronting African governments in their national tuberculosis programmes, produced salutary warnings and practical advice that might well be re-echoed and heeded by those engaged in leprosy campaigns. The main difficulties in the 23 countries from which the participants came seemed to be more organizational than medical.

The old-type tuberculosis hospitals and dispensaries, expensive second-line drugs, and major ablative and mutilating surgery, all came in for well-merited criticism in the light of the growing dimensions of the threat in town and village. Agreement was voiced on the general safety of BCG vaccination without previous tuberculin testing, and on domiciliary treatment with inexpensive drugs given according to accepted standardized régimes by trained, competent, and enthusiastic paramedical workers. The seminar advised that tuberculosis control should be integrated as far as possible with other public health activities concerned with endemic disease, with the proviso that medical men with special knowledge and experience would always be needed to advise and direct. As with leprosy, patient co-operation over the long period during which treatment is

required is essential for the cure of the individual patient, the interruption of the cycle of transmission, and the success of the national campaign. Fortunately, with standard drugs, patients may be rendered non-contagious in a few months.

With so many problems in common, both medical and social, economic and operational, the advantages of combining national campaigns against the 2 widespread endemic mycobacterial diseases—tuberculosis and leprosy—are self-evident.

Leprosy Symposium, New York

Under the auspices of the New York Academy of Medicine, the Leonard Wood Memorial, the American Leprosy Missions, Inc., and the New York Society for Tropical Diseases, a highly successful symposium on "Leprosy—Newer Concepts" was held in New York on 1 April, 1969.

A note of sober realism pervaded the meeting. Dr. Oliver W. Hasselblad, President of the American Leprosy Missions, reminded the participants that the misplaced optimism of a decade ago was now giving way to a greater realization of the need for better drugs and a more thorough application of existing knowledge. Dr. J. Convit, President of the International Leprosy Association, gave a factual survey of the successful leprosy control project in Venezuela, but so far only half the probable total number of leprosy patients have been registered for treatment. Dr. R. C. Parlett, Washington microbiologist, emphasized the lacunae in our knowledge concerning the value of prophylactic BCG vaccination, and Dr. C. C. Shepard recounted his work in evaluating the protective effect of BCG vaccination when given to mice subsequently challenged by *Mycobacterium leprae* inoculation in the foot pads.

Current Problems in Tuberculosis

The points of contact between leprologists and their colleagues concerned with *Mycobacterium tuberculosis* are interestingly implied in the papers delivered at a conference on "Current Problems in Tuberculosis" held at the University of Edinburgh, 19–20 September, 1968, and now published as a supplement to *Tubercle, Lond.* (1969) **50**, 1-92. Gross similarities in microbiology, immunology and therapy serve to emphasize the considerable differences between the causative micro-organisms themselves, their physiology and pathology, and their response to drugs. The lessons of epidemiology and drug-resistance learned by our colleagues in tuberculosis, who in many ways are several years ahead of us—although the discovery of *Myco. leprae* antedated that of *Myco. tuberculosis* by a decade—should not be lost to leprologists engaged in either laboratory research or mass-treatment campaigns, and to the medica administrators planning the rational utilization of all-too-limited resources.

Dr. N. W. Horne reviewed the global prevalence of drug-resistant tuberculosis—not, or not yet, a problem in leprosy—and indicated that both co-operation of the patient and effective treatment regimens are necessary if this problem and menace are to be controlled.

Experimental work on capreomycin, ethambutol, and rifampicin was reported by Dr. F. Grumback, and on B 663 (Lampren) by M. L. Conalty. The last-named drug (abandoned as a treatment for pulmonary tuberculosis in man) is concentrated in phagocytes, which show reduced phagocytic activity, the intracellular drug remaining active against mycobacteria.

Clinical investigations of ethambutol and capreomycin, both useful drugs in patients

harbouring bacilli resistant to standard régimes, were reported by several workers. Wallace Fox, in a very practical paper reviewing the problems of drug-resistant tuberculosis in developing countries, suggests that so far the excretion of drug-resistant organisms is not a major menace, and the treatment of infected patients should not divert funds from the main attack on the huge reservoir of treatable infections.

The session dealing with atypical or "opportunist" bacteria was full of interest. Further investigations of these increasingly important and widespread pathogens may shed welcome light on the growth problems of *Myco. leprae*.

From Mycobacteriology to Leprosy Control

A Report on the 1969 East African Medical Research Council Regional Scientific Conference held at Dar es Salaam

"Leprosy is a social disease with medical aspects" (Wheate). This was well illustrated by the delegates to this Conference, who were medical assistants, nurses, leprosy control officers, and doctors from both government and missionary agencies. The Seminar on Leprosy Control demonstrated a wide measure of agreement among these varied workers.

In all the 12 control schemes represented, the key to control was considered to be early diagnosis and easily available treatment. This demands the changing of social attitudes and the long-term cooperation of the population. Workers must understand both the science of disease control and the psychology of the people. S. J. Mamuya, Dar es Salaam, pointed out that if, for example, the name used for leprosy meant "fingers" its recognition would be late; that if its cause was believed to be hereditary, fear of damaging marriage prospects would lead to concealment; that the isolation or segregation of patients led to late diagnosis; and that the necessarily prolonged treatment, a concept alien to the African, resulted in default. Leprosy control may be better practised by a paramedical assistant, conversant with the language and customs of his people, than by the specialist in the disease, not so conversant. However, the two must work in close co-operation if the benefits of their respective skills are to be fused. Control methods designed on a purely scientific basis, neglecting the human and psychological factors, are likely to fail. There is a need to study the psychology of leprosy control.

There was common agreement that the institutional approach was unsatisfactory. Epidemiologically the patient presents too late, medically the non-infectious case is not provided for, economically the method spends too much on too few, socially the patient may be debarred from returning to his community, and psychologically the idea of isolation of both patient and staff is perpetuated. The institutions were looking beyond even their out-patient clinics to their countries as a whole, and attempting by survey to define the extent of the problem. In some cases they found prevalence rates of the same order as had been reported a decade or more previously by men like Ross Innes in the same areas (Lea).

In most cases a prevalence rate of around 2% was found. The attempts at survey illustrated the difficulties of achieving a high enough examination rate of the population selected, thereby exposing the results to some doubt (Chum and Larsen). There was often a very poor subsequent attendance rate by patients for treatment, suggesting a mistaken psychological approach; the staff of one leprosarium reported a 75% default rate (Larsen). The need to be very circumspect in the interpretation of survey figures was emphasized by Wheate and Christie. The many social factors in this social disease could lead to considerable bias in the findings. In regard to prevalence the figures could vary widely from one area to another, not always for known epidemiological reasons. It would appear that a reliable survey can be

achieved only by meticulous planning and much hard work, and with provision for adequate statistical analysis.

In the midst of these somewhat gloomy findings on survey in the modern context much light was shed by Leiker, based on his work in New Guinea of 15 years ago. As leprosy invades a previously unaffected population a very high prevalence rate builds up, with an initially low type-rate for lepromatous leprosy. Later the prevalence falls but the lepromatous rate rises. It would seem that BCG vaccination has its main value in the high prevalence situation by reducing the number of self healing cases. But in any situation it is the progressive case that is epidemiologically important, and if a control scheme has to be limited there should probably be a much greater effort made to hold the relatively small number of progressive cases.

It was the common experience of workers from all areas represented that the most effective method of both case-finding and case-holding was the provision of an adequate number of treatment points. In a disease that requires such prolonged treatment this is probably the most important single factor in achieving control, overriding all other factors, psychological, social, and medical. The inadequate provision of treatment points is the main obstacle to leprosy control in the developing countries with their limited budgets and man-power, and many competing priorities. It was clear to conference delegates that special leprosy projects could not hope to overcome these problems on their own, and that integration with the general medical services was the only way of providing an adequate number of treatment points.

The fact that the leprosy patient is often neglected by the general service is in part a reflection on the teaching institutions, none of which, it was said, gave adequate attention to leprosy, if indeed they covered it at all. The first priority in leprosy control is to "teach leprosy" to those who teach clinical and preventive medicine. This academic ignorance and its effect on the students is probably more deleterious to leprosy control than the superstitions of the population.

While it could be argued that the training of special leprosy assistants could perpetuate the unfortunate isolation of the disease, it was felt they had a place in leprosy control, especially if used, not for the general control programme, but for special projects designed to boost the medical services of an area.

The problem of providing adequate treatment points was particularly severe in those areas where the population was widely scattered. One attempt at dealing with this was the leprosy village system originally suggested by Kinnear Brown and practised in the Teso District of Uganda (Stone). Even with this it was found necessary to send leprosy assistants out from the villages to scattered treatment points; but for how long can such assistants be expected to travel large distances on repeated occasions in a rapidly changing social situation? The possibility of enlisting the voluntary help of responsible members of the community without medical training must be considered. There was also, it became evident, pressing need to conduct trials to determine the best way to use dapsone, in terms of dosage, frequency, and duration. Fortunately one can expect that with increasing leprosy consciousness and earlier diagnosis the complications of treatment will diminish and it will come to be recognized as a skin disease which, treated adequately, causes little inconvenience to the patient and his contacts.

One encouraging aspect of the conference was its integration of leprosy with the other mycobacterial diseases. It is hoped that increasingly in the future the tuberculosis specialist will take more interest here rather than confine himself to diseases of the chest. The interest in Buruli ulcer, a crippling disease first described in 1948 in Australia and now recognized as common in several parts of Africa, perhaps indicates the future widening of this field of diseases. BCG is an obvious point of common interest, but Professor Meissner showed us how much we should be aware of the many

mycobacteria that can effect man's immunological condition and sometimes produce disease. In the more practical field of control, tuberculosis and leprosy have common problems in the long duration of treatment and the many social factors involved. The mycobacterial diseases provide the leprologist with one avenue of approach to the general medical community, while he himself, tending to become slack in his isolation, can be stimulated by the more scientific approach of his colleagues. The alternative is to allow urban tuberculosis to control rural leprosy.

If leprosy is indeed a social disease with medical aspects what should be the functions of a leprologist? A certain percentage of patients will require more than diagnosis and dapsone. Admitted to a hospital unit, they will be his clinical responsibility. As in other fields of preventive medicine where the doctor has given the civil engineer, the health administrator and the social worker the rationale for their work, so in leprosy control he will need to be responsible for the overall strategy until the epidemiology of the disease is more fully understood. With the help of a medical statistician he must interpret the information derived from diagnostic and treatment services. He must be the link between the research scientist and the pharmacologist on the one hand and the field worker and patient on the other. Above all he must *teach*. One regrets seeing him placed in a leprosarium far from the Ministry of Health where he can think his own thoughts and trouble no one. Equally, one regrets seeing him confined to the Ministry of Health, an administrator in an office expected to visit and advise other people about their patients while having none of his own. When integration comes one hopes he will be in the reference hospital, as is his colleague the tuberculosis specialist. Where a dermatologist is considered too great a luxury the leprologist would do well to cover dermatology also. In this situation he can use the clinical skills he has been taught, he can be in the mainstream of the teaching programme, and he can appreciate the need for the out-patient programme he guides, which is the key to control. There will never be enough doctors to control leprosy. In this situation he can use his particular abilities to the best advantage and delegate field-work to others often better fitted for it than himself.

David R. Clegg

Medical Officer

LEPRA Control Project, Malawi

Formation of an East African Leprosy Workers' Association (E.A.L.W.A.)

The Planning Committee appointed by some 60 members attending the Seminar on Leprosy, 31 January to 1 February, in Dar es Salaam, Tanzania, met at the close of the Seminar. The Committee consisted of Dr. D. L. Leiker, Dr. A. C. McDougall of Zambia, Dr. D. R. Clegg of Malawi, Dr. W. Felton Ross of Ethiopia, Dr. Y. Otsyula of Kenya, Dr. W. Blenska of Uganda, Dr. H. W. Wheate of Tanzania, and the Secretary, Mr. G. V. W. Anderson.

The several alternatives that were examined by the Committee were discussed and the following decisions were arrived at as the most promising.

(1) That there should be an East African Leprosy Workers' Association, which could at a later date be expanded to cover other mycobacterial diseases.

(2) That there should be National Bodies whose members would be automatically members of the E.A.L.W.A. on payment of the minimum subscription.

(3) Mr. G. V. W. Anderson undertook to do the preliminary secretarial work in Nairobi after he had retired from the E.A. Medical Research Council at the end of February, 1969.

(4) It was decided that all leprosy workers should be invited to become foundation mem-

bers, including also persons not professionally engaged in the work but interested in promoting it.

(5) The Secretary was asked to circulate all those working in leprosy and those who were interested, asking them if they would become foundation members of the Association.

(6) The membership fee was suggested to be a minimum of 5 shillings, but any member may offer a larger sum.

(7) An offer of £100, made on behalf of the Netherlands Leprosy Foundation by Dr. Leiker, to cover the initial expenses was gratefully accepted.

(8) It was also proposed that there should be a suitable Bulletin, or some such, issued quarterly carrying news items, staff changes where appropriate, scientific articles, and similar matter as from time to time might be acceptable. Further, it was suggested that a leading article by some outstanding leprosy specialist should be a feature of each issue. The early issues would be in the nature of a mimeographed booklet until such time as a printed bulletin became feasible or desirable.

(9) Certain people were to be approached to undertake the work of promoting the national societies and the international association. It was further suggested that Dr. R. G. Cochrane be asked to act as Honorary Consultant.

The Tanzania National Leprosy Advisory and Co-ordinating Committee

In July 1967 there was formed in Tanzania a National Leprosy Advisory and Co-ordinating Committee. For some years there has existed a Tanzania Christian Medical Association (T.C.M.A.), affiliating all the Christian Missions undertaking medical work—which naturally includes leprosy—throughout the country. As the primary objective of this Leprosy Committee was to foster co-operation between all these bodies and between them and the Government, it was deemed advisable that it should be, not a Government appointed body but a sub-Committee of the Tanzania Christian Medical Association on which Ministry of Health officials would sit *ex officio*. So with goodwill on all sides, this came about.

The German Leprosy Relief Association (D.A.H.W.) gave both moral support for the principle and a generous gift to cover the inevitable administrative expenses. Later, the Swedish–Norwegian Save the Children Fund, which is organizing a Leprosy Campaign in the West Lake Region of Tanzania, contributed a handsome donation.

The initial action has included: (1) the appointment, by the Government Regional Medical Officers, of Regional Leprosy Officers in each of the 17 Regions in the country. The majority of these are Voluntary Agency doctors (it must be borne in mind that there is a great shortage of Government Medical Officers); and (2) the disbursement of financial assistance to 6 Missions to enable them to maintain and/or extend the leprosy control work in their Regions.

Of urgent concern is the need for more trained staff, and arrangements have been made to give all the leprologists in Tanzania a share in this task according to their particular interests. In addition, with the assistance of Dr. Luther Fisher and Mr. David Ward of ALERT, one of the leprosy centres is to run an elementary course in physiotherapy.

Hospital beds are provided for leprosy patients at all Government Hospitals, in particular in Dar es Salaam at the Muhimbili Hospital, with its attached medical school. There are special leprosy hospitals in 13 out of the 17 Regions (in 3 of the others the prevalence rate is very low). The leprosaria are now all institutions for the short-term care of acute or otherwise complicated cases. They deal with approximately 3000 cases annually.

(*continued on p.* 183)

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Significance of Variations Within the Lepromatous Group*

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To the 5 classes of lepromatous leprosy defined by Ridley and Jopling (1966) the authors now add a sub-group, LI (Indefinite Leproma), which appears to occur most frequently among Chinese and Malay patients but has been seen in patients of many other races. The biological response to treatment of this sub-group is described.

INTRODUCTION

Patients in the Leprosy Research Unit at Sungei Buloh have for the last 10 years been classified on the 5-group TT–LL system (Ridley and Jopling, 1962, 1966). From an early stage it was clear that the histological and clinical picture of lepromatous leprosy as seen in Malaya (West Malaysia) differed in some respects from that of typical polar lepromatous (LL) patients, although the typical LL form was occasionally encountered. It was also known that the rate of fall of the biopsy index (Ridley, 1958*a*) was somewhat faster in Malayan patients than in Europeans, namely, 33% as against 25% for each period of 6 months (Ridley, 1958*b*; Ridley and Jopling, 1962). Nevertheless, lepromatous patients at Sungei Buloh continued to be classified as LL for a number of reasons: (1) histologically the majority were closer to LL than to the next group, BL; (2) they were highly bacilliferous and the rate of fall of the bacterial index (BI) in smears was consistent with LL; (3) clinically they were either consistent with LL or closer to LL than to BL; (4) they commonly developed erythema nodosum leprosum (ENL), sometimes of a severe form; and (5) most of them remained stable during therapeutic trials of 6 months' or a year's duration. More recently, however, when greater numbers of such patients were studied, and also were followed-up for longer periods, it became evident that an appreciable proportion were undergoing reversal reactions with a significant effect upon prognosis: there is an immunological shift in the direction of tuberculoid, followed by an increase in the rate of elimination of bacilli from the skin, with or without an obvious reaction in the lesions (Fernandez *et al.*, 1962; Ridley, 1969). Such reactions were previously regarded as a feature of borderline leprosy (BL or BB) and were an important reason why BL patients were not accepted for therapeutic trials (Ridley and Jopling, 1966; Waters *et al.*, 1967). It became necessary therefore to make a thorough analysis of the "Malayan" type of leproma (which incidentally is not exclusive to Malaysia) and for this purpose a sub-group called Indefinite Leproma (LI) was introduced. Although the LI sub-group was originally a histological concept, it was soon found that the majority of cases could be identified clinically.

MATERIALS AND METHODS

The following steps were taken. (1) After a preliminary trial run with the modified classification and a comparison of the clinical and

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histological diagnoses, all new patients admitted to the Leprosy Research Unit, Sungei Buloh, were classified on the new system. Each was placed in one of the five original groups, or in the new LI sub-group. (2) Former patients at Sungei Buloh Leprosarium who had taken part in 2 trials were re-classified on the basis of their clinical records and the histological findings in sections, and their subsequent progress rates were estimated by the logarithmic index of bacilli (LIB) in biopsy specimens (Ridley and Hilson, 1967). The 2 trials were of ditophal (Etisul) and DDS, as against DDS alone (Waters and Pettit, 1965) and DDS in low dosage (Pettit and Rees, 1967). They were chosen because patients in these trials had been followed up for a year. As there was no difference in the rates of fall of the LIB in the 2 trials the results were treated as a uniform series for the present purpose. (3) Patients, both past and present, at the Jordan Hospital, Redhill, England, were re-classified on the basis of their histological sections, but not clinically, and their progress rates under treatment were estimated by the LIB. All patients who had been followed-up for a period of at least 18 months, and whose lesions had a granuloma fraction of at least 0.2, were included in the analysis. All had been treated with sulphones or thiambutosine (Ciba 1906, DPT). (4) The distribution of patients among the 5 groups and one sub-group was calculated according to race. The great majority of Sungei Buloh patients were Chinese or Malay; those at the Jordan Hospital were predominantly of European or Eurasian origin, but there were also some patients of Indian, Negro, and other races. (5) The progress rates of patients in the different groups were compared. Although the LIB was regarded as the most useful index for this type of work, the bacteriological index (BI) and morphological index (MI) of smears were also noted.

DEFINITION OF THE LI SUB-GROUP

Clinical

The majority of patients present an appearance closely resembling LL leprosy. Almost all the lesions are lepromatous and symmetrical, and the smears are strongly positive. Infiltration may be heavy. However, on careful inspection, nearly always one or a small number of residual, asymmetrical, borderline lesions (BB type) may be detected (Fig. 1). The latter appear months or years before the lepromatous lesions; they are most commonly found on the lower limbs, although they may occur elsewhere on the body, especially on the extensor surfaces of the trunk and arms. The outer edge of such a residual borderline lesion is usually somewhat vague as a result of the surrounding lepromatous infiltration, but the inner edge may remain sharp with a small hollowed-out, hypopigmented, anaesthetic centre. In addition there may be asymmetrical nerve damage, e.g. a unilateral claw hand or drop foot; the nerve damage often occurs early, in association with a borderline lesion (Fig. 2) and before the onset of the symmetrical lepromatous lesions, but occasionally it develops much later in an asymmetrically-enlarged nerve, when the treated patient is suffering from ENL. The outer halves of the eyebrows are usually intact and the nasal cartilage and bone are often spared. However, the testis is frequently involved and leprous orchitis (usually associated with ENL) may occur; although true gynaecomastia is rare, pseudogynaecomastia due to heavy infiltration of the skin of the nipple without glandular enlargement of the breast has occasionally been noted.

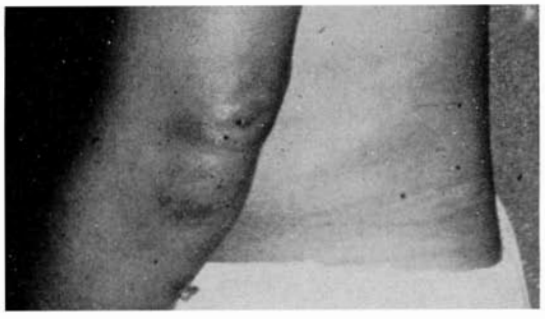

FIG.
Borderline lesion on left arm of patient who subsequently developed LI leprosy.

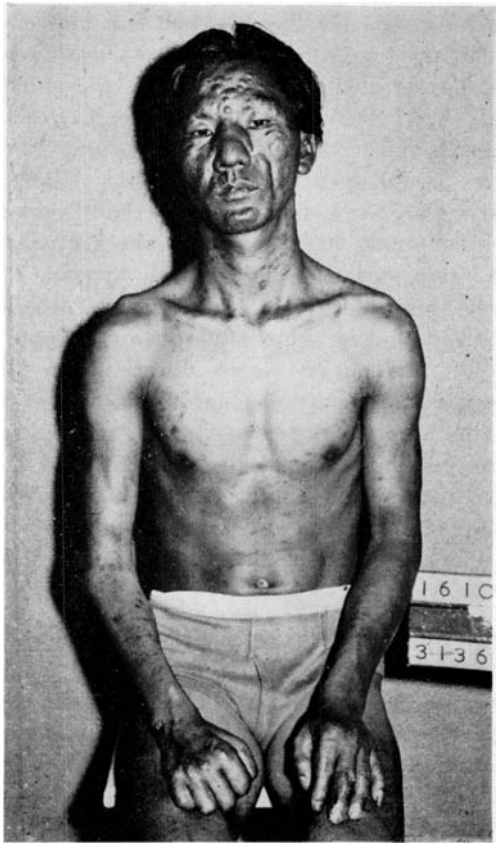

FIG. 2

Residual borderline (BT or BB) annular lesion encircling the right forearm; the distal (inner) edge remains sharp but the proximal (outer) edge is merged into the lepromatous infiltrate; the right hand is clawed with radial, ulnar, and median nerve paralysis. The borderline lesion and the nerve paralysis developed 7 years before the patient presented for treatment; at that time he had been developing LI lesions for the previous year, and some LI papules are visible on the right forearm.

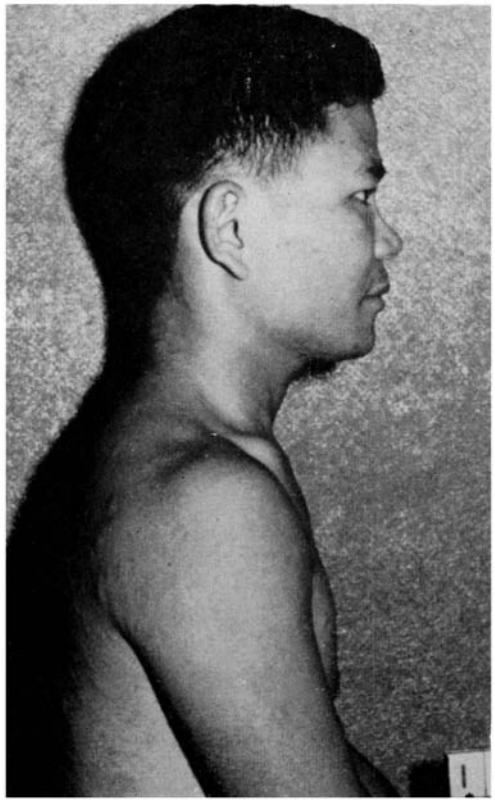

FIG. 3

Recently developed LI leprosy, with no appreciable enlargement of the ears and few lesions on the face. Eyebrows and nose are intact.

Some Chinese patients of the LI type, especially young adult males, show remarkably little deformity of the face; their ears are not enlarged (although a few tiny papules may be present), the eyebrows and nose are intact, and obvious lesions on the face are minimal (Fig. 3). Nevertheless, smears from the ear lobes are symmetrically and strongly positive provided that the lepromatous lesions have been present on the trunk and/or limbs for more than just a few weeks. In general, this "small-eared" type of lepromatous leprosy is of recent onset, associated with rapid multiplication of leprosy bacilli throughout the skin; if treatment is delayed for 2 to 3 months then the BI and the degree of infiltration are both considerably increased. Furthermore, under treatment these patients may develop severe ENL, even though they bear so few of the stigmata of lepromatous leprosy.

A third clinical type which is occasionally seen, more especially in older patients, is completely symmetrical. The face is mildly infiltrated, the ear lobes enlarged, and the trunk and limbs covered with multiple, erythematous, lepromatous macules or flat papules. However, the degree of underlying infiltration is relatively slight, the skin being less "succulent" than is typical of LL leprosy (Fig. 4). Such patients are

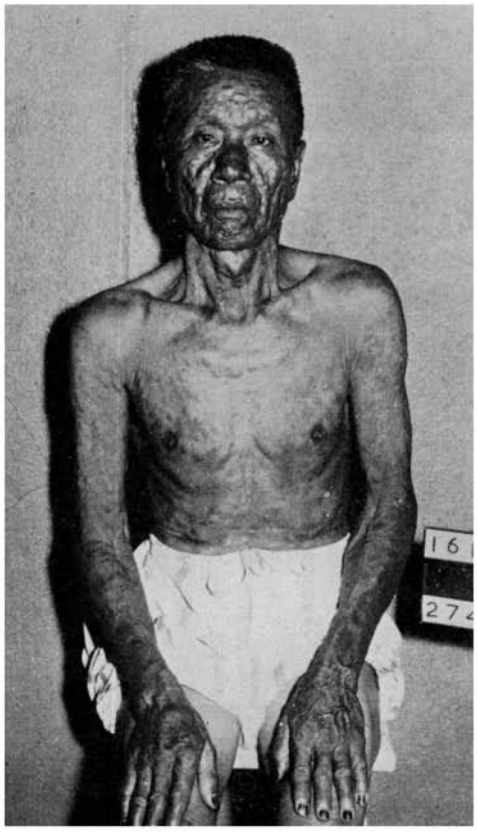

FIG. 4
Symmetrical, erythematous, LI maculo-papules, but with only slight infiltrate in the "normal" skin between the lesions.

difficult to classify clinically, although careful examination may reveal an asymmetrical anaesthetic area; histological diagnosis is essential to place them accurately on the leprosy spectrum.

Histological

As previously reported, the BL group is distinguished from the LL group either by an epithelioid tendency in the host cells of the bacilli, or by an increase in the number of lymphocytes in the granuloma. In addition, in BL there may or may not be a cuff of lymphocytes around nerves.

The same 3 characteristics are used to define the LI group. (1) The host-cell is a histiocyte. In the most active stage it takes the form of a macrophage, which is typically less rounded than the macrophage in active LL. Compression and flattening of the sides may give it some resemblance to an epithelioid cell. As it matures (a less active phase of the granuloma can sometimes be observed in another part of the same section), the host-cell appears as a fairly large histiocyte with no epithelioid tendency and no appreciable foamy change. In chronic lesions of longer duration, or after treatment, a foamy change occurs, though the accumulation of fat is not as great as in the corresponding stage of an LL lesion and there is less necrosis of the fatty cells in the granuloma. If large globi develop they are usually engulfed in a multinucleate giant-cell with fairly fleshy cytoplasm.

(2) Alternatively, or sometimes in addition to the above, there is an increase of lymphocytes in the granuloma. The number of these cells is then greater than would be found in an LL lesion but not great enough to justify a classification of BL. These lymphocytes are diffusely and fairly evenly infiltrated throughout the granuloma. Plasma cells are often fairly numerous and are a feature of LI lesions, though they are not a reliable diagnostic criterion. The mixture of histiocytes, lymphocytes, and plasma cells in the granuloma presents a pleomorphic picture which, together with its cellularity, is the most characteristic feature of LI (a lesion of this type is illustrated in Fig. 21 of Ridley and Jopling, 1966).

(3) The nerves in LI lesions, as in BL, may show nothing but fibrosis or loss of structure due to active involvement during an earlier borderline stage of the infection. More typically the nerves in LI cases, close to BL, are characterized by infiltration of the perineurium, though not of the nerve bundle itself, with histiocytes heavily laden with bacilli. In cases of LI near to LL, the infiltration disappears and the nerve sheath is split by vacuolar spaces, which presumably are due to disintegration of the histiocytic cells. Perineural infiltration is sometimes observed

also in BL patients, though it tends to be obscured by the cuff of lymphocytes around the affected nerve-bundle. In LL cases the perineural sheath is almost always normal.

There is, of course, no absolute point of distinction between LL and LI, or LI and BL and considerable experience of classification on this basis is needed before reproducible results are obtained. It is helpful to keep a small collection of classified slides as standards. There are two mains points of difficulty: (1) In very active lesions the histology, superficially at least, has a more borderline appearance than in less active ones. In LL cases there is merely an absence of fatty change in the swollen macrophages. In LI patients, however, the most heavily laden cells at the centre of a very active lesion may take on a somewhat epithelioid appearance. In BL one occasionally sees foci almost indistinguishable from epithelioid cell foci, except for the fact that they are found to be exceptionally heavily stuffed with bacilli, whereas in a true epithelioid cell focus bacilli would be fewer than elsewhere. There is a dual spectrum in histology, of BL to LL and of activity to regression. Allowance has to be made for the one in evaluating the other. (2) The foregoing account, although it describes both active and regressing lesions, refers mainly to untreated patients. After treatment the lesions regress in the manner described, but the histology is liable to be complicated by reactions which are usually associated with the influx of some lymphocytes at some stage (the possibility that reactions may occur in untreated patients must not be forgotten). In general, it should be quite possible to make a "blind" histological classification of an untreated patient; but if the patient has been treated it is desirable that the histologist should know this, and if possible that he should know the pre-treatment classification.

It is exceptional to find that the histological classification of 2 lesions taken at the same time from the same patient differs by as much as one group, when classification is based on a 5-group system, except possibly during a reversal reaction. When the LI sub-group is introduced it does happen occasionally that the classification of two concurrent biopsies differs; e.g. one may be LI and the other BL, even when there is no reaction. However, this is observed on less than 1 in 10 occasions.

RESULTS

Clinical—histological correlation in classification

Sections were available from 122 untreated patients at the Jordan Hospital. An equal number of patients were taken from the most recent admissions to Sungei Buloh, and of these the original clinical classification was available for 33 patients in the LL-BL range. There was complete histological-clinical agreement in 17 of the 33; and partial agreement in a further 11 cases in which there was some doubt on the clinical side, e.g. the clinical classification was given as LI or BL and the histological classification was one of these groups. There was disagreement in 5 cases concerning 2 adjacent groups, e.g. BL and LI, but in no case was there a disagreement concerning BL and LL. In cases of doubt the histological classification was accepted, partly because it appeared to be a little more emphatic than the clinical classification, and partly because at the Jordan Hospital clinical classification using the LI sub-group had not so far been undertaken.

Proportion of LI patients in different races

The distribution of patients between the 6 groups at Sungei Buloh Leprosarium and at the Jordan Hospital is shown in Table 1,

TABLE 1

Distribution of patients in 6 classification groups, at the Jordan Hospital and at Sungei Buloh Leprosarium, and according to race.

	LL	*LI*	*BL*	*BB*	*BT*	*TT*	*Total*
Jordan Hospital	30	26	20	13	25	8	122
Sungei Buloh	15	51	19	10	21	6	122
Chinese	8	26	8				
Malay	4	22	6				
Indian	8	10	8				
European	20	15	8				
Others	5	4	9				
Total	45	77	39	23	46	14	244

TABLE 2

Analysis of the mean falls of the logarithmic biopsy index (LIB) after treatment for 1 year, and in the 6 months following a reversal reaction

Leprosy group	*No. of patients*			*Mean fall in LIB at one year*			*% incidence of reversal reaction after*		*Fall in LIB in the 6 months following reversal reaction*
	*S.B.**	*J.H.*	*Total*	*S.B.*	*J.H.*	*Mean*	*1 yr*	*2-7 yr follow-up*	
LL	11	20	31	0.22	0.13	0.18	0	0	
LI	40	18	58	0.64	0.56	0.60	10	21	1.8
BL	19	6	25	2.2	2.2	2.2	36	60	2.1

* S.B., Sungei Buloh Leprosarium patients; J.H., Jordan Hospital patients.

which also shows the breakdown of patients from both centres according to race. The LL : LI ratio among European and Eurasian patients is 1 : 0.75; among Chinese and Malays it is 1 : 4; among those of Indian origin the ratio appears to fall between these 2 extremes, but the numbers are too small to give an accurate figure. At Sungei Buloh as expected, the proportion of LI patients appears to be exceptionally high by world standards, though there are other races about which more information is needed.

Rate of fall of LIB in LL, LI and BL patients

The fall of the LIB after one year's treatment is a little over 3 times greater in LI than in LL patients, and a little over 3 times greater in BL than LI (Table 2). Thus LI would appear to be a truly intermediate group, though numerically the fall in LIB for LI is closer to that for LL than for BL. The patients at Sungei Buloh Leprosarium and the Jordan Hospital could be compared, from the point of view of the fall in the LIB, only at one year. At this time there was good agreement in the results. The fall in LL and LI patients was marginally higher at Sungei Buloh than at the Jordan, showing that there was no bias in classifying patients as LI at Sungei Buloh and LL at the Jordan, possibly rather the reverse, although an alternative explanation lies in the different methods employed at the 2 hospitals for the treatment of ENL; in either case the differences are not statistically significant.

The fall of the LIB during the course of reatment is shown in Table 3 (these results

TABLE 3

Analysis of the mean fall in the LIB during treatment (Jordan Hospital patients only)

	Initial LIB	*Mean fall in LIB at (yr)*							
		½	1	1½	2	2½	3	3½	4
LL	5.27	0.06	0.13	0.34	0.80	0.81	1.2	1.8	2.5
LI	5.28	0.17	0.56	1.1	1.3	1.9	2.8		
BL	4.8	1.5	2.2	3.9					

were available only for the Jordan Hospital patients). The rate of fall in the 3 groups bears a constant relationship throughout the period of treatment during which biopsies were made. These conclusions were supported in the main by the results of the BI in the same patients' smears. But it was not possible to detect any significant difference between the LL, LI, and BL groups in respect of the rate of fall of the MI during the early stage of treatment.

Reversal reactions

The incidence of reversal reactions in the 3 groups is given in Table 2. The number in LI patients was relatively small; during the first year they occurred in 6 out of 58 patients, or 10%, of whom 2 showed only histological evidence of reversal; and on more prolonged follow-up there were a further 6 cases. Reversal reactions occurred more frequently in BL patients; they tended to be clinically more severe than in LI leprosy and to develop earlier in treatment (9 out of 25 BL patients, i.e. 36%, reacted within 6 months of starting treatment and a further 6 out of 25 (24%) after more than one year). However, one BL patient did not go

into reaction until he had completed 4 years of treatment, and he required strong reassurance that he had not undergone a relapse.

As a result of the reactions, LI patients usually converted to BL and BL patients to BB or even BT. The fall in the LIB as a result of the reaction was not usually so great in the early stages of treatment as in the later stages, but in almost every case it exceeded the reduction that would have been expected if there had not been a reaction. The accelerated fall in LIB did not take place until after the onset of the reaction. Thus, although there was evidence of reaction in 6 LI patients during the first year, only 3 of them showed a marked fall in the LIB during this period. There were mild lepra reactions bearing some clinical resemblance to reversal reactions in 2 of the 31 LL patients, but as there was no change in classification as a result of the reaction, nor any unusual drop in the LIB in either of them, they are not included in the Table.

The effect of reversal reactions is also shown in Fig. 5. LI and BL patients are noticeably more erratic in their response to treatment, as judged by the LIB, than are LL patients.

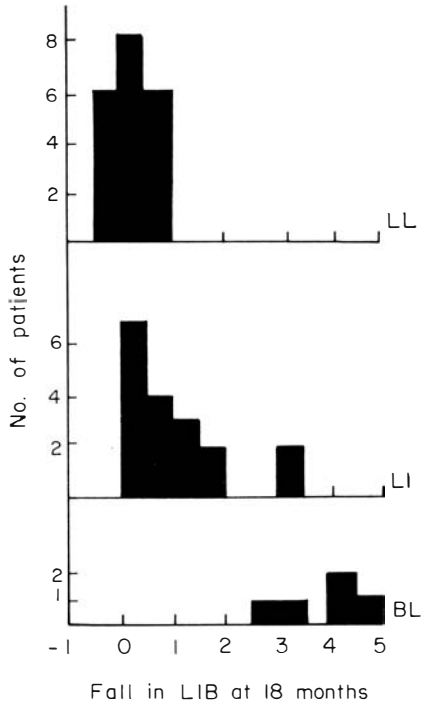

FIG. 5

Distribution of patients according to mean fall in the LIB after 18 months' treatment; 3 groups.

Erythema nodosum leprosum (ENL)

ENL tended to occur earlier and more frequently in LL patients than in LI patients. Of the 11 LL patients studied at Sungei Buloh Leprosarium and analysed in Table 2, 8 (73%) developed ENL within 12 months of commencing treatment; of the remaining 3, one subsequently developed undoubted ENL, another was seen to have one or 2 ENL-like papules at his 2-year out-patient review, which may have been a single mild episode of ENL, and only one of the 11 was never observed to develop any signs or symptoms suggestive of ENL during a relatively brief follow-up of 25 months. On the other hand, only 17 (42.5%) of the 40 LI patients developed ENL within one year of commencing treatment and a total of only 25 (62.5%) were known to have suffered from ENL during more prolonged follow-up.

ENL was least common in BL patients. Three out of 19 (i.e. 16%) developed this type of reaction within 12 months of starting treatment, and a total of 6 (32%) on more prolonged follow-up. Two BL patients who suffered from ENL subsequently underwent reversal reactions after 18 and 23 months' treatment respectively. Two LI patients who underwent reversal reactions to BL subsequently developed mild ENL. There did not appear to be any close relationship between the type of leprosy (LL, LI, or BL) and the severity of the ENL, although the duration of ENL tended to be shorter in BL leprosy; only one BL patient suffered from ENL for more than 2 years after the beginning of treatment.

Relationship of the type of leprosy and the lepromin test

Pre-treatment lepromin tests were performed on all Sungei Buloh patients. No significant

differences were discovered using Dharmendra-type lepromin between LL, LI, and BL patients. When Wade–Mitsuda lepromin was used, still no significant differences were detected between LL and LI patients, who were all uniformly negative at 4 weeks; however, 3 of 9 BL patients were weakly positive (± or +) at 4 weeks.

DISCUSSION

The analysis of lepromatous patients here reported has revealed a histologically and clinically distinctive sub-group designated indefinite leproma (LI). Prognostically, it is intermediate between LL and BL—the rate of elimination of bacilli from skin lesions, as shown by the LIB in biopsy samples, or the BI in smears, is intermediate between the other 2 groups; and a small but definite proportion of LI patients undergo reversal reactions. Histologically, the sub-group is intermediate between LL and BL. Clinically, the great majority of LI patients bear evidence that the disease has evolved from a pre-existing borderline condition.

It has often been said that the character of lepromatous (or tuberculoid) leprosy varies in different parts of the world (Browne, 1963; Ryrie, 1948). It would appear from the foregoing that much of this geographical variation is due to small differences in the distribution of patients along the immunological spectrum; and in particular that lepromatous leprosy which has evolved from the borderline type does not frequently or quickly descend as far as the lepromatous pole (LL). It is not surprising, therefore, that the majority of lepromatous patients in Malaya (West Malaysia) are found to belong to the LI sub-group. Primary lepromatous leprosy is rare among Chinese and Malays, certainly in patients aged less than 50 years; most cases are secondary, having developed from borderline disease (Ryrie, 1948; Waters, 1967), and Maxwell and Kao (1952) considered that in no more than one of 76 lepromatous patients at Hangchow was it of the primary type. The predisposition of patients to deteriorate from non-lepromatous to lepromatous is widely recognized in the literature, and in addition to China it has been reported from India (Dharmendra, 1960), Nigeria (Davey, 1960), Europe (Medina, 1949), and South America (Souza Lima and Rath de Souza, 1949). It is clear from Table 1 that LI leprosy is less common among European patients (including those of mixed racial descent) than it is in Malaya. The number of patients of other races in this analysis is too small to give much indication of the incidence of the LI sub-group among them, but cases have been observed among Aboriginal, Indian, Gurkha, Pakistani, African Negro and Indonesian patients, and there is no reason to doubt that it occurs, in varying numbers, in all races. We are not sure how closely Leiker's "non-diffuse lepromatous (L)" group (Leiker, 1966) is related to our LI group.

We do not wish to over-emphasize the importance of the LI sub-group. It is situated very close to the lepromatous pole of the spectrum and for most purposes there is no need to distinguish between LI and LL. The prognostic differences between them are, however, of some importance in therapeutic trials. During the first 6 months of therapy there is no significant fall of the LIB in LL patients, whereas there is a very small fall in LI patients. After one year the difference in the 2 rates of fall is more marked, and is statistically significant with groups of about 20 patients. The small but definite incidence of reversal reactions will significantly affect the prognosis of individual LI patients, especially in trials of more than one year's duration. The practice, adopted at Sungei Buloh during the last 10 years, of limiting the intake of patients for trials to the LL group (Waters *et al.*, 1967) as previously defined, has been followed also at a number of other centres. If now LI patients were to be excluded it is doubtful whether there would anywhere be a sufficient number of patients for controlled trials such as have been conducted in the past. At Sungei Buloh Leprosarium itself the number of LL patients is so small that the error of including LL and LI patients together in a single group would not be great; but ideally

they should be separated. The problem of the analysis of results obtained from combined LL and LI groups could be overcome by using the covariance method (Waters *et al.*, 1967), which might be considered for future trials.

It may be asked whether there is any longer any justification for using the rate of fall of the bacterial indices (LIB and BI) as a criterion of the potency of a drug. The elimination of dead leprosy bacilli has been found to be a function of the patient's immune mechanisms, and classification at the bacteriologically positive end of the spectrum has now been defined in considerable detail by reference to this fact. A correlation exists here by definition. On the other hand, none of the drugs so far used in leprosy has been shown to influence the rate of elimination of bacilli once they have been killed. The progressive fall in bacterial number is useful confirmation that bacilli have been killed and that drug resistance has not developed; it would be a criterion of potency only if a drug could be found that would hasten the process of resolution.

SUMMARY

A lepromatous sub-group (indefinite leproma, LI) has been identified histologically and clinically. The bacteriological response to treatment in this group is intermediate between that of LL and BL. LI patients differ from LL in being liable to undergo reversal reaction, though possibly at a later stage of treatment than BL patients; they differ from BL in being very prone to ENL.

The LI sub-group has been found among patients of many races, though with varying incidence. It is especially common in Chinese and Malays, among whom it greatly outnumbers LL and BL patients. LI patients are suitable for therapeutic trials under certain conditions. Clinicially, they present evidence of having evolved from a pre-existing borderline phase.

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Indomethacin in the Management of Erythema Nodosum Leprosum—A Double-blind Controlled Trial*

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This investigation of the efficacy of indomethacin in comparison with 3 other drugs (prednisolone, chloroquine, and aspirin) in the management of exacerbations of lepromatous leprosy (ENL) has shown that indomethacin and chloroquine were the most useful in decreasing the number of recurrences and that indomethacin was the most beneficial in improving vision but was no better than the other drugs in regard to arthralgia, acute exudative arthritis, and acute painful neuritis.

INTRODUCTION

Indomethacin is an indole derivative which was first synthesized in 1961 and found to have anti-inflammatory properties. It is a non-steroidal drug and is unrelated to any other known anti-inflammatory agent. Calculations based on animal tests have shown the drug to be between 10 and 85 times as potent as hydrocortisone (Winter *et al.*, 1963).

Clinical trials have demonstrated that indomethacin has anti-inflammatory, anti-pyretic, and analgesic properties when administered to patients with rheumatoid arthritis, osteoarthritis, and gout (Hart and Boardman, 1963; Smyth, 1965; Morkel, 1966). The results achieved by the use of the drug in these conditions have been encouraging.

While the role of steroids in the management of severely exacerbated phases of leprosy is well established their long-term use is hazardous, and the search for an alternative drug has to be continued. An open trial of indomethacin in our hospital gave encouraging results (Thomas *et al.*, 1968), and to further evaluate more fully its efficacy in the management of exacerbations in lepromatous leprosy, a double-blind controlled trial was carried out using prednisolone, indomethacin, chloroquine, and aspirin; from their initials the trial was known as "PICA" and this word was written on prescriptions ordered for patients entering the trials. The specific objectives of this study were to collect unbiased data on: (1) the role of indomethacin in controlling exacerbations of lepromatous leprosy, specifically erythema nodosum leprosum, fever, arthritis, periostitis, neuritis, iritis, lymphadenitis, and oedema; (2) its value in preventing further exacerbations while the patient was receiving maintenance doses of the drug; (3) the possibility of the early re-introduction of specific anti-leprosy therapy, following control of the exacerbated state, without precipitation of further attacks of exacerbation; and (4) the side-effects, if any, encountered during administration of the drug.

MATERIALS AND METHODS

During the 6-month period between November 1967 and May 1968, all lepromatous leprosy

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patients admitted to the Schieffelin Leprosy Research Sanatorium for control of exacerbation ("reaction" with erythema nodosum leprosum (ENL)) were screened and accepted for the trial provided that they were over 12 years of age, had no history or radiological evidence of peptic ulceration, pulmonary tuberculosis, hypertension, diabetes, severe intercurrent infection, or exacerbation associated with acute peripheral nerve paralysis, and no medical condition requiring the use of other anti-leprosy agents, such as long-acting sulphonamides or streptomycin. On admission to the trial, all specific anti-leprosy drugs were stopped. Each patient admitted to the trial was given a serial number and treated with one of the 4 drugs according to a confidential, randomized list. The Nursing Superintendent was responsible for the dispensing of drugs according to the therapeutic régimes shown in Table 1.

All drugs were administered orally at meal times, indomethacin being given in 25 mg capsules, aspirin in the form of "Ascriptin" tablets (aspirin 5 gr, with magnesium aluminium hydroxide 2.5 gr), chloroquine as 250 mg tablets, and prednisolone as 5 mg tablets. During the exacerbated phases, restless patients were sedated with phenobarbitone, 60 to 90 mg at night, or with chlorpromazine ("largactil") 25 mg t.d.s. by day as needed. No anti-inflammatory agents other than "PICA" were prescribed and diuretics were prescribed only when oedema was progressive and obviously uncontrolled by "PICA"; appropriate clinical notes were made by the observer-clinician at the time. Specific anti-leprosy treatment (dapsone) was re-introduced only when a patient was free of symptoms of reactions for at least 4 weeks.

A total of 50 lepromatous patients were included in this study, of whom 13 received prednisolone, 11 indomethacin, 12 chloroquine, and 14 Ascriptin. The clinical status of each patient was assessed on admission and graded according to the system shown in Table 2.

Table 1
Therapeutic régimes

Drug	*Dosage*		
	First 2 weeks	*Third week*	*Maintenance*
Prednisolone (P)	5 mg t.d.s.	5 mg b.d.	5 mg o.d.
Indomethacin (I)	50 mg t.d.s.	25 mg t.d.s.	25 mg o.d.
Chloroquine (C)	250 mg t.d.s.	250 mg b.d.	250 mg o.d.
Aspirin (A)	1 g t.d.s.	1 g b.d.	0.5 g b.d.

Table 2
Grading of reactional status

Grade		*Symptoms and signs*				*Oral temperature (°F)*
		Subcutaneous nodules	*Periosteitis neuritis and arthritis*	*Oedema*	*Others*	
1+	Few; superficial; not tender	Nil	Pain but not tenderness	±Minimal		99.0–101
2+	Scattered; mostly superficial; a little tender	±	With some tenderness	±Moderate		99.0–103
3+	Multiple; superficial and deep; painful and tender	±Tender	Painful and tender	±Gross	±Iritis ±Tender and painful lymphadenitis	99.0–105
4+	Multiple; superficial and deep; very painful and tender; nectrotic	±Tender	Very painful and tender	±Gross	Iritis; very painful and tender lymphadenitis; toxic state with distress	99.0–105

Clinical assessments were made on alternate days throughout the acute period and thereafter at monthly intervals until the trial period of 90 days had been completed.

The distribution of patients in each drug group according to the severity of presenting symptoms is shown in Table 3. Personal experience has led us to the belief that exacerbations of Grades 1 and 2+ differ from those of Grades 3 and 4+, not only in their clinical features but also in the degree of systemic disturbance which they cause and their response to anti-inflammatory drugs. It has thus been found convenient to discuss the findings in Grades 1 and 2+ as one category and Grades 3 and 4+ as another.

TABLE 3
Distribution according to severity of exacerbation in each drug group

Drug group	*Reaction*				*Total*
	Mild		*Severe*		
	1+	2+	3+	4+	
P	1	11	–	1	13
I	–	5	1	5	11
C	–	6	2	4	12
A	2	3	4	5	14
Total	3	25	7	15	50

It is somewhat unfortunate that by chance the majority of patients in the less-severe reaction group were receiving prednisolone, despite the statistically randomized grouping.

RESULTS

The number and percentage of patients in whom the reaction was successfully controlled in each of the 4 groups under study are presented in Table 4. While all the patients given prednisolone showed early response, the overall response to indomethacin was only 64%, which was not significantly different from that obtained in the chloroquine and aspirin groups. Among those who had severe exacerbations (3 or 4+) there was a higher response to indomethacin than to chloroquine, but the difference was not statistically significant.

TABLE 4
Responses to therapy in each of the 4 groups under trial

Drug group	*All cases*			*Severe cases*		
	Studied	*Responded*		*Studied*	*Responded*	
		No.	%		*No.*	%
P	13	13	100	1	1	100
I	11	7	63.6	6	4	66.7
C	12	8	66.7	6	3	50.0
A	14	10	71.4	9	5	55.6
Total	50	38	76.0	22	13	59.1

In terms of control of individual symptoms, differences were observed between the 4 drug groups, and these are shown in Table 5. None of the differences was significant statistically except in the case of neuritis, for which a significantly longer time to control the symptoms was required with indomethacin than with either prednisolone or chloroquine ($P<0.01$).

The side-effects of the various drugs were judged mainly by the subjective complaints made by the patients, except in the case of visual disturbance, where refraction studies were carried out monthly to give an objective parameter by which to judge the changes in vision. The group receiving aspirin had the least proportion (29%) of patients complaining of various side-effects, whereas 69.2% of those receiving prednisolone complained of some adverse effects. The corresponding percentages in the indomethacin and chloroquine groups were 63.6 and 58.5%. About one-quarter of the patients receiving indomethacin complained of headache, but only one complained of abdominal pain. In contrast, one-third of those receiving chloroquine complained of abdominal pain and nausea. Table 7 shows the changes in visual acuity as determined by refraction studies during the period of trial. All these patients had clinical evidence of iritis and were treated with local application of hydrocortisone and atropine eye ointment. It appears that indomethacin has a beneficial effect on vision in leprosy patients with acute iritis and iridocyclitis, and this effect appears to be greater than that of prednisolone. The recurrence of exacerbations among patients whose initial episode of ENL was controlled is presented in Table 8. This shows that the recurrence rate in the prednisolone

TABLE 5

No. of days required for the control of individual symptoms among patients in each of the 4 drug groups

(No. studied, modal values, means and standard deviations)

Symptoms	*Prednisolone*					*Indomethacin*					*Chloroquine*					*Asprin*				
	No.	*Mode*	*m*	±	S.D.	*No.*	*Mode*	*m*	±	S.D.	*No.*	*Mode*	*m*	±	S.D.	*No.*	*Mode*	*m*	±	S.D.
	11	7		±	10	6	14	15	±	3	8	7–14	14	±	11	9	7	12	±	7
Fever	8	3–5	9	±	13	4	6	14	±		8	7–9	8	±	3	8	5–7	11	±	8
Periostitis	7	7	11		12	4	7	9	±	3	4	7	9	±	3	5	7–14	14	±	8
Arthralgia	8	7	13	±		3	14	14	±	6		7	14	±	13	3	7	14	±	10
Neuritis	8	7	8	±	5	4	14	20	±	7	4	7	9	±	3	8	7		±	8
Oedema	8	7–14	13	±		4	14–21	18	±	4	8	7–14	15	±		4	21	17	±	

No., number studied; mode, modal values; m, means; S.D., standard devisions.

TABLE 6

Side-effects noticed in the 4 drug groups under trial

Drug group	*Side effects*								*Total studied*
	Abdominal pain		*Nausea*		*Headache*		*Dimness of vision*		
	No.	%	*No.*	%	*No.*	%	*No.*	%	
	2	15.4			2	15.4		7.7	13
		9.1			3	27.3			
	4	33.3	3	25.0		8.3			12
		14.2	1	7.1	3	21.3			14

and aspirin groups was nearly 70%, whereas among those given indomethacin it was only 57% and in the chloroquine group 50%. These findings were similar even among those with severe exacerbations.

As all cases receiving prednisolone showed an early initial response, patients in this group could have been restarted on anti-leprosy treatment early during the study. However, since the design of the study entailed waiting for 4 weeks after the initial response before beginning anti-leprosy therapy, the relatively early recurrence of reactions in this group meant that anti-leprosy therapy could not be introduced in all instances. In fact, in the one case of severe exacerbation in the prednisolone group no anti-leprosy drug could be introduced at all since this patient was practically continuously in reaction. Out of the 4 severe cases which responded to indomethacin, only in one case could DDS be introduced. Of the severe cases which responded to chloroquine and aspirin anti-leprosy therapy was begun in all.

TABLE 7

Changes in refraction during ' PICA' trial

Drug group	*Significant deterioration noticed*	*Significant improvement noticed*
P	4	
I		2
C		
A		
Total	7	3

TABLE 8

Recurrence of exacerbations among those who responded in each of the 4 groups under trial

Drug group	*All cases*			*Severe cases*		
	Studied	*Recurred*		*Studied*	*Recurred*	
		No.	%		*No.*	%
P	13	9	69.2	1	1	100
I	7	4	57.1	4	2	50.0
C	8	4	50.0	3	1	33.3
A	10	7	70.0	5	4	80.0

TABLE 9
Introduction of DDS in patients who responded in each of the 4 groups under trial

Drug group	*Total studied*	*Total responded*	*Among those responded DDS introduced in*	
			No.	%
P	13	13	8	61.5
I	11	7	3	42.9
C	12	8	4	50.0
A	14	10	5	50.0
Total	50	38	20	52.6

The introduction of specific anti-leprosy drugs once the exacerbation was under control was one of the criteria of the efficacy of the drug. The findings regarding this aspect are shown in Table 9; the differences were not statistically significant. The continuation of anti-leprosy therapy has depended on the recurrence of of exacerbations. Owing to the short duration of this trial, namely 12 months, and the stipulation that no anti-leprosy therapy was to be initiated until 4 weeks after control of an exacerbation, it was not possible to study the relationship between introduction of specific anti-leprosy therapy and recurrence of ENL in this group.

DISCUSSION

Lepromatous leprosy patients undergoing episodes of exacerbations present an extremely variable and difficult therapeutic problem group. The picture presented varies not only in relation to the clinical manifestations but also with the clinical course of the illness and the response to therapy observed in these cases. In any study designed to evaluate the effectiveness of an anti-inflammatory drug in lepromatous leprosy, this fact should be kept in mind; also the investigation should include a sufficiently large number of cases and means devised by which observations can be made as objective and unbiased as possible.

In this particular trial we were interested in studying the efficacy of indomethacin in the management of erythema nodosum leprosum. Choice of the controls was deliberate; though chloroquine was the chief drug for comparison, we wanted to use one very potent drug, prednisolone, and one drug which was expected to be least specific, namely aspirin. The findings as shown in the various tables are interesting and revealing. The number of cases studied was not large and in the event it so happened that the patients receiving prednisolone were, in general, in a milder grade of exacerbation than those receiving indomethacin. In spite of this advantage, the control of the exacerbations by prednisolone, though initially dramatic, was not wholly successful, in view of the early recurrences on reduction of the dosage and/or withdrawal of the drug. Comparison of the pattern of recurrences and side-effects of the 4 drugs shows that indomethacin compared favourably with the other drugs used in the trial in the dosages mentioned.

Visual disturbance was least in the indomethacin-treated patients as compared with those taking prednisolone or chloroquine. On the other hand, there was significant improvement in vision in 2 patients treated with indomethacin, while none of those in the prednisolone group showed improvement on refraction. It has been suggested that the rise in intra-ocular tension is subsequent to the use of steroids. The improvement in vision in patients treated with indomethacin could perhaps be attributed to early absorption of the plastic exudate that commonly occurs in lepromatous leprosy patients in reaction and with involvement of the eye.

The fact that symptomatic relief of painful neuritis associated with "reaction" took much longer to achieve with indomethacin than with the other drugs is somewhat surprising. Aspirin provided quicker relief in this group than did indomethacin (Table 5).

Despite the well-known effects of indomethacin in painful lesions of the joints, as for example in rheumatoid arthritis, the response of the arthralgia and acute exudative arthritis associated with ENL was less dramatic and indeed was practically the same in all 4 treatment groups.

SUMMARY

(1) A double-blind controlled clinical trial of indomethacin in the management of erythema nodosum leprosum ("reaction") and its associated clinical features was carried out, using chloroquine as the chief control drug and 2 other drugs also for comparison, namely prednisolone and aspirin. On the whole the therapeutic effect of indomethacin, in terms of its control of ENL, compared favourably with that of chloroquine and was superior to aspirin.

(2) Though initial control was most quickly achieved with prednisolone, indomethacin and chloroquine appeared to be slightly superior to the other drugs in decreasing recurrences.

(3) In regard to arthralgia and acute exudative arthritis associated with a reaction, there was no significant difference between the responses produced by the 4 drugs.

(4) Acute painful neuritis occurring in these patients appeared to respond least to indomethacin.

(5) The number of patients in whom specific anti-leprosy therapy could be reintroduced following subsidence of ENL was comparable in all 4 test groups.

(6) No significant side-effects were noted. However, there was a definite improvement in vision among the patients treated with indomethacin, while some patients receiving prednisolone showed a deterioration in vision on refraction. The significance of this difference is discussed.

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The Effect of Out-patient Dapsone in an Area of Endemic Leprosy*

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Following up the work of Charles Ross in Northern Nigeria the author has found that the prevalence of leprosy in one area in this region has fallen from a mean of 40 per 1000 of the population in 1952–5 to 1.6 per 1000 in 1967–8 after a campaign of treatment with dapsone in relatively low dosage. The limitations of the study and previously reported criticisms and drawbacks of sulphone therapy are discussed.

INTRODUCTION

Though the sulphones have been extensively used in countries where leprosy is endemic there is little information available regarding the effect of these drugs in controlling the disease. Cochrane (1964) considered there had been no decline in the world incidence of leprosy and that the widespread use of sulphone therapy for 15 years in certain areas of South India had failed to reduce the number of patients. However, no planned quantative study has yet been reported.

The work of the late Charles Ross in Nigeria is familiar to all interested in leprosy. His surveys in the early 1950's throughout the Northern Region give a good idea of the prevalence of the disease. Details of the initiation and progress of the mass treatment campaign based on the once weekly administration of dapsone have been fully described by him elsewhere (Ross, 1956, 1958, 1959, 1964). At present there are over 2000 out-patient clinics throughout the Northern Region of Nigeria where dapsone is being given.

This paper describes a study in an area of the Northern Region and attempts to assess the effect of sulphones on the prevalence of leprosy by comparing the present results with those in the pre-treatment surveys reported by Ross.

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MATERIALS AND METHODS

Area of study

Figure 1 shows the area of study and comprises the northern part of Zaria Province, including the villages of Igabi and Giwa, which Ross surveyed in 1952 before starting out-patient centres. The present study was carried out in 1967 and 1968. The results are given as prevalence rates, i.e. all the patients with leprosy at a particular time. This is in contrast to the incidence rate, which is the number of new patients over a specified interval of time. The prevalence rates have been assessed in 2 ways.

(a) *From out-patient clinics.* Twenty-nine clinics were studied in the area shown in Fig. 1. The majority of these had been visited regularly over the preceding 15 months for teaching and supervision. When it was found that patients with leprosy were much fewer than had been suspected, a decision was made to record the actual number. This was done by a single visit to each clinic at the end of 1967 and the beginning of 1968. Of these clinics 25 were visited personally and the numbers from 4 clinics were recorded by a leprosy inspector who had had 10 years experience in the diagnosis of the disease. In addition, in-patients of the Zaria Provincial Leprosy Settlement who originally came from the area under study were also included. Many people attended leprosy clinics in the hope of obtaining dapsone and, in fact,

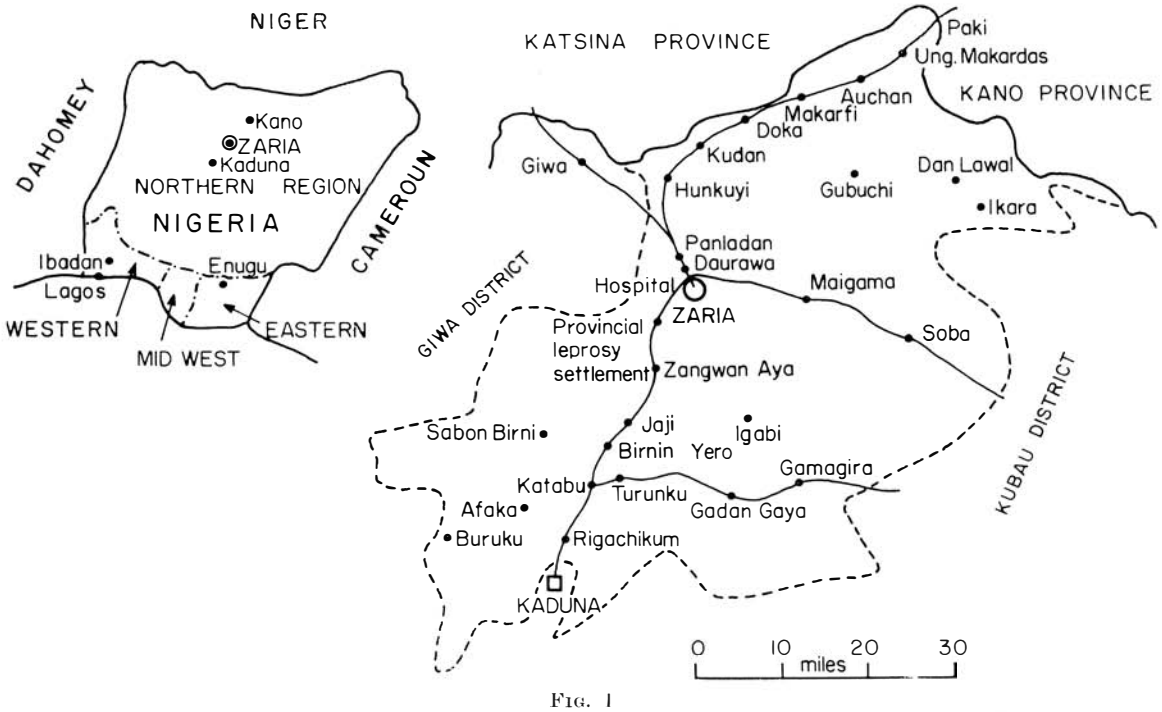

FIG. 1

Northern Zaria Province. The dotted line encloses the area from which prevalence rates have been calculated. The names indicate the position of leprosy clinics.

at some clinics 70 to 80% of attenders had no evidence of the disease; none of these persons were included in this study unless they had the signs listed below. The prevalence rate has been calculated from the total number of patients attending the out-patient clinics and from the 1963 census, in the area shown.

(b) *Village surveys.* These were carried out in Igabi and Giwa in 1967. The village headman had previously been contacted with the request that the people stay in their huts on the day of the survey. Teams of leprosy attendants, each headed by a leprosy inspector, examined all the people, and all those with any type of skin lesion or deformity were referred for diagnosis.

Diagnosis of leprosy

This was made on the clinical features of the various types, supplemented by bacteriological examination where possible.

In the lepromatous (multi-bacillary) type the features were infiltration of the ears and skin, especially of the face. Other accompanying signs often present were loss of eyebrows and nasal depression. A few patients showed acid-fast bacilli on bacteriological examination and in some there was evidence of mutilation of the extremities and thickening of the peripheral nerves.

In those non-lepromatous (pauco-bacillary) patients with discrete lesions the characteristic features were hypopigmentation with some alteration of the texture of the skin, anaesthesia to light touch—though this was not invariable—and absence of itching. The common skin conditions to be differentiated were birthmarks, pityriasis versicolor, other superficial fungous infections, the facial hypopigmentation which is common in children in Northern Nigeria, and macular hypochromia (Browne, 1964).

The neurological signs in those without skin lesions taken to be evidence of leprosy were a mononeuritis or mononeuritis multiplex (Brand, 1964) and a polyneuritis involving superficial

sensory modalities (Monrad-Krohn, 1923; Crawford, 1968) when this was accompanied by some evidence of loss of protective sensibility such as blistering or ulceration of the skin or mutilation of digits.

Bacteriological studies

Smears were taken by the standard split-skin method from 168 lepromatous out-patients and from 15 lepromatous patients in the leprosy settlement. Of the lepromatous patients, 34 were from the adjacent districts of Giwa and Kubau (see Fig. 1), but were included because the aim of the bacteriological studies was to test the effectiveness of out-patient treatment in rendering lepromatous patients bacteriologically negative. These cases are, of course, not included in the prevalence rates. Initially, 6 skin sites were chosen, but because of the consistently negative results from the trunk and limbs the examinations were finally restricted to both ear lobes and the forehead. The smears were stained with strong carbol fuschin, decolorized in 0.5% hydrochloric acid and 70% alcohol, and counterstained with brilliant green or methylene blue. All the slides were personally examined.

RESULTS

Table 1 shows the decline in the prevalence of the disease over 12 to 15 years in the area of Zaria Province studied. Ross's figures are derived from surveys and relate to the whole of Zaria Province. The prevalence rates in the adjacent provinces of Katsina and Kano are included to show the equally high levels prevalent in 1952–5. The number of patients attending the out-patient clinics with leprosy was 838. As the population of the area was 525,068, this gives a prevalence rate of 1.6 per 1000.

TABLE 1
Decline in leprosy prevalence in an area of Zaria Province

Year	*Study*	*Province*	*Prevalence rate*
1952–5	Ross	Zaria	46/1000
1952–5	Ross	Katsina	39/1000
1952–5	Ross	Kano	35/1000
1967–8	Present	Northern Zaria	1.6/1000

TABLE 2
Decline in leprosy prevalence in the villages of Igabi and Giwa by survey

Year	*Study*	*Population examined*	*No. with leprosy*	*Prevalence rate*
		Igabi		
1952	Ross	1422	94	67/1000
1959	Ross	1052	51	50/1000
1967	Present	1904	4	2/1000
		Giwa		
1952	Ross	410	16	39/1000
1967	Present	1187	3	2.5/1000

TABLE 3
Bacteriological status of lepromatous patients

	Out-patients	*In-patients*
No. of lepromatous patients examined	168	15
No. positive for acid-fast bacilli	19	11

Table 2 shows the decline in leprosy prevalence as assessed by survey in the villages of Igabi and Giwa. None of the patients in the present surveys had lepromatous leprosy.

The lepromatous patients in Table 3 have been divided into 2 groups, as the aim has been to show the effect of out-patient treatment on the bacillary state. Of the 11 positive in-patients, 6 had episodes of erythema nodosum leprosum (ENL) and 3 of these had in addition recurrent bouts of pain and tenderness in the ulnar nerve at the elbow.

DISCUSSION

The results show the marked decline in the prevalence of the disease. There seems little doubt that this is due to out-patient dapsone therapy, as, apart from the establishment of a segregation village at Giwa, no other means of control have been employed.

There are obviously several limitations to a study such as this. For example, not enough information was available to trace individual patients included in Ross's surveys; also the out-patient figures are recorded from a single attendance and census records are liable to be

inaccurate. However, the prevalence rates agree closely with the more accurate results from surveys. Despite these limitations, all the results point to a decline in the disease and are interesting if only to emphasize the need for planned studies on the subject. There is a danger that a potent method of eradicating leprosy may be needlessly abandoned, as the discussion of control methods has now shifted almost exclusively to the use of BCG vaccination and the administration of prophylactic sulphones to contacts (*Lancet*, 1966, 1968; *British Medical Journal*, 1966, 1968). The conflicting results to date of BCG vaccination will inevitably mean further delay before its efficacy can be decided. The results of giving sulphones prophylactically have been more encouraging, but even if both these methods are found in trials to be ultimately effective, there is still a practical point to be considered. In countries which have not conducted mass-treatment campaigns against leprosy, some way will obviously have to be devised to find the patients before their contacts can be treated.

Sulphone therapy has been criticized from a number of points of view. One of the main criticisms is the long time they take to render the patient bacteriologically negative. Thus Lechat (1961) found that, on average, it took 8 years to clear 50% of lepromatous patients of bacilli. However, Shepard *et al.* (1968) have recently demonstrated the decreased infectiousness for mice of bacilli from lepromatous patients beginning treatment with dapsone, and have emphasized how greatly reduced the chances are of these patients infecting others even after a few months of therapy. Further, the present study does show that lepromatous patients will attend regularly enough to become bacteriologically negative, even though this may take more than 10 years.

The lower dosage of dapsone now employed has led to a diminution of toxic effects, and in this study only one patient was observed with a mild dermatitis, although admittedly observation was limited. Heinz-body anaemia could not be excluded in the present study, but Smith and Alexander (1959) found that in patients taking dapsone in dosages comparable to those in leprosy there was no fall in the haemoglobin level. Erythema nodosum and pain, with swelling in the peripheral nerves occurred, as stated, in 6 of the in-patients, but was not seen in out-patients and thus were complications in only a small percentage of the total number of lepromatous patients. The sulphones have also been implicated in precipitating the onset, and producing exacerbations, of nerve damage in leprosy, but no definite conclusions can be drawn, as the natural history of nerve damage has never been studied. The most common and severe form of nerve damage encountered in Northern Nigeria is the acute onset of sensory loss associated with oedema of the hands and feet (Crawford, 1968). A similar process, also with oedema and nerve damage in the extremities, has now been reproduced experimentally (Rees and Weddell, 1968) without ingestion of sulphones, so that the syndrome in the leprosy patient is likely to be part of the natural history of the disease.

The reports of bacterial resistance to sulphones have led to justified concern. Pettit and Rees (1964) have, however, estimated the frequency to be of the order of only 3 per 1000 lepromatous patients and hence as a factor in mass treatment campaigns it is of little significance and nothing like the similar problem posed in the control of tuberculosis. The other virtues of dapsone, such as low cost and ease of administration, need no emphasizing here.

Any discussion about leprosy must take account of the social attitudes towards the disease. Ross (1964) from his experience in pre-treatment surveys made the following comments: "Survey has revealed that there is a degree of shame attached to infection by the disease; nevertheless, leprosy is tolerated in village and social life and any fear of detection has been associated with the dread of being segregated, which means divorce and separation from one's family". He also found that there was a good response to out-patient treatment facilities. In the present study there were few

patients who did not seek treatment where clinics were available. Leprosy is thus not a hidden disease, at least in this area.

The findings in this study and Ross's practical method of approach are relevant to the leprosy problem in the world as a whole. The latest estimate by the World Health Organization of the number of leprosy patients is 10.8 million, of whom only about 18% are receiving any form of therapy (Bechelli and Dominguez, 1966). Most of the remainder live in the rural communities of developing countries, and it is in these areas that a mass treatment campaign with dapsone should be seriously considered as a priority.

SUMMARY

A study in an area of the Northern Region of Nigeria has shown a marked decline in the prevalence of leprosy after a mass treatment campaign based on the out-patient administration of dapsone. The lack of information regarding the effect of sulphones in controlling the disease is emphasized. The properties of dapsone under conditions where leprosy is endemic are discussed.

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The Role of Microcellular Rubber in the Preservation of Anaesthetic Feet in Leprosy*

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In this paper the significant aetiological factors in the causation of plantar ulceration and its recurrence, particularly in patients with anaesthetic feet, are first briefly reviewed. Full details are then given for the construction of a type of sandal or chappal embodying a sole of microcellular rubber ("microporous compound") which when properly made and constantly worn gives excellent hope of preventing ulceration or its recurrence.

INTRODUCTION

Plantar ulceration is one of the major causes of disablement among leprosy patients. In the absence of protective footwear plantar ulceration continues to persist or recur with increasing frequency, gradually disabling the patient. The reported prevalence of plantar ulceration based on epidemiological studies have ranged from 15.7% of the feet examined (Noordeen and Srinivasan, 1966) to 36.41% of the patient population (Leprosy Centre, Polambakkam). In our own studies in Gudiyatham Taluk, North Arcot District, 17.7% of the patient population had a history of plantar ulceration (Rao *et al.*). Since anaesthetic feet is a permanent disability in the majority of these patients, the treatment and management of plantar ulceration need to be considered in terms of long-range care rather than on immediate results. Prevention of plantar ulceration will depend upon our ability to identify the major causes of the initiation and recurrence of ulcers, as well as on our ability to successfully protect the anaesthetic feet by designing a suitable type of footwear. In most developing countries footwear is either not used at all or the conventional closed footwear is impracticable becase of occupational and social considerations. In this paper a few significant aetiological factors in the causation and recurrence of plantar ulceration are described and methods of preventing such ulceration by the use of microcellular rubber footwear is discussed.

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PLANTAR ULCERATION

Causes of initiation of plantar ulceration

Plantar ulceration may be initiated by accidental trauma such as a thorn or nail prick. Its inability to appreciate pain makes the anaesthetic foot much more liable to such injuries during normal walking. The ulceration may also occur as a complication of the deep fissures that are frequently seen in unprotected, anaesthetic and anhydrotic feet. Plantar ulceration may also be initiated by deep pressure necrosis due to forces of thrust and shear which traumatize the soft tissue lying between the skin of the sole and the rigid bones of the foot.

Causes of recurrence of plantar ulceration

In describing the basic aetiopathology of recurrent plantar ulceration, Price (1959) has shown that trophic ulcerations occur in anaesthetic feet along the areas of maximum mechanical strain or high pressure during walking. That mechanical strain is an important factor is evident from the fact that plantar ulcer occurs along the "walking roll", and it heals as soon as the "walking cycle" of the foot is broken. Rest in bed, application of a posterior slab, or a plaster of Paris walking cast all result in interruption of the walking cycle and

healing of the ulcer. In fact, according to published reports, the majority of ulcers seem to heal with remarkable regularity despite a wide variety of methods of treatment (Price, 1961). The problem in the large majority of cases thus seems to be not one of initial healing of the ulcer but of preventing its recurrence.

Principles in the prevention of plantar ulceration

In order to prevent plantar ulceration, we have to offer protection against external trauma as well as to modify the mechanical stresses at each phase of the normal gait.

While external trauma can be easily avoided by wearing most types of conventional footwear, it is important to eliminate trauma due to the footwear itself when it is being used by patients with anaesthetic feet. Obvious causes of trauma, such as the nails with which the straps are fixed, the sharp edges of an ill-fitting strap or a heel counter, must be avoided. Friction between the skin and the leather strap should also be minimized. Footwear that squeezes the foot tightly around the metatarsal heads, thus increasing the pressure under them, should be avoided.

Mechanical stress during normal gait can be reduced by footwear that prevents concentration of the body weight in localized areas of the "walking roll" during each step. In a rigid soled rocker-shoe, reduction of peak pressure under the forefoot during the kick-off phase is achieved by adding a heel and a rocker under the sole. The addition of a moulded insole results in uniform distribution of the pressure throughout the sole, through all the phases of the walking cycle. However, a large number of patients are unwilling to wear such cumbersome footwear, which they find difficult to manage over rough terrain or on the narrow footpaths that divide wet fields. The time, expertise, and expense incurred in making individual footwear for each patient makes it also impracticable for general use in the management of a large number of patients with anaesthetic feet. Though such special footwear may be essential for the badly scarred and shortened foot, the majority of anaesthetic feet with minimal or moderate scarring do not need such extreme measures. However, the main principle on which the rocker shoe is designed is sound and hence should be adopted in the development of suitable footwear. Thus design of the footwear should be such as to enable reduction of peak pressure along the metatarsal heads by preventing excessive heel-lift and hyperextension at the metatarso-phalangeal joints.

Taking into consideration the various factors responsible for plantar ulceration, we have been able to develop a sandal (chappal) using microcellular rubber and a carefully designed upper, called the "Y"-strap microcellular rubber chappal, the features and effectiveness of which are described and discussed below.

MICROCELLULAR RUBBER

Microcellular rubber known technically as "microporous compound", is basically the same compound as that used in the "Hawaii chappals", except for certain changes in the physical properties to suit the particular requirements of the anaesthetic feet. The finished microporous compound has millions of individually enclosed tiny air spaces with thin walls closely packed together. The strength and resilience needed to sustain such a structure are obtained by the use of suitable chemicals and by achieving the optimum "cure" for the

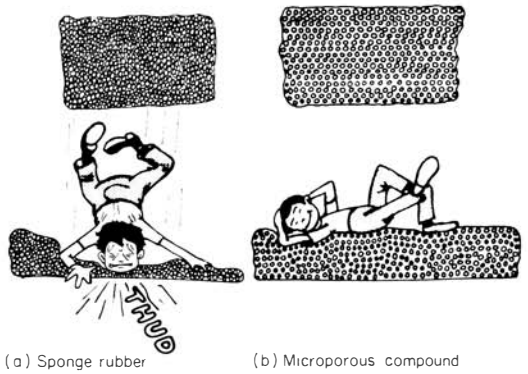
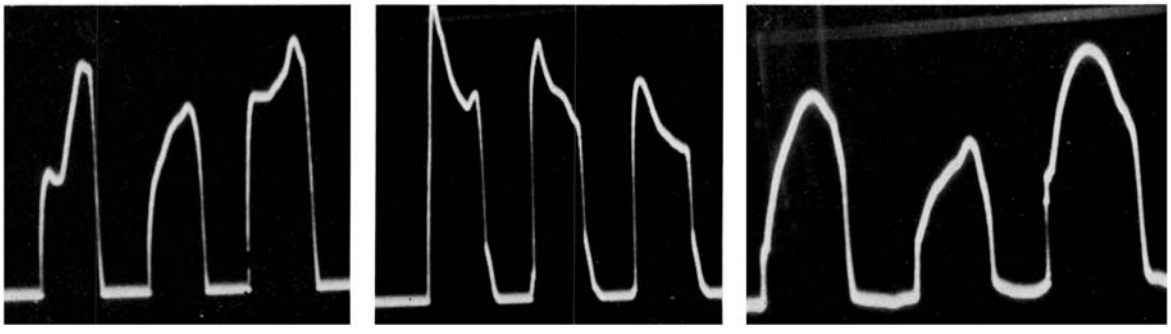


FIG. 1

(a) The inter-communicating spaces of the sponge rubber results in emptying of the spaces and total compression of the sponge on pressure.

(b) The individually enclosed air spaces in the microporous compound gives it the elasticity and buoyancy which allows the foot to "float" on it.



(a) (b) (c)

FIG. 2

Tracing on cathode ray oscillograph from a pressure senstive disc applied under first metatarsal head while walking. (a) Pressure tracing during 3 successive steps taken on 20 and 15°A microcellular rubber and on the floor, (b) Pressure tracing of 3 successive steps taken on the floor, 15 and 10°A microcellular rubber, (c) Pressure tracing of 3 successive steps taken on 3 mm thick microcellular rubber, $\frac{3}{4}$in. thick mircocellular rubber and on the floor. Note that no significant reduction in the peak pressure occurs in both 20°A microcellular rubber and 3 mm thick microcellular rubber.

rubber. The final product is soft and spongy, having an elastic buoyancy which enables the foot to "float" (Fig. 1). It is interesting to note that the subcutaneous fat of the normal sole is itself of a similar structure, each fat globule being enclosed in individual fibrous tissue compartments which impart elasticity and buoyance to the soft tissue pad next to the sole.

The unit of measurement of the resilience or compressibility of the rubber is the "shore A". The normal soles of people who habitually walk on bare feet measure from 15 to 20°A, and in those who walk with closed shoes from 10 to 20°A (personal observation). Most of the commercially available rubber measures more than 20°A and is too hard to provide adequate protection to anaesthetic feet. We have found that a soft, recently healed scar at the site of plantar ulceration, where the subcutaneous fat is destroyed, measures 20 to 50°A (personal observation, unpublished).

The microcellular rubber sole forms a protective, soft cushion under the anaesthetic foot, capable of effectively reducing peak pressures along the "walking roll". Its compressibility when combined with adequate thickness provides an instant mould under the walking foot. The high pressure points sink $\frac{1}{2}$ in. (1.25 cm) into the microcellular rubber, thereby increasing the available area of weight-bearing surface. This results in a reduction of the peak pressure per unit area, due to distribution of the pressure over a wider surface. In addition, when the foot sustains a heavy impact, as in jumping, the springiness of the rubber slows down the rate of deceleration and thus reduces the impact (Brand, 1966). It is important to ensure that the thickness and the softness are balanced in such a way that the rubber does not get totally compressed and become rigid under high-pressure areas at times of peak pressure; the remaining buoyancy of the rubber protects the soft tissue that lies between the unyielding floor and the rigid bone. A microcellular rubber sole of 10 to 15°A to $\frac{3}{4}$ in. (2 cm) in thickness is found to fulfil the above criteria (Fig. 2 (a) to (c)).

To maintain its spongy structure even after prolonged use, the microcellular rubber needs (a) abrasive resistance, (b) elastic recoil, and (c) tackiness.

(a) *Abrasive resistance*

Under high-pressure points, shearing force is added when the foot slips forward during acceleration and deceleration. The surface layer of the microcellular-rubber insole is thus subjected to the constant stress of friction. It is

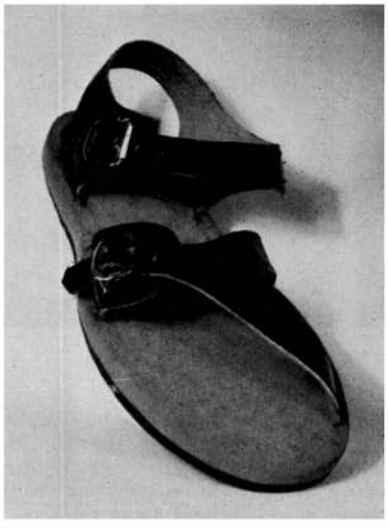


FIG. 3
The "Y"-strap microcellular rubber chappal.

important that the rubber should not wear out in this area where thickness and buoyancy are especially required.

(b) *Elastic recoil*

When the septa between the air spaces in the microcellular rubber are weak and lacking in resilience, they break down or become distorted when subjected to pressure. The softness and elastic recoil are then lost and the rubber gets compressed and hard under the foot. The softness and springiness of the microcellular-rubber compound are essential for reducing the compressive force on the soft tissue under the high-pressure areas and also to permit of instant moulding of the foot, which will then provide a larger area of the sole for weight-bearing.

(c) *Tackiness*

Ability to withstand tearing force is described as "tackiness". When this is lost, the rubber tends to tear easily wherever it is stitched or at the point of insertion of the straps. Occasionally, it may even split across the sole in the forefoot area where it has to bend frequently.

The above 3 properties depend on the quality of the materials and chemicals used and on the process of mixing and curing. A well-finished microcellular-rubber compound should be able to withstand constant wear for 18 to 24 months without losing its essential physical properties.

EFFECTIVENESS OF "Y"-STRAP MICROCELLULAR RUBBER CHAPPAL IN THE PREVENTION OF PLANTAR ULCERATION

In the "Y"-strap chappal (Fig. 3) the microcellular-rubber is lined underneath with a material that cannot be easily pierced by thorns or nails. Cow-hide, split car tyres, or a custom made vulcanized rubber sole may all be used for this purpose. No nail or metal is used to fix the upper to the sole. The strap across the forefoot is placed at the level of the mid-shaft of the metatarsals, thus avoiding "squeezing" the metatarsal heads. The straps are designed to fit the contour of the foot without the edges pressing abnormally, and are lined inside with "khaki" cloth so that the friction during walking is taken up partly by the movement between the cloth and the leather instead of between the skin and the leather. All straps in the sandal should have adjustable buckles so that when a foot is swollen or bandaged the straps may be re-adjusted to allow for the extra width needed around the foot (Fig. 4). Failure to provide for this will result in a new area of concentrated pressure which may initiate fresh ulceration.

The shearing force during acceleration and deceleration is markedly reduced by the

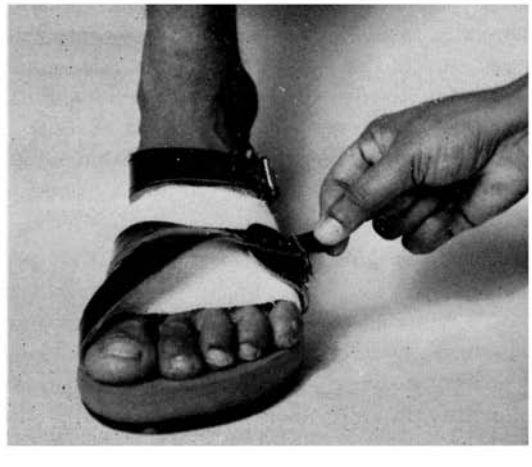


FIG. 4

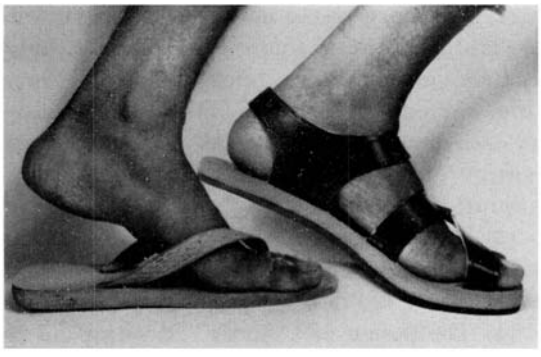


FIG. 5

sponginess of the microcellular rubber and also by the fact that as the foot slides forward in the footwear, the rubber yields and remoulds, thus eliminating the resistance of the "floor".

The principles used in the design of the rocker shoe can also be adapted to the microcellular-rubber chappal. Thus heel-lift and hyperextension at the metatarso-phalangeal joints during the "kick-off" phase are reduced by adding a back strap. When there is no back strap, the heel is raised awayfrom the footwear with a resultant reduction in the weight-bearing area and concentration of the weight of the body in the forefoot area (Fig. 5). In addition, the front strap of the "Y"-strap chappal is placed proximally, obliquely across the middle of the shaft of the metatarsals and not across the metatarsal heads. Thus the forefoot is held flat in the footwear at the mid-foot level, limiting hyperextension at the metatarso-phalangeal joints. An additional "limb" to the front strap helps to provide further support for the front part of the chappal.

The disadvantage inherent in a rigidly moulded insole is its inability to adapt to the altering contour and movement of the foot during walking. This disadvantage is effectively eliminated by the use of microcellular rubber, which not only forms an instant mould but also alters its contour to fit every change in the foot; one may call it a "mobile mould".

In our experience, this "Y"-strap microcellular-rubber chappal has given satisfactory results in preventing the initiation and recurrence of ulceration in the majority of patients with anaesthetic feet which are minimally or moderately scarred. However, such footwear does not withstand the rigours of wet farming and heavy field work. A simple "Y"-strap chappal is also not adequate for severely deformed feet which are mechanically unsuitable for normal weight-bearing. Recurrent plantar ulceration may appear in severely shortened and extensively scarred feet which are incapable of withstanding even the minimal stress of normal walking. Such problem feet need special adaptation to reduce the stress below the level that is "critical" to the particular foot. Thus, modifications that help to distribute pressure to the maximum available area and eliminate peak pressure during the walking cycle should be made use of. A moulded shoe that has a soft microcellular-rubber lining and a rocker is often adequate (Fig. 6 (c) and (d)). Very badly scarred feet which are totally incapable of even minimal weight-bearing may be fitted with a patellar-tendon-bearing prosthesis in which the weight is taken around the knee and the foot "floats" inside the prosthesis allowing easy mobility and stability.

High pressure areas across the metatarsal heads or forefoot may be relieved by a type of footwear which incorporates a metatarsal bar and a heel counter (Fig. 6 (b)). The heel counter is important to ensure that the metatarsal bar lies well behind the high pressure area; lack

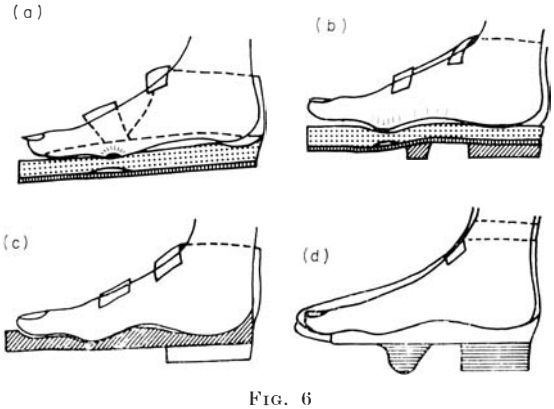


FIG. 6
(a) Scooped out microcellular rubber; (b) metarsal bar; (c) moulded insole; (d) rocker shoe.

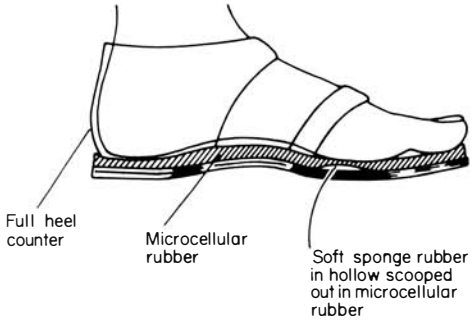


FIG. 7

of a heel counter allows the foot to glide backwards in the shoe, resulting in the metatarsal bar lying right under the high-pressure area.

A small localized high-pressure area may be relieved by partial scooping of the rubber from underneath the sole to give a smooth concave depression on the top (Fig. 7). Scooping on the upper surface leaves a rough edge and as a result of the friction the ulcer may "creep" forward. Again a heel counter to maintain the foot in position is essential.

In our experience we have found that a hard avascular scar that is liable to recurrent ulceration improves in quality when protected from excessive stress for a period of time. Often a more complicated type of footwear may be replaced by standard footwear after a period of a year or so when the texture of the soft tissue has improved.

A large majority of anaesthetic feet are capable of remaining ulcer-free when fitted with a standard "Y"-strap chappal. If patients with anaesthetic feet, with or without plantar ulceration, can be persuaded to use these microcellular-rubber chappals regularly, then we may be able successfully to eliminate a major disability in leprosy patients.

SUMMARY

(1) Plantar ulceration causing major disability in nearly 20% of leprosy patients will continue to persist in the absence of suitable protective footwear. The management of plantar ulceration should be in terms of long-range care rather than of immediate results, since we are dealing with permanently anaesthetic feet.

(2) The cause of the initiation and recurrence of plantar ulceration and the principles involved in their prevention are briefly indicated. Apart from the external trauma, mechanical stresses at each phase of the normal gait play an important role in the causation of plantar ulceration.

(3) The salient qualities of microcelluar rubber, known technically as "microporous compound", are described in detail.

(4) The design of a simple "Y"-strap microcellular-rubber chappal is presented and its effectiveness discussed in relation to the various grades of severity of plantar ulceration.

(5) It is maintained that if plantar ulceration is detected early and the type of chappal described is used regularly, the problem of plantar ulceration can be successfully minimized or even eliminated.

ACKNOWLEDGEMENTS

I am grateful to the Director and staff of the Madras Rubber Factory without whose help and co-operation we would not have been able to experiment and manufacture microcellular rubber for the use of a large number of patients all over the world.

My thanks are also due to Mr. Doorvasalu who has supervised the manufacture of the various types of microcellular-rubber chappals; and to Mr. Fred Morenas, Miss Indira and to Mr. S. Philip for secretarial help.

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The Use of Plastazote to Accommodate Deformities in Hansen's Disease*

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This paper gives some useful advice by an expert on the making of Plastazote insoles for leprosy patients with foot deformities and plantar ulceration, and describes the results achieved in 2 such severely disabled patients. Many readers who attended the Ninth Leprosy Congress in London will have seen the author demonstrating the speed and apparent ease with which Plastazote can be moulded.

It was early in 1967 that I discovered the use of Plastazote for orthopaedic purposes and my immediate reaction was to use this material for patients with leprosy. Many orthopaedic footwear manufacturers today are using Plastazote, and for grossly deformed feet this material has proved that it is not only light in weight and easy to mould and is something which has been sought for many years. Its introduction holds out great promise for the healing of trophic ulcers and in dealing with some gross deformities of the feet, particularly those with ulceration. Experience early showed that by using Plastazote in 1 in. (2.5 cm) thickness under ulcerated areas the ulcers soon became much smaller and in many cases healed completely.

My first encouragement outside my own hospital came from Dr. Paul Brand, who has dealt with leprosy patients in many parts of the world and who for years had been looking for a mouldable material which would be of help in dealing with these gross deformities of the feet. As soon as I had used Plastazote and found how useful it was, I told him about it, and received a reply saying that after he had used it he had seen for the first time a smile on his surgical bootmaker's face, which was very encouraging. Later, at the Ninth Leprosy Congress in London last year, Dr. Brand confirmed that he was very pleased with the results achieved with Plastazote for his leprosy patients with foot deformities, and was using it in conjunction with sandals.

The following 2 cases of my own may be of interest. The first was that of a leprosy patient who had had considerable trouble with his footwear over a number of years. About half his left foot had been amputated and he had also lost all his toes and part of the metatarsals from the right foot. The soles of the feet were in very poor condition due to ulceration, and when his feet became anaesthetic he suffered considerable anxiety, to which was added worry about his future condition. He was also very concerned about the appearance of his footwear. From the age of 36 for a number of years he had worn surgical shoes with a full $\frac{1}{2}$ in. sponge-rubber insole, sponge-rubber metatarsal pads, and sponge-rubber toe-blocks and wedges built in to accommodate the deformity. These orders were repeated every year and sometimes his feet were in a fair condition and at other times they were worse. He had periods in hospital, where he underwent some further amputations, and in 1965 he had to be re-admitted because of discharge from the deformities. Progress was very slow and unsatisfactory, however, until in 1967 I started to use Plastazote supports for him. A great deal of care was taken to obtain good plaster casts of both his feet and to mould the Plastazote to the base of his feet, under

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pressure. The present position is that since wearing surgical boots with well made insoles and with Plastazote made to come up to the forefoot, the patient is now much happier about his condition. There is no sign of ulceration and the soles of the remainder of his feet look very healthy. In spite of his being a somewhat despondent type of patient, he seems to have completely accepted the fact that his feet are as well as they are ever likely to be and he is able to earn his living quite satisfactorily.

The second patient, also with leprosy, had had all his toes amputated with the exception of the great toe. For a number of years he suffered from ulceration underneath the head of the fifth metatarsal and the foot generally had rather an unhealthy look. During this time he had his shoes made for him, these being fitted in the usual way with a toe block. This is typical of the type of foot that invariably required (when only sponge rubber was available) a very good, thick, sponge-rubber insole and a varus wedge to throw the weight back on to the great toe, because usually these patients cannot obtain a good balance. The problem with this patient was that he wanted more acceptable footwear, so we made for him a pair of sandals of 1 in. (2.5 cm) Plastazote with elastic across the top and the heel piece also made of Plastazote. On the left side, to counteract slipping, we put some extra padding inside to throw the weight back. He is now able to wear this type of sandal in the house and also on holiday, and he considers this to be a very real advantage. For a patient with this type of deformity it is a great comfort to obtain freedom from uppers over the foot, especially with the additional springiness of an inch of Plastazote underneath. In this patient there has been no sign of any ulceration at all since this support was supplied.

Patients with plantar ulceration are often in hospital for a considerable period simply because they cannot wear normal footwear. By using vacuum-formed Plastazote for the uppers and microcellular soles and heels directly attached to the Plastazote it is now possible to provide extraordinarily light and comfortable footwear, weighing for instance only 6 oz (170 g) for a pair of size 9 shoes (Fig. 1). Such footwear can be very quickly made, the vacuum forming being done over the cast or last of the affected foot. Most of the surgical footwear with leather uppers made in our workshops is made by the direct attachment method (not welted) and I have found that patients with partial amputations of the foot benefit considerably because the footwear made in this way is very much lighter than that made in the welted manner, and is also, by being firm but resilient, completely shock absorbing in walking.

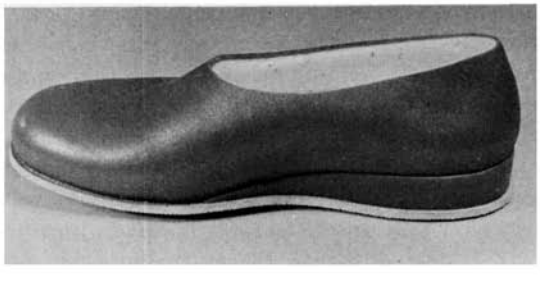

FIG. 1
Vacuum-formed Plastazote shoes, with microcellular soles and heels.

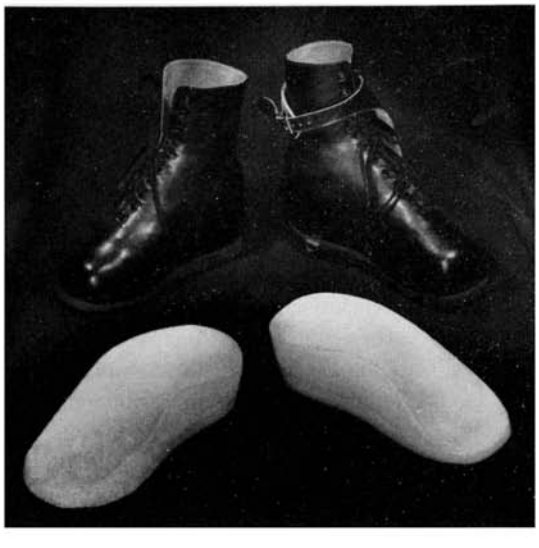

FIG. 2
Surgical boots and Plastazote insoles, for leprosy patient with grossly deformed feet.

To conclude, having described the old method of using sponge-rubber insoles with pads and toe blocks—until recently the best method available—which unfortunately did not entirely answer all the problems presented, there is no doubt that patients with deformed feet, prone to ulceration and with deformities that result in uneven balance, derive enormous benefit by having Plastazote insoles moulded directly to the base of their feet. This new method has been a major break-through in meeting the specialized requirements of these particular cases. Another advantage is that Plastazote is completely washable, although water repellent, and it can also be perforated for ventilation if required.

One important point worth stressing is that as Plastazote supports are less expense than normal supports and quick to make, they should always be supplied in duplicate to be worn on alternate days. It should also be emphasized that when Plastazote supports have been in use for a period of time, it is always necessary to reinforce the supports by adding another in $\frac{1}{4}$ in. (0.5 cm) thickness of Plastazote under the depressed area. This should be fixed to the original support by a rubber solution; the support itself need not be remoulded.

Lepr. Rev. (1969) **40**, 175-176

Observations on the Use of Plastazote Insoles in England

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Consultant Leprologist
Hospital for Tropical Diseases, London, N.W.1, England

The author reports the generally good results observed in 14 patients suffering from plantar ulceration, in most cases associated with arrested lepromatous leprosy, after their footwear had been expertly fitted with Plastazote insoles. The after-treatment of healed plantar ulcer is also briefly outlined.

Since the beginning of 1968, when Mr. Tuck drew my attention to the possible use of Plastazote for the prevention and cure of plantar ulceration, I have referred 14 leprosy patients to him. They were under treatment as out-patients and all had previously been fitted with orthopaedic shoes made of leather. Details are given in Table 1.

TABLE 1

To show effect of Plastazote insoles on plantar ulceration (established or threatened)

Initials of patient	*Sex*	*Type of leprosy*	*Disability*	*Period observed (months)*	*Result*
A.T.	M	Borderline (active)	Threatened breakdown of healed ulcer	10	No ulceration of sole, but dorsum of one toe became ulcerated
M.T.	F	Tuberculoid (active)	Chronic ulcerated plaque on one heel	8	Healed. No recurrence
J.E.	M	Borderline (arrested)	Threatened breakdown of healed ulcer	3	No ulceration
M.H.	M	do.	Large chronic ulcer, one foot	5	Improved, but not healed
B.L.	M	Lepromatous (arrested)	Small chronic ulcer, one foot Threatened ulceration of the other	12	Healed. Remained ulcer-free
P.G.	M	do.	Small chronic ulcers, both feet	12	Healed, but dorsum of one toe became ulcerated
D.S.	F	do.	Large chronic ulcer, one foot. Threatened ulceration of the other	12	Improved, but not healed. No ulceration of other foot
A.M.	M	do.	Threatened breakdown of healed ulcers, both feet	12	No ulceration
I.S.	F	do.	Moderate-sized chronic ulcer, one foot. Threatened ulceration of the other	12	Healed. No ulceration of other foot
R.D.	M	do.	do.	12	do.
A.H.	M	do.	Threatened ulceration of only foot (the other foot having been amputated)	12	No ulceration
S.H.	M	do.	Large chronic ulcer, one foot. Threatened ulceration of the other	10	Improved, but not healed. No ulceration of other foot
K.W.B.	M	do.	do.	6	do.
A.P.	M	do.	Small chronic ulcer, one foot. Threatened ulceration of the other	3	Healed. No ulceration of other foot

*Received for publication 29 April, 1969.

It is interesting to note that, in my work in England, lepromatous leprosy is far more important than tuberculoid or borderline leprosy as a cause of plantar ulceration, even though lepromatous patients constitute only one-third of the total number of leprosy patients under my care. The 10 lepromatous patients in this series had been under treatment for 10 years or more and could be classified as arrested cases; even so, they all had "glove and stocking" anaesthesia which had first appeared in the later stages of treatment and which, in some of them, was still increasing. The Plastazote insoles supplied by Mr. Tuck were placed inside the orthopaedic shoes with which the patients had previously been supplied, and this probably accounted for the fact that 2 of the patients developed ulceration on the dorsa of their toes as a result of the toes being rubbed against the uppers. It is hoped that in future this complication will be avoided by making new orthopaedic shoes, with good clearance for the toes, when fitting Plastazote insoles.

These insoles were effective in 10 out of 14 cases (70%) and partially effective in 4. In each case local treatment was unchanged after fitting of the insoles, normal activities were continued, and the only other treatment consisted of antileprosy drugs by mouth. An important part of local treatment was to scrape away the callus which formed over a healed ulcer or over a potential ulcer site; this had to be done regularly, and the patients were encouraged to soak their feet daily and to scrape with pumice while the callus was still soft. The soggy white skin which tended to form around the chronic ulcers was cut away with sterile scissors to allow healing from below. Probably an even higher success rate could be achieved by replacing leather soles by rigid ones, thus avoiding the damaging pressure on the metatarsal heads which occurs in walking when the rear foot thrusts the body forward at each step. It is significant that the partial failures in this series occurred in patients who had large ulcers which had been present for years; future policy in such cases will be to heal the ulcers by bed-rest or by the use of a "walking plaster" before fitting the Plastazote insoles.

Lepr. Rev. (1969) **40**, 177-181

The Use of Plastazote in Footwear for Leprosy Patients

A Preliminary Report*

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JEAN GARDINER
Physiotherapist
J. BISSET
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This further paper on Plastazote gives full details and instructions for the build-up of insoles for the shoes of leprosy patients afflicted with deformed, ulcerated, or insensitive feet, together with photographs to illustrate the various stages of the process and also of 2 patients who, thanks to Plastazote and skilled treatment, were able to walk unassisted for the first time for 4 and 15 years respectively.

INTRODUCTION

In leprosy patients anaesthesia of the feet and resultant plantar ulceration is a problem which continues to defy solution. Much has been written on the subject (Price, 1964; Brand, 1966) and much research has gone into producing suitable shoes and sandals which will offer protection to feet which have lost all sensation, as well as to feet which have actually undergone ulceration and even proceeded to deformity. The key to the problem, perhaps, is the elimination of all high pressure points on the sole of the foot, the starting point of many plantar ulcers. Microcellular rubber of 15-shore has been used widely in the making of sandals for such patients. The success of these sandals has varied in proportion to the degree of discipline in wearing them constantly exercised by the patient himself or by the institution where he was treated. In many places these sandals themselves became another stigma of the disease, and were reluctantly accepted by the patient and often discarded once he had returned to the home environment. Furthermore, lack of uniformity in the manufacture of the microcellular rubber, resulting in material that was too hard, was often a cause of failure.

Recently, a new plastic-foam material, marketed under the trade name of Plastazote, has been used to make built-up insoles, which when inserted into ordinary leather shoes or tennis shoes relieve all high pressure points; this also overcomes the objection of the patient that his footwear is different from that of non-leprous people.

PLASTAZOTE

Plastazote is a polyethylene-foam splinting material which, on being heated to suitable temperatures, is capable of being moulded. It is light in weight, readily washable, and does not encourage bacterial growth. The 2 main conditions in which Plastazote is most useful are (a) anaesthetic foot, with or without high pressure points or with or without plantar

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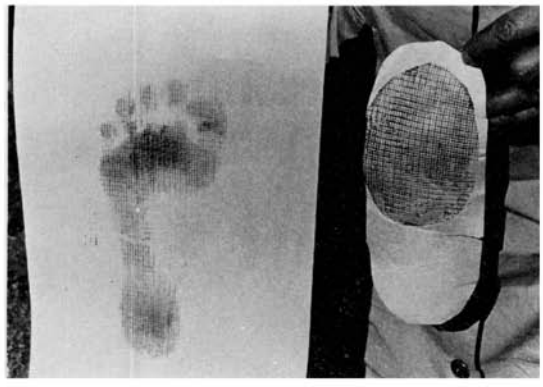
†A. Martin Mondl, Esq., is a retired shoe-manufacturer now residing in Wisconsin, U.S.A., who, at the request of Dr. Paul Brand, reviewed the above methods using Plastazote, and set up similar programmes in Taiwan, the Philippines, and Thailand. This is Mr. Mondl's third visit to McKean Leprosy Hospital.



(a) (b)

FIG. 1
Footprint taken before (a) and after (b) Plastazote build-up.

FIG. 2
Plastazote taken from oven after heating; now in a mouldable state.

FIG. 3
First stage in making Plastazote build-up.

FIG. 4
Build-up mixture being applied to under surface of Plastazote. Note drying build-ups, and last with build-up in background.

ulcers; and (b) anaesthetic foot with deformity, e.g. dropped foot, claw toes, or ankylosis of the ankle in inversion or eversion.

INITIAL FOOTPRINT STUDIES

Before using Plastazote build-ups it is essential to obtain footprints, using Harris footprint mats. These will show the high pressure points which have to be relieved. After Plastazote build-ups have been provided for either ordinary or custom-made shoes, or for tennis shoes or sandals, a further footprint is then obtained. If this is satisfactory, it will show that these high pressure points have been relieved and the patient thus protected from possible callouses and ulcers. Details of this procedure have been given elsewhere by Price (1964), Shipley and others. It should be noted that a 3-mm mat is used for the initial footprint and a 1-mm mat for that taken inside the actual shoe or sandal (Fig. 1).

PLASTAZOTE IN CONDITIONS LISTED UNDER (a)

A suitable piece of Plastazote, slightly larger than the foot, of $\frac{1}{4}$ or $\frac{1}{2}$ in. (0.5 or 1.25 cm) in thickness—the former is usually sufficient— is placed in an oven, at a temperature of 130°C for the former, 140°C for the latter, for a period of 3 to 5 minutes, by which time it becomes quite

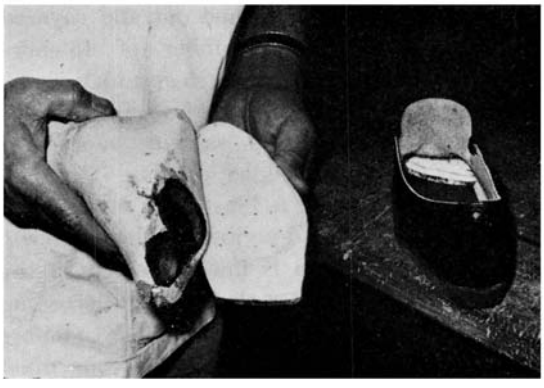


FIG. 5
Last with bubbles of foam rubber applied; Plastazote build-up and custom-made shoe. Note Plastazote cushion in toe of shoe.

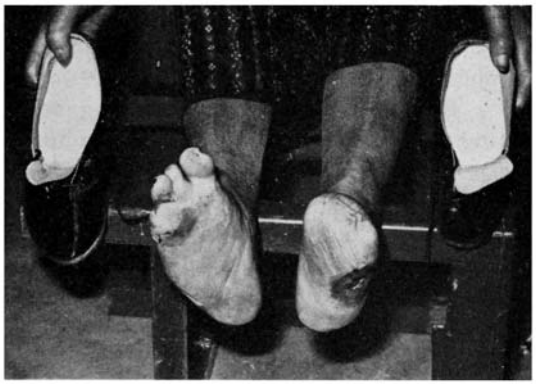


FIG. 6
Woman patient with finished footwear for chronically ulcerated feet.

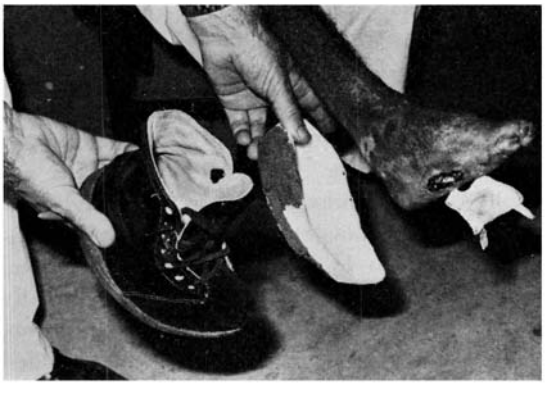


FIG. 7
Custom-made boot with Plastazote; lateral marginal ulcer on foot with ankle ankylosed in inversion.

FIG. 8
Patients whose feet are seen in Figs 6 and 7. The woman walks unaided for the first time in 15 years, the man after 4 years!

mouldable (Fig. 2). It is then placed over a sheet of 4 in. (10 cm) synthetic-foam rubber which is neither too hard nor too soft. On top of the Plastazote is put a thin layer of plastic sheeting, such as is used in making plastic bags, to prevent a possible burn. The patient is seated on a chair and places his foot on the Plastazote while the technician exerts an even pressure on the patient's knee and over the toes, for about one minute. A perfect impression of the sole of the foot is thus obtained (Fig. 3). The margins of the foot are then outlined on the Plastazote with a pencil.

The next stage is to build up the under surface of the Plastazote. For this purpose, the following mixture has been found suitable: 1 part rubber dust (from grinding any type of rubber); 2 parts sawdust (after sifting through a fine sieve to remove unwanted foreign bodies); and rubber cement to make a mixture similar in consistency to soft putty. This mixture is applied to the Plastazote in such a way as to fill in the depressions, adding a little extra in support of the longitudinal arch. A suitable tool for this purpose is an old, highly polished, kitchen knife. As the mixture tends to stick to the knife a small can of gasoline (petrol) is kept at hand and the knife dipped into it frequently as the

mixture is applied (Fig. 4). This build-up material, too, is applied a little beyond the periphery of the outlined foot. A period of 12 to 15 hours is allowed for drying before cutting along the outline with a sharp knife and then sanding to produce a smooth finish, paying particular attention to the natural contour of the heel portion. The Plastazote build-up is now placed in the shoe or sandal and another foot-print taken, as mentioned above. Any remaining high-pressure point can be dealt with by further sanding at the site of pressure on the under surface. A week later the foot is examined for any blisters or red spots resulting from pressure, especially on the dorsum of the foot. Leather shoes can be stretched; while tennis shoes should have their tongue slit distally on either side and laced loosely. (It should be noted that when Plastazote build-ups are being used, a shoe one size larger than normal should be obtained to allow for the additional bulk of the build-up.)

PLASTAZOTE IN CONDITIONS LISTED UNDER (b)

Here, a Plastazote build-up must be used in conjunction with a custom-made shoe or boot to compensate for a deformity which does not permit the use of an ordinary shoe or sandal. A plaster cast of the foot in question must be made first, in the following manner: high pressure points or bony prominences on the foot are outlined with indelible ink, and several layers of gauze impregnated with plaster of Paris are applied to the foot in order to form a shell. The foot is then withdrawn and the opened margins of the plaster of Paris shell taped together again. Freshly mixed plaster of Paris powder and water, still in fluid consistency, is poured into the shell; this will take about 45 minutes to harden. The original shell is now peeled off and the resultant cast is either allowed to dry in the sun or baked in an oven at 200°C (392°F). The cast is then pared down with a knife so that it now becomes a shoemaker's last. Gross abnormalities are filled out with the build-up material described in the previous section. Sites stained by indelible ink, representing high pressure points, are smoothed out and covered with bubbles of foam rubber of 15-shore cemented to the last, $\frac{1}{2}$ in. (1.25 cm) high in the centre which corresponds to the centre of the high pressure area, and sanded smooth to provide a regular moulded contour. The last is now used to make a Plastazote build-up in the same manner as described in detail above. The finished build-up is finally tacked to the last, from which a leather shoe is made according to routine methods of shoemaking. (Before building a shoe over a plaster cast one must add at least $\frac{1}{2}$ in. (1.25 cm) to ensure proper toe clearance, which will automatically help to blend a nice toe piece to the cast.) On completion the last is removed and the Plastazote build-up finished and inserted in the shoe, which is now ready for wear (Fig. 5).

Amputated or absorbed toes, fore-shortened feet, claw toes, and other deformities have to be compensated for by various methods which require some knowledge of shoemaking or prosthesis building. In brief, where toes are wholly or partly missing the cost is extended by adding $\frac{1}{2}$ in. of plaster of Paris, $\frac{1}{2}$ in. of Plastazote, and $1\frac{1}{4}$ to $1\frac{1}{2}$ in. (3 to 4 cm) of build-up material, in that order, before being finally shaped to conform to a normal last. In addition, where toes are absent a $\frac{1}{4}$ in. build-up is added to the under surface of the Plastazote at a point immediately behind the portion of the extension to the original cast.

When a deformity results in a sole which is not wholly plantigrade the build-up must be made so that the weight-bearing axis is always perpendicular, that is, the tibia and fibula are at right angles to the ground.

RESULTS

So far, 78 patients have been provided with tennis shoes and Plastazote build-ups at this institution, and 8 with custom-made boots or shoes and Plastazote build-ups. The latter group included a woman who had only been able to hobble around with the aid of crutches for the previous 15 years (Figs 6 and 8). There was also an elderly man with an ankylosed right ankle in a position of inversion and so

subject to chronic ulceration along the outer margin of his foot; he is now able to walk unassisted for the first time in 4 years (Figs 7 and 8). A few months of continual wear in urban and rural situations, together with their use in the paddy-fields during the rainy season, will be required to prove the effectiveness of these shoes.

SUMMARY

A new polyethylene-foam material, Plastazote, has been utilized in the making of built-up insoles in normal and custom-made footwear for patients with leprosy, subject to all the hazards of anaesthetic feet. With the help of this material it is now possible to provide leprosy patients with shoes of normal appearance which both give protection to their feet and at the same time are readily accepted by them. Economical to make, and cheaper than ordinary microcellular shoes, Plastazote build-ups may represent a significant advance in the care of the feet in leprosy.

ACKNOWLEDGEMENTS

Our thanks to Dr. Chinda Singhanet, Superintendent of McKean Leprosy Hospital, and staff and patients for their kind cooperation; to Smith and Nephew Ltd. of Welwyn Garden City, England, through their Bangkok agent Weelok & Marden, for their generosity in providing Plastazote for this trial; to Dr. Paul Brand and Mr. David Welch of the U.S.P.H.S. Leprosarium, Carville, La., whose original ideas have been incorporated in the making of the build-ups; and to Dr. Edwin McDaniel who took all the photographs accompanying this paper.

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Letters to the Editor

G 30 320 (B 663)

Anybody reading the paper by Dr. W. A. Vischer in the April issue of *Leprosy Review* (1969, **40**, 107) entitled "The Experimental Properties of G 30 320 (B 663)—a New Anti-leprotic Agent" might be surprised to hear that the synthesis and properties of B 663 and related phenazine derivatives have been the subject of more than 30 scientific papers published in various journals from this laboratory over a period of more than 20 years.

It may not have been Dr. Vischer's intention to mislead, but he nevertheless has succeeded in giving a very false impression. For a more complete account of the chemistry and biological properties of these interesting compounds and a detailed history of how they came to be developed, the following 2 papers should be studied:

BARRY, V. C. and CONALTY, M. L. (1965). The antimycobacterial activity of B 663. *Lepr. Rev.* **36**, 3.

BARRY, V. C. (1969). Synthetic phenazine derivatives and mycobacterial disease: A twenty year investigation. *Scient. Proc. R. Dubl. Soc.*, Series A, **3**, 153.

V. C. BARRY
M. L. CONALTY

Laboratories
Medical Research Council of Ireland
Trinity College, Dublin, Eire

23 July, 1969

We have shown the above letter to Dr. Vischer, who replies as follows:

Re: Letter of Dr. Barry and Dr. Conalty regarding the paper "The Experimental Properties of G 30 320 (B 663)—a New Anti-leprotic Agent".

It was certainly not my intention to depreciate the work of Dr. Barry and his collaborators done with B 663 and related phenazines. We have pointed out the importance of Dr. Barry's contributions within this field on other occasions (Vischer *et al.*, 1958; Vischer, 1968). It was felt that we should concentrate on that aspect of development of the compound with which we were intimately associated and that we should give a short account of the antimicrobial, pharmacological, toxicological and biochemical aspects of B 663. I completely agree with Drs. Barry and Conalty that the references cited in their letter given an excellent survey of the work carried out in their laboratories.

VISCHER, W. A., TIRUNARAYANAN, M. O. and BRUHIN, H. (1958). *Beitr. Klin. Tuberk.* **119**, 59, and references cited therein.

VISCHER, W. A. (1968). *Arzneim. Forschung* **18**, 1529.

WOLFG. VISCHER

N.A.E.O.

What effects have oral contraceptives on lepromatous leprosy? I have just re-read in *Leprosy Review* (1968, **39**, 173) a letter by Dr. Walter of Bangkok stating that he used norethisterone acetate ethinyl oestradiol (N.A.E.O.) in a series of 20 lepromatous women patients for a 3-months' trial, with a group of patients of about the same age and the same stage of the disease as a control. He states that no difference in the frequency of erythema nodosum (ENL) in the 2 groups was observed.

I would like to report that in a number of women patients we have been able to elicit a very definite history of crops of ENL which occur regularly 10 days before the menses are due. The first few days after menstruation begins, these ENL rapidly subside and for the next 2 weeks the patient is virtually reaction free and then starts showing crops of ENL. This ENL can be very severe, accompanied by fever, ulceration and gross oedema. The interesting factor is the definite cyclical pattern, though it takes quite a few months to establish the

pattern and casual enquiry will fail to reveal it. Also these patients will occasionally miss one month when reaction is minimal or absent.

We have attempted to investigate if this is connected with anovular cycles, but have not been able to obtain adequate patient co-operation to do regular temperature variation charts or vaginal smears. However, in a number of patients oral contraceptives have completely changed the pattern. I first realized this through giving stilboestrol to a patient with irregular cycles. Since that time we have used various contraceptives, but find that stilboestrol itself seems to be as effective as the others.

One patient previously developed gross oedema and when she was given various contraceptives, although her reaction was not so severe, she still continued to develop oedema but eventually we acquired Ethinyl-Oestradiol tab., 5 mg daily for 21 days in each cycle, and this completely controlled her reaction. However, it is no longer possible to purchase Ethinyl-Oestradiol tablets and we have now put her on stilboestrol, 2 mg daily for 23 days each month, commencing the second day of the cycle, and on this regime she remains reaction and oedema free. Twelve months ago she seemed so well that we stopped the stilboestrol and within 2 months she had resumed her pattern of ENL 10 days premenstrual. This is again under control, using stilboestrol.

This patient is the most dramatic case we have had, but there are several other patients in whom stilboestrol definitely reduces these episodes of reaction. Hence contraceptives may serve a useful purpose in the treatment of women with lepromatous leprosy, though for therapeutic purposes it would appear that the cheaper stilboestrol is quite adequate for this purpose.

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Hong Kong

23 July, 1969

THE TANZANIA NATIONAL LEPROSY ADVISORY AND CO-ORDINATING COMMITTEE

(*continued from p.* 142)

As the Government policy has been to treat leprosy within the framework of the general health service, except where a special leprosy control campaign is called for, virtually all the "bush" dispensaries (which come under the aegis of the Local Authorities, not under the Ministry of Health) hold regular leprosy clinics. One of the functions of the Regional Leprosy Officers is to supervize these clinics, which, together with the special leprosy campaigns and the Voluntary Agency dispensaries, treat approximately 60,000 cases per annum (that is, about 50% of the total estimated cases in the country).

H. W. Wheate

Corrigendum

Dr. A. B. A. Karat has written to say that owing to a mistake in the manuscript of the paper by Rao, Karat and Karat (*Lepr. Rev.* 1969, **40**, 93) the heading to Column 2 in Table 7, p. 95, is incorrect. It should read "Sex ratio (no. of females per 1000 males)".

Book Reviews

Précis de Léprologie. Clinique et Therapeutique de la Lèpre en Afrique Noire, by J. LANGUILLON and A. CARAYON. Masson & Cie, 120 Boulevard Saint-Germain, Paris VIe, France, 1969. xv+392 pages. Price: F70.

We extend a sincere welcome to this book, and have no hesitation in recommending it to our French-speaking readers. Those whose French is rusty could with profit study the photographs and try to follow the lucid language of the clinical descriptions.

The first part of the book bears the impress of General Languillon's extensive and accurate clinical observations and his vast experience not only in the conduct of chemotherapeutic trials but also in the day-to-day management of a wide variety of types of leprosy. The section on the long-acting sulphonamides is particularly good, and the "before-and-after" photographs confirm this author's excellent opinion of some of these promising drugs. While thalidomide comes in for mention, we miss all reference to the considerable amount of investigation of the riminophenazine derivative, Lampren (B 663).

The surgical sections show the wide range and experience of the surgical partner in this production, General Carayon. With clarity of exposition and detailed practical instructions, he adorns the theme and makes difficult surgical procedures appear straightforward, if not simple.

While most of the categorical statements on classifications are unexceptional, it is perhaps not out of place to indicate that low-resistant tuberculoid leprosy is not the same as "*lésions tuberculoïdes réactionelles*", and there is some confusion over the "immune areas" of borderline leprosy and the regions of skin that are but rarely invaded by leprosy lesions. Indeterminate leprosy, according to Languillon, could include a greater variety and range of lesions than many practising leprologists would admit. Painstaking and prolonged examination of serial sections of early tuberculoid lesions and indeterminate lesions will always disclose some acid-fast organisms, or some pathognomonic histological feature. Some of the abbreviations are subject to misprints, e.g. TBI should be TB 1. Some proper names are misspelt, and the quotations in English contain several errors.

However, these are small points when the excellent layout and the first-class photographic reproductions are considered in the light of an admirable text. We wish it a ready sale among our French-speaking colleagues, and dare to express the hope that our English friends might find it a salutary exercise to read what has been done elsewhere before venturing to publish their "new" findings.

Précis de Léprologie, by PIERRE HARTER. Oeuvres Hospitalières Françaises de l'Ordre de Malte, 52bis, due de Monceau, Paris VIII, 1969. 252 pages+ 73 black and white photographs. Special price for doctors: F45.

This well-produced and superbly illustrated handbook testifies to the dermatological background of its author, one-time consultant leprologist to the French Ministry of Foreign Affairs and well known to successive generations of students at the Paris Faculty of Medicine. The clinical sections are particularly well done, as is to be expected, and the detailed—even graphic—descriptions of the wide range of cutaneous lesions encountered, particularly in the Far East, have never been bettered.

The volume would have been greatly improved by removing typographical inconsistencies (e.g. B.H., mycobacterium leprae, *mycobacterium leprae*, M. Leprae, MYCOBACTERIUM LEPRAE, etc., etc.), by critical revision, and by careful proof-reading. The supplements, consisting of lists of periodicals, Associations, and principal leprosaria, unfortunately contain more than a few entries that are inaccurate or out-of-date, indicating the difficulties inherent in this kind of comprehensive compilation.

These blemishes, however, do not detract greatly from the value of the clinical observations and the practical advice that stand out on every page.

Obituary Notice

NEIL DUNCAN FRASER, 1900-1969

Neil Duncan Fraser, M.B., CH.B., D.T.M. and H., died in hospital at Perth, Scotland, on Sunday, 3 August, 1969, after suffering a coronary infarction. The news of his passing will be received with regret in each of the several areas in which he served so faithfully.

His interest in leprosy began in 1924 when he was appointed to the Presbyterian Hospital in Swatow, South-west China, by the English Presbyterian Mission. In 1928, Dr. Fraser accepted responsibility for the control and planning, first of the hospital and then of the medical missionary work, of the whole Swatow region. One of his colleagues has said that Dr. Fraser was "rightly dissatisfied until he had obtained better conditions under which modern methods could be practised and technical efficiency attained".

With the help from The Leprosy Mission, Neil Fraser developed a number of village clinics for the treatment of leprosy. Using methods of treatment recommended by Dr. H. W. Wade of the Culion Leprosy Colony, he obtained very satisfactory results and soon became a recognized authority on the disease.

When war conditions made work in Japanese-occupied China impossible, Dr. Fraser served in Hong Kong and, in 1946, with the goodwill of the English Presbyterian Mission, joined the staff of The Mission to Lepers as part-time Secretary for China and Hong Kong. Four years later he began to give his whole time to leprosy. In this capacity he accepted responsibility for The Mission to Lepers' Hong Kong leprosy venture, and saw it develop from small beginnings at Sandy Bay into the full-scale treatment and research centre on Hay Ling Chau (The Isle of Happy Healing) which it has now become.

Dr. Fraser had the full confidence of Hong Kong's foremost leaders, working happily with successive Governors, University chiefs and the principals of the Colony's commercial and business houses. Through the formation of the Hong Kong Auxiliary of the Mission and the Marianne Reichl Aid to Lepers Group, he ensured the continuity of interest which was to make the Isle of Happy Healing largely self-supporting.

In 1960, at the request of the Mission Council, Dr. Fraser joined the Headquarters' staff in London of The Mission to Lepers as its Medical Secretary, a post which took him on many extensive tours of investigation and demonstration. His period as Medical Secretary was marked by advances in medicine, surgery, and rehabilitation and he was one of the strongest advocates in favour of the Mission's change of name to The Leprosy Mission. His long experience and wide knowledge of leprosy care and leprosy control led Mission Boards and Government Departments to seek his help and advice, and both were freely given.

Even leprosy, which demanded so large a proportion of his time, could not fill his days or satisfy his enthusiasm and, through the years, he found relaxation and interest in archaeological investigation which has left public galleries and private collectors enriched by specimens which he discovered in the Far East.

Since he retired to Scotland in 1966, Dr. and Mrs. Fraser have lived at Pitlochry in Perthshire, to the encouragement of the Scottish Auxiliary of The Leprosy Mission and other good causes, all of which found Dr. Fraser ever willing to give his services. For many years he was a valued member of the Medical Committee of LEPRA.

The sympathy of his many friends and colleagues goes out to his widow, who so ably supported him in all his endeavours, and to his daughter and two sons.

WALTER FANCUTT

Lepr. Rev. (1969) **40**, 186 190

Abstracts

Unsatisfactory results with thalidomide as a specific treatment for leprosy, by J. Sheskin, F. Sagher, M. Dorfman and H. W. von Schrader-Beielstein. *Israel J. Med. Sci.*, 1968, **4**, 901.

This report concerns 24 patients (20 male and 4 female) who received treatment with thalidomide at a dose of 400 mg daily (given in 4 divided doses) for periods of from 3 to 19 months. Five patients improved as regards leprosy, 11 became worse, and the remaining 8 showed no change. The treatment had no antibacterial effect. In all 13 patients who began treatment when in reaction, the acute condition was controlled. The main side-effects noted were constipation, drowsiness, dryness of oral and nasal mucosa, peripheral oedema and psychiatric disturbance.

S. G. Browne.

A talidomida no tratamento da lepro-reaccao (Experiencia efectuada no Hospital Rovisco Pais) (Thalidomide in the treatment of reaction in leprosy), by A. Barbosa and R. Almeida. *Rovisco Pais*, 1969, **8**, 23.

The English summary appended to the paper is as follows:

"The results of the treatment of lepra reaction with thalidomide in 10 male in-patients of Rovisco Pais are presented.

All the patients had lepromatous leprosy and suffered from long lasting severe reactions with cutaneous and nevritic symptoms and fever. Almost all had previously been treated with corticoid drugs.

The initial dose was 300 mg a day (3 tablets), lowering as the patients got better.

Results: (1) Fast recovery of the general condition, followed by the cutaneous and nevritic symptoms, leading to the cure of lepra-reaction in one week. (2) Several weeks after suspending treatment, there were relapses that responded promptly to a new treatment. (3) There were no side effects with the doses used.

For these results, which agree with others referred to in the literature, thalidomide is considered as the most efficient drug for the control of lepra-reactions. It acts faster and more safely than the corticoids. Relapses, if any, respond promptly to a new course of thalidomide."

Histopatologia dos vasos cutaneos na lepra (Histopathology of the cutaneous blood vessels in leprosy), by H. Seabra Santos and M. L. C. de Matos Beja. *Rovisco Pais*, 1969, **8**, 3.

The English summary appended to the paper is as follows:

"From 2000 skin biopsies from leprosy patients, 90 were selected which contained sections of blood vessels. Preparations were stained by different methods, for studying vascular changes.

In lepromatous progressing lesions, from the earliest to the most evolved, the following changes were seen: 1st—Cells loaded with acid-fast bacilli (lepra-cells) in the endothelium. 2nd—Lepromatous endarteritis. 3rd—Lepromatous obliterative pan-arteritis; fragmentation of elastic fibres, fine network of reticular fibres.

In lepromatous regressing lesions, there was progressive substitution of the granuloma by collagen fibres, reticulin thickening and rebuilding of the elastic. As a residual change, after complete absorption of dermal granuloma, acid-fast bacilli were frequently seen, alone or in globi, in the *tunica media* and/or *tunica intima* of otherwise normal-looking arterise.

In dimorphous and tuberculoid leprosy, no significant changes were found in cutaneous blood v sels."

4. **Nasal care in leprosy: a means by which to help prevent deformity,** by C. W. Emerick. *J. Rehab. Asia*, 1969, **10**, 36.

The author issues a timely reminder that regular adequate cleansing of the nose in leprosy patients will reduce the risk of infection of soft tissue, cartilage and bone by septic organisms. While recognizing the role of *Myco. leprae* in specific destruction of cartilage, he has found that mechanical removal of crusts, and daily irrigation of the nasal cavity with ordinary saline solution, will prevent the nasal deformity that foll ws pyogenic infections.

5. **Protecting the patient from himself.** *Wld Medicine*, 1969, **4** (18), 38.

This short unsigned article reports recent work conducted at the United States Public Health Service Hospital at Carville, Louisiana, under the direction of Dr. Paul W. Brand, Chief of Rehabilitation. With the co-operation of the Southwest Research Institute in San Antonio, a polyurethane foam has been developed which is impregnated with microcapsules containing various dyes. The capsules are so made that they rupture when subjected to certain well-defined pressures. It is possible to make capsules that will rupture at different pressures, releasing minute amounts of coloured liquid. When a sock, or glove or prosthetic stump sock, lined with the dye-impregnated foam, is worn by a patient with cutaneous anaesthesia, the colour that appears after use indicates the degree of pressure that has been exerted: green signifies safety, and blue means potential danger. Appropriate measures can then be taken to obviate actual tissue destruction.

At present, the dye-impregnated foam is being used experimentally at Carville, and as a means of educating patients in the use of their anaesthetic extremities. We understand that a group of leprosy patients at Carville are at present making slipper-socks and stump socks, and may soon embark on the making of gloves.

The following 3 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1969, **66**, 2:

6. **Caractères épidémiologiques de la lèpra en Haute-Volta** (Epidemiology of leprosy in Upper Volta), by H. SANSARRICQ, H. HELIES and B. LAGARDERE. *Méd. Trop.*, 1968, **28**, 327.

This interesting paper is based on reasonably complete and reasonably accurate statistics concerning the 4 million inhabitants of a country stretching from the sparsely-populated thorn-scrub of the near-Sahara in the north to the more densely-peopled and greener savanna of the south. The medical facts are based on systematic and regular examination of the population by medical assistants, who have latterly supplemented their clinical findings by microscopical examination of the skin for *Mycobacterium leprae*. Ethnic and climatic studies complete the picture. The average density of the population is relatively high for rural Africa, being 14.6 per square kilometre (or 37.4 per square mile). In spite of an infant mortality rate of 174 per 1000, the population shows a natural increase of 2% per year, the expectation of life at birth being 31 years. The demographic situation is complicated by the temporary or permanent migration of about 8% of the young men to neighbouring countries, principally the Ivory Coast and Ghana.

Each of the 65 doctors in the Upper Volta has about 62,000 people under his care. The health of the people generally is poor; malnutrition is widespread, and there are deficiencies particularly of animal protein and animal fats, and even of calories.

The number of patients with leprosy is over 140,000, giving a gross prevalence rate of 35.01 per 1000, and ranging from 100 to 8.5 per 1000. The sex rate is unusual: females are affected more than males at all ages (39.20 against 30.85 per 1000), the difference being more marked in children than in adults. The authors attribute this preponderance of women to the greater opportunity the Upper Voltaic woman has of both intra- and extra-familial contacts with people suffering from open leprosy. Another unusual feature is the low child rate; for every 1000 adults with leprosy there are but 55 children. The lepromatous index (probably too low) is reported to be 1.51 per 1000 for males, and 1.27 for females. In both children and adults, males preponderate.

The prevalence of leprosy does not apparently depend on the density of the population, but it is correlated with rainfall—the greater the rainfall, the higher the prevalence. There is much variation between one ethnic group and another, but the reasons for the observed differences are by no means obvious.

S. G. Browne.

Troubles spastiques des membres inférieurs en milieu lépreux mélanésien. A propos de 12 cas observés en Nouvelle-Calédonie (Spastic disorders of the lower limbs among Melanesian leprosy patients. A report on 12 cases observed in New Caledonia), by G. DESMOULINS and G. ZELDINE. *Méd. Trop.*, 1967, **27**, 663.

The authors draw attention to a neurological condition of unknown aetiology appearing only among patients with leprosy in New Caledonia who have been treated within the past 20 years with sulphones. It is essentially an upper motor neurone type of spasticity of the lower limbs, with the usual symptoms (sensation of weight in the legs, difficulty in walking, progressive weakness and spasticity, muscular cramps), and signs (accentuation of the deep reflexes, Babinski response, marked ankle clonus and occasionally patella clonus). In the patients studied, the condition usually appeared a variable time after the cessation of sulphone treatment.

All enquiries into possible causes have so far proved abortive: trauma, infection (including syphilis), nutritional deficiencies, heredity, and anaemia appear to play no part. In the absence of post-mortem material—the disease is not fatal—further lines of investigation are suggested.

The authors reject the possibility that such a relatively common condition (12 cases in 879 leprosy patients) could be due to the extremely rare varieties of damage to the central nervous system reported in leprosy, in which leprosy bacilli are found only exceptionally. It is only since 1956 that the condition has been seen. No case has been reported among the 40,000 inhabitants not suffering from leprosy. They suggest tentatively the possibility that sulphone treatment of leprosy might, in the particular ethnic context of Melanesia, facilitate the emergence of some nerve disorder, recalling the "kuru" of New Guinea or the amyotrophic lateral sclerosis of the island of Guam. [Further investigation of this condition is called for, cluding the search for organic and inorganic toxins.)

S. G. Browne.

8. **BCG vaccination of children against leprosy in Uganda: results at end of second follow-up,** by J. A. K. BROWN, M. M. STONE and I. SUTHERLAND. *Br. med. J.*, 1968, *i*, 24.

This important controlled trial of BCG vaccine in the prevention of leprosy, begun in Uganda in 1960, is carried a stage further by this report.

The present total intake of child contacts of known leprosy patients now numbers 19,169, the majority of whom have been followed up for 3½ years. All the children were allocated randomly to a BCG vaccinated and an unvaccinated group, and at subsequent follow-up examinations precautions were taken to ensure that the observer was unaware of the vaccinal status of the individual children. The protection against leprosy apparently and solely attributable to BCG vaccination is of the order of 87% after 3½ years, as against about 80% after 2 years. Of the 162 cases of leprosy dis-

covered in children with initial tuberculin grades 0 to II, 143 were in the unvaccinated and 19 in the vaccinated group, giving attack rates of 15.8 and 2.1 per 1000 respectively. The efficacy of the protection afforded against the appearance of overt leprosy lesions in this context is thus not reduced after a further period of observation.

The percentage reduction of leprosy infection afforded by BCG vaccination was similar for children who initially had either weak degrees of tuberculin sensitivity or none. On the other hand, the incidence of leprosy in the unvaccinated children varied with the initial tuberculin sensitivity, those with the strongest tuberculin reaction having the lowest incidence of leprosy. Infection with other mycobacteria (apart from *Mycobacterium leprae*) apparently confers little or no protection against leprosy.

Further observation of this trial population is necessary to confirm that the substantial protection afforded by BCG vaccination will persist. If these findings can be shown to be applicable to other situations, particularly where the proportion of patients with lepromatous leprosy is higher, then a potent and practicable control measure will be available for large-scale application in countries where leprosy is still a formidable problem.

[For a preliminary account of this trial see *Trop. Dis. Bull.*, 1963, **60**, 1123; see also *ibid.*, 1960, **57**, 1181; 1965, **62**, 537; for the interim report, see *ibid.*, 1966, **63**, 413.]

S. G. Browne.

he following 3 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1969, **66**, 3:

9. **Intradermal tests with mycobacterial substances and normal tissue suspensions,** by D. L. Leiker. *Int. J. Lepr.*, 1968, **36**, 52:

The author sets out to illustrate the fact that in patients with leprosy there is a common pattern of reaction to various mycobacterial substances, and that those with the lepromatous type of the disease are less capable of reacting than are healthy subjects to intradermal injections of mycobacterial suspensions. He proposes the hypothesis that the size of the reactions could depend firstly on a genetically determined potential capability of reacting to a common component of mycobacteria; secondly, on the degree of sensitization to this component; and thirdly, on the quantity of the common component in the test material.

This hypothesis suggests that a substitute for lepromin might be found, that there is little hope of developing a vaccine to immunize against the lepromatous type of leprosy, and that the decline of leprosy in Europe may have been due to a marked reduction in the leprosy-susceptible stock of the population because of a killing mycobacterial disease—tuberculosis.

[See also *Trop. Dis. Bull.*, 1962, **59**, 160, 1068.]

W. H. Jopling.

0. **Streptomycin combined with sulfones in the treatment of relapsed lepromatous leprosy,** by R. C. Hastings and J. R. Trautman. *Int. J. Lepr.*, 1968, **36**, 45.

This paper purports to show that when patients with lepromatous leprosy relapse, in spite of continuous sulphone therapy, a satisfactory response can be obtained by the addition of streptomycin injections. Ten patients were selected for the trial, all having been on long-term sulphone therapy with an average duration of 14.7 years prior to relapse. 1 g of streptomycin was given intramuscularly 3 times a week and oral sulphone therapy was continued. Blood levels of sulphone were determined throughout the trial. Satisfactory clinical and bacteriological progress was recorded during the 21 months of treatment; 8 of the patients developed erythema nodosum leprosum; no toxic effects of streptomycin were encountered.

[The abstracter's criticism of this paper is that the authors omitted the important first step of observing the response to parenteral sulphone before instituting streptomycin therapy, for it is well known that the longer a patient has been free from signs and symptoms of leprosy the more likely he is to neglect treatment. It is significant that blood levels of sulphone were recorded after commencement of the trial, not before.]

W. H. Jopling.

1. **Leprosy control in Australia.** *Med. J. Aust.*, 1967, **2** (27), 1209.

This report, made by the members of the Tropical Medicine and Health Committee (with the collaboration of several locally knowledgeable experts) and endorsed by the National Health and Medical Research Council of Australia, is an authoritative document embodying both factual information and guidance for the medical practitioner and administrator. The definitions take cognizance of recent work on the non-viability of morphologically abnormal forms of *Mycobacterium leprae*, and, in general, reflect modern conceptions of leprosy control. Thus, it is stated that "every attempt should be made by the States and Territories to avoid unnecessary isolation of cases", and "isolation should be applied only to patients with whole or viable bacilli in their smears". [Exception might be taken to the inclusion of "nerve pain or tenderness" as indubitable indications of "activity", since it is recognized generally that this symptom may persist for years in the absence of clinical or bacteriological activity.] It is considered that the protective value of BCG vaccination in leprosy is now established, and that vaccination should be offered to all children born into households in which a parent has leprosy.

At the end of 1966, there were 1557 patients with leprosy in Australia: 792 in the Northern Territory, 549 in Western Australia, and 185 in Queensland. The great majority of the patients are aborigines, but in Queensland the disease is found in all racial groups. Since many patients when diagnosed and notified appear to be suffering from relatively advanced leprosy, a salutary warning is issued that there must be many with active disease who are unsuspected and un-

diagnosed, and that others are in the long incubation or latent period. The recommendation is made that the words "leper", "lazaret" and "leprosarium" should no longer be used. [The enlightened modern outlook shown in this document will commend itself to all.]

S. G. Browne.

following 4 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1969, **66**, 4:

12. **L'endémie lépreuse en Republique Centrafricaine** (Leprosy in the Central African Republic), by J. Saugrain. *Med. Trop.*, 1968, **28**, 143.

This detailed report on the anti-leprosy campaign (1959-1965) in the Central African Republic (ex-Oubangui Chari) provides practical information concerning the well-known French methods of attacking leprosy in an area of high prevalence. These consist of repeated whole population surveys, and mass treatment by teams of supervised auxiliaries working either at fixed centres or cycling to visit patients regularly over a pre-determined route. The prevalence rates of leprosy increased from north to south, and from west to east, reaching 10%; the overall figure was as high as 55 per thousand.

In spite of a decline during the past 4 years both in the total number of persons examined and in the proportion of the population responding to the call to be medically examined, there has a gratifying reduction in the numbers of new patients. Interesting features of the report concern the low proportion of patients with lepromatous leprosy (less than 5%), and the relative increase of this form among recently diagnosed patients, the approximately equal male/female ratio and the low child rate (14% in 45% of the population).

Bacteriological examinations are apparently confined to the nasal "mucus" [is this a misprint for *muqueuse* = mucosa?] and to skin biopsies. The nasal "mucus" contains bacilli (whether viable or not is not indicated) in 1-2% of patients, but the skin biopsies are positive in 4-6%.

Treatment consists of weekly oral sulphone for the majority of patients, and bimonthly injectable sulphone for the rest. The average annual dose of oral dapsone works out at about 150 tablets each containing 100 mg of the drug, which is quite adequate, and suggests that an acceptable regularity of treatment (90% of the patients making over 75% of possible attendances) is being attained.

Costly Land Rover treatment runs have been abandoned, as have attempts at providing patients with stocks of tablets to take when weather conditions made regular visits impossible for long periods.

Patients are discharged from treatment 2 years after clinical arrest of the disease, as judged by itinerant teams capable of differentiating between the sequelae of leprosy and active progressive disease. There follows a period of 3 years of observation without treatment, but with regular bacteriological examinations before the patients are finally pronounced cured.

S. G. Browne.

13. **Comparison in man of lepromins prepared from leprosy infections in man and mice,** by P. Draper, R. J. W. Rees and M. F. R. Waters. *Clin. Exp. Immunol.*, 1968, **3**, 809.

"Two methods for preparing a suspension of *Mycobacterium leprae* from tissues of infected mice, using enzyme digestion, are described. The suspensions of mouse "lepromin" were compared with standard human lepromin as skin test antigens in 49 leprosy patients with various types of the disease. The reactions to mouse 'lepromin' were closely similar to those produced by standard lepromin, and patients with lepromatous leprosy failed to react to either antigen. This helped to confirm that the same organism produced human leprosy and the infection in mice and that *Myco. leprae* was the main cause of the lepromin eaction.'

14. **Tratamiento de la reaccion leprosa con talidomida. Primeras observaciones en la Republica Dominicana** (Treatment of the lepra reaction with thalidomide), by H. Bogaert Diaz, G. Herrera and M. Fernández Henriquez. *Revta Dominicana Derm.*, 1968, **2**, 36. English summary.

The authors, in the Dominican Republic, treated 35 patients suffering from lepra reaction with thalidomide [see also *Trop. Dis. Bull.*, 1968, No. 8, abstr. 2232]. Ten patients were treated in hospital; 2 groups (5 and 20) were ambulatory.

The first group included 7 men aged from 27 to 51 years and 3 women aged 40 to 48 years. They received 200 mg of the drug daily in 2 divided doses for 15 days, then a rest of 1 week; this was followed by combined therapy beginning with 25 mg of dapsone (DDS) and 100 mg of thalidomide daily, the doses being adjusted every 15 days so that at 60 days the daily doses of dapsone and thalidomide were respectively 100 and 25 mg; thereafter dapsone alone was used.

The second group, of 2 men each aged 35 years and 3 women aged between 40 and 54 years, were treated on similar lines, but the initial dose of thalidomide was given for 1 week only and the final dose of dapsone was 50 mg only.

The third group, 8 men aged 15 to 54 years and 12 women aged 40 to 51 years, received 100 mg thalidomide only, daily for 1 week, after which it was reduced weekly until a daily dose of 25 mg was attained.

Details of all 35 patients are given. In general, manifestations of reaction disappeared rapidly. Eighteen patients were able to renew treatment with dapsone without further treatment with thalidomide, 3 patients required a second course and 14 needed a maintenance dose of 25 mg thalidomide daily in conjunction with dapsone. Tolerance was good in all patients. The authors note that improvement was more complete and stable in patients having an initial daily dose of the drug of 200 mg than in those receiving only 100 mg.

[The authors refer very briefly to the danger of thalidomide to the products of conception, but it is

noted that while most of the women in this series were aged more than 45 years, a number of them were aged only 40 years. The warning against the inclusion of women in trials of this kind, given by Jopling (see abstract quoted above), needs to be underlined.]

H. J. O'D. Burke-Gaffney.

5. **Cell walls from** *Mycobacterium tuberculosis* **(BCG) as vaccine against** *Mycobacterium leprae* **infections in mice,** by C. C. Shepard and E. Ribi. *Proc. Soc. Exp. Biol. Med.*, 1968, **127**, 517.

The cell walls from BCG used in this study were prepared by the method described by Ribi *et al.* [*Bull. Hyg.*, 1966, **41**, 1146]. After lyophilization 100 mg of the preparation were mixed with 0.48 ml 7-*n*-hexyloctadecane and suspended in 40 ml saline containing 0.2% Tween 80; the mixture was then heated at 65°C for 30 minutes, and was referred to as the oil-treated vaccine. A similar vaccine was also prepared but without the treatment with oil.

Groups of CFW mice were vaccinated either intravenously or intradermally with the oil-treated vaccine, with the vaccine without oil-treatment, or with viable BCG, and after 34 days the mice were inoculated into the footpad with 5×10^3 *Mycobacterium leprae*. At 6 months, when the count in unvaccinated control mice had reached more than 10^6 bacilli, the number of bacilli in the vaccinated mice was determined and again 3 months later; these counts were made on pools of up to 8 mice.

The results showed that intradermal vaccination with the oil-treated cell wall preparation gave less protection, as judged by depression of multiplication of the leprosy bacilli, than did intravenous vaccination, and that at 6 months the degree of protection was similar to that produced by viable BCG, although at 9 months it was somewhat inferior. Cells walls without treatment with oil afforded no protection.

The amount of local induration produced by the intradermal vaccination was less with the oil-treated cell wall preparation than that produced by the viable BCG vaccine; the enlargement of the draining lymph glands was also less. Intravenous injection of the oil-treated vaccine and the viable BCG produced pulmonary nodules with a peripheral zone of macrophages.

S. R. M. Bushby.

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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.

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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*)".

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