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Editorial

INTEGRATION–PRESENT PROSPECTS

A recent editorial in this journal (1971, **42**, 1) commented on certain trends in the relation between leprosy control programmes and the health services of developing countries. The provocative, controversial, idealistic watchword "integration" is fast becoming more than a talking point in many circles.

The Fourth Report of the World Health Organization (WHO) Expert Committee on Leprosy (1970) observed that "the need for integration of leprosy control programmes into the structure of the general health services is widely recognized", but pessimistically concluded that "full integration will be attained only as a result of a long drawn-out process". Lukewarm support for the theoretical desirability of integration was given by the WHO Regional Office Seminar in Kampala, but at a more recent meeting held in the same town (East Africa Leprosy Working Conference, April 1970), the principle of integration was "generally accepted" and some of the difficulties encountered at supervisory and local level were realistically faced and discussed. The responsibility of governments to plan national health programmes in the interests of all citizens has been urged and admitted by the World Health Organization, and also by such meetings as that convened by the United Nations at Geneva (September-October, 1971) on "National programmes for rehabilitation of the disabled in developing countries". Many governments have in principle accepted these various recommendations, but many face difficulties in their attempts to pay more than lip-service to them.

On another page of this issue (p. 255) we publish *in extenso* a valuable account of discussions held in Bhopal at the 12th All-India Leprosy Workers' Conference and 9th Biennial Conference of the Indian Association of Leprologists. The understandable prudence and circumspection of this account will commend themselves to those acquainted with the Indian scene. Local knowledge and sympathy should prevent precipitate action that would leave the leprosy sufferer worse off than he is. Over-rapid and ill-considered attempts at premature integration of a functioning leprosy programme into an unwelcoming rural health service could all too easily result in a return to the *status ante quo* of neglect. There might be some initial reduction in the number of leprosy patients receiving treatment, which, in these circumstances, would indicate failure rather than success.

In this matter, the social milieu and climate are factors just as important as the coverage of the health services. Such non-medical factors affect the speed and even the possibility, at the present time, of full integration of leprosy into the health programme. In some countries prejudice against leprosy and the leprosy sufferer still appears to be as strong (and as groundless and irrational) as ever, while in others gradual erosion of age-long beliefs is making gratifying headway.

The quality of the basic health services, the resources available in men and means, the apportionment of effort between curative and preventive measures, and between prestigious central hospitals and rural health centres—all have a bearing on the gravity of the leprosy endemic and the forces actually deployable for meeting it. When a specialized campaign of leprosy control has achieved a notable degree of success, the thorny and inescapable question arises: how can the residuum of patients still needing treatment be adequately cared for? It is possible that leprosy could insidiously and silently re-establish itself in such a community if existing medical services were too thin on the ground, or were otherwise unable or unwilling (for diverse reasons) to cope with this extra load.

Voluntary organizations have a continuing responsibility in this business: with their history of dedicated and competent service, their present resources, and their capacity for local initiative, they can influence policies and practices in many ways.

The debate continues.

Lepr. Rev. (1972) **42**, 237-251

News and Notes

TENTH INTERNATIONAL LEPROSY CONGRESS, 1973

DATES: From Monday, 13 August to Saturday, 18 August, 1973, both dates inclusive.

PLACE: Bergen, Norway

CHAIRMAN OF LOCAL COMMITTEE: Professor Erik Waaler
Address: Gade Pathological Institute,
University of Bergen,
Bergen 5000,
Norway

OFFICIAL CARRIERS: S.A.S. (Scandinavian Air Lines)

LANGUAGES: The official languages of the Congress are those of the International Leprosy Association, viz., English, French and Spanish.

SIMULTANEOUS TRANSLATION: At the Scientific Sessions of the Congress, main and concurrent, simultaneous translation will be provided in English, French and Spanish.

If a participant wishes to present a paper in, or to speak in, Portuguese or Japanese, he shall not be precluded from so doing. It is hoped that Portuguese and Japanese participants will themselves be responsible for the provision of facilities for simultaneous translation should there be a need.

ABSTRACTS

Language: Abstracts of all papers submitted should be in English, French or Spanish.

Length: The maximum length of abstracts is 200 words.

Date of submission: All abstracts must be in the hands of Dr S. G. Browne, Secretary-Treasurer of the International Leprosy Association, *before 1 December, 1972,* and should be sent to him at the following address:

57a Wimpole Street,
LONDON, W1M 7DF,
England.

Number of copies, etc.: Abstracts must be submitted in *four* typed copies, double-spaced.

Submission of abstracts and papers: Authors may submit, personally or conjointly, more than one paper, but the Selection Committee reserves the right not to accept any paper (and hence any abstract) submitted.

Papers may be submitted on any aspect of leprosy.

Publication: Abstracts accepted will be published in English, French and Spanish.

SCIENTIFIC SESSIONS

The titles of the Sessions proposed are as follows:

(1) Advances in experimental leprosy.
(2) Advances in the microbiology of *Myco. leprae.*
(3) Advances in experimental chemotherapeutics.
(4) Advances in immunopathology.
(5) Advances in epidemiology.
(6) Therapy.
(7) Control.
(8) Rehabilitation.

The time allotted to the individual sessions will be determined by the number of papers accepted on the above topics. The form of the programme will therefore not be known until the final apportionment of time has been made. Papers will be selected on the basis of the abstracts submitted, by a group of Councillors nominated by the Special Advisory Committee appointed by the President, together with co-opted members.

SUBMISSION OF PAPERS

Four copies of each paper in its final form, typed in double spacing, must be delivered to the Organizing Secretary of the Congress in Bergen so as to reach him before 13 June, 1973. They should be addressed to:

The Organizing Secretary,
10th International Leprosy Congress,
c/o Professor Erik Waaler,
Gade Pathological Institute,
University of Bergen,
Bergen 5000,
Norway.

POST-CONGRESS SEMINAR IN COPENHAGEN

It is proposed to hold a short seminar on medico-historical aspects of leprosy in Copenhagen, immediately following the Congress. The Organizer is Professor Wilhelm Møller-Christensen,

The Medical Historical Museum,
University of Copenhagen,
62 Belgrade,
1260 Copenhagen K,
Denmark

to whom all enquiries should be addressed. Further particulars will be made available at a later date.

COMMITTEES

Small groups of nominated members, chosen solely by reason of their expert knowledge, will meet before the Opening Session of the Congress. The named members will be hearing personally from the respective Chairmen in the near future.

The Committees will meet in Bergen on the day or days appointed by their respective Chairmen, on Thursday 9, Friday 10, and Saturday 11 August, 1973. The main language of these Committees will probably be English, but it is hoped

to provide facilities for translation from and into the three official languages of the Congress.

The Committee Chairmen are empowered to co-opt, to invite a co-opted member to attend meetings of the Committee, and to invite or to receive written contributions on the topic. Each Chairman will draw up a Report, of a maximum length of 2000 words, on the work of his Committee, and will prepare a résumé of this Report, of about 300 words, to be read at the Closing Session of the Congress. The full report will be prepared in time to be translated, and duplicated, before the end of the Congress, so that each participant may have a copy before he leaves Bergen.

J. CONVIT
President
STANLEY G. BROWNE
Secretary-Treasurer

PRE-CONGRESS TOURS

Tours of Norway and Scandinavia, of various lengths and itineraries, to take place before the opening date of the Congress, will be organized by the Bergen Committee. Full particulars of these will be available at a later date.

LEPRA—CHANGES AT HEADQUARTERS

Sir George Seel, KCMG, has relinquished the office of Chairman of the Executive Committee of LEPRA, the British Leprosy Relief Association. During the period of reappraisal of LEPRA's activities and its expansion into Malawi his wise leadership and urbane counsel have been much appreciated. *Leprosy Review* gives a warm welcome to his successor, Sir Gawain Bell, KCMG, CBE.

At a luncheon party given by the Rt Hon. Viscount Boyd of Merton, CH, LEPRA's President, at the Royal Commonwealth Society on 9 November, sincere greetings were voiced to both Sir George Seel and Sir Gawain Bell. Leave was taken of Air Vice-Marshal W. J. Crisham, CB, CBE, who has, by his initiative and dynamism, changed the face of LEPRA during his tenure of office as General Secretary.

As Mr G. Francis Harris, MC, now assumes the responsibilities of General Secretary, he brings to his task both wide administrative experience in West Africa, and a detailed knowledge of the many leprosy programmes supported by LEPRA. Facing new opportunities and changing emphases, the new General Secretary is assured of the good wishes of *Leprosy Review* and all its readers.

THE WORLD HEALTH SITUATION, 1965-1968
LEPROSY TAKES ITS PLACE IN THE QUEUE

The Fourth Report of the World Health Organization on the world health situation makes heavy and exciting reading. It should be required reading for those leprosy workers whose vision is oft-times so limited by the trees that they fail even to suspect the existence of the wood.

There are facts here, objectively reported by the governments of member-countries, as well as statistics and tables, shrewd comment and salutary warnings. Leprosy is scarcely mentioned; with tuberculosis, it continues "to cause concern"—an understatement that may either disturb us or challenge us. But the threat posed in the developing countries by communicable diseases in general is well recognized and well documented. Notwithstanding continuing economic growth during the period under review, the relative neglect by many governments of social considerations and matters of health and well-being is unfortunately all too obvious.

Much of the increase registered in health man-power and material facilities has been more than swallowed up by the spectacular rise in population—as is apparent in many rural leprosy-control programmes. However fast we run, we appear unable to do more than remain in the same place.

The report rightly stresses the part that can be played by the trained health auxiliary, in both the developed and the developing countries; "the balanced health team, composed of professional health personnel and their auxiliaries, provides a pattern of health care to be followed wherever and whenever this is possible". Leprosy campaigns have both pioneered and profited from this development, now recognized as providing the only possible means for mediating health care to the millions who need it.

Cause for satisfaction is registered in the partial success of the global smallpox eradication campaign and of malaria control schemes. Poliomyelitis is no longer a threat in the developed countries, but it is still so in countries of the Third World where immunization procedures are at best sporadically and patchily undertaken. Schistosomiasis, venereal diseases, infective hepatitis and measles are frequently mentioned by member-governments as major health problems. In addition, and particularly among children, the helminthiases and protein-calorie malnutrition continue to cause concern, if not alarm.

The section on medical man-power, education and training contains statements of fact and inference that will evoke regretful agreement among leprosy workers in under-doctored rural populations that are still denied even the rudimentary medical benefits available to their brethren in the burgeoning urban conglomerations.

We note with satisfaction that in several countries a critical review has been undertaken of the health services on the basis of criteria of "efficiency and productivity". More germane to our immediate interests are the comments concerning the integration of diseases in a comprehensive medical service. In the past, each disease was regarded as a distinct and separate problem, demanding its own organization and staff for investigation and control. Now, governments are devoting more attention to the planning of health services, and, in their laudable desire to bring the greatest good to the greatest number, they are organizing their immunization and control programmes in the light of such general factors as adverse environmental conditions, widespread undernutrition (especially among children), accelerating population pressures, lack of pure water, and unhygienic disposal of wastes.

This is all to the good. The whole "wood" should by now be glaringly obvious, even frighteningly and inescapably evident. Perhaps the time has come to suggest that such important and hardy "trees" as leprosy, often overlooked and ignored amid the sheer dimensions of the killers, the epidemic and the acute diseases, may be accorded their rightful place in the conscience and resources of individuals and governments.

REHABILITATION OF THE DISABLED

The United Nations convened in Geneva from 27 September to 6 October, 1971, a meeting of experts on the planning, organization and administration of national programmes for rehabilitation of the disabled in developing countries. The voluntary organizations were represented by a delegation from the Council of World Organizations interested in the Handicapped, of which the International Leprosy Association is a member.

The meeting saw little evidence of systematic planning for rehabilitation services in the developing countries, and advised the creation of national boards or councils, which would be officially responsible for planning and co-ordinating, for recommending any necessary legislative measures, and for establishing where indicated a pilot demonstration project, preferably in an urban centre and attached to a university. It was agreed that rehabilitation of the disabled was ultimately the concern of the state: voluntary bodies, however, still have an important rôle to play in many countries. Education of professional staff in all aspects of rehabilitation, and particularly the training of medical auxiliaries should be the first priority in any national campaign.

Those especially concerned with the medical and social rehabilitation of leprosy patients will doubtless maintain a watching brief in their own countries to ensure that, in any proposed scheme, the needs of the sizeable proportion of the handicapped whose disabilities are due to leprosy will not be overlooked among the more obvious and more publicized sections of the underprivileged community.

ALERT POST-GRADUATE COURSE FOR DOCTORS

We are indebted to Dr W. Felton Ross for the following report:

From 13 September to 9 October, 1971, 27 doctors attended a full-time course in clinical leprology at ALERT (the All African Leprosy Rehabilitation and Training Centre), Addis Ababa, and of this number, 17 stayed for further studies, for periods of up to 2 months, in leprosy control, surgery, ophthalmology, pathology, and the principles of administration. The course covered all the main facets of clinical leprology, including relevant aspects of the basic sciences, such as functional anatomy and immunology. In addition to the permanent staff of ALERT, lectures and demonstrations were given by Dr John Pearson on reaction and neuritis, Dr Dick L. Leiker on leprosy control, and Dr Margaret Brand on ophthalmology. Professor Charles Leithead, Chairman of the Board of Directors of ALERT, spoke on the rôle of medical educational institutions in developing countries, and Dr Chasles of WHO and Dr Meyer-Lie, Ministry of Public Health, participated in discussions.

Nine of the participants were citizens of the African continent; with the exception of one citizen from Pakistan, one expatriate working in India and another working in New Guinea, the remainder were expatriates working in Africa. The African doctors included three senior registrars from teaching schools.

All the participants were accommodated in the ALERT Guest House, and the hospital and teaching facilities, recently completed, proved more than adequate. Most of the comments from participants were favourable. The following are typical:

"For me the course was extremely important as I was just starting to work in a

leprosy control scheme. I should like to recommend the course to every doctor starting in this field."

"The duration of the course is too short as it hardly gives much time for us to learn everything in leprosy in detail. There are so many different aspects and one must get more ample knowledge of the whole subject . . . For newcomers, I think three to six months should be spent in this leprosy training centre."

It is probable that a course of this type will become an annual event for ALERT and certainly there will be such a course during 1972, beginning on Monday, 2 October, and continuing until 28 November. The first week of the course will introduce doctors without previous experience in this field, to clinical leprology, and the remainder of the course will cover the more advanced teaching that was included this year.

LEPROSY JOINS "HAND"

A combined international meeting, sponsored jointly by G.E.M. (*Groupe d'Etude de la Main*), which is an association comprising mainly French surgeons interested in the hand, and the *Association de Léprologues de Langue française* (A.L.L.F.), was held in the Val de Grâce Hospital, Paris, on 6 and 7 June, 1971. For the orthopaedic surgeons from many countries, this meeting formed part of a series that began with a course on hand surgery organized in Paris by Dr R. Tubiana, and ended in a Congress on Hand Surgery in Gothenburg, Sweden. The guests of honour were Drs Paul Brand (now at Carville, Louisiana) and Stanley Browne, representing The International Leprosy Association (who is also *Conseiller Technique* to the A.L.L.F.). The dynamic leadership of Général A. Carayon was everywhere evident: his contributions in papers and discussions were particularly appreciated. Although the two days were very full and many papers were presented, time for discussion—both at the sessions and between them—was not lacking.

The main themes centred around "trophic" lesions (considered in the widest and perhaps inaccurate sense), and lesions of nerve trunks. The foot and face came in for study and comment, as well as the hand. To an audience composed in the main of orthopaedic surgeons working in the affluent West and interested in traumatology, rheumatology, and other common conditions of importance in Europe and North America, the extent and variety and sheer pathological interest of the hand deformities seen by the thousand in countries where leprosy is rife, must have come somewhat as a surprise—even as a shock. However, the presentations of the clinical findings, the histological and immunological basis, and accounts of the therapeutic and surgical possibilities available in some few highly favoured centres all evoked lively interest. Attention was more than once focussed on simple operative interventions that could be applied in mass treatment campaigns.

For too long, there has been insufficient cross-fertilization of ideas and exchange of knowledge between French- and English-speaking doctors, leprologists as well as surgeons. This happy meeting on common ground revealed an unexpected overlapping of professional interests and activities, and opened the way to further contacts that should prove helpful to the cause of leprosy.

In his concluding remarks Dr Paul Brand stressed the point that experienced hand surgeons wishing to devote themselves for a time to helping developing countries with their skill and expert knowledge, should first learn about leprosy;

its pathology and clinical manifestations; the indications for (and contra-indications to) operative interference; the frequency of almost painless low-grade cellulitis; and the relentless progress of nerve damage in some forms of leprosy. Education, propaganda, the co-operation of auxiliary workers recruited and trained locally, the supreme value of *prevention* of deformities, the importance of accurate records, the provision of simple and cheap protective footwear and appliances—all formed part of the combined attack on the results of nerve damage in leprosy. Orthopaedic surgeons were forcefully made aware of "the million sufferers from leprosy, needing some kind of hand surgery", and the untold numbers who would—unless something more was done than is being done—inevitably develop some deformity of face, feet or hands in the coming years.

24th WORLD HEALTH ASSEMBLY

Another World Health Assembly has come and gone. From 4 to 20 May, 1971, representatives of Member-states, the United Nations and related organizations, and intergovernmental and non-governmental organizations met to discuss and deliberate. The account of their plenary meetings and subcommittees is embodied in a 600-page compendious document—Official Records of the World Health Organization (WHO), No. 194. The International Leprosy Association is one of the non-governmental bodies having a special relation with WHO.

As might be expected, leprosy figures but incidentally in the addresses made by the offical representatives to the Assembly, but the following references would indicate that the disease that concerns the readers of *Leprosy Review* was not entirely forgotten.

In *Sierra Leone* (pp. 48 and 49) the Endemic Diseases Control Unit, which was established primarily to combat trypanosomiasis, has more recently included smallpox, measles, and leprosy within its purview, and will shortly be transformed into a comprehensive service to deal with all types of communicable disease. For the time being, however, vaccination against cholera, smallpox and measles, and leprosy control measures will absorb all available resources. Satisfaction is expressed that the target of 11,000 patients under treatment for leprosy has been exceeded by 4000, and deep appreciation is voiced at the considerable help afforded by various voluntary agencies, the British Leprosy Relief Association (LEPRA) among others. The results so far achieved should be viewed against the background of the considerable number of leprosy sufferers still without treatment.

Nepal (pp. 80 and 81) registers some success in its malaria eradication campaign and in the efforts to eradicate smallpox by vaccination; control programmes for tuberculosis and leprosy are receiving governmental encouragement. Survey, education and treatment programmes, on the Indian pattern, are being implemented in the Kathmandu Valley and some other districts. Case-finding is mainly through school surveys, and treatment and follow-up are the responsibility of local health institutions. (The deep-seated prejudice against leprosy is a major factor in the slow progress of the best laid plans). Nepal is drawing up a master plan for its health services (p. 383), with help from WHO and UNICEF.

The representative from *Malawi* (pp. 85-86) confessed that the limited financial resources of his country were insufficient to give more than "rather a low

priority" to the social services. For some years, his government had felt "the need for a comprehensive health plan", and with advice and financial help from WHO in the development of basic health services, the control of communicable diseases, and the provision of technical assistance, he hoped that the present rather sombre picture would brighten. Meanwhile, he quoted with some feeling Professor Abel-Smith's comment: "ascertaining the cost of health services and relating them to national resources is only a modest beginning in the growing field of international health economics",

The *Central African Republic* (pp. 87 and 88) is achieving "very interesting results" in the matter of leprosy control: "26,749 patients were on the books at the end of 1970, including 5579 arrested cases and 8260 under observation without treatment. Since 1 January, 1970, 831 new leprosy cases have been detected while 3116 have been cleared from supervision, which brings the total number of patients released from supervision since the start of the campaign to nearly 30,000".

Zambia (p. 91) confessed that the communicable diseases (tuberculosis, leprosy, malaria and viral infections) still posed the greatest threat to the health of its people, together with undernutrition. However, the national health development plan was due to be inaugurated in January,1972, and a serious attempt would be made during its first 5 years of operation to solve the more pressing health problems of the country.

Togo (p. 99) mentions leprosy specifically as the first of the major endemic diseases to warrant a special control programme. Over 10,000 leprosy patients are at present receiving treatment, either under the domiciliary scheme or at the 4 residential leprosaria. At the same time, a network of health establishments is being developed, based on a central national hospital and 3 new regional hospital centres. Primary and secondary health centres are being equipped and modernized in an attempt to bring some kind of medical service within the reach of all, but chronic staff shortage and slow economic growth seem to hamper the implementation of official plans.

Gabon (pp. 155 to 157) considers itself favourably situated as regards its campaigns against smallpox, yellow fever and cholera. Malaria remains the major endemic disease. In 1970, considerable attention was given to the problem of leprosy in an effort to clarify the situation: some 7640 sufferers were under treatment at the end of the year, and tribute is paid to the preventive medicine services, which are accorded priority in government health planning.

In *Mauritius* (p. 178) the leprosy endemic is considered no longer to pose any threat. In 1925, the incidence was 12.5 per million, but in the years 1968-70 it had fallen to less than 1 per million.

The Assistant Director-General of WHO (p. 365), referring to the suggestion made by Tanzania that WHO should set an example to the world by integrating the tuberculosis and leprosy units, considered that the experience gained in tuberculosis and leprosy control was indeed being exchanged and that the control programmes that had been successful in tuberculosis might be applied in the case of leprosy.

In *Ceylon* (p. 383) leprosy control was being undertaken with much-appreciated help from WHO.

The differences between the affluent countries of the West and the developing countries of the Third World were stressed by the representative from *Hungary* (p. 553)—"malnutrition, morbidity caused by environmental pollution, malaria,

smallpox, syphilis, tuberculosis and leprosy were paramount" in precisely those countries beset by chronic shortages of specialized technical and auxiliary health staff, inadequate health institutions, and lack of funds. Here in a nutshell is the problem stated. It is to be hoped that amid the depressing weight of platitudes the plight of the forgotten millions of leprosy sufferers may receive increasing attention from those who plan the health services of the world and who channel the resources for their implementation.

TEN YEARS OF LEPROSY CONTROL AROUND BUSOGA, UGANDA

This bright, 28-page report, well-written and well illustrated, summarizes interestingly the main features of the control programme operating around the leprosy hospital at Busoga, Uganda, under the auspices of a Franciscan Order, among a population of about 1 million persons scattered over a land area of approximately 3500 square miles (8000 sq km).

There are 49 treatment centres caring for a total of 15,000 leprosy patients, some 9% of whom have lepromatous leprosy and 30% borderline disease. Case-finding whole-population surveys, contact examinations and BCG vaccination for child contacts under 5 years of age are all part of the programme. Treatment is, for the most part, oral once-weekly dapsone, but some patients are having fortnightly injections with a suspension of dapsone.

A happy co-operation exists between the Uganda Government (which pays the salaries of the district leprosy staff) and the voluntary agency responsible for the programme, with much-appreciated financial assistance from the German Leprosy Association (DAHW), LEPRA, OXFAM, St. Francis Leprosy Guild, and other bodies.

In accordance with recommendations of the World Health Organization, the emphasis has been on ambulatory care of leprosy patients in the rural areas; every opportunity is taken to offer general medical care both to leprosy patients and to those not suffering from leprosy, to facilitate the gradual and desirable integration of leprosy in the general health services of the region.

A 2-year course of training is offered at Buluba (the Control Headquarters) for intending leprosy assistants. Final-year medical students from Makerere Medical School spend some time at Buluba in order to become acquainted with clinical leprosy and the principles of leprosy control. Small district leprosy dispensaries, each with a small ward for 8 leprosy in-patients, have been erected in each of the 8 counties. From these centres the control work radiates into the surrounding villages and hamlets.

NOT ONLY THE MOUSE

Another animal has been found to be susceptible to experimental infection with *Myco. leprae, viz.* the armadillo. This is reported by Dr W. F. Kirchheimer, the well-known pathologist of the United States Public Service Hospital at Carville, Louisiana, who has been collaborating with Dr Eleanor E. Storrs, Director of the Department of Biochemistry at the nearby Gulf South Research Institute, New Iberia.

One of the 44 armadillos inoculated with material obtained from patients in South America, the Philippines and Africa, suffering from lepromatous leprosy

and untreated, developed widespread progressive "lepromatous" leprosy after 16 months, and subsequently died, presumably as the result of generalized mycobacteriosis. Post-mortem examination revealed the presence of highly bacilliferous granulation tissue throughout the body. Significant factors in the production of this infection may be the low body temperature of the armadillo and its life-span (some 15 years). The successful clinical and histological reproduction of the human disease in a small proportion of animals raises many questions and invites further investigations.

"PARAMEDICAL"–TO THOSE WHOM IT MAY CONCERN . . .

A recent press release informs the public that the World Health Organization will not in future use the term "paramedical" for the various university level health professions allied with medicine. In the past, the term has been used in some countries to designate such professional workers as nurses, physiotherapists, radiographers, laboratory technologists, etc., who have been regarded as people duly qualified in their own special branch of the health service and working alongside, or with, registered doctors. In other countries, and especially in the field of leprosy, the word as commonly used embraces the auxiliary and "middle level personnel".

VOLUNTARY AGENCIES FINANCE LEPROSY RESEARCH

LEPRA (the British Leprosy Relief Association) has, since its inception (as BELRA) in 1924, actively encouraged and sponsored leprosy research in the field and in the laboratory. At a recent meeting of its Executive Committee, grants were approved for covering the cost of transport of tissue recovered from leprosy patients at Dichpalli, India, to the National Institute for Medical Research at Mill Hill, London. At the same meeting, a travel grant to Dr Ralph Abrahams was approved to enable him to investigate the occurrence of amyloidosis in patients with lepromatous leprosy in Papua and New Guinea.

The Federation of European Anti-leprosy Organizations (ELEP) recommends from time to time that an increasing proportion of funds raised by voluntary organizations in Western Europe should be devoted to research in leprosy. The Medical Commission of ELEP, through its Secretary (Monsieur Pierre Van den Wijngaert, 4 rue Saint-Geoffroy, F 80 Amiens, France) is issuing a *Memorandum on Leprosy Research* in English, French, German, and Spanish. Copies will soon be available from the Secretariat.

The electronmicroscope now being used by Professor C. K. Job at the Christian Medical College, Vellore, South India, was purchased with money subscribed to commemorate the 90th anniversary of The Leprosy Mission.

ZAMBIA

The Permanent Secretary of the Ministry of Health, Zambia, and the Government leprologist (Dr B. Jogan) have expressed their gratitude for LEPRA's help in the provision of motor transport for the leprosy control scheme in the Eastern Province, and for the services of a Leprosy Control Officer (Mr Iorworth Rogers, S.R.N.) in the Luapula Province.

Since the population density in the country as a whole (including the denser concentrations of Lusaka and the Copper Belt), is less than 20 per square mile, with 46% of the population under the age of 15 years, the estimated leprosy prevalence of 2 per 1000 (in children) and 5 per 1000 (in adults) is considered to be a problem in finance and logistics rather than one of overriding medical priority.

UNICEF AND LEPROSY

As UNICEF celebrated on 11 December, 1971, the 25th anniversary of its foundation, *Leprosy Review* extends its congratulations, expresses its thanks, and dares to hope for a continuation of its beneficent activities.

From the beginning, leprosy control has figured among UNICEF's priorities. Many Government-sponsored schemes have been assisted by the joint UNICEF-WHO programme and have received drugs, transport and expert advice. In the past 25 years, no fewer than 415,000 children have been discharged as cured of leprosy in the schemes aided by UNICEF. In some instances, as is the case with tuberculosis, the facilities established for leprosy, the staff trained and the transport provided have formed the nucleus of a basic health service for the deprived rural populations of developing countries.

The task is by no means finished: leprosy is but one of the endemic threats to the 800 million children under 15 years of age in the countries assisted by UNICEF, but of these, there may be as many as 2 or 3 million needing treatment for leprosy.

NOVEL MEANS OF RAISING FUNDS

Many voluntary organizations are discovering novel means of raising funds. In addition to the conventional methods, sponsored walks have, of recent years, brought in many thousands of pounds for specific projects.

One that has captured a great deal of publicity has been the sponsored climb up to the summit of Snowdon, the highest mountain in England and Wales, by a group of Scout Cubs. The intriguing feature was not the age of these boys, or their affiliation to the Boy Scout Movement, but the fact that they were all blind.

No less a sum than £8250 was raised for the funds of LEPRA, the British Leprosy Relief Association. Other countries have higher peaks: can they too not be climbed to the benefit of leprosy?

RESEARCH IN DISEASES OF THE TROPICS

From time to time, the *British Medical Bulletin* publishes a quarterly issue that appeals to a wider audience than specialists engaged in a restricted field of medical activity. Such an issue has recently appeared: it is the first number, 1972, of Volume 28, and it is entitled "Research in Diseases of the Tropics". Under the able editorship of Dr C. E. Gordon Smith a notable team of contributors provide accounts of recent advances in many of the branches of medicine that daily impinge upon those whose chief concern is leprosy. Malaria, schistosomiasis, leishmaniasis, filariasis, onchocerciasis, sprue—all are embraced in this symposium. The changing pattern of disease, the problems of protein-calorie malnutrition,

diseases of the heart and anaemias, and arbovirus disease also come in for detailed consideration.

Of special interest to readers of *Leprosy Review* is the chapter entitled "Recent trends in leprosy research", which is contributed by R. J. W. Rees and M. F. R. Waters. This chapter provides a useful summary of recent work, bringing the fascinating story up to date with references to research in immunology and to treatment with clofazimine and rifampicin.

Copies of this "exhilarating and stimulating number" are obtainable from the Medical Department, The British Council, 97 and 99 Park Street, London, W1Y 4HQ, at a cost of £2.50.

LEPROSY IN NORWAY

Only 4 leprosy patients remain in Norway—the sole representatives of the last bastion of the disease in continental north-western Europe. Three of them live in Bergen and work in the State Rehabilitation Institute for the Handicapped, while the oldest patient, now aged 85, actually lives in the Institute. It was on 28 February, 1873, that Dr G. H. Armauer Hansen saw the brownish rods that he suspected of being the cause of leprosy. Some Scandinavian emigrants to the United States of America took leprosy with them to the New World; it is thought that only one of their descendants living today has the disease.

LEPRA's LEPROSY CONTROL PROJECT IN MALAWI

The total number of leprosy patients registered for treatment under the aegis of this Project is now 11,774. New patients are still being discovered by the case-finding teams during whole-population examinations, at the skin clinics in Blantyre and Zomba, while some present themselves voluntarily as the result of press or radio publicity. Dr S. G. Browne, in his capacity as Medical Secretary of LEPRA, visited Malawi in January, 1972, to observe the working of the Project and review its progress. Now that the Project has entered on the 7th year of its 10-year course, the rhythm of discharges should accelerate.

The Central and Northern Provinces of the country still lack an effective leprosy control service, but there are hopes that a recent report by a World Health Organization team may provide the practical basis for a programme of control of endemic disease (including leprosy) through a network of dispensaries, and a concerted attack on malnutrition and infantile morbidity and mortality.

The fact that bench space is available in the laboratory of the Project Hospital in the grounds of the Queen Elizabeth Hospital, Blantyre, should be more widely known. Anyone wishing to make use of these investigative facilities is invited to write direct to: Dr B. David Molesworth, LEPRA Control Project, P.O. Box 496, Blantyre, Malawi.

GANDHI MEMORIAL LEPROSY FOUNDATION ANNUAL REPORT, 1970-71

The Report provides a useful summary of the activities of the Foundation during its 20th year. In addition to research and teaching at Wardha (Maharashtra, India) itself, the Foundation is responsible for several leprosy control programmes and a valuable chemoprophylaxis investigation. Methods of control that are proving

successful in rural areas are being adapted to the more difficult urban conglomerations, where the co-operation of private medical practitioners is encouraged. Health-education units are active in all areas, making contact with schools, teacher training colleges, and groups of doctors as well as the general public. They reach out beyond Maharashtra State and into West Bengal, Orissa, Kerala, Mysore and Gujarat. The provision of training for paramedical workers and refresher courses for medical officers has been increased during the year.

The chemoprophylaxis project continues to evoke interest beyond the borders of India, and statistically significant results are becoming available as the period of investigation increases. During the year, the Foundation organized a Conference for leprosy workers within the State of Maharashtra, and a three-day Leprosy Workshop for the study of the medical, social and administrative aspects of the leprosy problems of India.

Under the vigorous leadership of the new Director, Dr M. S. Nilakanta Rao, the Gandhi Memorial Leprosy Foundation enters another decade of fruitful and useful activity, the results of which will be seen beyond the immediate area of its operations.

HIND KUSHT NIVARAN SANGH

The Annual Report for 1970 of the Indian Leprosy Association provides an encouraging and sober review of the activities of government and voluntary agencies in the campaign against one of the major scourges of the subcontinent. The estimate of the total number of leprosy sufferers still stands at 2.5 million, notwithstanding the increase in population, and of these just over 800,000 are at present receiving treatment, mainly through the S.E.T. (Survey, Education and Treatment) programmes.

The Report stresses the advances made in our knowledge of leprosy and its treatment, the need for training of doctors and auxiliary workers, the gaps in medical curricula, the value of the courses provided at various institutions (notably Chingleput, Wardha, and Vellore, among others), and the diverse investigations being pursued. It also includes an account of work being done by non-government agencies.

KUMI LEPROSY CENTRE ANNUAL REPORT, 1970

The dynamic medical superintendent of the Kumi Leprosy Centre, Uganda, summarizes in his Annual Report for 1970 the new emphases on domiciliary treatment for leprosy covering 7 districts with a total population of just under 3 million. Out of the estimated number of sufferers (42,768—based on a probable prevalence rate of 1½%) 11,112 were under more or less regular treatment. There were 298 discharges during the year.

Appreciative reference is made to the early whole-population surveys by Dr J. A. Kinnear Brown of representative samples of the area now covered, and the opinion is expressed that such surveys should be repeated in the near future so as to provide an objective basis for the evaluation of the efficacy of present methods of leprosy control. The training and supervision of the leprosy assistants attached to the programme are an important part of the activities of the medical and expatriate staff. More facilities are being provided in district hospitals for the

in-patient treatment of leprosy patients needing special care—surely a most desirable development.

Reference is made to the much-appreciated work of Dr Kinnear Brown and Miss M. M. Stone in connection with the BCG trial in the Teso District, which was supported by the Uganda Government, the Ministry of Overseas Development and the (British) Medical Research Council.

The Kumi-Ongino Leprosy Service owed its origin largely to the Church Missionary Society, its early development to the British Leprosy Relief Association (LEPRA) and The Leprosy Mission, and now obtains over 43% of its running costs from voluntary agencies overseas. Considerable sums for capital expenditure were received during 1970 from Holland and West Germany. The cost of the service in 1970 was near 712,000 shillings (East Africa).

LEPROSY IN TANZANIA
ANNUAL REPORT OF THE GOVERNOR CONSULTANT LEPROLOGIST FOR 1970

Dr Harold W. Wheate surveys the progress of the leprosy control scheme in Tanzania during the year, where co-operation between the government and the voluntary agency hospitals continues. In addition to routine activities, special mention is made of 2 new leprosy control schemes, in Tanga and Kasulu. A health campaign conducted in Mafia Island has resulted in the registration for treatment of probably 90% of those suffering from leprosy. Dr Wheate concludes that if future immigrants to the island can be routinely checked and treated for leprosy where necessary, "the eradication of leprosy from Mafia is eminently feasible".

Future co-operation with Professor Johs Andersen in the Orthopaedic Department of the Kilimanjaro Christian Medical Centre will assure leprosy patients suffering from deformity of the services of an experienced expert.

The Save the Children Fund Leprosy Campaign in the West Lake Region reports a definite downward trend in the number of new leprosy infections, the result of 10 years of intensive work. More generally, it is noted with satisfaction that the number of newly-diagnosed leprosy patients presenting with deformity is practically *nil,* and that there is a steady decline in the lepromatous: tuberculoid ratio among them.

LEPROSY IN THE BRITISH SOLOMON ISLANDS PROTECTORATE

The Annual Report for the year 1969 of the Director of Medical Services of the British Solomon Islands Protectorate expresses general satisfaction with the leprosy control programme. The numbers of annual notifications show a progressive decline from 110 in 1965 to 33 in 1969, giving a total on the register of 612 cases. Patients are presenting themselves for diagnosis and treatment at a much earlier stage of the disease. The real and dramatic reduction in the size of the leprosy problem in the Protectorate is attributed to the widespread BCG vaccination campaign conducted during the 1960's, together with the treatment of all known cases. Tribute is paid to the value of the surgical rehabilitation of leprosy sufferers, the co-operation of the voluntary agency medical services, and the drugs supplied by UNICEF.

LEPROSY IN RHODESIA

The Annual Report of the Secretary for Health for the year 1970 mentions that 411 cases of leprosy were notified during the year, compared with 287 in 1969. The increase is thought to be due to greater case-finding activities in all provinces, both by medical staff and by leprosy scouts from the "Friends of Ntemwa", a voluntary organization concerned with the discovery of people suffering from leprosy and with their welfare. The availability and popularization of the domiciliary treatment of leprosy are having a beneficial effect on the leprosy campaign, and the Secretary for Health (Dr M. H. Webster) considers that the present trends point to an acceleration of the process of leprosy eradication in Rhodesia.

Lepr. Rev. (1972) 42, 252

Letters to the Editor

It was refreshing to read "Epidemiology and Leprosy Control" by Dr Meade (*Lepr. Rev.*, 1971, 42, 14) and his assertion of a long-awaited need to apply epidemiological fundamentals to the control of leprosy. Especially important is the need to focus our attention on *primary prevention.* We have long preached, and correctly so, early diagnosis and treatment, which Dr Meade points out is unlikely to contribute much towards the ultimate eradication of leprosy. Appropriately, our efforts should be paying attention not alone to reducing the established infectious reservoir, but to primary prevention directed at high-risk groups and the reduction of incidence. Unfortunately, even secondary prevention has not been, and is not being, extensively practised, and large sums of precious human and material resources are being drained from needy control efforts by institutional programs and poorly administered control programs which contribute nothing to control.

More please.

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Regional Advisor on Leprosy

23 November, 1971

LEPROSY OR HANSENIASIS?

I was very interested in the correspondence relating to a proposed new terminology to replace the stigmatizing word "leprosy".

Being a simple microbiologist, and not a leprologist or Hansenologist, I am curious to know why workers in this field propose to use the appellation "hanseniasis" and not "hansenosis"; the latter appears to me to be slightly but decidedly less of a tongue-twister and moreover would fall in line with other commonly used bacteriological nomenclatures such as Shigellosis and Salmonellosis, Listeriosis and Brucellosis as against Amoebiasis, and Leishmaniasis, and Schistosomiasis (Bilharziasis).

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Assistant Professor of Pathology

30 November, 1971

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Obituary

MARGARET FITZHERBERT, OBE
(1906-1971)

Although it was only in 1959 that Dr Margaret FitzHerbert became really interested in leprosy, she carved for herself a unique niche in the esteem of colleagues and patients in the Princess Zenebeworq Leprosy Hospital, Addis Ababa, Ethiopia. She died on 27 October, 1971, at the age of 64. At her funeral in Addis Ababa, members of the Ethiopian Royal Family, Ambassadors and Cabinet Ministers came to pay tribute to one who had spent herself in selfless service for others in Ethiopia; also present were crowds of leprosy patients, beggars and students, all come to pay their last respects to a real friend.

Margaret FitzHerbert had qualified as a doctor (MRCS, LRCP) in 1935, from the Royal Free Hospital Medical School, London, but it was only after serving for 4 years on the staff of the Bible College of Wales that she resumed medical practice. She gained the specialist diploma in obstetrics (MRCOG) in 1948, and then responded to the appeal of Emperor Haile Sellassie I to found the first midwifery unit in Addis Ababa. The Emperor showed his recognition of her sterling work by conferring on her the Order of Menelik II. In 1966, she was elected a Fellow of the Royal College of Obstetricians and Gynaecologists.

In 1959, concerned with another area of human need, she joined the Sudan Interior Mission staff at the leprosarium in Shashemane, Ethiopia, and later entered government service as medical officer to the Princess Zenebeworq Leprosy Hospital in Addis Ababa. It was here that her life-work was abundantly fulfilled. She quickly became very proficient and skilled in the diagnosis and treatment of leprosy, and endeared herself to her friends, the patients, by reason of her deep sympathy and tireless devotion. When others might legitimately plead age or a "weak heart" as excusing them from exhausting journeys and long, tiring clinics, "Dr Fitz" was always avid for work and eager to take her full share and more of responsibility.

She was a good teacher, as students attending the various courses offered by the All-Africa Leprosy Rehabilitation and Training Centre would testify, but it was as a clinician that she excelled. A Christian through and through, she not only delighted in teaching (in Amharic) in Sunday School, but did much good by stealth, devoting her salary to helping fifty or more Ethiopian students through secondary school.

In the press account of her funeral, the following sentence occurs: "Something that she kept from the public was that in the last years of her life she herself contracted leprosy and was under treatment".

Her Majesty Queen Elizabeth II honoured her by making her an Officer of the Order of the British Empire. Thousands of people in Ethiopia feel and know that

they have lost a real friend. Her total assets at her death realized less than £100. She was poor, but she had made many rich indeed by sharing with them not only her worldly goods, but also her deep faith.

S. G. BROWNE

Lepr. Rev. (1972) 42, 255-259

The Ninth Meeting of the Indian Association of Leprologists and Twelfth All-India Leprosy Workers' Conference Held at Bhopal, Madhya Pradesh*

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INTRODUCTION

A well-known map showing leprosy prevalence throughout the world paints some countries black. India, along with some other countries, appears a dull shade of grey, and the impression gained by the inexperienced observer could well be that leprosy in India is less important a problem than it is, for instance, in Nigeria. Such an impression is grossly in error. World maps of leprosy prevalence have little virtue unless they are considered side by side with the actual numbers of people infected and at risk, and with the fact that leprosy is not a disease of uniform severity the world over.

With an estimated 2½ million sufferers, India may well have more people at risk of contracting leprosy than any other nation in the world. Furthermore, in India every problem in leprosy seems to present itself in its most acute and difficult form. The nature of the disease, its persistence, its disabling effects, and its social and psychological consequences all combine to give leprosy in India a particular importance. The small army of dedicated workers, while certainly inadequate to bring the disease under control, have given much thought over the years to the problems of leprosy and its control, and many ideas and no little wisdom are the result. The experience of leprosy workers in India is thus of interest and significance to leprosy workers everywhere.

The 9th Meeting of the Indian Association of Leprologists and the 12th All-India Leprosy Workers' Conference took place at Bhopal between 24 and 29 October, 1971, at the invitation of the State Government of Madhya Pradesh. The occasion followed the well-established tradition, so aptly expressing Indian concepts of democracy, that leprosy workers of all types and levels were welcome. The presence of large numbers of paramedical and social workers, on whom falls the brunt of fighting leprosy at ground level, was an important feature. While sitting respectfully during the scientific sessions of the Indian Association of Leprologists' Meeting, they came into their own during the Leprosy Workers' Conference, and contributed to this latter a concern with basic practical issues which was very important.

* Received for publication 20 December, 1971.

The Leprologists

The 9th Biennial Conference of the Indian Association of Leprologists met first, under the distinguished Presidency of Dr V. P. Das, and was inaugurated by Shri Shyama Charan Shukla, Chief Minister, Madhya Pradesh. As papers and discussions presented at the scientific sessions will in due course appear in *Leprosy in India,* only a brief summary is indicated here, drawing attention to points of general interest and scientific progress.

Epidemiology and Control

The long tradition of epidemiological study founded by Lowe and Dharmendra in the 1930's continues to find expression at each succeeding conference. There are particular difficulties in the way of securing data of statistical significance in the Indian rural setting. Some interesting figures regarding leprosy incidence in an area covered by substantial leprosy control work were given in the paper by Drs P. S. S. Rao, A.B.A. Karat and Mrs Karat on estimates of the incidence of leprosy in Gudiyatham Taluk. In this area, with a total population of 400,000, the population survey was complete and all known cases of leprosy registered by 1966. During 1967-69 the number of new cases registered was 1922, giving an annual incidence rate of 0.8 per 1000, a lepromatous rate of 6%, and male : female and adult : child ratios of 1 : 1. These rates come much closer to the findings in other countries than do some others reported, but the incidence found gives little ground for complacency. Dr P. N. Neelan reported on relapse in lepromatous leprosy under sulphone treatment in rural conditions. As may be expected, the maximum risk of relapse occurred during the first 3 years after bacterial negativity; over a 10-year period, the figure was 1.9% per year among 2833 patients. This is not very significant, as in India bacterial negativity is often achieved only after long periods of treatment, and intermittent treatment is all too common; a finding of 3.3% relapse per year among 151 patients known to have taken irregular treatment is of more concern.

Dr S. K. Noordeen drew attention to the frequency of mono- and poly-neuritic leprosy, which he found in one-sixth of all cases detected. A lower limb was involved more frequently than an upper, and spontaneous regression of nerve lesions was quite common.

Surgical Aspects

India is proud of her pioneering rôle in reconstructive surgery in leprosy, and a whole session of the Conference was devoted to this aspect. Dr Srinivasan reported on a new corrective procedure for claw hand, described as an Extensor Diversion Graft Operation. The management of the paralysed thumb was discussed by Professor A. J. Salvapandian, including a new method of assessing the degree of thumb-web contracture, and new modifications in procedures for restoring the function of the paralysed thumb. Dr Ranney reported on a post-operative study of temporalis transfer for the relief of lagophthalmos in leprosy patients.

Reconstructive surgery in leprosy has now been accepted by surgeons in various parts of India as a legitimate challenge to their skill and ingenuity. We are now far removed from the days when one or two pioneers in this field held a leprosy

workers' conference enthralled as they opened up new vistas of hope to patients. This session could easily have taken place in a conference of orthopaedic and plastic surgeons, and there seems little doubt that with increasing sophistication that would be the right setting for the exposition and discussion of new surgical procedures, now that the basic principles and standard practice have become widely recognized.

The open forum led by Dr T. F. Davey on "Problems of therapy, with special reference to reactional states and sulphone resistance" evoked much useful discussion. The following points were made:

(1) In India only a minority of lepromatous patients are of the anergic LL variety. The dominant type is the type designated by Ridley as LI, in which an earlier dimorphous type of response has broken down, not necessarily permanently or completely. This is potentially an unstable form of leprosy, very reaction-prone, and frequently presenting very severe nerve involvement.

(2) The response of these patients to dapsone treatment tends to be slower than is usual elsewhere. Whereas it was expected in Nigeria that with good chemotherapy the Morphological Index would fall below 10% within 6 months, this is exceptional in central India, and often at least one year is needed to achieve this result.

(3) Chemotherapy with dapsone thus needs to be very prolonged. As yet we have not the basic *in vivo* data to establish that drug resistance to dapsone exists in India, but there is strong clinical evidence that it does. Many patients respond to quite low doses of dapsone (e.g., 30 mg per week) just as well as they do to the high doses still widely used (600 mg per week). Cases have been encountered in which after many years of high-dose dapsone therapy, fresh exacerbation has occurred. It seems wise, as routine, to aim at a maintenance dose which is calculated to be effective against partially resistant bacilli and, as suggested by Rees, a figure of 300 mg per week appears reasonable. There are no logical grounds for intermittent treatment–indeed this could contribute to the development of drug resistance. Once initiated, chemotherapy should be regular and persisted with for long periods. A negative skin smear is an artificial criterion for stopping chemotherapy. Apart from its intrinsic unreliability as an index that the infection has come to an end, the skin smear, because of the limitation of its technique, can never reveal the situation in muscles which can be reservoirs of the bacillus. The patient needs to accept that chemotherapy must be continued for life if he has suffered from lepromatous leprosy.

(4) Reaction in India takes several forms, some of which are not clearly understood. We need to remember that erythema nodosum leprosum (ENL) is not necessarily always induced by dapsone. More than 30 precipitating causes of ENL are known, and quite a number of these are operative in India. We should not incriminate dapsone as the cause of this complication until we have considered the other bacterial, viral, fungal, chemical, metabolic, and psychological factors which may be determinative factors.

(5) Too hasty recourse to corticosteroids in cases of reaction is to be deplored. Corticosteroids certainly have their place in acute types of reaction, especially where antimony preparations have no immediate effect. Where there is an underlying cause, we must obviously treat it. Nowadays we have in clofazimine (Lamprene, or B 663) a much more valuable remedy for reactional states, not only for controlling reaction, but as on-going chemotherapy for patients who

cannot tolerate dapsone. What is now urgently needed is the manufacture and distribution of clofazimine in India at a price the average patient can afford.

The remaining sessions of the conference had to be curtailed as some of those presenting papers could not be present. Dr Job gave a scholarly paper on the ultra-structural study of nerve lesions. Dr Parikh described leprosy lesions on the scalp. Dr Desikan described the distribution of *Myco. leprae* in various structures, Dr Pandya discussed "Electrodiagnostic aids in the differential diagnosis of leprosy", and Dr Ghosh spoke on "Leprosy and tuberculosis", while a range of papers covered other topics. Altogether, the Conference proved to be a useful forum for the sharing of experience and provided a meeting point for leprologists who in this large country often have little opportunity to meet one another.

The Leprosy Workers

In an outstanding Presidential address at the opening of the Twelfth All-India Leprosy Workers' Conference, Professor T. N. Jagadisan referred to the "disenchantment" that had come from expecting too much of the sulphones. "Unfortunately, over-enthusiasm led to over-simplification and there was an all-round expectation that through widespread administration of sulphones leprosy will quickly disappear. But it soon became apparent that the organization of control campaigns was not a soulless reaching out of drugs, but a complex, dynamic process in which many human factors were involved." He insisted that any leprosy control programme that ignores the felt need of the individual patient is doomed to failure, and pleaded for a whole view of the leprosy problem, which does not lose sight of the patient in its concern for the community.

The Conference addressed itself to three topics:

(a) Integration of leprosy control with the general medical and health services; (b) Health education for leprosy control; (c) Social and administrative aspects in relation to rehabilitation.

A. The Integration of Leprosy Control with General Medical and Health Services

This is an issue of universal interest. In some countries, leprosy has already been absorbed into the planning and practice of the general health services. India, along with some other countries, is not yet at this point of development. While all acknowledge the desirability of freeing leprosy from its peculiar significance as quickly as possible, there is real danger that precipitate action, taken before the general public are ready for it, could put the clock back by decades and cause tremendous suffering to patients. The subject was discussed at length, and a memorandum prepared by an expert committee, and addressed to the Government, was endorsed by the full conference. It is worth quoting in full, and appears as an appendix to this report (see p. 260).

B. Health Education for Leprosy Control

Much has been written in recent years on the importance of health education of the public where leprosy is concerned, and the rehabilitation of leprosy sufferers into the community. The two themes are intimately related. Behind all the problems of leprosy control and the care of patients, there broods the evil

angel of public prejudice against leprosy sufferers, and prejudice can only succumb to the enlightenment which effective health education can bring. The problem is not one of principle but of method. Where both health education and rehabilitation are concerned, we have guidance galore. What we lack is the means of effectively changing public opinion. We cannot expect more rapid progress in India than, say, in Britain in this respect. Where leprosy is concerned, prejudice dies extremely hard, whatever the form of the society involved in it. Until the truth is presented convincingly and consistently over the mass media of communication we can expect very little progress.

This is very much the case where India is concerned. Among the hundreds of millions of people in rural society the impact of the mass media is as yet minimal, and prejudice is likely to persist for a long time. In the cities, where the level of literacy is higher, and rapid social change is reducing the bastions of caste, progress could be much more rapid, but it is as yet making little headway. In Bombay, a private group of concerned professional men has made a promising entry into radio, with a regular and popular feature designed to present the truth about leprosy. Here is a noteworthy example of what can be done, but it needs widespread emulation.

In the Conference session on Health Education, these issues were recognized. Emphasis was laid on the importance of recruiting the practical interest of professional groups, and the importance of the urban situation as a point where progress could be hoped for fairly speedily, was emphasized.

C. Administrative and Social Aspects, including Rehabilitation

This session covered several points of interest.

The first paper, by G. S. Dalmia on "The changing pattern of leprosy institutions" gave welcome recognition to the place of leprosy institutions in a comprehensive national leprosy control programme. Experience in India has confirmed the importance of this. We may cope with leprosy on a domiciliary and outpatient basis to a large extent, but patients from time to time have real and urgent needs for the degree of medical care which can only be given on a hospital and residential basis. In the present situation, some specialist institutions are necessary if patients are not to be treated as second-class citizens.

The theme of the psychological rehabilitation of leprosy patients was taken up by Dr Davey in a paper which evoked much discussion.

Papers by S. W. Gokhale, Smt. Indumati, S. Rao and P. S. Damie all pinpointed and stressed the need in rehabilitation programmes not to treat our patients as a socially isolated group, but to integrate them with wider groups of the physically disabled.

Appendix

The Integration of Leprosy Control with General Health and Social Services

PREAMBLE

It is the natural evolution of specialized health services, called into being to deal with a particular problem, ultimately to be integrated into the general medical services of a country. What has already been the case with malaria control could at the proper time also be the rightful way ahead for the leprosy control programme, and then be both conducive to leprosy control and in the best interests of patients.

Undertaken precipitately, for administrative reasons only, and without due regard to the issue involved, integration could however be damaging to the best interests of patients, detrimental to leprosy control, and destructive of the progress in leprosy control achieved during the past 15 years.

The Twelfth All India Leprosy Workers' Conference gave considerable thought to this matter. After due consideration, a Committee of experienced leprologists and administrators was appointed to clarify and stress the issues which must be regarded if the integration of leprosy control work with the General Health Services is to be successful. Their findings are here presented, endorsed by the Conference, and offer outlines of the measures considered necessary if integration is to be promoted successfully without affecting the quality of the Leprosy Control Service.

Leprosy control work does not consist simply in the distribution of dapsone tablets. It involves on the one hand the comprehensive care and treatment of patients, with adequate record-keeping for assessment purposes, and on the other hand the enlightenment and protection of the general public through all that is involved in case finding and health education.

Integration means that leprosy takes its place, along with other communicable diseases, in the daily routine of every hospital, dispensary, and health centre, not only in respect of treatment, but also, as appropriate, in respect of case finding, case holding, domiciliary care and rehabilitation. It follows that the entire Health Establishment, from the Director of Medical and Health Services down to junior nurse and basic health worker, must ultimately become interested in leprosy and concerned in its control, and where personal contact with the disease is concerned, be competent in its recognition and basic treatment, and also ready to pursue the compassionate approach which alone wins the acceptance by the general public of leprosy sufferers as people like themselves. A revolution in popular thought is involved.

Recommendations

A . GENERAL POLICY

(1) Sufferers from leprosy should be accepted for treatment at all hospitals, dispensaries, and primary health centres without discrimination.

(2) Sufferers from leprosy should also be accepted without discrimination at general hospitals at Taluq, District, and other levels, and be treated for whatever disease made their admission necessary, especially when referred by doctors in charge of Control Units and S.E.T. (Survey, Education and Treatment) Centres. Necessary directives should be given in respect of both these measures.

(3) In hyperendemic areas (prevalence greater than 10 per 10,000), the work of Leprosy Control Units should continue, but no new Units should be created.

(4) In areas of lower prevalence (less than 10 per 10,000) existing leprosy control units should be replaced by a suitable number of S.E.T. Units, and adequate medical and non-medical supervision should be ensured.

(5) In areas where leprosy control work has not yet been established but there is nevertheless need for it, the S.E.T. unit has an essential rôle in the first place in breaking the ground and preparing the way for an integrated service.

(6) While most medical needs of leprosy patients should be catered for at general hospitals, there remains a residue of cases needing highly specialized diagnosis and care, including intensive physiotherapy to prevent deformity. For these, referral hospitals are needed, which can also be valuable centres for teaching. It is noted that most of the leprosy colonies are trying to become referral hospitals, and it is hoped that this process will be speeded up. In this rôle of referral and teaching centres, Voluntary Agency hospitals have an important part to play.

B. ORIENTATION AND TRAINING

(7) It is most essential to sustain the programme of integration by the orientation and training of all Medical Officers at all levels. A start should be made with Medical Officers in charge of S.E.T. Units, 6-day programmes (Monday to Saturday) being organized, utilizing all centres, whether run by Government or Voluntary Agencies, where suitable facilities can be offered.

(8) Workshops in leprosy for the benefit of Senior Medical Staff from District Medical Officer/District Health Officer and Deputy District Medical Officer/ District Health Officer level up to Director's level are also regarded as essential.

(9) Importance needs constantly to be given to the training in leprosy of medical students. Leprosy should be regarded as a part of general medicine, and training in it needs both to be emphasized and undertaken only by those who are fully competent.

(10) Short educational courses in leprosy should be arranged for Senior Administrators and Social Leaders engaged in all other community activities.

(11) Ultimately, more effective training and orientation in leprosy must progressively be envisaged for non-medical grades of general health and technical staff, including health visitors, sanitary inspectors, laboratory technicians, and physiotherapists.

(12) *Health Education:* Much more effective education of the general public is essential if progress is to be made towards integrating leprosy into the Health and Social Services. Both urban and rural populations must be reached. The object must be to encourage patients to seek sound medical advice and treatment in the early stages of their infection. Only with enlightened and sustained effort will the fear of leprosy melt away and the unique status of this disease gradually disappear from the minds of the people.

C. ADMINISTRATION

(13) It is essential for the State Leprosy Officer to continue to function, his work however becoming increasingly more that of Leprosy Consultant, related to the offering of advice, the organization and carrying out of advanced training in leprosy, and the inspection of medical units.

(14) This officer and his assistant need to be given the status of official inspecting officers, responsible not only for visiting specific leprosy units, but also for inspecting the leprosy activities of general medical units.

(15) Senior Medical Officers, from District Medical Officer/District Health Officer upwards, should ensure that Medical Officers of general hospitals, District Hospitals, Taluq dispensaries and Primary Health Centres are treating patients without any discrimination.

D. SOCIAL ASPECTS

(16) It must be emphasized that the integration of leprosy into the Social Services is as important as its integration into the Health Services.

E. PILOT STUDIES

(17) In order to gain experience in all aspects of integration, a pilot project is recommended in each State, whereby full integration is initiated on an experimental basis in one or two Districts.

(18) For the above purpose it will be necessary to organize suitable training courses which can be effective in preparing *all grades* of health staff for participation in a fully integrated health service. The subsequent assessment of such training, and of the usefulness of junior grades of worker, is essential.

(19) In pilot integrated projects it is also necessary to include the rehabilitation of handicapped leprosy patients along with other handicapped people.

F. CONCLUSION

We conclude on a note of caution. Malaria was controlled by simple mechanical procedures capable of being applied by health workers of junior grade, and without appreciable social complications. In leprosy, the situation is not at all comparable. Deeply entrenched social attitudes militate against leprosy control, and are inherited by medical and health workers just as much as by other people. The psychological effects of these on the patient, as well as the depressing experience of the disease itself, tend to lead to a diminished capacity of the patient to co-operate. Without his co-operation, there is no progress. The way of approach is thus all important. That is why so much emphasis must be placed on health education and adequate safeguards. We sincerely believe that integration is the right way ahead, but this must come in stages, and only after adequate preparation.

The Committee consisted of:
Dr T. F. Davey (Chairman),
Prof. T. N. Jagadisan, President of the Conference, and Drs V. Ekambaram, P. Kapoor, M. S. Nilakanta Rao, Shanti N. Mathur and V. K. Sharma.

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The Results of Physiotherapy in Leprosy Patients with Early Paralysis*

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A total of 142 patients who had suffered from different types of leprosy (having, in all, 180 nerve lesions) were given physiotherapy. The majority of them, irrespective of the type of leprosy, improved markedly from regular physiotherapy, and the benefits persisted after treatment had stopped. The improvement was much less marked when therapy was irregular.

Introduction

A perusal of the literature on physiotherapy in leprosy reveals much information on techniques, appliances and equipment. In comparison, detailed analyses of the results of physiotherapy are scanty. In the present study an attempt has been made to determine the extent of recovery and maintenance of muscle function in patients with early paralysis.

Materials and Methods

A total of 142 patients with some muscle paralysis of less than 3 months' duration were selected for physiotherapeutic treatment; all of them had either isolated or combined nerve damage affecting 180 principal peripheral trunks. All were assessed clinically and electrically both before and after treatment, and then followed up. The treatment was given daily for 3 to 6 months.

Evaluation of muscle power, based on the International Scale, was combined with an assessment of nerve function, to give a scale of I to IV in order of increasing severity of damage. Two patients showed neuropraxic lesions—clinical paralysis, and no electrical evidence of degeneration.

The physiotherapeutic procedures adopted were as follows: prevention of deformity (by splinting); encouragement of function (by active exercises); maintenance of full range of joint movements (by passive exercises); maintenance of good circulation (by wax baths and oil massage); and prevention of muscle atrophy (by electrical stimulation).

Results

Table 1 gives details of the number of patients assessed before treatment and the improvement or deterioration observed.

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TABLE 1

Grade before treatment	Total no. of nerve lesions	Grades after treatment				
		0	I	II	III	IV
0	2	2	–	–	–	
I	10	7	–	–	–	3
II	109	33	3	–	–	73
III	59	9	26	4	–	20
Total	180	51	29	4	–	96

To determine the reason why patients with early lesions deteriorated (3 with Grade-I and 73 with Grade-II lesions) these cases were further analysed, with the results shown in Table 2.

TABLE 2

Grade before treatment	Type of leprosy	No. of patients	Treatment					
			Regular			Irregular		
			Impr.	Unimpr.	Total	Impr.	Unimpr.	Total
I	T	10	7	–	7	–	3	3
	I	–	–	–	–	–	–	–
	L	–	–	–	–	–	–	–
		10	7	–	7	–	3	3
II	T	95	26	2	28	5	62	67
	I	6	2	–	2	–	4	4
	L	8	3	–	3	–	5	5
		109	31	2	33	5	71	76

T, tuberculoid; I, indeterminate; L, lepromatous.

It would appear that the sole reason for failure to improve in the case of the 3 patients originally classed as Grade I lay in the fact that they were irregular in following the treatment offered. But among the patients in Grade II, 2 did not recover in spite of regular treatment, while 5 of those whose treatment was irregular recovered. The 59 patients in Grade III are similarly analysed with respect to regular and irregular treatment, with the results as shown in Table 3.

TABLE 3

Grade before treatment	Type of leprosy	Regular			Irregular		
		Impr.	Unimpr.	Total	Impr.	Unimpr.	Total
III	T	30	1	31	2	15	17
	I	7	–	7	–	–	–
	L	–	–	–	–	4	4
		37	1	38	2	19	21

The majority of patients whose original assessment was Grade III showed some degree of improvement: 39 lesions out of 59.

From among the 84 patients who had improved and had ceased having physiotherapy, 26 were seen again after 2 years. In only 3 of them was the improvement not maintained. It would seem that physiotherapy is of benefit not only temporarily, or for as long as it is continued, but also for a variable time afterwards.

Acknowledgements

I thank Dr N. Figueredo, Ex-Special Officer, Acworth Leprosy Hospital, for valuable guidance, and Dr N. D. Katdare, Superintendent, Acworth Leprosy Hospital, for permission to use the hospital records and for his helpful suggestions. I also wish to thank Dr (Mrs) S. S. Pandya (Tata Department of Plastic Surgery, J.J. Group of Hospitals, Bombay) for her help in the preparation of this paper.

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Intravenous Regional Analgesia for Hand Surgery in Leprosy*

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Introduction

The production of surgical analgesia in the limbs by intravenous injection of a local anaesthetic, was introduced by Bier (1908). The procedure involves exsanguination of the extremity by elevation and compression, and the application of a tourniquet. The anaesthetic solution, which is injected into the vein, diffuses into the tissue and blocks the nerve endings.

Technique

A sphygmomanometer cuff is placed high on the upper arm of the limb to be operated on, and the hand is prepared and draped. A Mitchell's needle is then introduced into a prominent vein on the dorsum of the hand, the arm is elevated for 5 min, and if necessary the extremity is exsanguinated with a sterile Esmarch bandage. The sphygmomanometer cuff is inflated to a pressure of 220 mmHg, and 15 ml of 1% Xylocaine solution is injected through the needle. We prefer Xylocaine solution to procaine because it seems to diffuse more easily across the endothelium. Some anaesthetists apply two tourniquets on the arm in an attempt to avoid discomfort, since the pressure of the tourniquet is felt by the patient after about 50 min. At the end of the operation the tourniquet is released intermittently in order to allow the drug from the exsanguinated area to enter the systemic circulation slowly. Too rapid a release may produce a generalized response resulting from flooding of the tissues with anaesthetic solution.

During the past 5 years, of the 1472 operations performed on the hand at this institution, regional anaesthesia was used in 1124 cases; 80% of the operations were for tendon transplantation, and the remainder were for fractures and other injuries. Plantaris tendon required as graft for tendon transplant was removed under Trilene anaesthesia. Four wrist fusions, and several reductions of fractures of the forearm bones, both open and closed, were also performed under intravenous regional anaesthesia. Since the anaesthesia lasts for about 15 min after the tourniquet is deflated, this was done before the skin sutures were inserted.

With good technique, 100% success rate is achieved; our failures were due to a leaking tourniquet. Out of this large series, systemic response has occurred on a few occasions only. In one case the patient developed convulsions and

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hypotension as the tourniquet was deflated 5 min after the injection. He was given 2 ml of Thiopental intravenously (100 mg) to control the convulsions, together with 8 mg of Dexamethasone and inhalations of oxygen; he remained disorientated for over 1 h after recovering.

Four patients developed hypotension, but this was of a degree that did not require treatment. If the forearm is not exsanguinated sufficiently the venous pooling of blood may hamper the surgeon.

In persons over 12 years of age, we have used a 1% solution, instead of 0.5% of Lignocaine to produce intense analgesia in the forearm. No systemic response was observed after releasing the tourniquet suddenly after 40 min. The low incidence of central nervous system and cardiovascular effects is, according to Knapp and Weinberg (1967), due to the rapid tissue uptake of the drug from the blood. Mazze & Dunbar (1966) have shown in man that with intravenous regional anaesthesia the plasma concentration of the drug is actually less than with conventional axillary block. Foldes *et al.* (1960) also found that the blood levels of the drug after release of the tourniquet were much lower than those associated with central nervous system toxicity.

This technique is particularly useful in hospitals like ours where the surgeon has to work single-handed. It is simple and safe, and with a good tourniquet and proper exsanguination of the extremity complete analgesia is achieved.

References

Bier, A. (1908). Über einen neuen Weg Localanasthesie an den Gliedmassen zu erzeugen. *Arch. klin. Chir.* **86**, 1007.

Földes, F. F., Molloy, R., McNall, P. G. and Koukal, L. R. (1960). Comparison of toxicity of intravenously given local anesthetic agents in man. *J. Am. med. Ass.* **172**, 1493.

Goodman, S. and Gilman, A. (1968). *The Pharmacological Basis of Therapeutics,* 4th ed. New York: Macmillans.

Knapp, R. B. and Weinberg, M. (1967). Drug distribution following intravenous regional anaesthesia. *J. Am. med. Ass.* **199**, 760.

Mazze, R. I. and Dunbar, R. W. (1966). Plasma lidocaine concentrations after caudal, lumbar, epidural, and axillary block and intravenous regional anaesthesia. *Anaesthesiology* **27**, 574.

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Serum Complement (C3) in Leprosy*

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Serum complement (C3) was estimated in fresh sera of 45 leprosy patients and 10 healthy controls. Most of the patients with lepromatous leprosy showed an elevated complement level, but 4 out of 6 patients during the first 2 weeks of acute erythema nodosum leprosum (ENL), with or without proteinuria, showed a depressed complement level. Follow-up of one of the latter patients showed that such reduction in complement is only temporary. This suggests that there is an antigen-antibody reaction, with utilization of complement, during the early stage of ENL, which is often associated with proteinuria.

Introduction

Evidence that antigen-antibody reactions may be occurring in a patient can be gained from the amount of complement present in the serum. Thus in serum sickness, acute nephritis, and systemic lupus erythematosus, diseases in which antigen-antibody reactions presumably occur *in vivo,* complement titres are depressed (Boltax & Fischel, 1956; Gewurz *et al.,* 1966). However, complement titres are raised in a number of acute inflammatory conditions, such as acute infectious diseases, rheumatic fever, rheumatoid arthritis, and myocardial infarction (Gewurz *et al.,* 1966; Rapp & Borsos, 1966).

While most authors (Sheagren *et al.,* 1967, 1969; Saitz *et al.,* 1968; Wemambu *et al.,* 1969; Sacher *et al.,* 1970; Mayama, 1971) have reported complement to be elevated in leprosy, others have reported it to be absent (Eliasberg, 1911), normal or slightly depressed (Bonatti & Castro, 1945), or depressed in many patients undergoing severe leprosy reactions (Azevedo & Melo, 1966; Bonomo & Dammacco, 1968, 1969; Meneghini C-Trimigliozzi *et al.,* 1969). The study on serum complement in leprosy was therefore repeated, special emphasis being accorded to its presence in different stages of the lepra reaction.

Materials and Methods

Serum complement (C 3) (βic-βia) estimations were carried out on fresh sera collected from 45 leprosy patients at the Hospital for Tropical Diseases, London. The sera of 10 normal healthy subjects (also from the tropics) were included in the study as controls. One patient with acute erythema nodosum leprosum (ENL) and proteinuria, in whom the level of complement was found to be depressed, was

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followed at monthly intervals for 3 months. The estimation of complement (C 3) was carried out by the radial diffusion method (Mancini *et al.*, 1963), using the specific antibody in agar gel plates, and the standard C 3 complement purchased from Hyland Laboratories, California, U.S.A. Sera were diluted for retesting when the diameter of the precipitation zones was greater than that of the highest standard complement. The levels of complement are expressed in mg per 100 ml.

Results

The patients with non-lepromatous leprosy had a mean serum complement level close to that of the controls, viz: 133.0 and 139.4 mg per 100 ml respectively.

Among patients with lepromatous leprosy a wide range of the level of complement was recorded. Most of the patients, with or without ENL reaction, had a raised serum complement level, but among the patients with acute and severe reaction of recent onset there was a reduction in serum complement in 4 out of 6 patients. The difference is significant when this group of patients is compared with other lepromatous leprosy patients with no reaction or to those with chronic ENL ($P < 0.01$) The results are summarized in Table 1 and Fig. 1.

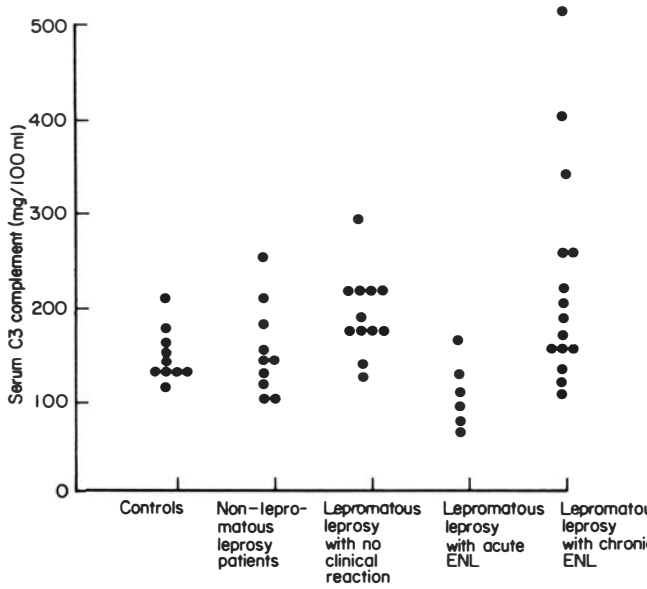

Fig. 1. Serum complement (C3) in different groups of leprosy.

A follow-up study of one patient showed that serum complement was reduced (to 65 mg per 100 ml) only in the early stage of ENL and proteinuria. During the course of the reaction the serum complement level rose again (Figs 2 and 3).

TABLE 1
Serum complement (C3) in different leprosy groups

Group	No. of patients studied	Serum complement level mean (standard deviation) (mg/100 ml)	
Controls	10	134.9	(34.9)
Non-lepromatous leprosy	10	133.0	(48.2)
Lepromatous leprosy with no lepra reactions	12*	183.1	(41.2)
Lepromatous leprosy with chronic lepra reactions	17**	222.4	(120.1)
Lepromatous leprosy with acute lepra reaction	6***	100.0	(37.2)

* includes 2 patients with chronic renal failure.
** includes 7 patients with proteinuria.
*** includes 3 patients with proteinuria.

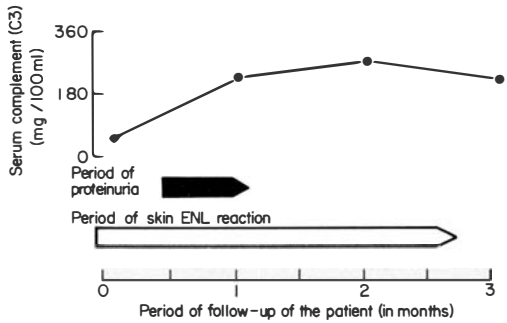

Fig. 2. Follow-up study of a patient showing the relation between the fall in serum complement, ENL, and proteinuria.

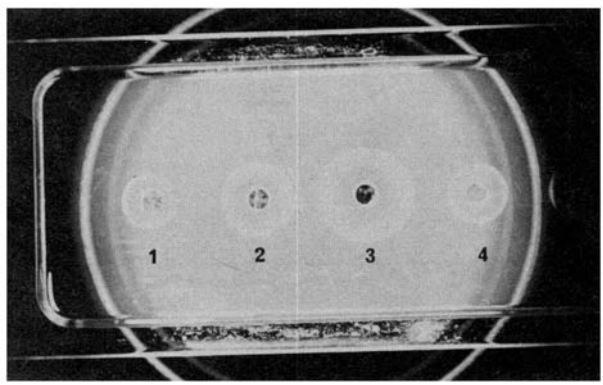

Fig. 3. Immuno-diffusion plate for assay of human complement C3 (βic-βia) after incubation with 3 reference standards and serum from a patient with lepromatous leprosy during the first 2 weeks of reactions and proteinuria, showing the fall in complement level of patient's serum. The first 3 wells belong to reference standards 60,185 and 360 mg per 100 ml respectively. The 4th well, which contains the patient's serum showed the diameter of the precipitation ring equivalent to 65 mg per 100 ml.

Discussion

In this study a depressed level of complement (below 90 mg per 100 ml) was recorded in 4 out of 6 patients within the first 2 weeks of acute ENL, with or without proteinuria. Among other patients with lepromatous leprosy, including those with no lepra reactions, the serum complement value was raised in most cases.

In leprosy, conflicting results have been reported as regards the level of serum complement. Sheagren *et al.* (1967, 1969) reported the concentration of C 3 complement as normal in all patients with uncomplicated leprosy, but found it elevated in lepromatous leprosy patients with ENL or amyloidosis. Saitz *et al.* (1968) reported that C 2 complement levels were within the normal range among lepromatous leprosy patients without ENL, but the titres were distinctly raised in most borderline cases and in cases with an ENL type of reaction. Wemambu *et al.* (1969) reported that 5 out of 17 patients with ENL had a serum complement value (C 3) over 250 mg per 100 ml, and none of them had levels below those found in normal subjects. Sagher *et al.* (1970), in their study on more than 300 sera, reported that complement levels tended to be elevated in patients with active lepromatous leprosy, as well as in patients suffering from lepra reactions, though they tended to be lower during the quiescent phase of reaction. Mayama (1971), in a study of 38 patients with leprosy, also found a marked increase in serum complement in lepromatous leprosy patients with ENL.

On the other hand, other workers have reported serum complement in patients with leprosy as absent (Eliasberg, 1911) or normal or slightly diminished (Bonatti & Castro, 1945). More recently Bonomo and Dammacco (1968, 1969) reported that 50% of lepromatous leprosy patients had low complement levels, and Meneghini C-Trimigliozzi *et al.* (1969) in their study on 80 leprosy patients found low complement levels as measured by serum haemolytic activity, in many cases with strong leprosy reactions.

Such differences could be due to the differences in the method of estimating serum complement, and also to the stage of the ENL reaction. In the present study the fall in serum complement during the early stage of ENL and proteinuria provides indirect evidence that an antigen-antibody reaction, with utilization of complement, occurs in patients with lepromatous leprosy. Serum complement is raised in a number of inflammatory conditions, and therefore the increase in serum complement which is found in most patients with lepromatous leprosy is not altogether surprising.

This finding is in agreement with the reports of Wemambu *et al.* (1969) who demonstrated granular deposits of immunoglobulins and complement in the skin of patients with acute ENL and suggested that ENL reaction is a manifestation of the Arthus phenomenon; and also of Tin Shwe (1971) who has demonstrated granular deposits of immunoglobulins and complement in the glomeruli of 3 out of 7 patients with lepromatous leprosy and proteinuria, and suggested that the chronic renal failure so common in leprosy is possibly due to deposition of antigen-antibody complexes in the kidney. It also confirms the findings of Tin Shwe and Petty (1971) who demonstrated activation of complement (C 3) by immuno-electrophoresis in fresh plasma of 6 lepromatous leprosy patients with proteinuria, and suggested that in lepromatous leprosy there is a stage of antigen-antibody complex formations.

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References

de Azevedo, M. P. and de Melo, P. H. (1966). A comparative study of the complementary activity of serum in the polar forms of leprosy and in leprosy reaction. *Int. J. Lepr.* **34**, 34.

Boltax, A. J. and Fischel, E. E. (1956). Serologic tests for inflammation. Serum complement, C-reactive protein, and erythrocyte sedimentation rate in myocardial infarction. *Am. J. Med.* **20**, 418.

Bonatti, A. A. and Olmos Castro, N. (1945). Dosaje del complemento en sueros leprosos. *Rev. Argent. Dermatosif.* **29**, 301. Quoted in Saitz, E. W., Dierks, R. E. and Shepard, C. C. (1968). *Int. J. Lepr.* **36**, 400.

Bonomo, L. and Dammacco, F. (1960). Protein changes in immunity in some chronic infectious diseases. In "Proceedings of the International Symposium on Gummapathies, Infections, Cancer, and Immunity", p. 12 (eds Clini, V., Bonomo, M., and Sirtori, C.). Carl Erbo Foundation, Milan.

Bonomo and Dammacco (1969). Personal communication. Quoted in Wager, O. (1969). *Bull. Wld Hlth Org.* **41**, 793.

Eliasberg, J. (1911). Über das Fehlen freien komplementes im Blute Leproser. *Dtsch. Med. Wschr.* **37**, 302. Quoted in Saitz, E. W., Dierkes, R. E. and Shepard, C. C. (1968). *Int. J. Lepr.* **36**, 400.

Gewurz, H., Pickering, R. J., Muschel, L. H., Mergenhagen, S. E. and Good, R. A. (1966). Complement dependent biological functions in complement defiency in man. *Lancet*, ii, 356.

Mancini, G., Vaerman, J. P., Carbonara, A. O. and Heremans, J. F. (1963). In Proceedings of the 11th Colloquium on *Protides of the Biological Fluids*. Edited by H. Peeters. p. 370 Amsterdam: Elsevier.

Mayama, A. (1971). Complement factors in lepromatous patients with erythema nodosum leprosum (Abstract). *Int. J. Lepr.* **39**, 91.

Meneghini C-Trimigliozzi, G., Lospalluti M-Angelini, G. and Bonifazi. (1969). Immunological and haematological research in leprosy. Second World Congress of the International Society in Tropical Dermatology. (Abstracts). Kyoto, Japan. p. 29.

Rapp, H. G. and Borsos, T. (1966). Complement research. Fundamental and applied. *J. Am. Med. Ass.* **198**, 1347.

Sagher, F., Sheskin, J., Zlotnik, A. and Turk, J. L. (1970). Complement and immunoglobulins in leprosy and leprosy reactions. (Abstract) Summaries of International Leprosy Colloquium. Forschungsinstitut Borstel. p. 67.

Saitz, E. W., Dierks, R. E. and Shepard, C. C. (1968). Complement and second component of complement in leprosy. *Int. J. Lepr.* **36**, 400

Sheagren, J. N., Block, J. B., Trautman, J. R. and Wolff, S. M. (1967). Immunologic reactivity in leprosy. (Abstract). *Clin. Res.* **15**, 300.

Sheagren, J. N., Block, J. B., Trautman, J. R. and Wolff, S. M. (1969). Immunologic reactivity in patients with leprosy. *Ann. intern. Med.* **70**, 295.

Tin Shwe. (1971). Immune complexes in glomeruli in patients with leprosy. *Lepr. Rev.* **42**, 282.

Tin Shwe and Petty, R. E. (1971). Activation of complement (C 3) in patients with leprosy. *Lepr. Rev.* **42**, 277.

Wemambu, S. C. N., Turk, J. L., Waters, M. F. R. and Rees, R. J. W. (1969). Erythema nodosum leprosum a clinical manifestation of the Arthus phenomenon. *Lancet* ii, 933.

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Hepatitis Associated Antigen (HAA) in Leprosy*

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This report confirms earlier findings of the increased frequency of HAA in leprosy patients. This association is investigated in relation to various characteristics of the sample studied. It is concluded that the impaired immune mechanism in lepromatous leprosy is mainly responsible for the observed association, rather than other factors such as treatment or confinement of the patient

Introduction

The close association of the hepatitis-associated antigen (HAA) with viral hepatitis has been well established (Blumberg *et al.*, 1967*a*; Memorandum, 1970; Papaevangelou *et al.*, 1971). Its increased frequency in lepromatous leprosy and in other chronic diseases characterized by impairment of the immune mechanism, has been reported (Blumberg *et al.*, 1967*b*; London *et al.*, 1969; Salazar Mállen *et al.*, 1970). However, Salzano and Blumberg (1970) suggested that this is true only for areas where HAA is common in the general population. We have therefore studied the distribution of HAA in 427 leprosy patients in order to investigate its possible relation to the various characteristics of these patients. The findings of this study are here reported.

Materials and Methods

We examined 427 leprosy patients born and living in various regions of Greece. They comprise one-third of all the leprosy patients in Greece under close observation; 363 of them were in-patients at the only residential institution for leprosy in Greece, the Infectious Diseases Hospital, Athens. The remaining 64 patients were under treatment at the out-patient clinic of the same institution.

Patients were carefully examined and a complete questionnaire about their past history and present condition was completed. Thus, we were able to classify them by leprosy type, viz: lepromatous 187, tuberculoid 153, and indeterminate 87 and to cross-classify them by age, sex, duration of the disease, bacteriological status, and type of treatment received. The differences in the incidence of HAA among the various subgroups of each characteristic studied were compared after standardization for the type of disease (Armitage, 1971). The presence of *Myco. leprae* was determined by special examination of the leprosy lesions as well as from the naso-pharyngeal mucosa and the blood.

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The double immunodiffusion technique in 0.9% agarose, as described by Prince (1968), was used for the detection of HAA. Blood samples were collected under aseptic conditions and sera were separated immediately and kept at −20°C till tested. The serum of a patient with polytransfused thalassaemia served as the source of antibody; its titre varied between 1/16 and 1/64. Reactions of immunological identity were obtained with reference antisera kindly provided by Dr Blumberg and Prince.

Results

HAA was detected in 17 (4.0%) out of the 427 patients examined. Its frequency was equally high in the lepromatous (5.9%) and indeterminate (5.7%) type of leprosy, but significantly ($P< 0.05$) lower (0.7%) in the tuberculoid type of the disease. Table 1 shows the incidence of HAA by the characteristics studied

TABLE 1

Comparison of the frequency of HAA by various epidemiological characteristics before and after standardization for the type of leprosy

Comparison		No. Patients	HAA positive	Crude frequency (%)	Frequency (%) after standard. For type of disease
Sex	Males	241	11	4.6	4.1
	Females	186	6	3.2	3.8
Age (years)	<30	24	1	4.2	3.7
	30-49	167	7	4.2	3.6
	>50	236	9	3.8	4.1
Duration of disease (years)	<5	89	1	1.1	1.0
	5-14	158	7	4.4	5.2
	>15	180	9	5.5	4.5
Confinement to Institution	In-patients	363	15	4.1	4.2
	Out-patients	64	2	3.1	3.0
Bacteriological status	Positive	112	1	0.9	0.7
	Negative	315	16	5.1	5.8
Treatment	Parenteral	70	4	5.7	5.4
	Oral	357	13	3.6	3.7

before and after adjustment for the type of leprosy. HAA is more common in males (4.1%) than in females (3.8%), but the difference does not reach the 5% level of significance. HAA frequency does not vary significantly ($P> 0.1$) with the age of the leprosy patients. The frequency is slightly higher in the in-patients (4.2%) than in the out-patients (3.0%) and also in patients treated parenterally (5.4%) than in those under oral treatment (3.7%), but in both comparisons that difference is not statistically significant ($P< 0.05$). The frequency of HAA increases with increasing duration of the disease, being lowest in those with disease of less than 5 years' duration (1.0%). HAA is not associated with the detection of *Myco. leprae.* Its frequency is significantly ($P < 0.05$) higher in the absence (5.1%) than in the presence (0.9%) of *Myco. leprae.*

Discussion

HAA is common in the general population of Greece; its frequency in a representative sample of healthy persons was found to be 1.9% (Papaevangelou & Kourea, 1972). In the present study we were able to confirm the increased frequency of HAA in leprosy patients previously reported (Blumberg *et al.*, 1967*b*; Salazar Mállen *et al.*, 1970). Thus HAA was more common in the leprosy patients studied (4.0%) than in the general population. Comparisons among the patients showed that this association was apparent for those with the lepromatous and indeterminate types of the disease. However, HAA was less common in patients with tuberculoid leprosy than in the general population.

Alterations in some aspects of immunological reactivity, including decreased reactivity to lepromin, generalized impairment of delayed hypersensitivity (*Wld Hlth Org.*, 1970), and impaired lymphocyte transformation have been reported (Sheagren *et al.*, 1969). Salzano and Blumberg (1970) suggested that the increased frequency of HAA in lepromatous leprosy, as well as in other chronic diseases (such as Down's syndrome, etc.), is due to an inadequate immune mechanism, which renders such patients more susceptible to chronic infection with hepatitis.

We studied the effects of the other factors after correcting for the observed different frequency of HAA in relation to type of leprosy. Our results are not much at variance with the findings of Blumberg *et al.* (1967*b*) as far as the sex distribution of HAA in leprosy patients is concerned, although the observed increased frequency in males did not reach the 5% level of significance in our sample. However, we were not able to confirm the reported decrease in the frequency of HAA with increased age of leprosy patients (Blumberg *et al.*, 1967*b*).

The majority of the patients were confined in a residential institution, but some patients with lepratomous, indeterminate or tuberculoid disease were treated as out-patients. After correction for the type of leprosy, the frequency of HAA was not significantly higher in in-patients than in out-patients ($P > 0.1$).

HAA is associated with the serum hepatitis (B) type of virus (Krugman & Giles, 1970). In the sample studied HAA was more common in patients under parenteral treatment than in those treated orally, but the difference was not significant ($P > 0.1$). It is believed therefore that neither admission to hospital, which helps the spread of infectious diseases transmitted through the oral-faecal route, nor iatrogenic transmission is mainly responsible for the increased frequency of HAA observed in leprosy patients.

HAA does not seem to be related to the presence of *Myco. leprae* or to products of the host's reaction to it. The presence of this organism was not associated with the detection of HAA; on the contrary, in the patients negative for *Myco. leprae*, HAA was more common. This is in agreement with the increased frequency of HAA observed in patients who had had the disease for more than 5 years.

The observed increased frequency of HAA in lepromatous leprosy patients is thus mainly due to impairment of the immune mechanism, which renders them more susceptible to infection with the hepatitis virus and also interferes with its elimination. Iatrogenic transmission, lower health standards associated with confinement, or other factors seem to be of less importance.

References

Armitage, P. (1971). In *Statistical Methods in Medical Research.* p. 388. Oxford: Blackwell Scientific Publications.

Blumberg, B. S., Gerstley, B. J. S., Hungerford, D. A., London, W. T. and Sutnick, A. I. (1967*a*). A serum antigen (Australian antigen) in Down's syndrome, leukemia and hepatitis. *Ann. intern. Med.* **66**, 924.

Blumberg, B. S., Melartin, L., Lechat, M. and Guinto, R. (1967*b*). Association between lepromatous leprosy and Australian antigen. *Lancet* **ii**, 173.

Krugman, S. and Giles, J. P. (1970). Viral hepatitis. New light on an old disease. *J. Amer. med. Ass.* **212**, 1019.

London, W. T., Sutnick, A. I. and Blumberg, B. S. (1969). Australian antigen and acute hepatitis. *Ann. intern. Med.* **70**, 55.

Memorandum. (1970). Viral hepatitis and tests for the Australia (hepatitis-associated) antigen and antibody. *Bull. Wld Hlth Org.* **42**, 957.

Papaevangelou, G. J., Kourea, T. and Tsoukas, S. (1971). Hepatitis-associated antigen in acute viral hepatitis in Greece. *Path. Microbiol.* **37**, *361.*

Papaevangelou, G. J. and Kourea, T. (1972) Frequency of HAA in a representative sample of healthy Greek persons. *Acta Microb. Hell.* **17**, 99.

Prince, A. M. (1968). An antigen detected in the blood during the incubation period of serum hepatitis. *Proc. nat. Acad. Sci., Wash.* **60**, 814.

Salzano, F. M. and Blumberg, B. S. (1970). The Australia antigen in Brazilian healthy persons and in leprosy and leukemia patients. *J. clin. Path.* **23**, 39.

Sheagren, J. N., Block, J. B., Trautman, J. R. and Wolfe, S. M. (1969). Immunologic reactivity in patients with leprosy. *Ann. intern. Med.* **70**, 295.

World Health Organization (1970). WHO expert committee on leprosy: Fourth report. *Wld Hlth Org. Techn. Rep. Ser.* No. 459, Geneva.

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Activation of Complement (C3) in Patients with Leprosy

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Evidence of activation of complement (C3), detected by altered mobility on immuno electrophoresis, was found in the fresh plasma of patients with lepromatous leprosy and proteinuria, with or without lepra reactions, but not in patients with other forms of leprosy. This may result from circulating antigen-antibody complexes. Such immune complexes if deposited in the capillary walls of the skin might cause erythema nodosum leprosum, and if deposited in the kidneys might cause proteinuria.

Introduction

Proteinuria is frequent in leprosy patients with a high bacterial index in skin smears, an acute erythema nodosum leprosum (ENL) reaction or reversal type of reaction, and occurs in some patients with lepromatous leprosy without skin reactions. Using the indirect fluorescent antibody technique, Wemambu *et al.* (1969) demonstrated deposition of immunoglobulins and complement in the skin lesions of patients with acute ENL. Also, by the fluorescent antibody technique, Tin Shwe (1971) has demonstrated the depositions of immunoglobulins and complement in renal glomeruli of 2 patients suffering from proteinuria and reversal reaction, and in one other patient with proteinuria without skin reaction.

Since such immune complexes activate complement, a study of C3 levels and immuno-electrophoretic characteristics of this complement component (βic in immuno-electrophoresis nomenclature) was undertaken.

Patients and Methods

Twenty-one leprosy patients attending the Hospital for Tropical Diseases, London, were chosen for study. All the patients were classified according to the criteria of Ridley and Jopling (1966). A control group of 4 members of the staff of the Hospital for Tropical Diseases was included in the study. Specimens of

blood from patients and controls were collected at the same time in tubes containing EDTA (ethylenediamine tetra-acetic acid). After immediate centrifugation, the fresh plasma specimens were subjected to electrophoresis on the same agar slide (barbitone buffer I = 0.9, pH = 8.6) at +4° C for 1 hour (Soothill, 1967). Specific anti-βic-βia antisera prepared by Behringwerke were used. The slides were examined 24 h after electrophoresis. Two of the patients in whose serum alteration of the complement component was detected were followed at intervals for up to 4 months.

Quantitative estimation of C3 was made on the same plasma samples using Hyland immunoplates for radial diffusion. The results were expressed in mg per 100 ml, using the standards supplied with the plates. Proteinuria was detected by the sulphosalicylic acid test.

Results

Immuno-electrophoresis of plasma of all normal subjects used as controls revealed a single normal (uncoverted) β ic arc (Fig. 1). This normal result was also obtained in the 4 patients with non-lepromatous leprosy and in the 7 patients

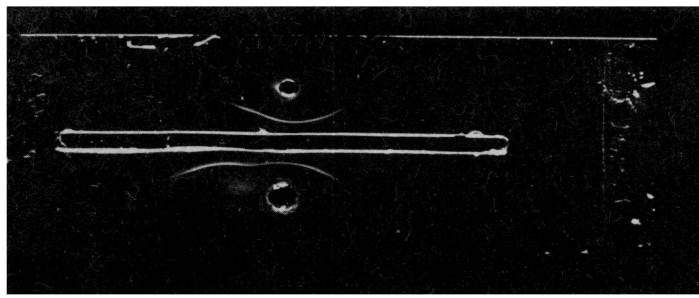

Fig. 1. Altered complement component in leprosy patient with proteinuria and reactions (above) compared with normal control (below).

with lepromatous leprosy but with no skin reactions and no proteinuria. Altered βic was detected in all 3 patients with recent ENL (duration less than 2 weeks) and proteinuria. The patient who had lepromatous leprosy and ENL for 18 months but no proteinuria did not show the reacted β-ic.

Of the other 6 patients with lepromatous leprosy and proteinuria, 3 showed this complement change. One had a reversal reaction, but the other 2 had no present skin reaction. Of the 3 who were negative, one had had a renal transplant for chronic renal failure and was receiving immunosuppressive treatment, one had renal failure due to amyloid, and the 3rd patient, who had had leprosy for 30 years, suffered a relapse.

Immunochemical estimation of C3 gave a wide range of results (Table 1). Only patient No. 25, who had had reacted βic, gave a low value, and he had had ENL for the shortest time, namely one week.

Two patients were followed sequentially. In patient no. 23 (LL with proteinuria and skin reactions), altered βic was detected 3 months prior to, and also during, the period of clinical skin reaction (ENL). The βic electrophoresis

TABLE 1

Clinical and immunological features of patient groups

Patient group	Serial No.	Age	Sex	Classification	Special clinical features	Serum C3 level (mg/100 ml)	Altered complement component βic/βia
Controls	1	36	M			135	–
	2	47	M			132	–
	3	31	F			110	–
	4	20	M			145	–
Non-lepromatous leprosy	5	36	M	BB		148	–
with no proteinuria	6	20	F	BB		130	–
	7	38	F	TT		142	–
	8	23	M	BT		105	–
Lepromatous leprosy, no reactions	9	34	M	LL	No ENL for 1 yr	80	–
and no proteinuria	10	47	M	LL	Trophic ulcer 6 months	170	–
	11	39	F	BL	Reversal reaction 1 yr. ago	285	–
	12	71	F	LL	Trophic ulcer 8 yrs	210	–
	13	62	M	LL	No reactions in the past	120	–
	14	71	M	LL	No ENL for 3 yrs	196	–
	15	38	M	LL	No reactions in the past	185	–
Lepromatous leprosy with chronic ENL–no proteinuria	16	46	M	LL	ENL 18 months	150	–
Lepromatous leprosy and proteinuria	17	21	F	BL	Reversal reaction	152	+
	18	25	M	LL	Hepatosplenomegaly, no skin reaction	210	+
	19	31	F	LL	No reaction in skin	200	+
	20	33	M	LL	Renal transplant; 6 yrs on immunosuppressives	85	–
	21	52	M	LL	Renal failure due to amyloidosis for 9 months	160	–
	22	64	M	LL	Leprosy 30 yrs, in relapse hypertension 20 yrs	210	–
Lepromatous leprosy with acute ENL and proteinuria	23	23	M	LL	Acute ENL 2 weeks	220	+
	24	47	M	LL	Acute ENL 2 weeks	165	+
	25	46	M	LL	Acute ENL 1 week	60	+

then became normal as the ENL subsided, but abnormal βic was again detected prior to and during the period of proteinuria which followed. Subsequently, further studies gave normal results (Fig. 2). Patient no. 24 (LL with proteinuria and skin reactions) had proteinuria and ENL at the time when electrophoretically altered βic was first detected. This disappeared after the ENL and proteinuria cleared up.

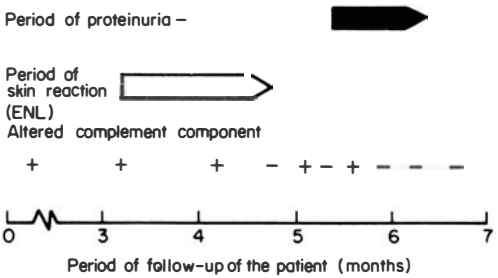

Fig. 2. Time relationships between the presence of altered complement in the plasma and the presence of skin reactions and proteinuria in patient no. 23.

Discussion

It is believed that the low serum complement level frequently found in patients with acute glomerulonephritis is partly due to utilization of complement components in an antigen-antibody reaction. This provides indirect evidence for an immunological basis for glomerulonephritis. Electrophoretic alteration of βic can be induced by *in vitro* exposure of normal plasma to an antigen-antibody reaction (Müller-Eberhard & Nilsson, 1960). Soothill (1965, 1967) has demonstrated that this change occurs *in vivo* in patients with acute glomerulonephritis (with or without low complement levels) and in some patients with the nephrotic syndrome due to proliferative glomerulonephritis, and membranous glomerulonephritis. Morse *et al.* (1962) and Lachmann (1963) had also demonstrated a similar phenomenon in patients with active systemic lupus erythematosus. One possible cause could be the presence of circulating soluble antigen-antibody complexes. In the present study we have demonstrated the presence of electrophoretically altered complement in all 3 of the 3 patients with a recent ENL reaction and proteinuria, and in 3 out of 6 lepromatous leprosy patients with proteinuria. The 3 patients with proteinuria, but no reacted complement, had other likely explanations for their proteinuria, namely renal transplant, amyloid, and hypertension respectively; 12 other patients without proteinuria showed no βic changes.

Towards the end of the first year of treatment most patients with lepromatous leprosy have ENL and some have reversal reactions. During this phase, bacterial morphology in skin smears changes from the solid to the granular form, indicative of cell death. This is presumed to be associated with antigen release and formation of complement activating antigen-antibody complexes. Clinically, this phase coincides with the development of ENL, reversal reactions, and proteinuria. The demonstration of altered βic at this stage in the disease is consistent with this hypothesis. Indeed the electrophoretic change may precede proteinuria or skin reaction. As recovery occurs the βic electrophoresis becomes normal.

In patients with chronic lepromatous leprosy, although the acid-fast bacilli may still be present as dead granular forms, there is no more active degranulation and possibly there is no further release of antigen into the circulation. In these patients and in those patients with no bacilli in skin smears such altered complement was not detected.

This study provides evidence of complement activation, perhaps by circulating antigen-antibody complexes. It is suggested that such immune complexes when deposited in the capillary walls of the skin cause ENL, and when deposited in the glomeruli of the kidneys cause proteinuria.

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References

Lachmann, P. J. (1963). The formation of βia-globulin *in vivo*. In *Clinical Aspects of Immunology* (eds Gell, P. G. H. and Coombs, R. R. A.), p. 260. Oxford: Blackwell Scientific Publications.

Morse, J. H., Müller-Eberhard, H. J. and Kunkel, H. G. (1962). Antinuclear factors and serum complement in systemic lupus erythematosus. *Bull. N.Y. Acad. Med.* 38, 641.

Müller-Eberhard, H. J. and Nilsson, U. (1960). Relation of βi-glycoprotein of human serum to the complement system. *J. exp. Med.* **111**, 217.

Ridley, D. S. and Jopling, W. H. (1966). The classification of leprosy, according to immunity. A five group system. *Int. J. Lepr.* **34**, 255.

Soothill, J. F. (1965). The detection of altered form of the complement component C3a (βic-βia) in the serum of patients with various forms of glomerulonephritis. *Nephron* **2**, 63.

Soothill, J. F. (1967). Altered complement component C3a (βic-βia) in patients with glomerulonephritis. *Clin. exp. Immunol.* **2**, 83.

Tin Shwe (1971). Immune complexes in glomeruli of patients with leprosy. *Lepr. Rev.* **42**, 282.

Wemambu, S. C. N., Turk, J. L., Waters, M. F. R. and Rees, R. J. W. (1969). Erythema nodosum leprosum, a clinical manifestation of the Arthus phenomenon. *Lancet* ii, 933.

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Immune Complexes in Glomeruli of Patients with Leprosy*

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Renal biopsy specimens from 7 patients with leprosy were studied by fluorescence microscopy after staining with fluorescein *iso*thiocyanate-labelled anti-human immunoglobulins IgG, IgM, and third component of human complement βiC. Bound immunoglobulins and complement were observed in the form of granular deposits along the glomerular capillary walls in 2 patients during reversal reaction and in one other active patient. It seems reasonable to conclude that renal impairment in some patients with leprosy may be regarded as an immune-complex disease.

Introduction

Autopsy studies on leprosy patients have shown that lesions in the kidney are a major cause of death. In this respect they are second in importance only to tuberculosis. Thus from the 5458 cases reported in the literature it has been possible to ascertain that at least 17.6% of these patients had pathological changes in the kidneys (Table 1), but the mechanism of the production of these changes was unknown.

From retrospective studies of the clinical histories of 498 patients from Argentina it is clear that renal complications shorten the lives of patients with lepromatous leprosy, especially those with lepra reactions (Brusco & Masanti, 1963). To date, however, specific granulomatous lesions of the kidney due to *Myobacterium leprae* have not been recorded.

The question was asked, whether deposition of immune complexes is responsible for the lesions, and in a clinical and pathological study made in an attempt to answer this problem, 7 patients were submitted to renal biopsy and investigations to detect the presence of immune complexes in the kidney.

Materials and Methods

The 7 patients were chosen from among the patients undergoing treatment at the Hospital for Tropical Diseases, London. All the patients were classified according to the method of Ridley and Jopling (1966) and their skin smears were assessed according to Ridley's bacterial and granularity indices (Ridley, 1964). The bacterial index, that is the logarithmic index, ranges from 0 to 64, while the

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TABLE 1

Summary of the autopsy findings in patients with leprosy

Name of worker and year reported	Country from which reported	No. of cases studied	Common pathological condition found at autopsy associated with leprosy			General remarks
			Tuberculosis of the lungs	Amyloidosis in any internal organ	Renal changes including amyloidosis of the kidney	
Hansen & Looft (1895)	Norway	89	40	52	67	Nodular leprosy cases
		36	14	10	13	Maculo-anaesthetic cases
Pineda (1924)	Culion, Philippines	300	72	nil	49	Nephritis in nodular type is 25.5%, neural type almost nothing
de Souza Arauja (1929)	Culion, Philippines	—	—	—	—	Same as Pineda (1924)
Ryrie (1934)	Malaya	33	not mentioned	not mentioned	32	
Muller *et al.* (1936)	East Java	225	61	not mentioned	18	
Mitsuda & Ogawa (1937)	Japan	150	82	not mentioned	20	
	Culion, Philippines	3155	1533	not mentioned	411	
Fujita (1938)	Japan	1200	456	not mentioned	240	
Kean & Children (1942)	Panama	103	24	not mentioned	22	16 chronic and 4 acute cases of glomerulonephritis
Powell & Swan (1955)	Carville, U.S.A.	50	7	23	19	
Shuttleworth & Ross (1956)	Carville, U.S.A.	20	0	9	9	
Franca (1961)	Brazil	30	not mentioned	1	30	
Wu Li Tien *et al.* (1962)	China	2	0	0	0	Borderline cases only
Hosaka Sakuri *et al.* (1964)	Japan	115	6	not mentioned	see remarks	On basis of histopathology the main causes of death were contracted kidney and pneumonia
Krishnamurthy & Job (1966)	India	25	not mentioned	2	2	
Desikan & Job (1968)	India	30	15	3	24	Lepromatous cases
		7	0	0	2	Non-lepromatous cases
Sachdev *et al.* (1969)	India	3	0	3	3	Report of 3 cases of amyloidosis

granularity index varies from 1 to 10. A granularity index of 1 is given if all the bacilli are in solid form, and 10 if all the bacilli are in granular form. Skin biopsy specimens were also taken from one or two skin sites.

From each of the above patients 2 kidney biopsy specimens were taken at the same time. One was snap frozen in liquid nitrogen, stored at $-70°$ C overnight, and on the next day sections 5μ in thickness were cut with a cryostat at $-18°$ C, using a guide plate to ensure flatness. The sections were transferred to separate slides at room temperature and dried for 2h in a current of air; no fixation was carried out. The sections were moistened with a drop of Coon's buffer and then stained with sheep fluorescein labelled anti-human immunoglobulin IgG, IgM (Wellcome Reagents) adsorbed with pig's liver powder to reduce non-specific staining, or with anti-βiC globulin respectively (the anti-βiC was kindly supplied by the Department of Immunology, Middlesex Hospital, London). Fluorescent-labelled anti-rabbit immunoglobulin (Wellcome Reagents) and anti-rat fluorescein-conjugated animal antiglobulin GAR/FITC (Fraburg Ltd.) were used as control staining solutions.

After staining for 30 min the slides were washed in Coon's buffer for 45 min. They were then dipped in 1% photographic gelatin and finally mounted in 75% glycerol buffer. The other kidney biopsy was fixed in S.U.S.A. and paraffin sections were prepared 5μ in thickness and stained by haematoxylin, eosin, periodic-acid Schiff, congo red for amyloid, and modified Fite-Faraco (Lowy & Ridley, 1954) for acid-fast bacilli.

The clinical details of the patients studied were as follows.

Case 1. An Indian male aged 30 years, suffering from near lepromatous leprosy for 2 years, had a severe reaction of 21 days' duration. The skin biopsy was

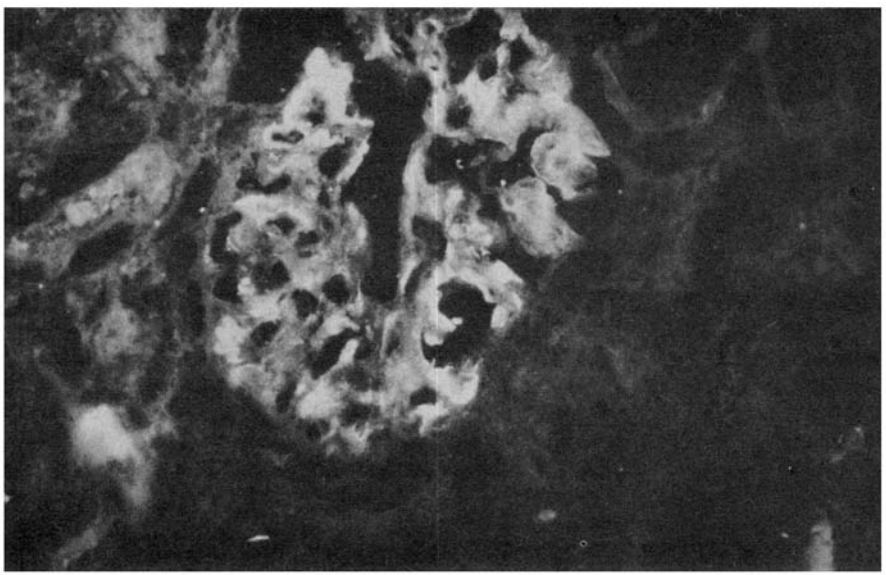

Fig. 1. Frozen section of kidney from patient no. 2, stained for IgG, showing irregular granular deposits of IgG globulin in the glomeruli.

reported as showing a reversal reaction, with a change from the original classification of BL to BB or BT. Skin smears revealed a bacterial index of 2.7 and a granularity index of 7.5. There was a trace of albumin in the urine, approximately 2 g in 24 h. The creatinine clearance rate was 76 ml per min. Renal biopsy examination showed normal glomeruli, but chronic inflammatory cells were present between the tubules.

Case 2. An Anglo-Indian female aged 39 years had been suffering from lepromatous leprosy (LI) for 4 years, and had had lepra reactions for 2 years. For the previous 3 months an acute reversal reaction had been present. Skin biopsy revealed suppuration and micro-abscess formation. A satisfactory clssification was not possible at this stage, but the condition was considered likely to move to BT. Skin smears taken 3 months prior to the renal biopsy showed a bacterial index of 2.7 and a granularity index of 8.2. It was also possible to demonstrate a few acid-fast bacilli engulfed within the monocytes in the blood during this reaction. The results of renal function tests were normal except for the presence of a trace of albumin in the urine; renal biopsy showed proliferation of cells in the glomeruli.

Case 3. A Cypriot male aged 57 had been suffering from borderline leprosy for 10 years. He came to hospital with oedema of the face and extremities. The skin biopsy showed an almost healed lesion with only one acid-fast bacillus in muscle; skin smears were persistently free from acid-fast bacilli. There was a trace of albumin in the urine, and the creatinine clearance rate was 68 ml per min. The patient had had no lepra reaction for the past year, and the cause of the oedema of the face and extremities was not clear. The kidney

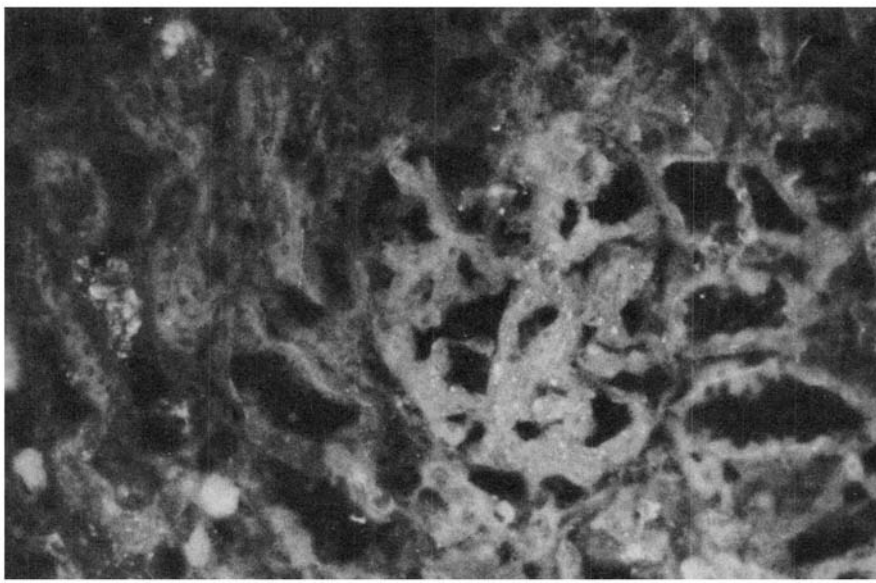

Fig. 2. Frozen section of kidney of patient no. 6, stained for anti-human IgG globulin. No deposits are seen.

biopsy showed chronic inflammatory cells between the tubules, with increased interstitial fibrous tissue.

Case 4. An Anglo-Burmese male aged 47 had a history of lepromatous leprosy of 32 years' duration. He had had leprosy reactions in the past, and at the time of renal biopsy showed signs of a mild reaction consisting of a few erythema nodosum leprosum lesions in the skin, redness of one eye, and swelling of the metacarpo-phalangeal joint of the thumb of one hand. His main problem was trophic ulcers of the legs and fingers. Skin smears showed a bacterial index of 1.0, and he had intermittent albumin in the urine. The creatinine clearance rate was 68 ml per min. Renal biopsy revealed that one third of the glomeruli were replaced by hyaline material.

Case 5. An Indian male, aged 26, had been suffering from lepromatous leprosy (LL) for 1 year. He was admitted to hospital with general wasting and with palpable spleen, liver, and some of the lymph glands. His skin smears showed a bacterial index of 3.8 and a granularity index of 8.6. His calves and thighs were tender and there were a few nodules in the muscles of the leg. Biopsy examination of one of these nodules showed extensive leprous interstitial myositis, with large foam-cell foci between the muscle bundles. Non-solid acid-fast bacilli were numerous in the lepra cells of one specimen. The clinical appearance of the patient suggested leprosy of the "diffuse lepromatous type", He had intermittent proteinuria, but renal function tests, as well as the kidney biopsy, gave normal results.

Case 6. A European male, aged 63, with a history of lepromatous leprosy of 34 years' duration. In response to treatment with DDS for 15 years he had become bacteriologically negative at one stage, but at the time of examination he was suffering a relapse. The bacterial index was 3.5 and the granularity index 5.2. He had also had hypertension for 20 years (blood pressure 180-200/110-120 mmHg). There was oedema of the legs and body and also a trace of protein in the urine. The glomerular filtration rate was 57 ml per min. He had no clinical or histological evidence of lepra reactions. Renal biopsy showed hypertensive nephropathy.

Case 7. An Indian male aged 51 years, who had suffered from lepromatous leprosy for the previous 28 years. He had been receiving regular antileprosy treatment for the past 6 years, but his progress was slow and interrupted due to reactions of the erythema nodosum leprosum (ENL) type. He also had had hypertension (blood pressure 180-150/110-190 mmHg) for the previous 4 years. He remained free from lepra reaction for 1 year, but 2 months before admission he collapsed at work and developed a right hemiplegia due to cerebral thrombosis. Later he developed the nephrotic syndrome. His blood urea level was 77 mg per 100 ml, creatinine clearance rate 77 ml per min, plasma cholesterol level 238 mg per 100 ml, urinary protein excretion 10 to 17 g per day, serum total protein value 5.3 g—albumin 1.8 g and globulin 3.5 g. Skin smears showed a bacterial index of 1.5, all in granular form. As only one kidney biopsy was obtained paraffin sections could not be prepared, but when the patient died 4 months after the biopsy the kidney showed amyloid deposits in all the glomeruli and on the blood vessel walls.

Results

In the kidney specimens of patients nos. 1, 2, and 5 immunoglobulins and complement were demonstrable by immunofluorescence on the glomeruli. The fluorescence was in granular form and was localized along the walls of the glomerular blood vessels. Fluorescence was observed on all the glomeruli, but apart from the glomeruli no deposits were seen on other areas of the kidney section. Both fine and coarse deposits were observed and there was not much variation in the size and distribution of the glomerular deposits. In general the fluorescence was stronger on sections stained with IgG than on those stained with IgM and βiC. The sections from patient no. 5 showed comparatively weak fluorescence deposits. Sections from the remaining patients showed no specific fluorescence after staining with either conjugate. None of the control sections stained with either anti-rabbit or anti-rat fluorescein-conjugated globulin showed any deposits.

Discussion

In a disease in which antigen persists over a long period of time and antibody response to the infecting agent develops, conditions are favourable for the formation of circulating soluble immune complexes. That antigen-antibody complexes in the blood stream can lead to serious tissue injury is unquestioned (Weigle, 1961). So in leprosy it is possible that such antigen-antibody complexes may be found in patients with lepromatous leprosy, in whom numerous leprosy bacilli are spread all over the body, and this especially during treatment, when much disintegration of bacilli takes place.

Epidemiological studies recently undertaken at the Hospital for Tropical Diseases, London, have shown that proteinuria in such patients is common, especially in those suffering from severe ENL as well as in those with reversal reactions. There are also records of patients with proteinuria without clinical reactions.

ENL is thought to be due to an Arthus reaction. It is often associated with acute vasculitis in the skin, iridocylitis, arthritis, epididymo-orchitis, and even glomerulonephritis (Turk, 1970). Histologically, the presence of polymorphonuclear leucocytes is the essential and predominant feature, especially in the early stage, and there is much cellular disintegration (Job *et al.*, 1964; Mabalay *et al.*, 1965). In this type of reaction Wemambu *et al.* (1969), using the indirect fluorescent antibody technique, had demonstrated the presence of granular deposits of immunoglobulin and complement in the acute lesions of the skin, but not in older forms of the skin lesions. During this type of reaction there is every likelihood of immunoglobulins and complement being deposited in the glomeruli of the kidneys. In this study patient no. 4, though suffering from a mild form of ENL, had no deposits of immunoglobulins and complement, probably because the lesion was old. There were no other patients with ENL in the series.

The second type of reaction is the reversal reaction in which the main infiltrating cell is the lymphocyte. This reaction, which resembles a tuberculin reaction, is the result of a recovery of the patient's cell-mediated immune response towards *Mycobacterium leprae* (Ridley, 1969; Turk, 1970).

Patients with acute reversal reaction can be very ill, but the reaction occurs primarily in the clinically apparent lesions of the skin—unlike ENL, in which the

reaction often occurs in crops of new lesions. It has not so far been postulated, therefore, that reversal reactions are due to a humoral mechanism. Nevertheless, reactions of this type are characterized by the elimination of bacilli from the skin lesions, and it is probable that much antigenic material is discharged into the blood circulation and filtered off by the renal glomeruli. This is probably the explanation for the finding of fluorescent deposits of immunoglobulin and complement in the glomeruli of patients nos. 1 and 2, both of whom had a severe reversal reaction associated with a sharp diminution in the number of bacilli in the skin and elsewhere, with an erythrocyte sedimentation rate (ESR) of over 100 mm in 1 h.

Patient no. 5 was in the early months of treatment, and though not in reaction his skin smears showed a granularity index of 8.6, indicating that most of the bacilli in his body were in fragmented or granular form, a condition which is seen in ENL. So the finding of weak immunoglobulins and complement in the renal glomeruli of this patient was not altogether unexpected.

Immunoglobulins and complement were not found in any of the other patients. In patient no. 3 the leprosy was almost cured, and there were no acid-fast bacilli (AFB) in his skin lesions. Patient no. 6 was suffering from relapse, probably due to drug resistance. His skin smears showed a bacterial index of 3.5 and a granularity index of 5.2, so antigenic breakdown was therefore limited; his proteinuria was probably secondary to hypertension. Patient no. 7 had long-standing chronic disease, with amyloidosis of the kidneys, but few signs of activity of his leprosy.

The sera of all the above patients gave a negative response to the test for Australia antigen and antibody, the anti-streptolysin-0 titre was less than 200 Todd units, and the malaria antibody titre less than 20. So it is not likely that the present finding of immune complexes in the kidneys of Patients 2, 3 and 5 was due to any other antigen than leprosy.

All the above evidence suggests therefore that the renal impairment in some leprosy patients is due to deposition of antigen-antibody complexes in the glomeruli.

Acknowledgements

I am deeply indebted to Professor A. W. Woodruff, Professor of Clinical Tropical Medicine, London School of Hygiene and Tropical Medicine, and to Dr D. S. Ridley, Pathologist, Hospital for Tropical Diseases, London, for their supervision, guidance, and encouragement throughout this work. My gratitude is also due to Dr W. H. Jopling, Consultant Leprologist, Hospital for Tropical Diseases, London, for unceasing guidance and help in allowing me to carry out this study on his patients.

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References

Brusco, C. M. and Masanti, J. G. (1963). Causes of death of leprosy patients; influence of lepra reactions and renal disease. *Int. J. Lepr.* **31**, 14.

Desikan, K. V. and Job, C. K. (1968). A review of postmortem findings in 37 cases of leprosy. *Int. J. Lepr.* **36**, 32.

de Souza-Arauja, H. C. (1929). "Leprosy survey made in 40 countries, 1924-1927". Rio de Janeiro.

Franca, H. H. (1961). Contribuicao do estudo do rim na leprolgia. (Study of the kidney in leprosy). *Revta Brax. Leprol.* **29**, 43.

Fujita, K. (1938). Review of the autopsy protocol of Zensei Hospital. *Lepro.* **9**, Suppl. 39.

Hansen, G. A. and Looft, C. (1895). *Leprosy and its Clinical and Pathological Aspects,* (translated by Norman Walker), p. 138. Bristol: John Wright and Sons.

Hosaku Sakurai, Masazo Kawaguchi and Eiji Nakada (1964). Histopathological findings on 115 corpses of leprosy. *Nagashima Arch. Lepr.* **4**, 22. (Abstract in *Int. J. Lepr.* **1965**, **33**, 50.)

Job, C. K., Guda, S. and Macaden, V. P. (1964). Erythema nodosum leprosum, a clinico-pathologic study. *Int. J. Lepr.* **32**, 177.

Kean, B. H. and Children, M. E. (1942). A summary of 103 autopsies on leprosy patients on the Isthmus of Panama. *Int. J. Lepr.* **10**, 51.

Krishna Murthy S. and Job, C. K. (1966). Secondary amyloidosis in leprosy. *Int. J. Lepr.* 34, 115.

Lowy, L. and Ridley, D. S. (1954). The acid-fast staining properties of *Mycobacterium leprae. Trans. Roy. Soc. Trop. Med. Hyg.* 48, 406.

Mabalay, M. C., Helwig, E. B., Tolentino, J. G. and Binford, C. H. (1965). The histopathology and histochemistry of erythema nodosum leprosum. *Int. J. Lepr.* **33**, 28.

Mitsuda, K. and Ogawa, M. (1937). A study of 150 autopsies in cases of leprosy. *Int. J. Lepr.* **5**, 53.

Muller, H. and Mertodidjojo, S. (1936). Causes of death and visceral infection in East Java. *Geneesk. Tijdschr. Nederlandsche-Indie* **76**, 2174. (Abstract in *Int. J. Lepr.* (1937) **5**, 401.

Pineda, E. V. (1924). Pathological survey of the causes of death in lepers at Culion. *J. Philippine Islands Med. Assoc.* **4**, 169.

Powell, C. S. and Swan, L. L. (1955). Leprosy pathogenic changes observed in 50 consecutive necropsies. *Amer. J. Path.* **31**, 1131.

Ridley, D. S. and Jopling, W. H. (1966). The classification of leprosy according to immunity. A five group system. *Int. J. Lepr.* **34**, 255.

Ridley, D. S. (1964). Bacterial indices. In *Leprosy in Theory and Practice.* 2nd ed., p. 620. (eds Cochrane, R. G. and Davey, T. F.). Bristol: John Wright & Sons.

Ridley, D. S. (1969). Reactions in leprosy. *Lepr. Rev.* **40**, 77.

Ryrie, G. A. (1934). Leprosy in Malaya. *Int. J. Lepr.* **2**, 77.

Sachdev, J. C., Vevinder Puri and Surinder Bansal (1969). Secondary amyloidosis in leprosy. *Lepr. India.* **41**, 73.

Shuttleworth, J. S. and Ross, H. (1956). Secondary amyloidosis in leprosy. *Ann. intern. Med.* **45**, 23.

Turk, J. L. (1970). Immunological aspects of clinical leprosy. *Proc. Roy. Soc. Med.* **63**, 1153.

Weigle, W. O. (1961). Fate and biological action of antigen-antibody complexes. In *Advances in Immunology,* Vol. 1, p. 283. (Eds Taliaferro, W. H. and Humphrey, J. H.). New York: Academic Press.

Wemambu, S. N. C., Turk, J. L., Waters, M. F. R. and Rees, R. J. W. (1969). Erythema nodosum leprosum, a clinical manifestation of the Arthus phenomenon. *Lancet* ii, 933.

Wu li-Tien, Chin Kuang-Yu and Liu Tze-Chun (1962). Leprosy lesions of internal viscera, with special reference to the lesions of borderline leprosy and lepromatous reaction. *Chinese Med. J., Peking.* 81, 30.

Lepr. Rev. (1972) 42, 290-291

Book Reviews

Reconstructive Surgery in Leprosy by Ernest P. Fritschi; xiv + 225, illustrated. 1971. Bristol, John Wright & Sons Ltd. £3.25.

All doctors working in leprosy need this book. They should get it, and read it, and keep it handy for ready reference. Dr Fritschi has brought together, within the convenient compass of 216 pages of well-illustrated text, a vast amount of very practical observations and helpful advice.

The book is intended primarily for doctors who have had some training in, and flair for, surgery, and will be especially appreciated by those who have followed short courses under expert guidance. It will remind them of salient points in operative technique that they may not have appreciated until they themselves are facing real problems on the operating table. The well-tried and classic procedures are here described, often with practical comments drawn from the author's extensive experience.

The book will also be of value to those budding surgeons who from time to time have to do more than treat series of plantar ulcers. If some of the diagrams are rather too diagrammatic and make surgery look a little too neat and easy, salutary experience (and hints and warnings scattered in the text) should make the unwary surgeon conscious of the pitfalls and problems in his path. It is practice under experienced guidance, and not infrequent—and perhaps ill-considered—surgical intervention, that will lay the foundations of knowledge, judgement, and technique.

While we cannot exactly subscribe to the statement in the "blurb" that "this book constitutes a real breakthrough in tropical medicine", it is a pleasure to commend it to readers of *Leprosy Review.* Those who constantly refer to the chapters by Brand in Cochrane and Davey's *Leprosy in Theory and Practice,* and surgeons conversant with the fine work of their French and South American colleagues, will nevertheless welcome this very practical and handy résumé of the application to leprosy of the established principles and procedures of reconstructive surgery.

The text and the diagrams are on the whole clear, but a critical revision would have eliminated the rather numerous verbal infelicities and misprints. In places, also, more precise advice could have been given regarding, for instance, the indications for operative interference; the rather bald statement "the presence of lagophthalmos", as the indication for a Gillies type of temporalis transfer, is not sufficiently helpful to the puzzled surgeon.

These quibbles apart, this is a book to buy, to refer to, and to put into the hands of the local surgeon, who has not appreciated what can be done—and what ought to be done—in the way of reconstructive surgery for the benefit of those whose preventable leprosy deformities have not been prevented.

S. G. Browne

Health, Manpower and the Medical Auxiliary by the Intermediate Technology Development Group. Published in London, 1971. £1.50.

The pivotal rôle of the medical auxiliary or paramedical worker has for years been recognized by doctors engaged in leprosy control schemes. Without them, the majority of such programmes would grind to a halt. Some developing countries, however, have been slow to see that it is quite impossible and unrealistic to imagine that health care and preventive medicine

can be provided for the mass of the people, unless recourse is had to the services of trained and supervised auxiliary workers.

This little book examines some of the parts that can be played by such auxiliaries. For most leprosy workers it is a preaching to the converted, but the chapters on "Towards an appropriate health care technology" (by Dr Oscar Gish), "Intermediate technology in medicine" (by Prof. Kenneth R. Hill), and "Using medical auxiliaries: some ideas and examples" (by Dr Katherine Elliott) all provide salutary reminders and useful suggestions to the most convinced and experienced readers.

Units, Symbols and Abbreviations—a Guide for Biological and Medical Editors and Authors. Edited by George Ellis. Published by the Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE. Price 54p per copy, post free.

We draw the attention of our readers and potential authors to this guide, which embodies the recommendations of a Working Party set up at a Conference of Medical Editors held in London in December, 1968. It is practical, compact, comprehensive, and clear. With the advent of metrication, and the wider diffusion of scientific knowledge through the medium of the printed word, it is more than ever necessary that clarity and uniformity should be the hallmarks of our communicating with each other and with the outside world.

We give this booklet an unqualified welcome, and hope that all future contributors to the pages of this *Review* will buy it, read it, and use it.

Lepr. Rev. (1972) 42, 292-299

Abstracts

1. **Leprosy, Echinococcosis and Amulets : A Study of a medieval Danish inhumation**, by D. L. WEISS and V. MØLLER-CHRISTENSEN. *Med. Hist.* 1971, **15**, 260-267.

The authors give a description of skeletal remains of exceptional diagnostic interest. The bones are those of a female of about 16 years of age, buried *c.*1450 A.D. in the Danish mediaeval leprosy hospital at Naestved.

Although the leg bones are missing (because of disturbance due to a later inhumation) and no pathognomonic features are present in the skull or face, typical changes were found in the terminal phalanges of three fingers. Further study revealed a very small stature for the bone age, early spinal osteoarthritis, lumbar lordosis, and bones of unusually light weight. The authors deduce from this evidence that the girl was rendered inactive by reason of severe leprosy, and suffered from osteoporosis, possibly associated with renal amyloidosis. Many calcified cystic structures were present in the abdominal cavity. After discussing the various diagnostic possibilities, the authors conclude that the cysts were probably echinococcal in origin and represented abdominal dissemination of daughter cysts following rupture of a hepatic primary cyst.

The third group of intriguing diagnostic clues consisted of calcified structures which were identified as sesamoid and pisiform bones of sheep, and phalangeal bones of a small pig. The apparently careful disposition of these bones suggests that they were arranged in the form of amulets and served some magical or therapeutic function.

S. G. Browne

2. **Sporadic ulcero-osteolytic neuropathy in the Bantu**, by I. F. ANDERSON and E. J. SCHULZ. *Br. J. Derm.* 1971, **85**, Supplement 7, 18-26.

The authors report a series of 7 adult male patients seen within a period of one year in Pretoria (South Africa), complaining of a sensori-motor (global, not dissociate) neuritis of the legs accompanied by painless multiple ulcerations of the feet, partial destruction of the phalanges, erosion of the metatarsal heads, and osteo-arthrosis of the small joints of the feet.

No vascular insufficiency was demonstrable by arteriography. Histological examination of the sural nerves (macroscopically atrophic) revealed no evidence of leprosy, but some reduction of myelin. It was considered possible that functional impairment of the liver, with accompanying moderate to severe cirrhosis and siderosis (demonstrated by liver function tests and histological examination of specimens obtained by needle biopsy) may have contributed indirectly to the neuropathy. The only positive findings in the history were a heavy consumption of alcohol over many years, and trauma to the feet. It is probable that this latter condition accounted for the neuropathy present in the legs and the consequent picture of peripheral damage to bone and soft parts.

Since no residual signs of leprosy were discovered in the skin or nerves, and in view of the histological findings in the sural nerves, the diagnosis of leprosy could be definitely excluded.

[The clinical photographs and radiographs would be considered typical of the lower limb peripheral neuropathy and its sequelae seen in leprosy.]

S. G. Browne

3. **Cutaneous granulomas responding to dapsone therapy,** by A. C. PARIKH, S. S. NAIK, R. GANAPATI and B. I. KAPADIA, *Punjab Med. J.*, 1970, **20**, 55-60.

Chronic skin lesions resembling leprosy in which no sensory impairment is demonstrable may arise from a variety of causes, and in some cases no cause can be found. The authors record 6 such cases in patients who attended their leprosy clinic. All were treated with dapsone.

Histological examination at intervals revealed changes that ran parallel with the clinical improvement. The authors advocate histological studies and the administration of dapsone in all such doubtful lesions, where the true aetiology of a granulomatous condition is not disclosed by standard investigations.

S. G. Browne

4. **L'acide epsilon-aminocaproique dans les états lépreux réactionnels. (Epsilon-aminocaproic acid in reactional states in leprosy),** by Y. MAFFART and M. DUCLOUX. *Bull. Soc. Med. Afr. noire Lang Fr.*, 1970, **15**, 300-304.

In view of the known anti-enzyme activity of epsilon-aminocaproic acid in diverse allergic phenomena in which antigen-antibody reactions are thought to be involved, the authors used this compound in 2 patients undergoing prolonged and severe bouts of exacerbation—one with the typical erythema nodosum leprosum of lepromatous leprosy, and the other with a degenerating near-lepromatous form of leprosy. Within a few hours of the beginning of an intravenous perfusion of the product (5 g in 250 ml of isotonic glucose saline every 6 h) the acute erythematous skin lesions disappeared. Subsequent oral treatment at a high dose, diminishing to 2 g daily, was continued for 15 and 9 months respectively, without return of the signs of acute exacerbation.

[Further study of this compound is indicated.]

S. G. Browne

5. **Mpilo Hospital Case Report—A Case of Sarcoidosis in an African,** by J. E. P. THOMAS. *Centr. Afr. J. Med.*, 1971, **17**, 111-112.

The paucity of "proved" cases of sarcoidosis in Central Africa enhances the value of this report. The patient, a female aged 55 years, presented at Mpilo Hospital (Rhodesia) complaining of painful swollen fingertips that were beginning to ulcerate. General clinical examination and routine laboratory investigations yielded no clue to the diagnosis, but radioscopy revealed bilateral hilar lymph-node enlargement, with a slight nodularity of both lung fields, and punched-out cystic lesions of the terminal phalanges of the fingers and the proximal phalanges of the 4th finger on both hands.

Microscopical examination of tissue removed from a finger-tip showed a granulomatous lesion composed of epithelioid cells, lymphocytic infiltration, and scanty giant cells. No specific changes were noted in a small portion of liver examined histologically. Treatment, which was rapidly successful, consisted of high doses of prednisolone for 2 weeks, followed by a single morning dose of prednisolone (10 mg).

[The matter is referred to in an Editorial in the same Journal, p. 255.]

S. G. Browne

6. **Cultivation of the Douglas strain of *Mycobacterium lepraemurium* in continuous culture,** by L. SULA and J. DUBINA. *Bull. Wld Hlth Org.*, 1971, **45**, 209-212.

Attempts at cultivating mycobacteria in cell-free media frequently fail because of the accumulation of toxic products derived from effete organisms or from metabolites of nutrients. This paper describes a continuous culture technique that involves regular removal of potentially inhibitory products in the medium, and the replacement of the liquid thus removed. The medium was derived from human placenta.

The authors were able to demonstrate active fission of *Myco. lepraemurium* and the production of elongated forms, but no macroscopically visible colonies appeared, even after incubation for a period of 8 months.

S. G. Browne

7. **Infection caused by *Mycobacterium fortuitum*** by R. C. OFFER, A. G. KARLSON and J. A. SPITTELL. *Mayo Clin. Proc.*, 1971, **46**, 747-750.

A case is reported of a deep-tissue infection caused by *Mycobacterium fortuitum,* following a penetrating wound caused by a gardening implement. The cavity was scraped and drained surgically; healing was uneventful.

The causative organism was isolated in pure culture from a chronic subcutaneous cavity. Identification was on cultural characteristics and mouse inoculation (with production of typical lesions in the kidneys). The possibility of infection by this organism at intramuscular injection sites must be borne in mind.

S. G. Browne

8. **An unusual case of leprosy with pathological features common to Lucio's Phenomenon,** by E. TAUBE and B. P. B. ELLIS. *Cent. African J. Med.*, 1971, **17**, 119-122.

The authors give a good clinical description of an African female patient aged about 45 years who had treatment for early lepromatous leprosy from 1954 to 1958. She apparently remained well until 1966, when signs resembling closely the classic features of the acute exacerbation of Lucio leprosy began to appear. The histological picture in the blood vessels of the dermis was confirmatory. The patient responded well to dapsone, given at first in small doses, which were prudently increased. Corticosteroids were not needed.

This is the first reported instance in Rhodesia of a patient exhibiting many of the clinical and histological features associated with the Lucio phenomenon in diffuse lepromatous leprosy.

S. G. Browne

9. **A note on the presence of *Mycobacterium leprae* in the central nervous system of a mouse with lepromatous leprosy,** by M. C. VAIDYA, E. PALMER, G. WEDDELL and R. J. W. REES. *J. med. Microbiol.* 1970, **3**, 194-196.

Although it is a commonly held belief that *Myco. leprae* does not cross the blood-brain barrier of the choroidal plexus or invade the spinal axis, well-corroborated *post mortem* findings of the bacilli in the central nervous system have long been recognized. The present paper reports the occurrence of *Myco. leprae* singly, or in typical globi, in every twentieth of 600 serial sections through the brain of a mouse experimentally infected with leprosy after thymectomy and whole-body irradiation. Both white and grey matter of cerebrum and cerebellum contained organisms. In the spinal cord, globi were found in cells of the anterior horn and dorsal root ganglia. The disposition of these bacilli in association with blood vessels suggests that the route of entry of bacilli into ganglion cells was from the bloodstream. Whereas some evidence of damage was present in the anterior horn cells, no focal damage to the brain tissue was seen.

S. G. Browne

10. **The Kveim Test in Crohn's Disease,** by D. N. MITCHELL, P. CANNON, N. C. DYER, K. F. W. HUNSON, and J. M. T. WILLOUGHBY. *Postgrad. med. J.*, 1970, **46**, 491-494.

The interest to leprologists of investigations into tissue granulomata is shown by this paper. Some of the similarities (and differences) of the most diverse conditions characterized histologically by a non-specific "sarcoid" response—as in tuberculoid leprosy—are exemplified by Crohn's disease. The specificity of the Kveim test has been called into question before. This communication records that of 45 patients clinically diagnosed as having Crohn's disease, no

fewer than 23 had a positive Kveim test. It is possible that Crohn's disease is caused by a similar agent to that causing sarcoidosis, or the findings may be an expression of cross-reactivity between the antigens of both diseases. The particulate matter present in the testing material may also be responsible for the reported results.

S. G. Browne

The following abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1971, Vol. 68.

11. **Thalidomide in the treatment of erythema nodosum leprosum. With a note on selected laboratory abnormalities in erythema nodosum leprosum,** by R. C. HASTINGS, J. R. TRAUTMAN, C. D. ENNA and R. R. JACOBSON. *Clin. Pharmacol. Ther.*, 1970, **11**, 481-487.

The authors concur in the generally accepted conclusions that thalidomide is of value in controlling the pyrexia and the acute skin manifestations of erythema nodosum leprosum. The value of their work lies in careful laboratory studies of 22 patients with typical clinical features, who were subjected to 44 trials of thalidomide or an apparently identical placebo. They investigated the acute anaemia, the sudden leucocytosis and the shift to the left in the differential count—during or after the acute apisode. They demonstrated an increase in direct and indirect serum bilirubin, and a fall in total serum cholesterol.

The authors discuss the possible mechanism and sites of action of thalidomide in controlling the manifestations of acute exacerbation, and compare it with the corticosteroids in these respects. They consider that thalidomide is less toxic than the corticosteroids, and that it possesses distinct advantages over the corticosteroids in the treatment of erythema nodosum leprosum.

S. G. Browne

12. **Leprosy in the [U.S.] military services,** by C. D. ENNA and J. R. TRAUTMAN. *Milit. Med.*, 1969, **134**, 12, 1423-6.

Leprosy was imported into North America in the 16th century by soldiers and settlers from Spain, and later by immigrants from Germany, Czechoslovakia and France. More recently, slaves from Africa, and Scandinavians added to the total. Excluding patients in Hawaii and Puerto Rico, the number of sufferers from leprosy registered in the continental United States (45 out of 50 States) over the past 75 years is 3461, of whom about 1800 are alive today.

Records of leprosy among persons having served abroad in the armed forces suggest that in most cases the infection was probably acquired before the foreign assignment. After World War I, 97 veterans (ex-service men) are known to have had leprosy; 137 veterans from World War II and 25 from the Korean War (1950-53) contracted leprosy, but in fewer than 50 was it considered that the disease was "probably related" to military service overseas.

Of the 11 veterans from the Vietnam war (which began in 1964) who have been reported as having leprosy, none is thought to have caught the disease as the result of exposure in Vietnam.

The precise effect of dapsone, taken as a prophylactic measure against malaria, is unknown, as is that of the practice of bringing troops back to the United States after a year's service abroad.

S. G. Browne

13. **Further experience with the kinetic method for the study of drugs against *Mycobacterium leprae* in mice. Activities of DDS, DFD, ethionamide, capreomycin, and PAM 1392,** by C. C. SHEPARD. *Int. J. Lepr.*, 1969, **37**, 389-397.

The author reports further results obtained by the application of his kinetic method [this *Bulletin*, 1968, **65**, abstr. 2828] to investigate the activity of more drugs and of dapsone given

in different doses and for different periods. [For details of this elegant technique the original paper should be studied.]

By this method, the following drugs showed no activity against *Myco. leprae* inoculated into mouse footpads: aminosalicylic acid (PAS), isoniazid (INH), and the quinazoline PAM 1392. Some drugs were found to be bacteriostatic as long as they remained in effective concentration in the neighbourhood of *Myco. leprae*; examples are streptomycin, capreomycin, and probably thiambutosine. Other drugs showed such antimycobacterial activity that even after their disappearance from the tissues the residual effect on the bacilli was sufficient to impair multiplication, transiently or permanently: into this category fell dapsone, ethionamid and probably DFD (4,4-diformyl-diaminodiphenyl sulphone).

A significant finding in one series of experiments was that human tissue from patients with lepromatous leprosy lost its infectivity for mice after 90 days of treatment with dapsone, the morphological changes in the bacilli indicating loss of viability.

A further finding of interest to clinicians is that where varying concentrations of dapsone are given to the experimental mouse for 3 months, bacterial multiplication is impaired after a shorter period with higher concentrations of drug: this is the only difference observed whatever the dosage levels employed.

S. G. Browne

14. **Some recent laboratory findings on *Mycobacterium leprae*. Implications for the therapy, epidemiology and control of leprosy,** by L. M. BECHELLI and R. S. GUINTO. *Bull. Wld Hlth Org.*, 1970, **43**, 4, 559-69.

The burden of this well-documented paper is to offer a salutary warning against the indiscriminate application of experimental findings in the laboratory mouse to the complex problems of leprosy control in the field. In particular, the authors consider it premature and unwarranted to assert that leprosy bacilli that fail to multiply in the artificial micro-environment of the mouse footpad would also prove to be non-viable if given the chance to grow in human tissue. The conclusions that are currently drawn from the experimental findings have widespread repercussions on the control measures being advocated, since patients harbouring reputedly non-viable leprosy bacilli should not be subject to the restraints imposed upon those patients regarded as contagious.

The authors support their arguments with evidence drawn both from the laboratory and the field. *Mycobacterium leprae* infections in the mouse footpad are said to "die off after reaching a certain level". (Many of the bacilli obtained from footpad infections, in the plateau phase, are viable.)

The fact that a certain proportion of patients, adequately treated and bacteriologically negative, relapse after treatment has been discontinued for a variable period, is taken to indicate that viable bacilli may persist for years in deep or unexamined tissues. Even continued dapsone treatment is no guarantee against bacteriological and clinical relapse.

Low-dose dapsone treatment meets with critical review, as possibly favouring the emergence of dapsone-resistant strains of *Myco. leprae*. Another—and more cogent—argument concerns the appearance of signs of overt leprosy among child contacts of persons who have at some time had a contagious form of leprosy, notwithstanding the fact that some of them have taken dapsone prophylactically. [In view of the prolonged silent period of leprosy, the difficulty of recognizing early lesions, and the incomplete information concerning the putative index case, the occurrence of leprosy among child contacts of a patient no longer contagious is, however, not germane to the argument.]

The authors also suggest that since dapsone has been used "very extensively in the treatment of leprosy for about 20 years", and that BCG vaccination has also been in vogue (for purposes of tuberculosis control), these two measures should by now have led to some obvious reduction in the worldwide prevalence of leprosy. The fact that no such reduction is apparent is held to show that the success of dapsone treatment in experimental infection in the mouse may not be applicable to the human situation. [It may be argued, however, that noticeable reductions in

leprosy prevalence have followed the widespread application of adequate control measures, which include dapsone treatment of all patients with contagious forms of leprosy.]

The experimental and field work on BCG vaccination is also referred to, again with the salutary warning that the complex clinical situation contains elements that cannot be reproduced in the experimental animal.

Amid the wealth of clinical and experimental data adduced, the authors assert that "in all the forms of leprosy, lepromatous, borderline or tuberculoid, clinical improvement coincides with a fall in the BI [Bacterial Index] rather than the MI [Morphological Index]" [but such an improvement occurs in tuberculoid leprosy, in which the extremely scanty bacilli are all morphologically abnormal, that is presumably non-viable.]

[This thought-provoking paper deserves detailed study.]

S. G. Browne

15. **A study of age at onset of leprosy**, by V. N. SEGHAL. *Int. J. Derm.*, 1970, **9**, 3, 196-9.

The author investigated 954 patients attending leprosaria in Varanasi district, eastern Uttar Pradesh, India. They were asked the duration of the disease and their age at its onset. Where possible, corroboration was sought from relatives and other observers.

In both lepromatous and non-lepromatous patients (men and women) the peak age of onset was between 20 and 34 years. Onset of leprosy under the age of 10 years is less common than in the two series reported from Chingleput district (Madras State) by COCHRANE [*A Practical Textbook of Leprosy*, 1947– this *Bulletin*, 1947, Vol. 44, 1026] and by MOHAMED ALI [this *Bulletin*, 1964, Vol. 61, 1145].

The author's figures were obtained by interrogating patients with established leprosy, and are not population surveys.

H. V. Morgan

16. **Eighth cranial nerve affection in leprosy**, by F. EL ARINI, M. A. SHEHATA and S. A. ABDOU ZEID. *Int. J. Lepr.* 1970, **38**, 164-9.

A study of 102 patients suffering from different types of leprosy in various stages of the disease revealed a relatively high incidence of eighth cranial nerve affection. The ages of the patients ranged from 11 to 85 years. Loss of hearing was perceptive in type and was considered to be due to bilateral eighth nerve damage without any detectable lesions in the middle ear, inner ear, or in the central connexions of hearing.

H. W. Jopling

The surgical treatment of lower facial palsy in leprosy, by J. B. A. VAN DROOGENBROECK. *Ann. Soc. Belg. Méd. Trop.*, 1970, **50**, 6, 653-87.

"Upper and lower facial palsies, both uni- and bi-lateral, and even nearly complete facial paralysis, are not exceptional in the Far East.

"It is possible to rehabilitate patients suffering from these paralysis, according to the nature of the individual case, by isolated or combined transfers of temporalis and masseter muscles (examples are given).

"Although our work is essentially clinical, its aim being the treatment and rehabilitation of patients, there can be no doubt that there is much room for research in fields of leprosy and lower facial palsy."

18. **Bacterial negativity and reactivation (relapse) of lepromatous outpatients under sulfone treatment**, by R. QUAGLIATO, L. M. BECHELLI and R. M. MARQUES. *Int. J. Lepr.*, 1970, **38**, 3, 250-63.

This is a retrospective study from Brazil of 815 patients treated for lepromatous leprosy with various sulphones throughout the period 1946 to 1968, giving the numbers of patients becoming bacteriologically negative, the time taken to reach this stage, the numbers relapsing, and the number of relapses. Presumably, irregularity of treatment among out-patients was the factor chiefly responsible for relapses judging by the proportion regaining bacterial negativity when treatment was supervised, but bacterial reactivation occurred in a number of patients "despite apparently continuing sulfone therapy". No attempts were made to discover the incidence of bacterial resistance to sulphone.

The authors conclude that their findings support the view that, with present antileprosy drugs, patients with lepromatous leprosy should be treated for life.

W. H. Jopling

19. **Leprosy in Ethiopian society**, by R. GIEL and J. N. VAN LUIJK. *Int. J. Lepr.*, 1970, **38**, 2, 187-98.

This study was undertaken primarily with the object of predicting which patients diagnosed as suffering from leprosy would persevere with treatment when advised to attend either a rural clinic near their home or the out-patient department of the Princess Zenebework Hospital in Addis Ababa. Although it failed in its primary purpose, the authors record the interesting results of an hour-long, in-depth interview with 100 patients, and 20 patients not suffering from leprosy.

The patients, whatever the ethnic background, were mainly peasant farmers. Most recognized the signs of leprosy, but postponed seeking medical advice for several years, visiting priests, indigenous "specialists" or native healers, holy water shrines and so on, before eventually travelling several days to Addis Ababa. The wide range of beliefs and superstitions among the patients interrogated is recorded. The authors discuss at length the significance of their findings, referring to lay recognition of leprosy, the stigma of the disease, attempts at concealment, and the various psychological reactions displayed by individual patients to the infection and its symptoms, as well as to their family and society in general.

It is concluded that, among the many human variables investigated, the unidentified factor or factors that eventually impelled the patient to seek help would probably determine his willingness to submit to a long period of treatment.

S. G. Browne

20. **Leprosy in society. V. "Leprosy" in occidental literature**, by O. K. SKINSNES and R. M. ELVOVE. *Int. J. Lepr.*, **1970**, **38**, 3, 294-307.

The authors pursue their studies of the social phenomena surrounding leprosy, with this interesting paper on the word "leprosy" in occidental literature. [The term "occidental" has been taken to indicate "mainly English" to the virtual exclusion of the rich literature existing in the French, German, Italian, Spanish and Scandinavian languages where cognate expressions are found.]

Extensive quotations from Chaucer, Shakespeare and less well-known writers indicate the wide and diverse connotation of the term and the imprecision of much that passed for "leprosy" in past centuries and more recently. The authors consider that the social reaction to true leprosy (as at present understood) is so characteristic as to be almost pathognomonic, but they quote such references as that to "the furious burning itch". They hold that in ancient literature, as well as in the Old Testament, the existence of true leprosy can be inferred from the accompanying social reaction, notwithstanding both the absence of references to signs of

skin and nerve damage, and also the inclusion of scaly conditions of cloth and walls within the meaning of the single word used in the Old Testament.

[Passing reference might have been made to the good descriptions of leprosy in ancient Indian literature and in Greek writings from the 3rd century B.C., and to the absence of specific leprosy lesions in ancient skeletons from the Fertile Crescent.]

S. G. Browne

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