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News and Notes

RIFAMPIN-RESISTANT LEPROSY

Letter to *The Lancet*, 11 December, 1976*

The rifamycin antibiotics have been used in the treatment of leprosy since 1963 (Opromolla, de Souza Lima and Caprara, 1965). The orally active rifamycin, rifampicin, or rifampin has been utilized more recently (Rees, Pearson and Waters, 1970; Shepard, Levy and Fasal; Opromolla and Tonello, 1975). Rifampin exerts a rapid bactericidal effect on *Myobacterium leprae* in man (Shepard *et al.*, 1972; Levy, Shepard and Fasal, 1972), but concern has been expressed regarding the possible development of rifampin-resistant *M. leprae* (Shepard *et al.*, 1972; Opromolla and Tonello, 1975; Ellard, 1975; Rees, Waters and Pearson, 1976).

We have seen a patient with sulphone-resistant lepromatous leprosy who experienced clinical and bacteriological relapse while on rifampin monotherapy. The patient is a 49-year-old male of Scandinavian extraction who has had lepromatous leprosy since the age of 18. He was treated with sulphones, glucosulphones ("Promine"), and, later, sulfoxone ("Diasone") both of which he took irregularly from 1946 until 1968. In 1968 he developed clinical relapse despite sulfoxone therapy and mouse foot-pad studies by Dr Charles Shepard in

TABLE 1

Drug sensitivities in mouse foot-pads

Treatment	% w/w in diet	No. of pads positive for acid/fast bacilli/total	Acid-fast bacilli/foot-pad
Controls		6/6	$1.750\ (\pm 0.810) \times 10^5$
Dapsone	0.0001	6/6	$1.033\ (\pm 1.013) \times 10^5$
	0.001	6/6	$4.502\ (\pm 3.406) \times 10^4$†
	0.01	0/6	$<7.298 \times 10^3$‡
Clofazimine	0.0001	0/6	$<7.298 \times 10^3$‡
	0.001	0/6	$<7.298 \times 10^3$‡
	0.01	0/6	$<7.298 \times 10^3$‡
Rifampin	0.001	6/6	$3.773\ (\pm 0.857) \times 10^4$†
	0.01	6/6	$8.757\ (\pm 8.648) \times 10^4$
	0.03	6/6	$5.718\ (\pm 2.669) \times 10^4$†
	0.06	0/6	$<7.298 \times 10^3$‡
Ethionamide	0.01	0/6	$<7.298 \times 10^3$‡

† $0.01 > P > 0.001$, Student's *t*-test, compared with controls.

‡ $0.01 > P > 0.001$, χ^2_1, test with Yates' correction, compared with controls and compared with any group with 6 of 6 positive harvests.

Values are means (S.D.) of acid-fast bacilli harvested from individual animals $6\frac{1}{2}$ months after inoculation with 5×10^3 *M. Leprae*.

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Atlanta, Georgia showed intermediate levels of sulphone resistance (multiplication in mice fed 0.0001% and 0.001% w/w dapsone in the diets but no growth in animals fed 0.01% dietary dapsone). The patient was put on high doses of dapsone (up to 200 mg daily) from 1968 to 1970, and, because his disease continued to progress, he was then treated with streptomycin from 1970 to 1972. His disease responded to streptomycin, but in July 1972, it became progressive once again despite continued therapy, and treatment was changed to rifampin 600 mg daily. The patient took 93.5% of his prescribed doses of rifampin from July 14, 1972 to July 10, 1976. In February, 1976, after 43 months of rifampin therapy, a new nodular skin lesion developed on his left lower chest. Biopsy was done and mouse foot-pad drug-sensitivity studies were started. The patient had slow progression of his lepromatous leprosy despite rifampin until July, 1976, at which time he was placed on clofazimine ("Lamprene") 100 mg daily. The results of drug-sensitivity tests are given in the table.

To our knowledge this is the first case of rifampin-resistant leprosy confirmed by mouse foot-pad studies. The pattern of rifampin resistance in *M. leprae* appears to be of a streptomycin type or single-step mutant. This contrasts to our experience with 75 dapsone-resistant strains in which the pattern of growth in mice fed dapsone indicates a penicillin or multiplestep type mutation. The spectre of multiple drug-resistant leprosy bacilli suggests that consideration be given to routine multiple drug therapy of lepromatous leprosy, particularly in regimens including rifampin.

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11th INTERNATIONAL LEPROSY CONGRESS MEXICO CITY, 13-18 NOVEMBER, 1978

The special Advisory Committee, nominated by the President of the International Leprosy Association, Dr J. Convit, to advise him on the content and form of the Scientific Sessions and general arrangements for the 11th Congress, met in Mexico City on 7 and 8 January, 1977.

The Committee waited on Dr Emilio Martinez Manautou, the newly appointed Secretary for Health. Like his predecessor in office, he expressed warm interest in the Congress and assured the delegation of his Government's support.

The Committee met with the active participation of Drs Latapi, Saúl and Rodriguez, local President, Vice-President and Secretary respectively, and also had a session with the full local Organizing Committee.

The President's Advisory Committee considered the numerous suggestions that have come since the Bergen Congress from members of the International Leprosy Association and others. While many of these suggestions cancelled each other out,

and others were quite impracticable for various reasons, the Committee arrived at a series of compromises which, it is hoped, will augment the value of the Congress to the majority of the participants without impairing its scientific purpose and content.

An innovation that will commend itself to many will be the designation of named workers to present papers on a given theme, of a didactic or review nature. Unfortunately, this will mean that fewer proffered papers will be read.

Another innovation will be the introduction of "poster sessions" at which designated authors of abstracts will speak of their material, prepared in the form of posters (photographs, charts, graphs, letterpress, etc.) suitable for hanging in the Exhibition area.

The deadline for the receipt of abstracts is 28 February, 1978 (to Dr S. G. Browne, 57a Wimpole Street, London W1M 7DF). Full details of all matters concerned with the Congress will appear in the preliminary announcement, now in course of active preparation.

Pre-Congress Workshops will be held. Members suggested by the President's Advisory Committee, and those nominated by the respective Chairmen, will be notified personally by letter.

The new format of the Scientific Sessions will permit of more time for open discussion.

Since it is not possible (for various reasons) for the afternoon sessions to begin before 1500 h, it is suggested that groups with a common interest may wish to meet in suitable rooms at the Congress Centre, between the hours of 1400 and 1500.

While the President's Advisory Committee dares not hope to have reconciled the irreconcilable, it has tried in its suggestions for the Scientific Sessions at the forthcoming Congress to please most of the people most of the time.

Correspondence regarding the Congress should be addressed to: Dr Amado Saúl, Dermatologo, Insurgente Sur 363–303. Mexico 11, DF, Mexico.

WHO SPECIAL PROGRAMME FOR RESEARCH AND TRAINING IN TROPICAL DISEASES

At a meeting at WHO Headquarters, Geneva, on 7-8 December, 1976, representatives of health ministries, bilateral and multilateral aid agencies, missions and private foundations reviewed developments during the past year in the WHO Special Programme for Research and Training in Tropical Diseases. The 35 delegations were unanimous in expressing support for the Special Programme, and US $7.5 millions was pledged for 1977 by, The UN Development Programme; ILEP; The Sasakawa Memorial Health Foundation; The Japan Shipbuilding Industry Foundation; and Governments or Aid Missions of Austria, Belgium, Denmark, Finland, Nigeria, Norway, Switzerland and the United Kingdom. This is good news for all concerned with leprosy, for it indicates that the financial backing for the IMMLEP and THELEP programmes is secure.

SECOND REGIONAL CONFERENCE OF DERMATOLOGY
Bangkok, 17-21 January, 1977

This Conference, organized by the Dermatological Society of Thailand at the instigation of the International Society of Tropical Dermatology proved to be a

resounding success. It attracted more than 300 participants from 15 countries, mainly from Asia and Australasia, but also from Europe and the United States of America. The joint sponsors were the Thailand Ministry of Public Health and SEAMEO Tropical Medicine, whose indefatigable co-ordinator is Professor Chamlong Harinasuta.

In addition to discussions on matters of general interest to dermatologists working in the area, leprosy came in for a very fair share of attention. One of the concurrent scientific sessions was entirely devoted to leprosy, under the chairmanship of Dr John Pettit (of Kuala Lumpur) and Dr V. R. Mehta (of Bombay).

The 2 guest speakers at the closing plenary Session were Dr Stanley Browne, who spoke on "Recent advances in leprosy of general and dermatological interest" and Dr William Jopling, whose subject, illustrated by an abundance of coloured transparencies, was "The differential diagnosis of leprosy in the tropics".

It is planned to hold the Third Regional Conference in Indonesia towards the end of 1978.

C.I.O.M.S.

As a Founder-Member of the Council for International Organizations of Medical Sciences, the International Leprosy Association was represented at the recent (November 9–11, 1976) Tenth General Assembly of the Council in Geneva by its Secretary Treasurer, Dr S. G. Browne. Under the dynamic presidency of Dr Alfred Gellhorn and its newly-appointed Executive Secretary, Dr Z. Bankowski, the Council is actively pursuing its role of ethical watchdog on the progress of medical sciences throughout the world.

During the Geneva meeting, the ethical and moral repercussions of drug trials were discussed, and the meaning in practice of "informed consent". Delegates were encouraged to discover if the principles of the Declaration of Helsinki and other internationally recognized pronouncements were being observed in medical publications in which they had an interest or which were published in their countries.

The Council was empowered by its General Assembly to develop a programme on the role and functions of ethical review committees for research involving human subjects. It will work closely in this programme with the WHO and UNESCO. Initially, information will be collected from certain countries where ethical review committees have already been established, such as Ireland, Sweden, the United Kingdom and the Unites States of America. Reference was made at the meeting to the valuable pioneering work in this field of the Medical Research Council of Great Britain.

Any relevant experiences of members engaged in drug trials, which might be of value in the compilation of the report, would be welcomed by Dr S. G. Browne.

Future activities of the Council will include further debates on medical education and on various aspects of biochemical ethics, and an investigation (on the invitation of the WHO) of the views of medical scientists and other health workers on the protection of prisoners and detainees against torture and other cruel, inhuman or degrading treatment or punishment.

The Secretary-Treasurer of the International Leprosy Association, who was elected Vice-President of the CIOMS at its General Assembly will welcome any comments from members (under confidential cover if thought advisable) to

enable him to represent their views. The reactions of all CIOMS Member-Organizations, now numbering 90—including 68 international organizations and 22 national bodies representing national academics of science and research councils—will be sought and studied.

TRAINING OF LEPROSY WORKERS IN ASIA

The First International Workshop on Training of Leprosy Workers in Asia was held in Thailand from 25 to 28 November, 1976, under the auspices of the Ministry of Public Health of Thailand and the Sasakawa Memorial Health Foundation. A total of 36 delegates and observers from 10 Asian countries and 8 international anti-leprosy organizations, as well as representatives from the Leprosy Division of Thailand Department of Communicable Disease Control, spent a very full 4 days in Bangkok and Pattaya, discussing and debating in a very practical fashion the problems posed by the training of leprosy workers in countries where the disease is a major health hazard With the exception of Japan, Taiwan and Singapore the countries represented at the workshop might be described as poor and developing, and they all had to cope with other diseases that numerically took precedence over leprosy.

After the inaugural ceremony, at which Mr Kyoichi Sasakawa himself spoke, Dr Stanley Browne gave the opening paper entitled "The Training of Health Workers in Leprosy—ILEP's approach", after which Dr J. Walter from the WHO Headquarters in Geneva read a paper on "Manpower formation for leprosy control".

In addition to very able presentations from delegates from Thailand and other countries of South-East Asia, and some excellent sessions on "How to teach" by Thai medical education experts, Dr Ernest Fritschi (Karigiri), Dr J. Cap (ALERT, Addis Ababa), and Dr Felton Ross (now Medical Adviser to the American Leprosy Missions, Inc.) contributed not only in papers they read but also in the discussions that occupied a commendable part of each session.

After the Workshop, the delegates were taken by coach to the Provincial capital of Khonkaen, where they saw the Nonsumboon Leprosarium, the Miramon Medical and Social Centre, and the Provincial Training School and Health Department Headquarters. A concluding visit was paid to the Pharpradeung Leprosarium and Training Centre just outside Bangkok.

This valuable seminar will have considerable influence upon the standards of training of health workers in leprosy for years to come in the countries of South-East Asia.

CHEMOTHERAPY OF LEPROSY IN ASIA

The first International Workshop on the Chemotherapy of Leprosy in Asia was held in Manila (Philippines) from 26 January to 2 February, 1977 under the joint sponsorship of the Department of Health of the Republic of the Philippines and the Sasakawa Memorial Health Foundation, Japan. Governments of countries in South-East Asia had been invited to send delegates to the Workshop, and in addition there were guest lecturers from England, Belgium, the United States of America and the Philippines, as well as a number of local observers.

With an appreciation of the size of the leprosy problem in the countries represented, and conscious of the threat of the emergence of sulphone-resistant

bacilli on a wide scale, the Workshop reviewed the very practical problems of the treatment of huge numbers of patients within the context of meagre financial resources and, in most of the countries, of incomplete medical coverage.

The Workshop stressed the importance of regular treatment, and was gratified to be assured that monotherapy with dapsone was still considered to be adequate for patients suffering from paucibacillary forms of leprosy. The menace of sulphone-resistance called for a comprehensive prevalence study of the condition, since in many areas where it should be occurring its existence was not yet suspected. This study would presuppose accurate records of treatment given before the appearance of relapse due to resistant organisms.

Rifampicin or clofazimine should be given in addition to dapsone at the beginning of treatment to all patients suffering from multibacillary forms of leprosy. The financial implications of this recommendation to the poorer countries of Asia faced with a considerable leprosy problem, would be brought to the attention of governments and voluntary agencies.

As in previous workshop sponsored by the Sasakawa Memorial Health Foundation, the importance of adequate training of health workers was stressed, as well as the necessity to treat adequately all cases of reaction arising when optimally large doses of dapsone were given daily to patients in danger of developing reversal reaction.

THE CLASSIFICATION OF LEPROSY

A very useful series of 35 mm transparencies on the classification of leprosy has been produced by the Institute of Child Health, 30 Guilford Street, London WC1N 1EH, U.K. That these have been prepared by Dr Jopling and Dr Ridley is sufficient testimony to their authority. Microscopic photographs illustrating the various type of leprosy are matched by clinical photographs, and there are 2 accompanying scripts, one by Drs Jopling and Ridley the other by Dr C. McDougall which includes a questionnaire. The set is available from Foundation for Teaching Aids at low cost, c/o The Institute of Child Health at the above address, for a small charge.

RESEARCH IN LEPROSY CONTROL

A vacancy exists at Schieffelin Leprosy Research and Training Centre, Karigiri, Tamil Nadu S. India, for an Epidemiologist to work in the Leprosy Control Project. The Control Project, established in 1962, is one of the best documented projects in the world. A very high level of co-operation between local population leprosy patients and the staff of SLR and TC has been achieved. The project offers unrivalled opportunities for use as a field laboratory. The basic control procedures are undertaken by 20 trained paramedical workers, most of whom have been with the project since its inception, supervised by 3 supervisors and 2 doctors. 8600 patients are registered in a population of 426,000. The appointment will be for 3-5 years.

Successful applicants should have an M.P.H. or equivalent in addition to medical qualifications. Field experience in endemic disease control in the tropics will be an advantage. Further information about this appointment may be obtained from Mr A. D. Waudby, The Leprosy Mission, 50 Portland Place, London W1N 3DG, England, to whom application should also be addressed.