REPORTS

The Leprosy Research Fund

The objects and achievements of this fund are described by Dr. R. G. Cochrane. The headquarters of Dr. Cochrane and of the Leprosy Research Fund (LRF for short) are at 11A Weymouth Street, London, W.1, England.

In 1953 the American Leprosy Missions appointed Dr. Cochrane as their technical medical adviser, wisely giving him full freedom to develop his lines of investigation and the stimulus to and aid for research in leprosy by other workers. From this the LRF and its beneficial activities have grown. One of the contentions by Dr. Cochrane was that leprosy research could enrich the basic knowledge in other diseases and branches of science, and in this he was proved correct.

The first financial grant for the LRF came from the American Leprosy Missions, and later the Wellcome Foundation granted £500 for three years because of their interest in the histology section of the programme, and by October 1953 the LRF came into being in 11A Weymouth Street, under the administration of a committee under the Chairmanship of Dr. W. A. R. Thomson (a joint editor of *The Practitioner*). The LRF does not aim to raise public subscriptions nor to finance large long term research projects. Its limited resources are used to stimulate pilot research projects and enquiries, and to assess the probable value of such approaches to basic research problems, as well as in new therapeutics. For practical early therapeutic trials of new drugs there is the norm of efficiency of the sulphones for comparison, few cases are necessary, and proved lepromatous leprosy cases are the most informative, and efficient pilot trials can save a lot of money later. The LRF is in touch with a large number of leprosaria throughout the world and finds ready co-operation in arranging such pilot therapeutic trials.

Some interesting activities of the LRF are as follows. Dr. V. R. Khanolkhar, Director of the Indian Cancer Centre in Bombay, by 1954 had re-focused attention on the histopathology of early lesions in leprosy, especially in regard to the cutaneous nerves. The LRF helped Dr. A. G. M. Weddell (Reader in Human Anatomy, University of Oxford) to visit India to study cutaneous sensibility in relation to leprosy, with results which advance our knowledge of cutaneous sensibility as well as of leprosy. As a direct result of Dr. Weddell's work, Dr. D. G. Jamison (Lecturer in Physiology, Corpus Christi, Oxford) was appointed to a research fellowship sponsored by the Royal Society, and in company with Dr. Cochrane visited Nigeria, January to March 1957, and collected material. This visit was under the auspices of the Colonial Medical Research Committee, and the subsequent studies promise to advance knowledge of the

histopathology of leprosy and in particular of the path of invasion and evolution of the disease.

The electronmicroscopic studies of *M. leprae* since 1955 by Dr. E. M. Brieger of the Strangeways Laboratories, Cambridge, were likewise fostered and financed by the LRF. He visited and obtained material from Oicha Leprosarium in the Belgian Congo. This fruitful work of Dr. Brieger and colleagues has been further supported by a two-year grant from the C.M.R.C.

Similarly in 1956 Dr. S. W. A. Kuper (Consultant in Clinical Pathology at the Brompton Hospital, London) visited Westfort Institution, South Africa, and obtained material for a detailed study of the lepromin test, and his journey was financed by the LRF. A second visit was made in 1957.

Dr. John Hanks, Bacteriologist to the American Leprosy Foundation, visited London in 1955, and the LRF had some hand in arranging this.

Because of Dr. Cochrane's long continued interest in the histopathology of leprosy, the LRF is particularly well equipped with histological slides and specimens, and clinical photographs. It has been a natural step therefore for Dr. Cochrane to suggest that a formal registry now be developed: the cost of the improvements and staff and running costs for such a registry is estimated to be £2,300 per annum. Dr. Cochrane emphasizes that the LRF is itself a pilot organization and would cheerfully disappear if some larger body took over or absorbed its functions, or independently organized itself to perform similar functions.

The 83rd Annual Report of the Mission to Lepers deals with the year 1957, and reveals a far-flung assistance to leprosy work in many countries, based on a total ordinary income of £355,680 from the free donations of the people of Great Britain and other countries. Medical statistics give some idea of this magnificent work. From 89 of the Mission's own or aided leprosaria in India, Africa and the Far East, 18,899 patients had received treatment, and of these 3,488 had progressed to the arrest of the disease (1,844 without deformity). In addition, 6,582 were much improved and it had been suitable to discharge 1,401 of these. The disease had become stationary in a further 1,409 patients. The outpatients brought under treatment numbered 38,840 and of these 3,155 had become 'arrested' and 14,604 had received some degree of improvement.

Lecture by Mr. Paul W. Brand, M.B., F.R.C.S., on Reconstructive Surgery in Leprosy. (Reported by Dr. J. Ross Innes, who was present.)

Mr. Brand is Director of Orthopaedic Work of the Mission to Lepers and is stationed in Vellore, South India. On the 18th

June, 1958, under the auspices of the Mission to Lepers and the Friends of Vellore, he lectured on reconstructive surgery in the Royal Society of Medicine, under the chairmanship of Professor H. J. Seddon, C.M.G., of the Institute of Orthopaedics.

Mr. Brand said that proper understanding of the nature of the deformity in leprosy is vital. Eleven years ago, he tried to find out why leprosy eats away tissues in hands and feet, and by studying 2,000 hands found that leprosy destroyed only digits and did that in two different ways: (*a*) by the direct activity of leprosy and (*b*) by the effect of trauma, sepsis, and burns on digits rendered anaesthetic by the leprosy. In the history of the loss of their digits, patients recalled early incidents which suggested that their loss was always due to a secondary trauma. Peculiar to leprosy among the diseases which produce granulation tissue is the great tendency to the loss and destruction of fibres. In other diseases, the part attacked by the morbid process is carefully protected, but not so in leprosy, and the loss of tissue goes on unchecked. The introduction of protection to the hands and feet in leprosy is entirely successful, even in cases where the nerves have been grossly damaged. There is no doubt that the leprosy patient uses the hand too freely and carelessly, and the blisters which appear are *not* typical of uncomplicated leprosy but of unregarded trauma. Mr. Brand checked this in a clinical experiment designed to avert trauma by splintings and dressings and general watchfulness. It was found that in 15 men after five years, only two had lost any length of finger because of associated septic infection. Special care will prevent the loss of segments of fingers. The chief causes of loss of the bones of the hand are the continuation of the use of the hand after minor injury and infection, too vigorous use of the hand at any time, or lepra reaction which tends to set up osteoporosis. The control of the force of natural movements of the hands and feet was previously thought to be due to control exerted in the muscle spindles, but it has been shown that it is almost entirely controlled by the skin reflexes. Anaesthesia of the skin of the hand abolishes or damages the pressure sense. It has been found that lack of control of even small original forces has led to pressure of 24 lb. per square inch (about 1.8 kg. per sq. cm.), and this pressure would be extremely painful in a normal hand.

Mr. Brand described the correct picture of the motor disability of the claw hand, which leads to the finger-tip clasp in leprosy patients. This also leads to concentration of force on a small area, so that the finger tips may receive 100 lb. per square inch (about 7 kg. per sq. cm.). Each day the use of a claw hand in work may set up a crushing action on the terminal phalanges and even tiny bone fractures. In one experiment, a boy was forbidden to work in farming and taught carpentry instead and given careful instruction

how to use his hands safely. He lost no part of his digits. Even when he went back to farming, he used the care of his hands that he had been taught and did not injure his hands badly, though there was some slight shortening later in his fingers. The same things apply to the feet. Special soles and sandals are devised to protect against uneven and concentrated strains on the feet in walking.

In motor paralysis in leprosy, there is a pattern and always some muscles are exempt. It seems that leprosy can affect every nerve that is near the surface of the skin but not those well protected by tissues, and there seems to be some connection with the bulk of the nerve. Thus, all thick nerves near the skin are liable to paralysis and deep nerves are not so, in spite of the thickness. In the limbs, the thickness goes with nearness to surface and hence the limbs have a great liability to paralysis in leprosy.

Mr. Brand described the fascinating features of the surgical reconstruction of leprosy deformities and successful operations for tendon transplantation and showed an instructive film of an operation of this nature, which dealt with the standard procedure for claw hand.

East African Leprosy Research Centre, Annual Report covering 1st July, 1956 to 30th June, 1957.

Dr. J. M. B. Garrod, who has been Director since 22nd January, 1957, when he replaced Dr. J. Ross Innes on his translation to Medical Secretary of BELRA, reports on the progress of this new Centre. Therapeutic trial of the diphenylthiourea (DPT or SU 1906), which was started in July 1956, has continued and 45 patients now remain on the trial. The Centre obtains patients from the adjoining leprosarium of the Kenya Medical Department. Because it is proving difficult to get large numbers of patients, Dr. Garrod has made arrangements to extend the drug trial to two other leprosaria. As well as a large share of the capital cost of the Research Centre, and the recent special expenses of biochemical work, BELRA shares in the recurrent costs and gave a special grant of £4,000 to defray the cost of connecting the Centre to mains electricity. Dr. Ralph Naylor of the Department of Chemistry of Makerere College, Uganda, has visited the Centre and is pursuing studies with tetrazolium compounds as applied to staining the human leprosy bacillus, and in applying chemical methods to observation of the growth of mycobacteria in presence of sulphones. (An interim report on the diphenylthiourea compound, by Ross Innes, Smith and Smith, was published in East African Medical Journal, July 1957, **34,** 2, pp. 395–402.)

Nigeria Leprosy Research Unit, Uzuakoli, Annual Report, 1957

This unit concentrates on problems of chemotherapy and

immunology. They had four new drugs under investigation in 1957.

(*a*) *Diphenylthiourea*, compound SU 1906 (DPT).

A report on this drug appeared in *Leprosy Review*, **29,** 1; January, 1958, pp. 25–44. At a dosage level of 25 to 40 mg./kg., there was complete freedom from toxic action and a very satisfactory therapeutic response. It was found especially useful in cases of intolerance to the sulphones and in cases with severe neuritis and persistent lepra reaction and also in cases of DDS psychosis. Trial of the drug was extended to six other centres, and the total number of patients receiving DPT rose to 167. All these centres confirmed the favourable opinion of the drug. It has also been shown that DPT combines safely and effectively with DDS and with INH. So far no satisfactory laboratory method has been devised for the estimation of DPT in body fluids. A trial has been made of twice weekly dosage, with the result that there seems to be some loss of efficiency except in some patients for whom it is satisfactory.

(*b*) *Diameno Diphenyl Sulphoxide* (DDSO).

This drug has been studied for 26 months in a dosage of 100 mgm. daily. It has a certain amount of toxicity and does not appear to be as active as DPT, but in some cases it gave good results. It has been tried also in twice weekly doses of 300 mgm. and has been found quite effective. It seems similar to DDS in both activity and toxicity, but does not seem to have notable advantages over DDS, but further study is needed.

(*c*) *Pyrazinamide.*

This was given in a small trial of 11 patients in doses of 250 to 500 mgm. daily. At this lower dosage than that used in tuberculosis, the therapeutic action was erratic. The trial was brought to an end when two cases, after 15 months, showed clear signs of drug resistance.

(*d*) *Diethyl-dithiol-isophthalate*, compound 15688.

The trial of this drug is in its early stages. It has a high antituberculous activity and the same seems to apply to leprosy but it has a very offensive odour, which is a great trouble to the patient. It is given by inunction.

Immunology.

The tuberculin-lepromin relationships have been studied and reported in *Leprosy Review*, **29,** 2: April, 1958, pp. 81–101. The association between tuberculin and lepromin sensitivity found in these areas seems apparently to be due to non-specific geographical and constitutional factors. In another trial of BCG in indeterminate and early lepromatous leprosy, it was found that it completely failed to induce lepromin sensitivity. Dr. Davey thinks that these findings

make it very doubtful whether mass BCG inoculation offers any ready means of eradicating leprosy.

For the year 1957, Dr. T. F. Davey, Director of the Unit, was assisted by Mr. S. E. Drewett, and records the visits of Dr. R. G. Cochrane, Dr. J. Ross Innes, Dr. D. S. Ridley, Dr. D. G. Jamison, Dr. V. Ekambaram and Dr. Khushu.

UZUAKOLI, 1957

GROUP DECLINE IN BACTERIAL INDEX DURING CHEMOTHERAPY