REPORTS

Annual Report, Leprosy Research Unit, Uzuakoli, 1961.

Introduction

The Leprosy Research Unit at Uzuakoli is under the administrative control of the Ministry of Health, Eastern Nigeria. It is an integral part of the Regional Leprosy Service, being intimately associated with this Service in the Owerri Province and related to that in other Provinces through Settlements that co-operate in drug trials.

The financial support, which used to come from the Colonial Welfare and Development Fund, through the Federal Government, is now assured directly by the Federal Government.

The research projects of the Unit are made possible and greatly facilitated in all ways by the Settlement at which it is located. The advantages of the complete fusion of administrative, medical and laboratory activities, are everywhere apparent.

A. Chemotherapy

Therapeutic trials have been completed on the following drugs:

(*a*) Diamino-diphenyl sulphoxide;
(*b*) An azulene derivative: AZ-8;
(*c*) A long-acting Prednisolone.

Trials are still in progress on the following drugs:

(*d*) Thiambutosine; Diphenyl thiourea; DPT or Compound SU 1906;
(*e*) Ditophal; Diethyl-dithiol-*iso*phthalate;
(*f*) A substituted Anilino-*apo*safranin;
(*g*) Methimazole; Tapazole (Lilly).

As opportunity offers, studies are proceeding on other drugs of possible use in the dyschromias of leprosy (especially persistent hypopigmentation in quiescent and resolved lesions) and other conditions;

(*h*) Mono-benzyl ether of hydroquinone (Boots Chemists, Limited);
(*i*) 8-methoxy-psoralen; 'Oxsoralen' (Paul B. Elder);
(*j*) Dihydroxyacetone (Boots Chemists, Limited).

(*a*) *Diamino-diphenyl sulphoxide.*—All patients who had received this drug were reviewed clinically and bacteriologically, both those still in the Settlement and those who had been discharged. Particular attention was paid to possible signs of residual nephrotoxicity. It was gratifying to note that there was little indication of permanent kidney damage among the patients who had during the course of treatment shown albuminuria and haematuria. Dr. Davey co-operated in the

publication of a paper which summarized the findings and contained a warning regarding the nephrotoxicity of the drug. Similar conclusions have been reached when the drug was employed in high doses for the treatment of dermatitis herpetiformis.

(*b*) *An azulene derivative:* 1.4 *dimethyl-7-isopropyl-azulene; AZ*-8 (*Beris Laboratories*).—The 23 patients who took part in this trial were reviewed. The initial improvement noted, though not maintained, is suggestive that the anti-inflammatory action of the drug may possibly potentiate anti-leprosy therapy if given in conjunction with standard treatment, e.g., dapsone. The patients have since responded to accepted treatment for lepra reaction, most of them having had severe and persistent episodes.

(*c*) *A long-acting Prednisolone* (*Pfizer*).—Despite the recognized limitations and side effects and disadvantages of prolonged corticosteroid therapy, there is an unfortunate class of patients with severe lepromatous leprosy who respond only to these drugs. They are subject to persistent lepra reaction that fails to respond when anti-leprosy therapy is stopped and other treatment instituted. When indicated, the long-acting prednisolone under trial, given by injection at weekly intervals, not only controls the distressing clinical manifestations of lepra reaction, but also in some cases permits of the resumption, in carefully graduated doses, of anti-leprosy therapy. A publication summarizes the results of our enquiry.

(*d*) *Thiambutosine; a Diphenyl thiourea, DPT, Compound SU* 1906 (*Ciba*).—Work has continued on this useful drug, and a trial of an injectable compound will shortly be instituted. The occurrence of a modified form of drug 'resistance', observed towards the end of the second year of treatment, is confirmed. It is therefore advisable to introduce another drug during the second year, with a view to postponing the onset of resistance and in order to assure that adequate anti-leprosy therapy may be continued.

(*e*) *Ditophal: Diethyl-dithiol-isophthalate;* '*Etisul*' (*I.C.I.*).—The patients who have taken part in previous trials have continued under observation; it is particularly important to discover if ditophal given alone has a beneficial effect on lepromatous leprosy, and if the addition of ditophal to standard therapy reduces the total time necessary for treatment and accelerates bacteriological negativity.

Five patients were given ditophal in addition to the Rimino-compound, B 663.

It would appear that ditophal in certain cases has a definite effect in lepromatous leprosy; and that it may reduce the period of treatment. Several aspects of this problem remain obscure.

(*f*) *Rimino-compound: a substituted Anilino-aposafranin B* 663 (*J. R. Geigy, S.A.*).—In view of the distinctly encouraging early results obtained in the small pilot trial of this compound (6 untreated lepromatous patients, of whom 3 received dapsone in addition), more

patients were added to the trial when further supplies of the drug were made available by the manufacturers. Twenty-two additional patients receive the drug, of whom 7 received dapsone in addition and 5 received ditophal ('Etisul' I.C.I.). Further investigation suggests that the beneficial effect of the drug may not be maintained and that a modified form of drug 'resistance' may develop. Unfortunately, in view of the expense and technical difficulties of manufacturing this promising compound, it is probable that no more will be available for trial or therapy, since it could never replace such an inexpensive and chemically simple drug as dapsone.

(*g*) *Methimazole:* 1-*methyl*-2-*mercaptoimidazole;* '*Tapazole*' (*Eli Lilly and Company Research Laboratories*).—In view of the fortuitous observation that a patient suffering from leprosy benefited from Tapazole (given for hyperthyroidism), a South American worker reported favourably on the use of the drug in leprosy. Notwithstanding the paucity of bacteriological supporting evidence, it was decided to proceed cautiously with a small pilot trial to ascertain if the drug was worthy of fuller investigation. Five patients willingly agreed to co-operate, though the tentative nature of the trial was explained to them, as also the necessity for frequent blood examinations. The clinical and bacteriological findings do not suggest the advisability of further trial, and the risk of disabling side-effects and even leucopenia and agranulo-cytosis would render the drug unsuitable for mass treatment even though it should have some value in leprosy therapy.

B. Other Investigations

Several studies in the diverse fields of immunology, classification and differential diagnosis have been pursued in the Unit during the year.

1. *Immunology.*—Investigations have continued on the tuberculoid response to the intradermal injection of particulate matter in patients suffering from polar forms of leprosy. In particular, and in continued collaboration with Dr. D. S. Ridley, Pathologist at the (London) Hospital for Tropical Diseases, the efforts of the inoculation of micronised Bentonite have been studied histologically.

2. *Classification.* Further studies have been undertaken with a view to shedding light on certain controversial matters: borderline leprosy (especially its unstable clinical and immunological features); the maculo-anaesthetic variety of tuberculoid leprosy (*vide* India leprologists); the macules of dimorphous leprosy.

3. *Differential* diagnosis necessarily occupies a prominent place in the daily Diagnostic Clinic in the Unit, where approximately half the patients thought to have leprosy are found in reality to be suffering from a wide variety of tropical and non-tropical cutaneous and neural conditions.

4. *Miscellaneous* investigations covering a wide field in tropical medicine continued to be pursued in the Unit for their possible help in the elucidation of some of the outstanding problems of leprosy, its epidemiology and its clinical manifestations.

Laboratory Aspects

The laboratory is an essential part of the work of the Unit, and its maintenance at a high level of efficiency is a primary concern. More good work could be done, and more varied investigations attempted, if staff and equipment could be augmented.

Within the limits imposed, however, the laboratory undertakes the routine procedures necessary for the cover of drug trials, immunology and diagnosis.

(*a*) Skin biopsy, the preparation of sections, clinical photography, tuberculin and lepromin reactions; these are undertaken for research patients, and as necessary for other patients on admission;

(*b*) Laboratory cover for drug trials proceeds according to a standardized schedule involving blood, urine and liver function;

(*c*) Bacteriological examination of multiple smears is carried out routinely on all patients in the Settlement, and on all patients presenting themselves at the Diagnostic Clinic. All patients under treatment with new drugs are smeared at regular intervals, and the detailed morphology of the *M. leprae* is recorded for each site examined. This information is of great value in indicating degenerative changes presumably due to therapy, even when the actual bacteriological index may show little change.

Statistics

	1960	1961
Patients smeared for *M. leprae*	3,042	3,049
Lepromin test	187	153
Tuberculin test	142	143
Examinations:		
Blood	2,197	3,204
Serology	—	230
Urine	3,731	3,249
Faeces	763	1,599
Sputum	107	107
Biochemical (various)	719	677
Histological: Blocks	114	74
Slides	336	238
Miscellaneous	128	143
Radiographic	147	122
Bentonite	—	4

Training

The benefits accruing from the short courses of training given for laboratory workers from other Leprosy Settlements in Eastern Nigeria where drug trials are in progress, and elsewhere, have been apparent during the past year. More trainees have followed these courses during 1961.

The existence of these facilities should be more widely known.

Personal

Mr. O. U. Osoagbaka, F.I.M.L.T., has continued in charge of the Laboratory. During his leave (6th June to 4th September) Mr. E. A. Okpo assured this service.

Deep appreciation must be expressed for the continued valuable co-operation of Dr. L. M. Hogerzeil in assuring the administrative oversight of the Settlement. His sharing of the clinical work of the Unit, his lively interest in the various research projects undertaken, and his assumption of responsibility for these projects during the absence on leave of the Senior Specialist (from 11th November) are here gratefully acknowledged. He is joint author of a number of scientific papers prepared in the Unit during the year.

Help has also been forthcoming from Medical Officers attached for a time to the Settlement: Drs. J. C. Uzoma, F. O. C. Peters and E. Fern.

Dr. S. G. Browne was elected to the Fellowship of the Royal College of Physicians of London early in the year.

During the year, he gave a course of lectures and demonstrations on Leprosy to the clinical medical students and senior student-nurses at Ibadan University. He also gave lectures to the medical staff of University College Hospital, Ibadan, on 'Some Observations on Onchocerciasis' and to the Ibadan Medical Society on 'Medical Services in the Belgian Congo before Independence'. Dr. Browne gave courses of lectures and demonstrations in Leprosy to Leprosy Inspectors at Oji River and Ekpene Obom, and twice addressed Conferences of doctors from the southern half of Eastern Nigeria (at Ikot Okoro and Ekpene Obom) on 'The Differential Diagnosis of Leprosy', and 'Clinical Varieties of Leprosy'. While on leave, he addressed various scientific bodies, including the Edinburgh Branch of the Royal Society of Tropical Medicine and Hygiene ('Present Perspectives in Leprosy'), and the School of Pharmacy of the Glasgow College of Science and Technology ('Problems and Prospects of Chemotherapy in Leprosy').