EDITORIALS

Drug Resistance in Leprosy

One of the chief bugbears in modern medicine, especially in diseases which require prolonged treatment, is the development of strains of the infecting organism which are resistant to the drug used. What evidence is there that drug resistance may develop in leprosy? As *Myco. leprae* has not so far been effectively cultivated outside the human body, there is no bacteriological indication as to whether there is more than one strain, or as to whether a universal strain varies under certain circumstances. Nor is there any clinical or epidemiological evidence that the gravity of the disease, and the variety in its types and forms, correspond with different strains. These diversities appear rather to be contingent on degrees of resistance—on the soil rather than on the seed. One child of an infective mother will develop the lepromatous type and another a mild tuberculoid, although both have been subjected to intense infection from the same source. The fact that the majority of advanced lepromatous cases under treatment with sulphones continue to improve steadily over long periods, sometimes of ten years or more, would have led to the hope that *Myco. leprae* was incapable of forming resistant strains; but there seems to be general agreement that under treatment with thiosemicarbazone initial improvement comes to an end after a few months, and the patient tends to relapse. Is this the result of drug-resistant strains, or is there something else that blocks the early effectiveness? In our present ignorance of the mode of action it is impossible to say with any certainty.

An important question arises as to whether the sulphones produce drug resistance, and if so under what circumstances. Most of those with any extensive experience of sulphone treatment of leprosy have had patients who improved up to a point and then appeared to make very little or no further progress. In the writer's experience this has generally been connected with two things: irregularity of treatment and absence of physical exercise. Wolcott and Ross[1] found a number of instances of rapid extension of the leprous process in patients receiving continuous sulphone and other treatment, in whom the disease had reached a stage of apparent quiescence. The only possible cause found was that a few of these had experienced some increase of emotional strain. Elsewhere Doull and Walcott [2] reported relapse in 6 of 33 patients who were followed up for one to five years after apparent arrest.

This is in marked contrast to the findings of Lowe[3] in Nigeria. Out of 139 lepromatous patients discharged there was slight

bacteriological relapse in 13. Of these, four became rapidly negative under treatment five became negative without treatment, but in none was there a serious relapse. Garrett[4], after discharging for 3½ years an average of 3,000 patients a year, found an average relapse rate of 7 per cent. These were in three types of patients: (a) In those previously treated with hydnocarpus oil and apparently inactive, many had had a course of dapsone of only one year or less; (b) in clinically tuberculoid cases, not completely typical, either with not very clearly defined edges or with lack of healing centre, in whom response to treatment is usually dramatic. Lesions disappear in a few months, but lacking an initial positive smear, they were given a relatively short course of dapsone, usually 18 months; (c) those not attending regularly for treatment due to laziness or personal difficulties. See also the Owerri Report, page 119 of this issue.

The Editor would welcome evidence and experiences from other workers under the following headings: (1) patients who have become bacteriologically negative (routine examination) under sulphones and have then relapsed; (2) whether such patients have yielded to further treatment with sulphones; (3) patients who improved at first up to a point with sulphones and then failed to make further progress over years of further sulphone treatment; (4) whether these patients undoubtedly *had absorbed* regular treatment; (5) other particulars.

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VII International Congress

At the Madrid Congress in October, 1953, an invitation was received from the Indian Government, and accepted, to hold the seventh international congress on leprosy in India. The first international congress was held in Berlin in 1897, where there was a pronouncement in favour of rigorous isolation of leprosy patients, which was followed by a marked diminution of leprosy in Germany and Central Europe. The second congress was in Bergen in 1909, where the same pronouncement was ratified. This was followed by complete control and near disappearance of leprosy in Norway. The third congress was in Strassburg in 1923, where the tuberculoid form of leprosy was described, leading to a modification of measures for prophylaxis. In 1931 a number of leprologists were invited to a conference in Manila under the auspices of the Leonard

(1) Internat. Jl. of Lep. (1953), Vol. 22, p. 437.
(2) New England Jl. of Med. (1956), Vol. 254, p. 20.
(3) Internat. Jl. of Lep. (1955), Vol. 23, p. 183.
(4) Lep. Rev. (1956), Vol. 27, p. 59.

Wood Memorial, which led among other things to a new classification of leprosy, and to the foundation of the International Leprosy Association. One of its functions was to arrange for quinquennial international congresses in different countries, the governments of which would act as hosts and invite other countries to send delegates. The first of these, that is the **fourth** international congress, was held in Cairo in 1938. There, it was arranged that the next congress should be held at Paris in 1943, but this was rendered impossible by the war, and the fifth Congress met in Havana in 1948 at the invitation of the Government of Cuba. There invitations for the next congress were received from India and from Spain, but by a majority vote it was decided that the sixth congress should be held in Madrid in 1953. There the invitation from India was received for the 1958 congress, and a new invitation was received from Japan. The former of these was accepted, the hope being expressed that a subsequent congress would meet in Japan.

It is understood that the location of the seventh congress will probably be **New Delhi** and that it will probably meet in **November, 1958.**

There was considerable criticism of the last two congresses, and steps are being taken to modify accordingly the arrangements for the Delhi meeting. The chief modifications suggested are as follows:—(1) the scientific preparations to be in the hands of the International Leprosy Association from the first; (2) preparatory panels on as many as possible of the subjects chosen to be formed beforehand, with the object of collecting, discussing and co-ordinating information and opinions prior to the congress; (3) selected workers to be asked to prepare and read papers on each of the selected subjects at the main sessions of the congress, these papers thereafter to be open to general discussion; (4) the results of these papers and discussions would then be co-ordinated with draft resolutions by selected commissions, the nucleus of each commission being the corresponding preparatory panel. Provision would be made for reading of other papers provided they conformed to the regulations regarding length, and were received before the dated decided. We hope to publish further information as soon as it is available.

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Testing New Drugs for Leprosy

A sub-committee of the Colonial Medical Research Council has been formed to initiate and co-ordinate research in leprosy in the U.K. and the colonies. One of its activities is to form panels (a)

to advise on drugs considered suitable for " pilot " testing as to their value in the treatment of leprosy; (b) to arrange for further controlled tests of drugs, the pilot tests of which had given evidence of hopeful results; and (c) to assess statistically and otherwise the results obtained in these controlled experiments.

The compound of diphenylthiourea reported on in this number is a good example o
testing but in a limited controlled experiment, that it is well worthy of wider trials. Arrangements for these trials are already under way. The three chief weaknesses of sulphone treatment are occasional toxicity, erythema nodosum or more severe lepra reaction, and the slowness of elimination of bacteria. If the findings with this new compound on these three scores are widely confirmed, and if its usefulness is not limited by the development of drug resistance, then another considerable advance may be recorded in the treatment and control of leprosy.