ABSTRACTS

Preliminary Report on DPT (Ciba–1906) in the Treatment of Leprosy. (Name of Author not given.) The Med. J. of Malaya, **14,** 4: June, 1960, p. 249.

This brief report is of a trial of Ciba–1906 in 12 leprosy cases at 1 g. to 2 g. per day orally, with control cases given DDS by injection. The results were very good in borderline cases and considerable in lepromatous. The drug seemed non-toxic and is considered worth expanded trials. The higher cost, and the inconvenience of daily administration, are not thought to be of importance.

Leprosy in Papua and New Guinea. D. A. RUSSELL, Papua & New Guinea Med. J., **4,** 2; July, 1960, pp. 49–56.

Dr. Russell, who is specialist m.o. (leprology) has given this interesting study of the problem in those countries. He recognises leprosy as endemic in most parts, and quotes various preliminary survey figures which gave leprosy incidences from 36 to 39 per thousand, with lepromatous rate low, and tuberculoid rate high. The policy of control is on the "*open-up*" modern lines, based at present on oral DDS and Avlosulphon therapy, and other drugs will be tried. There is enlightened recognition of the need to introduce physiotherapy and reconstructive surgery to assist in rehabilitation of those with deformities and stigmata. Dr. Russell also is keen on *training* in leprosy work for nurses and medical auxiliaries, education and propaganda, extension of rural aid and care, and on continued practical research. His refreshing article should be studied in detail by all workers.

The Application of Quantitative Electronmicroscopy to the Study of M. lepraemurium *and* M. leprae. R. J. W. REES and R. C. VALENTINE and P. C. WONG, Journal Gen. Microbiol, **22**, 2; April, 1960, pp. 443–457.

The authors refer to previous reports by HANKS, 1955, and MCFADZEAN and VALENTINE, 1960, who showed that *M. lepraemurium*, when kept in a phosphate buffer loses its viability and shows morphological changes under the electron microscope. The uniform density of the bacilli is lost and the picture changes to an empty cell wall, except for some disorganised material. The present authors confirm the morphological changes and further show that the proportion of degenerated bacilli is inversely proportional to the infectivity of the suspension. The change was also noted in bacilli in tissue cultures in which the tissue cells had degenerated, but not in healthy cultures. The authors also found a third distinct morphological change in which the bacillus divided into many bodies clearly outlined and often dense. This change took place in a medium con-

taining a high percentage of citrate—viability tests showed that such bacilli were dead.

The beading seen in human leprosy bacilli under Z.N. stain seems equivalent to the degenerative change seen under electron microscopy. Death of the bacilli in the host and during storage can thus be detected under the electron microscope. Death in the host but not during storage can be detected by a study of the bacilli under the light microscope after Z.N. staining.

Serological Findings in Leprosy. H. G. S. RUGE, G. FROMM, F. FUHNER and R. S. GUINTO, Bull. World Health Organization, **23,** 1960, pp. 793–802.

The authors seem unaware that The V International Leprosy Congress of Havana in 1948 recommended the abandonment of the word "leper" for a patient of leprosy, and it creates a painful impression in their paper to read phrases like "sera from lepers" instead of "sera from leprosy patients". They have studied the serological finding in leprosy. Leprosy sera often give biologically false positive reactions in serological tests for syphilis, which may be due to the presence of lipid antibodies in the sera, or of errors in technique or unfavourable working conditions in the laboratory. The authors investigated several hundred sera from leprosy subjects by means of 4 of the standard serological tests for syphilis with cardiolipin or crude lipid antigens. They used also the PR test with Reiter treponemes, and the Trep. pallidum immobilization test. It was found that the number of biologically false positives was not so high as expected, and that the lipid antigens were those mainly responsible for the non-specific reactions. They think the PR test will give sufficiently accurate results in the serodiagnosis of treponematoses, but it is not able to differentiate between syphilis and yaws infections.

Leprosy and Coccidiomycosis. J. GONZALEZ, Dermatologia, Rev. Mexicana **4,** 2; June, 1960, pp. 113–119.

The author describes the clinical history and successful treatment by Amphotericin B. of a case of borderline leprosy who also had coccidiomycosis of the neck. The case was seen in Monterrey, Mexico, and is the first case of the diseases combined. The treatment of the leprosy at the same time was carried on with Avlosulphone with success.

Biochemical Aspects of the Chemotherapy of Leprosy. G. A. ELLARD, East African Med. J., **37,** 12; Dec., 1960, pp. 765–775.

The author has been working for 2 years at the East African Leprosy Research Centre at Alupe, Kenya.

He opens his paper by stating that quicker acting drugs are urgently needed for the treatment of leprosy, and sets out to study the biochemical aspects involved in the choice of potential new

drugs. He points out that because of the similarity of the causal agents of tuberculosis and leprosy, almost all the promising antitubercular drugs have been tried in leprosy. This has had partial success, for the best antitubercular drugs are of little value in the treatment of leprosy, while the best antileprosy drugs are not now used in tuberculosis (with a possible exception in the case of Etisul). No drug has yet been found effective in leprosy which is entirely without activity in tuberculosis. Testing of antileprosy drugs in rat leprosy has been done by some, with good but by no means sure correlation with human leprosy. Others think that antileprosy drugs should have metal-chelating properties, lipid solubility, and antifungal activity. The general approach of using antitubercular drugs did result in the discovery of a curative drug, DDS. With the sulphones, leprosy became curable, though slowly, but *if sulphones alone are used* the author thinks that *the eradication of the disease in this generation will be impossible. New drugs are urgently needed, which will cure the disease in a year or less.*

The requirements of a good drug for the treatment of leprosy are very exacting. It should be well absorbed but slowly excreted, so that blood levels do not diminish rapidly. As most leprosy cases are treated on an outpatient basis, drugs active by administration only once or twice a week are desirable. As most leprosy occurs in the poorer countries of the world, a good drug should be cheap to produce (though cheapness in a drug is a factor secondary to effectiveness: it will be more economical to use a very effective drug which is dearer, as it will be needed for a shorter time—Editor). An anti-leprosy drug should be non-toxic in therapeutic doses, because of the paucity of skilled staff. Biochemical approaches include:
(1) *The designing of antimetabolites is proving a very profitable approach in the search for new chemotherapeutic compounds.* Antimetabolites are compounds which inhibit the pathogen by interfering with some vital enzymic process in which the antimetabolite is bound on to an enzyme in place of the metabolite it mimics. Consequently only small molecular changes are needed to turn a metabolite into an antimetabolite. Examples are sulphonamides derived from PAB, and PAS from benzoic and salicylic acids. Sometimes combining two antimetabolites in one compound gives a potent new one, e.g. INH from the active chemical groupings of INH and thiosemicarbazones. The difficulties in the way of the cultivation and transmission of *M. leprae*, perhaps from the lack of some vital growth factor, reduce the chances of its synthezising an antimetabolite, but mycobacteria possess permeases and also have adaptive enzymes so there are yet possibilities. By synthezising antimetabolites, new classes of antimycobacterial compounds may be discovered, which must then be tailored into a suitable form for absorption by the bacillus.
(2) *For effective in vivo activity* a drug must be well abso bed, and

the absorption processes are highly specific. At present, many compounds have to be made and the best absorbed found by experiment. Absorption in man is often very different from in the animal, and after absorption there are differences in metabolism which will cause variation in therapeutic action. To obtain *in vivo* action, a drug must reach the infective agent. In both tuberculosis and leprosy this is particularly difficult because the bacilli are intracellular and maybe walled in by fibrous tissue or lipid.

(3) *The evasion of drug resistance* in leprosy at present depends on the hope that such strains will be few and slow to appear; so it is with the slower sulphones in therapy. For quicker drugs, the appearance of drug-resistant strains may often be prevented by the concurrent use of two or more drugs, with the extra benefit of synergic action to be expected.

(4) *Personal variations:* every human being is now thought to have a virtually unique biochemical constitution; biochemistry applied to chemotherapy must take account of this. Individual human variations in drug response must never be forgotten, e.g. there are rapid, medium, and slow inactivators of INH, and the inactivator-type is genetically controlled.

Present Antileprosy Drugs were then discussed by the author, viz. chaulmoogra oil, the sulphones, DDSO, TB_1, DPT and Etisul. As regards DPT and Etisul he drew attention to the finding that a decline in the proportion of normal staining bacilli precedes the decline in numbers of bacilli. Both these drugs seem to act by rendering the bacilli susceptible to phagocytic destruction. He states that Etisul causes a rapid diminution of the numbers of normal staining bacilli and the bacterial index.

Angiography in Non-lepromatous Leprosy. S. P. BASU, S. K. GHOSH, N. MUKERJEE, and K. P. ROY, Bulletin of the Calcutta Sch. of Trop. Med., **8,** 4: Oct., 1960, pp. 166–167.

From investigations by angiography and other means findings led the authors to believe that vascular stasis and consequent failure to dissipate heat are noticeable in the human body parts in non-lepromatous leprosy. The experiments of CHATTERJEE on blister formation led to a similar conclusion. The authors now report angiographic results in the hands of 20 non-lepromatous cases. All the cases had slight or moderate polyneuritic changes in the upper limb. They injected 10 ml. of 30% Dionine into the brachial artery above the bend of the elbow and X-rays were taken. There was violent spasm of the arteries in almost all the cases, probably due to the dionine. The dye was seen well distributed in the arteries, with good visualization in most cases. Some cases showed *stasis* of the dye, engorgement of parts of the vessels, thinning of the digital vessels and delayed emptying.