EDITORIAL.

The sulphones, using this term to cover the parent substance as well as its derivatives, have become the accepted routine treatment for leprosy. It is necessary, however, when considering the therapeutic battle against leprosy, to remember the hard and up hill task which preceded the search for new and more powerful remedies against this disease. We therefore should not too readily assume that, because we have cracked the armour of this obstinate invader of the human tissues, the victory over leprosy is complete. Those who remember the work on the Hydnocarpus (Chaulmoogra) derivatives, will recall the arduous labours of the early pioneers —particularly Mercado and Heiser in the Philippines, and Sir Leonard Rogers' brilliant work in India—before an effective method of treatment was evolved. It is a strange coincidence that the war years of 1914-18 saw the great advances in chaulmoogra therapy, while the war years 1939-45 saw the beginning of the sulphone era in leprosy. It seems as if when man's spirit is challenged to the greatest extent, at these times the mind of man turns his attention to scientific research into processes which appear to be most baffling.

In this number of *Leprosy Review* there has been an attempt to present different aspects of sulphone therapy, and the articles written or reprinted have this end in view—the maintenance of an adequate balance in the therapeutic approach to leprosy. Dr. Garrett's article shows the possiblity, as Dr. Lowe has previously contended, of using the parent sulphone as an out-patient method of treatment; whereas the Drs. Barnes issue a note of warning as to the possible dangers of using this drug in such a widespread manner. The article reprinted from the *Practitioner* endeavours to guide workers as to the dosage of the parent sulphone and its derivatives.

In this connection it is important to note that a group of medical men interested in leprosy work in Africa recently met Dr. E. Muir and the Medical Secretary of the Association in order to discuss the question of sulphone therapy, and issue a statement which could be accepted by all. We hope to publish this statement in our next issue of the Review. Suffice it to say that the unanimous feeling of the meeting was that if D.D.S. is chosen it is preferable to administer it in twice-weekly oral dosage, gradually increasing to a maximum of 800 mgm. a week, i.e.

400 mgm. twice a week, than in daily dosage. It was emphasised that tablets should never be given to a patient to take home unless the authorities were certain that he would not abuse this privilege. In this meeting parenteral Sulphetrone (50% aqueous solution) in a dosage gradually reaching 3.0 gms. divided into twice-weekly dosages, was also recommended. The question of the choice of sulphones for mass treatment can now be left to the discretion of the individual practitioner. The choice of sulphone which is most convenient to use so largely depends on conditions pertaining in different countries that all we can attempt is to set forth the various advantages and drawbacks of the sulphone preparations available.

It is salutary to remind ourselves that a similar situation arose many years ago regarding the mass treatment of yaws—the following passage from an article on this disease is worthwhile quoting, for we should not overlook the experience of others situated in similar circumstances:—

"Stovarsol or Fourneau 190, a pentavalent arsenical compound, was the first product used in the Ivory Coast in an attempt to suppress yaws with drugs. Advocated by Bouffard in 1924, it had the following advantages: it was in the form of 0.25 g. tablets, easy to transport and to administer; it was given by mouth and consequently required only simple supervision of its administration. Finally, it was very active, at least on the skin lesions. The distribution of stovarsol, without charge, by the Health Service of the Ivory Coast, rose from 20 kilos in 1925 to 100 kilos in 1929, and finally reached 200 kilos in 1934. The price of stovarsol was then about 1,000 francs per kilo. Bouffard had fixed the standard treatment as follows:—

Children, under 10 years old, 3 tablets on 2 consecutive days, i.e. 1.50 g., from 10 to 15 years, 4 tablets on 2 consecutive days, i.e. 2 g.

Adults, 4 tablets on 3 consecutive days, i.e. 3 g.

Later these doses seemed high to Salomon, who reduced them considerably, especially for children. Stovarsol has many disadvantages. Its great ease of administration had led to the idea that its administration could be entrusted to hospital attendants. This idea had to be abandoned because of the illicit traffic in which they indulged with this drug, so eagerly sought after by the natives, who quickly came to look on it as a panacea and would pay high prices for it. The drug moreover, is so potent that it is not suitable for the treatment of yaws without effective medical supervision . . . . When it was realised that medical supervision was necessary if one wishes to cure yaws, the secondary advantages of stovarsol all disappear, and there is no reason why it should be preferred to trivalent arsenicals which are less expensive, less toxic, more active, but require to be injected subcutaneously or intravenously. Whilst continuing to use the stovarsol still in stock, novarsenobenzol replaced stovarsol from 1934, and treatment was given on fixed days, at first as a trial at the Baule centre and later elsewhere. The price of the course is substantially the same for novarsenobenzol as for stovarsol, but there is no leakage due to illicit traffic." (Botreau-Roussel (1938) *Clinique chirurgicale des pays chauds*, 271, Paris, Masson et Cie.)

It seems appropriate at this point to draw attention to a statement which is frequently seen in connection with therapy in leprosy,

and that is the cost of syringes needed when injections are used in the treatment of leprosy. While admitting that this is an item of expenditure which can be high, we feel we must state that undue emphasis on the possible cheapness of the routine treatment of leprosy may give the wrong idea that this disease can be dealt with without sufficient attention being given to the need for adequate medical personnel. This would be disastrous, because leprosy will not attract medical workers if the impression is given that the problem can be easily tackled by non-medical personnel. Governments may then tend to reduce leprosy grants. A disease which has baffled mankind for so many centuries needs the best trained and the most enthusiastic workers, and any steps which discourage the recruitment of such personnel may be fatal to future research in leprosy, and nullify the great advances now within view.

The articles in this number of the Review bring out very clearly (1) the need for meticulous care in the administration of the sulphone remedies and (2) the relatively small margin between the therapeutically effective and toxic dose of D.D.S. Dr. E. Muir's article illustrates the first point. His approach to the clinical side of leprosy is worthy of emulation for he himself examined each patient daily and made certain that the right dosage was taken. When Dr. Muir gave D.D.S. tablets to be taken away he explained in detail in the local language, of which he is an expert, the need for caution, and, coming from him, his words would carry great weight. On the other hand, a relatively untrained person, particularly if not a doctor, would be greatly handicapped in this respect.

Dr. Barnes' article well emphasizes the second of the above points, for he has shown that in as low a dosage as 100—200 mgm. per day there may be serious toxic effects. In the twice-weekly regimen of dosages which is now generally advocated, we feel that these dangers are reduced to an absolute minimum. Further work will show whether there is any risk attached to this recommended line of treatment. It is for this reason that certain workers have maintained that if oral D.D.S. is to be the remedy of choice it should be given in bi-weekly dosages rather than daily. It may be found that parenteral sulphone (that is a suspension of D.D.S. in arachis, or preferably cocoanut, oil) can be given once a week, and be as effective as oral dosages, and thus further reduce the drawbacks of D.D.S. therapy.

Workers will be interested in the advocacy of Vitamin B12 by Dr. Muir, for if his observation is confirmed that this is not

only a method by which reactions can be controlled, but will increase the tolerance of the patients to sulphone therapy, a difficult problem will have been solved, and at the dosage recommended of 30 micrograms per week the cost would be extremely low.

This number of *Leprosy Review* is almost solely confined to sulphone therapy, but we would draw attention to Dr. Wheate's article on the granular form of the M. leprae. There is still some doubt as to the significance of the breaking down of M. leprae to granules under sulphone therapy. The phenomenon, which is most marked under sulphone therapy, has been observed with hydnocarpus treatment of leprosy. The M. leprae appear to assume the granular form when the tissue environmental conditions are inimical to its multiplication. It is tempting to conclude that these forms are dying or effete bacilli, but until more work has been done on the histopathology of M. leprae it is safer to assume that the granular form of the bacilli appears when conditions for its growth are adverse. We have seen severe lepra reaction after a patient has shown only a few granular forms for many months, and has had over two years treatment with the sulphones. Modern techniques may be able to differentiate between dead and living bacilli, but this is an aspect of research work which is highly specialised. A few reports of relapses under sulphone therapy are appearing in the press, and therefore some consider a maintenance dose of sulphones, e.g. 200 mg. D.D.S. bi-weekly, should be continued, preferably for life, but for at least two years after all signs of activity of the disease have disappeared.

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We publish the Order declaring leprosy to be a notifiable disease in this country. It will be seen that these regulations have been devised to assist the leprosy patients to get the best possible treatment and also to bring to them that sympathetic help which is available. The Association, in co-operation with the Red Cross Society, are considering a plan for the welfare and social assistance of the leprosy patient and we trust that this action on the part of the Ministry will mean not only better treatment for the leprosy patient, but afford an opportunity for the dissemination of up-to-date knowledge with reference to Hansen's Disease, and hasten the day when irrational fear and prejudice in this country will be banished.

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The Editor would like to add a personal note. It is sixteen

years since he left the Association to resume work in India, and he returns to his task in an era of great hope and optimism. Good wishes are extended to all readers of the journal, and assurance given that every endeavour will be made to fulfil the objects for which this Review was commenced, viz. a medium whereby a balanced account of the development of leprosy treatment and research in the Commonwealth and Empire may be found, and a magazine which will be helpful particularly to the lone worker who cannot resort to the specialist for advice with his problems. To Dr. G. A. Ryrie, who worked under an almost impossible burden of ill health, we extend our cordial good wishes and admiration for his courage in carrying on under such difficult circumstances.

Gratitude is extended to all those who have assisted in the publication of the Review, and a reminder is given that a journal of this kind cannot be maintained without a constant supply of original articles and annotations from workers in the field.