CORRESPONDENCE

This department is provided for the publication of informal communications which are of interest because they are informative or stimulating, and for the discussion of controversial matters.

DISTRIBUTION AND CONTROL OF THE SULPHONES

TO THE EDITOR:

We are witnessing at this time the worldwide distribution of proprietary compounds synthesized from 4,4′-diaminodiphenylsulphone. Such distribution is partly the responsibility of various charitable bodies, but apart from this the proprietary sulphones may now be purchased upon the open market—black as well as legitimate—in both America and Europe and probably elsewhere.

Any small hospital or leprosarium may purchase or receive these drugs, which are potentially toxic, require strict laboratory control, and for their maximum effect require the close supervision of an experienced medical officer. There are to my knowledge such small leprosaria which have received, and are receiving, supplies of sulphones from one or another of the sources mentioned but which have no facilities for blood sulphone estimations, and some not even for accurate blood counts or hemoglobin determinations.

The imagination can well picture what might happen under such conditions. Allow me to speculate. A patient receives a sulphone, together with routine administration of ferrous sulphate. The iron induces constipation and the sulphone accumulates in the bowel. No blood-level determinations being performed, the increase of blood sulphone to dangerously high levels passes unnoticed: the resultant high blood level induces a severe lepra reaction. The literature of the chemotherapy of tuberculosis affords evidence of a similar case which resulted in the death of the patient.

There are in this continent, if not elsewhere, many small colonies with no resident medical officers or adequate laboratory facilities. Such institutions are staffed by various mission workers whose enthusiasm is beyond question but whose ability to supervise the administration of sulphones is open to doubt. There are also large leprosaria which are badly understaffed, with one medical officer to 1,000 to 3,000 patients, and with

minimal laboratory facilities. The medical officer of such an institution has his general medical work plus the administrative matters to attend to, and he cannot be expected to give to the patients on sulphones the supervision they require.

It would be well if we reminded ourselves that the sulphones are toxic drugs and that the clinical and laboratory studies of them are by no means complete. Any institution, therefore, which commences sulphone therapy should have a resident medical officer who is not overworked, a qualified laboratory worker who is preferably a biochemist, and adequate laboratory facilities for blood sulphone estimations and routine hematological investigations. The institutions which have such facilities are by no means the usual ones.

The editorial by Dr. Doull on the need of proof of the superior value of the sulphones [THE JOURNAL **15** (1947) 88] deserves the closest attention, for the proposals therein point towards a solution of the situation which I have set forth. Has anything been done to implement the proposal for a Nuclear Central Committee? In my opinion the establishment of such a Committee with the powers and functions outlined by Dr. Doull would mark the greatest step forward in the treatment of leprosy that we have witnessed. In coordinated research and central planning lies the hope of any major advance in the chemotherapy of this disease.

I would plead for some restriction to be placed upon the present indiscriminate distribution of the sulphones. The Nuclear Central Committee might well organize the distribution of the sulphones to such institutions as they decide have proper facilities for control. Since the American Leprosy Foundation is in sympathy with Dr. Doull's proposals, let us hope that we shall see the implementation of these proposals in the near future. We may then see the sulphones given their true place in the chemotherapy of leprosy.

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[Mr. Smith has pointed out that the above communication was written by him in his capacity as a chemist and a member of the International Leprosy Association, and that the views expressed are purely his own and should not be construed as necessarily representing the official view of the British Empire Leprosy Relief Association.—EDITOR.]

397

To The Editor:

In reply to your inquiry about our experience in the light of the views of Dr. G. Brownlee on the anemias of sulfone treatment as given in a recent abstract in *Tropical Diseases Bulletin* [**45** (1948) 711 (Aug.)], it is believed that Dr. Brownlee's statement is based upon toxicity studies in rabbits. The picture which he draws involves (*a*) an early anemia of the hemolytic type, which he says is continuous while the drug is being administered. Shortly there develops (*b*) a hypochromic anemia due to the fact that an insoluble or nonabsorbable salt with alimentary iron is formed in the intestinal tract, thus causing the iron to be excreted; this form of anemia responds to iron. He also found (*c*) that, if large doses of sulfones are given over long periods of time, a nutritional anemia may develop due to modification of the intestinal microflora and consequent interference with the biosynthesis of vitamins of the B-complex group; this anemia responds to yeast treatment. [Statements by Brownlee appear in the discussions of a symposium on leprosy in *Trans. Roy. Soc. Trop. Med. & Hyg.* **41** (1948) No. 5 (Mar.), pp. 596-597; and *Proc. Roy. Soc. Med.* **41** (1948) 309-310 (Sect. Dermatol, No. 2, pp. 123-124).]

The idea of the development of a nutritional anemia in humans is based more on theory than on facts. The anemias observed at Carville due to sulfone therapy have all been of the simple, low-grade hypochromic type which responds to iron. Since high concentrations of the drug are produced in the blood stream, especially from intravenous use of promin, part of the anemia is undoubtedly due to hemolysis. While we do use vitamins freely at Carville, these have not been used to counteract the development of nutritional anemia as much as for building up the patient in general—and to some extent because of current vogue. It is believed that our dosages of the sulfones have not reached the level where nutritional anemias occur, if they do occur in humans from sulfone therapy. It is our feeling that Dr. Brownlee's statements, at least so far, are based entirely upon experimental work in rabbits from which he has advocated the use of yeast as well as iron as a routine in sulfone treated cases. It is my feeling that we can get along in many cases without using either iron or yeast, especially if promacetin is used and the patients are on an adequate diet.

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