## THE ANTI-PROTOZOAL ACTION OF THE SULPHONES AND THE ANTI-MALARIAL ACTION IN PARTICULAR Dr. G. Tarabini

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In a brief note, Leiker gives his observations on the possible antimalarial action of the sulphones in leprosy patients. He records that in a malarial endemic zone some years ago he noted that 10 leprosy inpatients and 25 outpatients did not show attacks of malaria, and throughout one year in the Miei leprosarium, which is also in a malarial area, 164 inpatients had no attacks of malaria, nor were there malarial parasites on examination of thick drop blood tilms. More than this, a patient who came in suffering from malaria became cured of it a short time after beginning to take a small dose of DDS. Leiker ends by saying '' it is permissible to conclude that DDS has a suppressive action against malaria '. He had made his remarks as the result of those of the Editor of '' Leprosy Review '' (**26**, 1, 1955, pp. 3-4) on the activity of the sulphone drugs against one protozoon at least, namely toxoplasma.

The argument is of great importance, especially for the areas in which these two grave diseases coincide, and where the treatment and prevention of leprosy are carried on by a country-wide and regional plan (a system such as in India, according to our conversations with Dr. Wardekar on the occasion of his visit to Fontilles) and where it would result in the treatment and prevention of malaria

In 1937 Diaz de León reported in the Boletin Sanat. Panamer. that the sulphamides which a short time before had appeared in the therapeutic arsenal had an evident antimalarial action in man. Niven in 1938 in England reported, though with less enthusiasm, that prontosil was more effective against *Plasmodium falciparum* than *Plasmodium vivax;* but Menk and Mohr in 1939 in the Institute for Tropical Diseases at Hamburg had less encouraging results with 10 patients, inasmuch as they confined themselves to saying that prontosil could not in any way be a substitute for quinine or the atebrine class of compound.

The second wave of these studies arose in America in 1941 with the work of Coggeshall, Mayer, and Best, who used promine in daily doses of 10g. or more and obtained very good results in human and experimental malaria. This study deserves special attention because it was carried out at a time when the sulphone derivatives were being investigated and it was being shown that 4-4'-diaminodiphenyl-sulphone which was previously abandoned was not only less toxic and more soluble than the glucoside derivatives but had a very efficacious action; on the other hand the glucoside derivatives of sulphapyridine were not so efficient because they did not break down fast enough in the blood, (Taylor *et al.*).

Patrono (1943) using a product of the promine type in dosage of 36 g. in 4 days and of 108 g. in 6 days obtained good results in human malaria. He noted the disappearance of the fever in I or 2 days in the cases with *Plasmodium falciparum* infection and in 5 to 6 days in those with *Plasmodium vivax*.

After the Congress of Dermatology and Syphilology held in Padua in 1943, where promine and tibatin were discussed, Messrs. Recordati in Italy manufactured the product called *reconan* which differed from promine (the sodium disulphonate of the diglucoside of DDS) in being the dextrose diglucoside of DDS, and thus being similar to tibatin which is the digalactoside of DDS.

In those years I had a fair number of malaria patients in the Tropical Diseases Clinic at Modena and I wished to try reconan to see if the simple dextrose diglucoside of DDS was as equally effective as promine which was a more complex product. I reported the results in February 1945 to the Medico-Surgical Society of Modena, together with Dr. Enzo Secreto. We adopted the dosage of 16 g. during 9 days and repeated the treatment after 10 days of rest. A definite fall in the fever occurred on the second day of treatment, and there were only 2 cases of relapse in the 12 patients treated with this dosage. In 10 other cases who were given only the first period of treatment, success was obtained, but somewhat less striking. Almost all our patients were parasitized by Plasmodium falciparum: we had no cases with the other plasmodia. It was noted that there was a much greater action against the schizonts than the gametocytes. In 2 patients we made check studies and found that the activity of the drug was due exclusively to the DDS.

It was also noted that a patient with diabetes complication had a striking definite cure in two days, notwithstanding an application of treatment for only 6 days; in this patient the degree of urinary elimination of the drug was less than in the others.

From what has been said, it can be concluded that the sulphones are very active against human malaria, and much more so than the sulphamides.

Other studies also carried out in Modena enabled us to note an ineffectiveness of reconan against the intestinal protozoa: we had some informative cases of colitis due to *Entamoeba histolytica*. However we now think that the sulphones given orally and for a long time can have a certain activity; for in the years I spent at Fontilles we often found intestinal protozoa and never *Entamoeba histolytica*, and hence there is some validity in the idea. In regard to cutaneous leishmaniasis we do not have enough data, but the case

which we studied (Contreras et al.) in a leprosy patient treated for some years with oral DDS in whom oriental sore developed, makes us think that this drug neither impedes nor cures infection by Leishmania tropica.

In short we can say that the observations of Leiker arouse interest in the use of the sulphones as antimalarials and there is confirmation in the studies of the authors quoted, and they suggest the use of this therapy at the one time for malaria and leprosy in the areas where these two diseases exist in association, and also as a prophylaxis for both diseases when DDS is given for a long time to the whole population of areas where these two great scourges exist.

## Summary

Emphasis is given to the observations of Leiker on the antimalarial action of the sulphones, and the studies are recalled of Coggeshall et al, of Patrono, of Tarabini and Secreto in the years 1941-45 carried out on the glucoside derivatives of DDS (promine and reconan) and which show a marked antimalarial activity.

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