

### Treatment of *Dipetalonema perstans* infections with mebendazole

Generally, *Dipetalonema perstans* infections are regarded as clinically silent, peripheral blood eosinophilia being the only indication of infection. Now and then, however, quite severe pruritis, abdominal pain, kalabar swelling and pleuritis seem to occur. The drug mainly used against this parasite has until now been diethylcarbamazine (DEC) (ADOLPH *et al.*, 1962) but it is not very efficient and side effects are common.

In Sweden we have recently had some patients with symptomatic *D. perstans* filariasis. As the DEC treatment given to six of them failed, we decided to try mebendazole in one patient in the dosage 100 mg twice daily for 30 days. She was subsequently cured and freed of earlier symptoms. A second patient was then given the same treatment and the circulating microfilariae disappeared. These two patients have already been described elsewhere (WAHLGREN, 1982). Although the number of patients infected with *D. perstans* in Sweden is small, further experiences in another seven patients with the new drug might be of interest as to dosage and maintenance of therapy, as well as to side effects which have been common, although mild.

second course of treatment when only half the dose was given. Mild side effects were also seen quite frequently in some other patients. Rashes (in five patients) and pruritis (in three) were the most common side effects, seen mainly during the third week of treatment. No haematological or other side reactions were observed.

In many of the patients there was a significant decrease in the eosinophil count. Follow-up examination could be performed in five of the patients only one month after the end of treatment as all of these patients decided to return to Africa. The three other patients have been free of microfilariae for more than nine months.

Since ADOLPH *et al.* (1962) described the successful, but very tedious, treatment of *D. perstans* with DEC, very little progress has been made. In 1975 the first report on mebendazole treatment of *D. perstans* was given by MAERTENS & WÉRY (1975), who showed that the microfilariae disappeared completely in one patient after seven weeks of mebendazole in a dosage of 100 mg twice daily. BERNBERG *et al.* (1979) reported that a combination of levamisole (100 mg b.d.) and mebendazole (100 mg. t.i.d.) for 10 days cured three of four patients in Rhodesia infected with *D. perstans*-like microfilariae. Some other patients

Table I—Age, sex and laboratory data of 9 patients treated with mebendazole for *Dipetalonema perstans* filariasis

Pat. No.	Age	Sex	No microfilariae/4 ml venous blood		Duration of Mebendazole 100 mg twice daily P.O.
			Before treatment	After treatment	
1	38	♀	253	0	4 weeks
2	34	♀	8	0	4 weeks
3	33	♀	592	0	7 weeks
4	27	♀	280	3	4 + 4 weeks
5	36	♀	10	0	7 weeks
6	32	♀	many	0	4 weeks
7	8	♀	22	0	4 weeks
8	6	♀	32	13	2 + (half dose) 2 weeks
9	6	♀	32	0	4 weeks

All the patients (eight Swedes and one African from Uganda) had been infected in tropical Africa, and most of them in Zaire. Age, sex and laboratory data are summarized in Table I which includes the first two patients previously reported. All were given mebendazole treatment orally, 100 mg twice daily. Six were cured, i.e., microfilariae were removed from the blood, when this dosage was given for 30 days. One patient (No. 4) had to be given a second course of treatment, after which only a few circulating microfilariae were seen. Two patients (Nos. 3 and 5) were given seven weeks' treatment and in one of them (No. 5) the microfilariae disappeared after 30 days. Patients No. 8, a six-year-old child, had to discontinue treatment due to severe side effects (high fever and angio-oedema) with recurrence of symptoms during a

have also been successfully treated with a combination of mebendazole and levamisole (MAERTENS & WÉRY, 1975; GOLDSMID & ROGERS, 1979) but levamisole can sometimes cause severe bone-marrow toxicity and has not been shown to be advantageous in the treatment of onchocerciasis (RIVAS-ALCALÁ *et al.*, 1981a, b). Our data, although based on very few patients, suggest that mebendazole alone could be sufficient in the treatment of *D. perstans* filariasis. Four weeks of 100 mg twice daily might, in most patients, be long enough but a second course sometimes seems to be necessary, as in patient No. 4.

At present we suggest that patients with *perstans*-filariasis are given mebendazole treatment. Several factors of interest have to be studied further on prospective larger numbers of patients; these include

the nature of side effects with a peak three weeks after the onset of treatment, the optimal dosage and the duration of therapy.

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#### Riboflavin status and malaria in infants in Papua New Guinea

We should like to comment on an interesting relationship between riboflavin status and malaria in

infants in Papua New Guinea which suggests that riboflavin deficiency in infants may be protective.

In studies to determine the role of riboflavin deficiency in the aetiology of anaemia, blood samples were obtained from 83 infants aged 0 to 18 weeks at well-baby clinics near Madang, a coastal town, during October to December 1981. The infants were afebrile and had not been sick in the two weeks before being seen. Riboflavin status was measured using the erythrocyte glutathione reductase test (THURNHAM & RATHAKETTE, 1982) and 70 measurements were outside the normal range (activation coefficient >1.30). Riboflavin status improved with age, i.e., AC values were higher at birth in both boys ( $r = -0.53$ ,  $P < 0.001$ ) and girls ( $r = -0.45$ ,  $P < 0.002$ ). The results were similar to those reported from the Gambia in infants of the same age (BATES *et al.*, 1982).

Five of 83 thick blood smears were positive for malaria and it was also apparent that the parasite densities ranked exactly the inverse of the AC values. Analysis of this data using the chi-squared test confirmed that the number of infants with malaria in the group with normal riboflavin status was significantly greater than would be expected by chance ( $P < 0.005$ ). In addition, using the Mann Whitney 'U' test and ranking the AC values, also confirmed that there was a tendency for infants who contracted malaria to have lower (normal) AC values ( $P < 0.02$ ).

There was no relationship between age and slide positivity in these infants. Furthermore, although breast milk has been reported to depress parasite multiplication due to its lack of 4-aminobenzoic acid (HAWKING, 1953), it would not appear to be protective in this environment since three of the babies with malaria were still reportedly being solely breast fed.

Although the number of infants with malaria parasites in their blood was small, the results are analogous to the experimental effects of riboflavin deficiency on both *Plasmodium lophurae* (SEELER & OTT, 1944) and *P. berghei* infections (KAIKAI & THURNHAM, in press) in which parasite numbers were inversely proportional to riboflavin status. Riboflavin deficiency lowers the potential activity of erythrocyte glutathione reductase and thus, in the face of oxidant stress which is increased in the malaria infection (ETKIN & EATON, 1975) may impair the synthesis of reduced glutathione and the survival of the red cell and hence the parasite. This is similar to the mechanism proposed by LUZZATO *et al.* (1969) whereby glucose-6-phosphate dehydrogenase deficiency is believed to protect against malaria and raises the question of whether riboflavin deficiency also protects young infants against malaria parasite

Table I—Riboflavin status of babies with malaria

Riboflavin Status	Malaria	Age	Solid Foods	
AC	Density	Species	Weeks	
1.12	'heavy'*	<i>P. vivax</i>	11-12	No
1.20	252/200WBC+	<i>P. falciparum</i>	14-15	No
1.24	176/200WBC	<i>P. vivax</i>	6-7	Yes
1.54	71/200WBC	<i>P. falciparum</i>	16-17	Yes
1.74	1/100WBC	<i>P. falciparum</i>	1-2	No

\*Heavy means approximately 100 parasites per high-power field. +White blood cells.