The mechanism of injury in patients with interferon induced cardiotoxicity is not known. Together, interferon and cardiac tissue may stimulate an auto-immune or inflammatory reaction, or the increased demand for oxygen caused by fever, chills, and tachycardia may precipitate infarction in a compromised myocardium, or interferon may induce coronary spasm. Since the effect of interferon was reversible in our patient we suggest that cardiomyopathy was induced through impaired myocyte metabolism rather than through histological damage.

Our patient's dramatic improvement could not have been due to drug treatment alone because diuretics do not greatly improve ventricular function, and most of his drugs had been stopped. It seems, therefore, that in the absence of pre-existing heart disease withdrawing interferon leads to cardiac function returning to normal.

A report has now appeared on reversible cardiac dysfunction associated with interferon treatment in a patient with AIDS.⁴ The potential cardiotoxicity of interferon was attributed to a synergistic interaction with HIV infection. Our case suggests that other mechanisms are responsible for the cardiotoxic effect of interferon.

We thank Amir Ben Moshe for secretarial help.

- 1 Quesada JR, Reuben J, Manning JR, Hersh EM, Gutterman JU. Alpha interferon for induction of remission in hairy cell leukemia. *N Engl J Med* 1984;310:15-28.
- 2 Cohen MC, Huberman MS, Nesto RW. Recombinant alpha-2 interferon related cardiomyopathy. *Am J Med* 1988;85:549-50.
- 3 Dickson D. Death halts interferon trials in France. *Science* 1982;218:772.
- 4 Deyton LR, Walker RE, Kovacs JA, et al. Reversible cardiac dysfunction associated with interferon alfa therapy in AIDS patients with Kaposi's sarcoma. *N Engl J Med* 1989;321:1246-9.

(Accepted 15 January 1990)

Falciparum malaria resistant to quinine and pyrimethamine-sulfadoxine successfully treated with mefloquine

Adam S Malin, Anthony P Hall

Hospital for Tropical Diseases, London NW1 0PE
Adam S Malin, MRCP, registrar
Anthony P Hall, FRCPED, consultant physician

Correspondence to: Dr Hall.

Br Med J 1990;300:1175

Falciparum malaria has become increasingly resistant to chloroquine. It must be treated with quinine (when this is available), which can be followed by a single dose of pyrimethamine-sulfadoxine (Fansidar). This three drug regimen is usually curative,¹ but we have recently observed an increasing number of recrudescences of disease.

Case reports

During the 12 months September 1988 to August 1989, 229 patients with falciparum malaria were seen at this hospital. Five were not cured by treatment with quinine followed by one dose of pyrimethamine-sulfadoxine (table). Four of these patients received treatment in hospital; one (case 4) took her last few days' treatment with quinine and the pyrimethamine-sulfadoxine at home. Blood films obtained at the end of the regimen were negative for parasites in cases 1, 2, 4, and 5; in case 3 the film showed scanty trophozoites on the day of discharge. The patients stayed in the United Kingdom throughout the study, and none had any medical condition that might impair the response to treatment.

Recrudescences occurred 17-77 days after the regimen was started; each blood film was examined by several experienced observers to confirm the finding of

parasites. All patients subsequently responded to mefloquine or quinine followed by mefloquine. One (case 2) developed a self limiting anxiety state 48 hours after taking mefloquine.

Comment

The development of resistance to a regimen comprising quinine and pyrimethamine-sulfadoxine is worrying. So far this resistance has presented as an initial clearance of the parasitaemia and clinical resolution followed by relapse and has been described in Thailand and east Africa.^{1,2} Three of the five patients reported on here contracted their disease in west Africa. We believe that these are the first cases of malaria resistant to quinine and pyrimethamine-sulfadoxine from that region to be described.

In cases of malaria resistant to quinine alternative regimens include either quinine in combination with tetracycline or one of several new drugs such as halofantrine or mefloquine; mefloquine is soon to be marketed in the United Kingdom. These new drugs may be used alone or after a course of quinine. Mefloquine alone cures about 98% of patients with falciparum malaria,³ but in our experience patients with severe infection should receive quinine before mefloquine. Quinine lowers the parasitaemia and leads to improved tolerance of mefloquine. To reduce toxicity at least 12 hours must elapse between the last dose of quinine and the first dose of mefloquine.⁴ Mefloquine may cause nausea and malaise, and some reports suggest that neuropsychiatric complications occur in 1-2% of patients treated.^{3,5} Thus patients should be kept in hospital during treatment.

Physicians should be aware that falciparum malaria is sometimes resistant to a regimen comprising quinine and pyrimethamine-sulfadoxine. As this is, however, rare we recommend that the regimen is used as first line treatment.

We thank Dr A D M Bryceson and Dr G C Cook for permission to report cases 1 and 5; Dr M G Brook for his help with the manuscript; and Dr P L Chiodini and Mr A H Moody and their staff for the parasitology reports.

Details of five patients who developed recrudescence of falciparum malaria after treatment with quinine and pyrimethamine-sulfadoxine (Fansidar)

Case No	Ethnic origin	Sex	Age (years)	Country visited	Quinine-Fansidar regimen*		Time to diagnosis of recrudescence (days)	Final treatment†
					Dose of quinine (mg)	Duration of quinine (days)		
1	African	F	32	Ghana	600 Thrice daily	7	17	Quinine, mefloquine
2	White	M	24	Zimbabwe	600 Twice daily	5	46	Mefloquine
3	White	M	24	Ghana	600 Thrice daily	4	34	Quinine, mefloquine
4	African	F	3	Nigeria	125 Twice daily	7	19	Mefloquine
5	Burmese	M	50	Burma	600 Thrice daily	10	22	Mefloquine

*A course of quinine was given orally (except in cases 2 and 4, in which the first two and first four doses, respectively, were given intravenously) and was followed by three tablets (total 75 mg pyrimethamine, 1.5 g sulfadoxine) of Fansidar (except in case 4, in which only one tablet was given).

†Mefloquine 750 mg was given on two occasions 12 hours apart (except in case 4, in which 250 mg was given twice).

- 1 Hall AP, Doberstyn EB, Mettaprakong V, Sonkom P. Falciparum malaria cured by quinine followed by sulfadoxine-pyrimethamine. *Br Med J* 1975;iii:15-7.
- 2 Warhurst DC, Hall AP, Tjokrosonto S. RI quinine-Fansidar resistant falciparum malaria from Malawi. *Lancet* 1985;iii:330.
- 3 World Health Organisation. Advances in malaria chemotherapy. Report of a WHO scientific group. *WHO Tech Rep Ser* 1984;711:105, 118.
- 4 Hall AP, Doberstyn EB, Karnchanachetane C, et al. Sequential treatment with quinine and mefloquine or quinine and pyrimethamine-sulfadoxine for falciparum malaria. *Br Med J* 1977;ii:1626-8.
- 5 Stuijver PC, Ligthelm RJ, Goud TJLM. Acute psychosis after mefloquine. *Lancet* 1989;ii:282.

(Accepted 9 February 1990)