SHORT REPORTS

Chloroquine resistant Plasmodium falciparum malaria in Zimbabwe

Resistance of *Plasmodium falciparum* to chloroquine in Africa was first reported from Kenya in 1979.[1] Since then reports of resistant strains from other parts of Africa have continued to appear. Drug sensitivity studies during the 1983 and 1984 malaria seasons in endemic areas in the north east and south east of Zimbabwe showed that *P falciparum* infections in these localities were fully sensitive to a standard course of chloroquine.[2] We report the first seven cases of confirmed chloroquine resistant *P falciparum* infection acquired in the Zambezi Valley of Zimbabwe.

Patients, methods, and results

Four of the seven patients (cases 1-4) were treated for malaria between May and September 1984 as inpatients or outpatients in various Harare hospitals. They had been in the Zambezi Valley (either Kanyemba or Chirundu) on holiday or work transfer from Harare, an area hypoendemic for malaria, and were taking chloroquine as prophylaxis before the onset of their illness. All four patients failed to respond to at least the initial two standard courses of chloroquine and were referred for chloroquine sensitivity tests. The remaining three patients were resident in the Zambezi Valley, an area hyperendemic for malaria, and had asymptomatic *P falciparum* infections confirmed during routine drug sensitivity tests conducted in Kanyemba in August 1984.

Blood samples from seven patients were subjected to the in vitro macro test for chloroquine resistant *P falciparum* malaria.[3] Before in vitro testing, all the patients underwent the Dill-Glazko test for chloroquine in urine.[4] Schizont maturation was expressed in relation to 300 leucocytes.

Blood smears from all seven patients before the in vitro tests disclosed parasitaemias ranging from 3020×10^6 to $21\,040\times10^6$ parasites per litre of blood, and this was considered suitable for in vitro studies (table). One patient (case 1) failed to respond to a single dose of 1500 mg sulfadoxine and 75 mg pyrimethamine (three tablets of Fansidar) and was finally cured with 4·5 g oral quinine and 5·25 g tetracycline administered concurrently over three and seven days, respectively. A single dose of Fansidar cured two patients (cases 2 and 3). Case 4 responded to a third course of chloroquine (1·8 g base parenterally) given five days after a course of sulphadimidine for a urinary tract infection.

Comment

Persistence of schizont maturation at chloroquine concentrations greater than 1·0 μmol/l (32·0 μg/100 ml) blood show that *P falciparum* isolates in the Zambezi Valley are resistant to a standard course of chloroquine, which agrees with the patients' failure to respond to the initial standard or multiple courses of chloroquine. In view of resistance already reported in parasites isolated from Zambia,[5] which verbal reports now give as being widespread, and the absence of mass chloroquine distribution in the Zambezi Valley of Zimbabwe, probably the resistant parasites reported here had spread into Zimbabwe from neighbouring Zambia in the north. The extent of chloroquine resistant malaria in the Zambezi Valley of Zimbabwe is unknown, and more surveillance of drug sensitivity must therefore be undertaken to obtain information on the changing pattern of sensitivity of *P falciparum* to chloroquine.

Fansidar, quinine, and tetracycline should be reserved for cases of chloroquine resistant infections. Chloroquine, however, remains the drug of choice for sensitive *P falciparum* infections by virtue of its efficacy, low cost, and ready availability. The use of chloroquine as prophylaxis should be under strict control throughout Zimbabwe so as to reduce drug selection pressure on *P falciparum*. Alternative agents such as a combination of pyrimethamine (12·5 mg) and dapsone (100 mg) should be used, though recommendations about appropriate prophylaxis must take many factors into account.

1 Fogh S, Jepson S, Efferse P. Chloroquine-resistant Plasmodium falciparum in Kenya. *Trans R Soc Trop Med Hyg* 1979;73:228-9.
2 Mutambu SL. Drug resistance of Plasmodium falciparum in Africa with particular reference to chloroquine resistance in Zimbabwe. *Cent Afr J Med* 1984;30:269-72.
3 Rieckmann KH, Antunano L. Chloroquine resistance of Plasmodium falciparum in Brazil detected by a simple in vitro method. *Bull WHO* 1971;45:157-67.
4 Lelijveld J, Kortmann H. The eosin colour test of Dill and Glazko: a simple field test to detct chloroqquine in urine. *Bull WHO* 1970;42:477-9.
5 Kofie-Ekue JN, Ulrick A, Njelesani EK. Plasmodium malaria resistant to chloroquine in a Zambian living in Zambia. *Br Med J* 1983;286:1315-6.

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The provenance of extradural haematomas

Extradural haematoma is a lethal, if uncommon, complication of minor head injury. Fear of its generation causes the admission to hospitals in England and Wales of about one quarter of a million patients each year. In 1982 in the northern part of the South Western region 4743 patients were admitted with head injury alone, 4343 for fewer than seven days. Nine cases of extradural haematoma were diagnosed, an incidence of less than 0·2% of those admitted, although an unknown number may have died on the way to hospital.

Guidelines for the management of head injury have been published by a group of neurosurgeons based on observed indicants of extradural haematoma and aimed at reducing unnecessary admissions with more effective care of those whose brain injury demands close attention.[1] We have assessed these in a retrospective study.

Methods and results

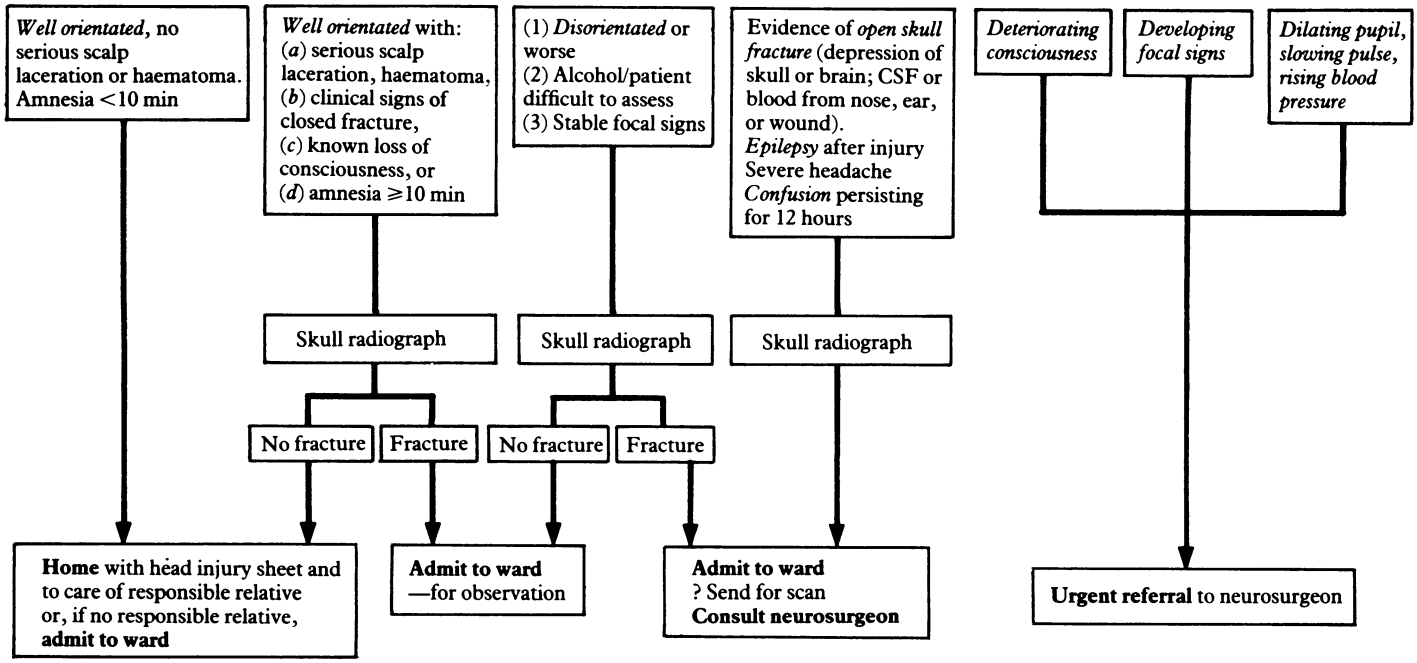
The records of 100 consecutive cases of extradural haematoma admitted to the neurosurgical unit at Frenchay Hospital, Bristol, over 10 years (1974-84) were analysed to test the strength of the guidelines.

Of the 100 patients, 32 were aged under 12, 18 were teenagers, and 65 were under 30. Some 52 had been in road traffic accidents, 16 having fallen from a bicycle; 23 cases had arisen from accidents at home and 13 from sport. Only three had been caused by assault, and in only five was alcohol a complication. One third (32) had presented to the district hospital for the first time with their extradural

Results of in vitro macro tets for sensitivity of P falciparum *to chloroquine, Zambezi Valley, Zimbabwe*

Case No	Age and sex	Preculture asexual parasite count in blood ($\times10^6$/l)	Schizonts per 300 leucocytes: Control 1	Control 2	Mean	Chloroquine concentrations (μmol/l blood) 0·25	0·50	0·75	1·00	1·25	1·50	2·00	3·00	Result of Dill-Glazko test before in vitro tests
1	25 M	3020	24	30	27	17	17	14	13	10	9	14	7	+
2	30 F	21040	14	14	14	14	10	8	5	7	6	7	6	+
3	29 F	16000	42	32	37	26	30	18	12	5	11	7	7	+
4	45 M	17307	28	22	25	22	14	10	8	10	8	5	6	+
5	10 F	11160	13	13	13	8	7	9	4	5	3	8	6	−
6	15F	11813	52	42	47	28	30	22	31	20	34	20	26	−
7	14 F	7013	17	23	20	15	18	12	11	9	13	8	8	−
Mean parasite density		12479	27	25	26	19	18	13	12	9	12	10	9	

Conversion: SI to traditional units—Chloroquine: 1 μmol/l≈32·0 μg/100 ml.



Flow chart showing guidelines for management of head injuries.

haematoma already clinically apparent (deterioration of consciousness (14) or localising signs (18, of whom 11 were conscious)), causing their immediate referral to the neurosurgical unit. A skull fracture was seen in 24 of the 32. Two thirds of cases (68) became clinically apparent after admission for observation without prior evidence of extradural haematoma.

Application of the guidelines to patients at their initial observation in the accident service would have resulted in failure to admit four cases. Two had skull fractures undiagnosed by the observer of the *x* ray film; one young motorcyclist with a good crash helmet did not need a skull *x* ray investigation; and one child aged 3 did not have a fracture but did have a definite scalp lesion.

Comment

The guidelines for the management of head injuries will pick up 96% of extradural haematomas. Careful consideration must be given to patients with local scalp trauma, and children, who may develop an extradural haematoma more readily in the absence of a fracture than adults, must be carefully assessed. With the addition of a serious scalp lesion, the guidelines can be presented as a flow chart for the help of junior staff (figure). We have used this for a year at the Bristol Royal Infirmary and have confirmed it as safe and effective.

1 Group of Neurosurgeons. Guidelines for the management of recent head injury in adults. *Br Med J* 184;288:983-5.

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Discrepancy between standard and low range mini Wright peak flow meters

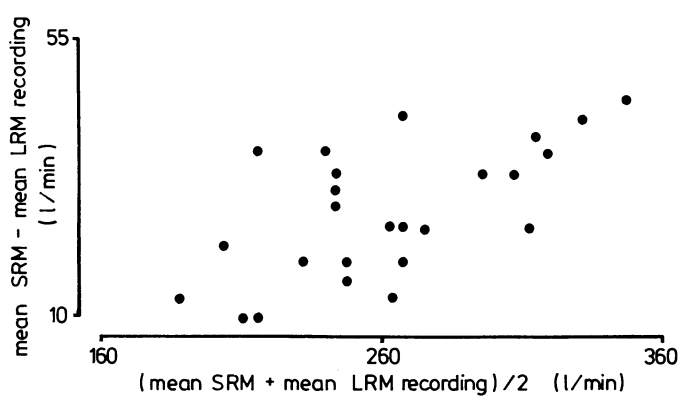
The mini Wright peak flow meter[1] is widely used as a cheap and convenient method of measuring peak expiratory flow rate[2] and monitoring this over time. It is available in two models with scales 60-800 l/minute (standard range) and 30-370 l/minute (low range). Variation between instruments exists for the standard range model, but this is of little practical importance.[3] The manufacturers claim that the scale of the low range meter is close to that of the standard Wright peak flow meter and hence to that of the standard range meter (Mini-Wright peak flow meters: notes for the doctor. Clement Clarke International Limited, London). Our recent experience with these instruments, however, suggests that the scale of the low range meter gives lower readings than the standard one in the same patient.

Methods and results

Two standard and three low range meters were drawn at random from a pool of new, unused meters. Thirty children aged 7-9 from a local school were each taught the technique of forced maximal expiration. Each then blew at least three times through a paediatric mouthpiece into each meter, in random order, finishing with the meter used first. The highest reading from each meter was recorded, and the data for that child were rejected if the two recorded readings from the meter used first differed by more than 10 l/minute. Records from 25 children were accepted.

The two sets of standard range and three sets of low range recordings differed little (mean (SD) difference for standard 0·8 (6·3) l/minute; mean (SD) difference for each low range pair 3·0 (12·6), 13·8 (10·7), and 10·8 (10·8) l/minute) and the means for each child and model (mean standard range meter range 195-371 l/minute; mean low range meter range 183-325 l/minute) were used in the subsequent analysis.[4]

The figure shows the discrepancy between the mean standard and low range meter recordings for each child; the mean low range recording was always lower (range of differences 10-46 l/minute), and the difference in scales between the two models was significant.



Difference between mean recordings obtained by standard range meter (SRM) and low range meter (LRM) for each child. Transformation of the ordinate by calculating proportional bias ((mean SRM−mean LRM recording)×2/(mean SRM+mean LRM recording)) for each data point abolished the positive trend. The mean (SD) proportional bias 0·102 (0·035) was significantly different from zero; $t=14·6$, df=24, $p<0·001$.

Comment

The discrepancy between the scales of the standard and low range meters is clinically important, particularly in the upper part of the range of the low range meter. Standardisation of physiological measuring instruments may be difficult, particularly if it requires the cooperation of many subjects. In