Amoebiasis. For a discussion of the treatment of amoebiasis with mention of chloroquine for hepatic amoebiasis, see p.822.

Inflammatory disorders. Chloroquine and hydroxychloroquine possess anti-inflammatory properties and they have been tried or used with some benefit in a range of inflammatory conditions which often have an immunological basis, although they rarely constitute first-line therapy in these disorders. Such conditions include rheumatoid arthritis and SLE (see under Hydroxychloroquine, p.604), ulcerative colitis,[1] infantile interstitial pneumonitis,[2,3] asthma,[4] giant cell arteritis,[5] and various skin disorders (see below). The mode of action in these conditions is unclear. Results of studies have been conflicting but it does appear that chloroquine and hydroxychloroquine might have some immunosuppressive effects.[6,7]

1. Mayer L, Sachar DB. Efficacy of chloroquine in the treatment of inflammatory bowel disease. *Gastroenterology* 1988; **94:** A293.
2. Springer C, *et al.* Chloroquine treatment in desquamative interstitial pneumonia. *Arch Dis Child* 1987; **62:** 76–7.
3. Kerem E, *et al.* Sequential pulmonary function measurements during treatment of infantile chronic interstitial pneumonitis. *J Pediatr* 1990; **116:** 61–7.
4. Charous BL. Open study of hydroxychloroquine in the treatment of severe symptomatic or corticosteroid-dependent asthma. *Ann Allergy* 1990; **65:** 53–8.
5. Le Guennec P, *et al.* Management of giant cell arteritis: value of synthetic antimalarial agents: a retrospective study of thirty six patients. *Rev Rhum* 1994; **61:** 423–8.
6. Bygbjerg IC, Flachs H. Effect of chloroquine on human lymphocyte proliferation. *Trans R Soc Trop Med Hyg* 1986; **80:** 231–5.
7. Prasad RN, *et al.* Immunopharmacology of chloroquine. *Trans R Soc Trop Med Hyg* 1987; **81:** 168–9.

Malaria. The overall treatment and prophylaxis of malaria and the place of chloroquine in current recommendations are discussed on p.594.

TREATMENT. In the treatment of patients with chloroquine-sensitive falciparum malaria studies have found chloroquine to be at least as effective as quinine in both uncomplicated and severe infections. However, very few areas exist where *Plasmodium falciparum* remains sensitive to chloroquine. There are also reports of resistance to chloroquine in *P. vivax*.[1]

Treatment with chloroquine is usually by mouth, adults and children being given the equivalent of 25 mg of chloroquine base per kg body-weight over 3 days. Any chloroquine lost through vomiting needs to be replaced by additional doses.[2]

Intravenous therapy has been used if the infection is severe or oral dosage is not possible. There should be close monitoring for hypotension and other signs of cardiovascular toxicity. The intramuscular or subcutaneous routes have been used if intravenous dosage is not possible. Patients should be transferred to oral therapy as soon as possible and treatment continued until a total dose equivalent to 25 mg of the base per kg has been given.

If injections cannot be given a chloroquine suspension or syrup appears to be well absorbed when given by nasogastric tube even in comatose patients. Rectal use in young children has also produced beneficial responses.[3,4]

PROPHYLAXIS. The widespread prevalence of strains of *P. falciparum* resistant to chloroquine has considerably diminished the value of chloroquine for malaria chemoprophylaxis and has made recommendations increasingly complex (see p.594). If chloroquine is used for prophylaxis it is usually given with proguanil. For **adults** a dose equivalent to 300 mg of chloroquine base is given by mouth once each week, beginning about one week before exposure and continuing throughout, and for at least 4 weeks after, exposure. Some countries advise the use of 100 mg daily for 6 days a week. For **children**, a weekly dose of chloroquine base 5 mg/kg has been recommended, although UK malaria experts[5] have suggested the following prophylactic doses for children based on fractions of the adult dose of 300 mg weekly:

- under 6.0 kg (0 to 12 weeks of age), one-eighth the adult dose
- 6.0 to 9.9 kg (3 to 11 months), one-quarter the adult dose
- 10.0 to 15.9 kg (1 year to 3 years 11 months), three-eighths the adult dose
- 16.0 to 24.9 kg (4 years to 7 years 11 months), half the adult dose
- 25.0 to 44.9 kg (8 years to 12 years 11 months), three-quarters the adult dose
- over 45 kg (13 years and over), the adult dose

They noted that body-weight was a better guide to dosage than age for children over 6 months.

1. Whitby M. Drug resistant Plasmodium vivax malaria. *J Antimicrob Chemother* 1997; **40:** 749–52.
2. WHO. *WHO model formulary*. Geneva: WHO, 2004.
3. Westman L, *et al.* Rectal administration of chloroquine for treatment of children with malaria. *Trans R Soc Trop Med Hyg* 1994; **88:** 446.
4. Antia-Obong OE, *et al.* Chloroquine phosphate suppositories in the treatment of childhood malaria in Calabar, Nigeria. *Curr Ther Res* 1995; **56:** 928–35.
5. Chiodini P, *et al.* HPA Advisory Committee on Malaria Prevention in UK Travellers. Guidelines for malaria prevention in travellers from the United Kingdom (issued 01/07). Available at: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1203496943523 (accessed 17/06/08)

Porphyria cutanea tarda. Chloroquine and hydroxychloroquine have been used with some benefit in the treatment of porphyria cutanea tarda (p.1448) and low doses (such as chloroquine phosphate 125 mg or hydroxychloroquine sulfate 200 mg given twice weekly) have been considered by some to be useful in patients unsuitable for phlebotomy.[1-4] However, the acute increase in urinary porphyrins and fall in hepatic porphyrin content produced by these drugs have been associated with a variable degree of hepatotoxicity[5,6] and others prefer to use desferrioxamine.[7]

1. Grossman ME, *et al.* Porphyria cutanea tarda. *Am J Med* 1979; **67:** 277–86.
2. Cainelli T, *et al.* Hydroxychloroquine versus phlebotomy in the treatment of porphyria cutanea tarda. *Br J Dermatol* 1983; **108:** 593–600.
3. Ashton RE, *et al.* Low-dose oral chloroquine in the treatment of porphyria cutanea tarda. *Br J Dermatol* 1984; **111:** 609–13.
4. Stölzel U, *et al.* Hemochromatosis (HFE) gene mutations and response to chloroquine in porphyria cutanea tarda. *Arch Dermatol* 2003; **139:** 309–13.
5. Scholnick PL, *et al.* The molecular basis of the action of chloroquine in porphyria cutanea tarda. *J Invest Dermatol* 1973; **61:** 226–32.
6. Rossmann-Ringdahl I, Olsson R. Porphyria cutanea tarda: effects and risk factors for hepatotoxicity from high-dose chloroquine treatment. *Acta Derm Venereol* 2007; **87:** 401–5.
7. Rocchi E. Treatment of porphyria cutanea tarda. *Br J Dermatol* 1987; **116:** 139–40.

Rheumatoid arthritis. For reference to the use of chloroquine in the treatment of rheumatoid arthritis, see under Hydroxychloroquine, p.604.

Sarcoidosis. Chloroquine and hydroxychloroquine have been tried in the management of sarcoidosis (p.1512) as alternatives or adjuncts to corticosteroid therapy.

References.

1. O'Leary TJ, *et al.* The effects of chloroquine on serum 1,25-dihydroxyvitamin D and calcium metabolism in sarcoidosis. *N Engl J Med* 1986; **315:** 727–30.
2. Adams JS, *et al.* Effective reduction in the serum 1,25-dihydroxyvitamin D and calcium concentration in sarcoidosis-associated hypercalcemia with short-course chloroquine therapy. *Ann Intern Med* 1989; **111:** 437–8.
3. DeSimone DP, *et al.* Granulomatous infiltration of the talus and abnormal vitamin D and calcium metabolism in a patient with sarcoidosis: successful treatment with hydroxychloroquine. *Am J Med* 1989; **87:** 694–6.
4. Jones E, Callen JP. Hydroxychloroquine is effective therapy for control of cutaneous sarcoidal granulomas. *J Am Acad Dermatol* 1990; **23:** 487–9.
5. Zic JA, *et al.* Treatment of cutaneous sarcoidosis with chloroquine: review of the literature. *Arch Dermatol* 1991; **127:** 1034–40.
6. Baltzan M, *et al.* Randomized trial of prolonged chloroquine therapy in advanced pulmonary sarcoidosis. *Am J Respir Crit Care Med* 1999; **160:** 192–7.

Skin disorders. In addition to their use in lupus erythematosus hydroxychloroquine and chloroquine have been tried in a number of other skin disorders including polymorphic light eruptions[1] (see Photosensitivity Disorders, p.1581), lichen planus[2,3] (p.1580), cutaneous symptoms of dermatomyositis (p.1510), erythema nodosum,[4,5] and recurrent erythema multiforme (p.1580). It has also been tried in mild type 2 lepra reactions (erythema nodosum leprosum, see p.176).

1. Murphy GM, *et al.* Hydroxychloroquine in polymorphic light eruption: a controlled trial with drug and visual sensitivity monitoring. *Br J Dermatol* 1987; **116:** 379–86.
2. Mostafa WZ. Lichen planus of the nail: treatment with antimalarials. *J Am Acad Dermatol* 1989; **20:** 289–90.
3. De Argila D, *et al.* Isolated lichen planus of the lip successfully treated with chloroquine phosphate. *Dermatology* 1997; **195:** 284–5.
4. Alloway JA, Franks LK. Hydroxychloroquine in the treatment of chronic erythema nodosum. *Br J Dermatol* 1995; **132:** 661–2.
5. Jarrett P, Goodfield MJD. Hydroxychloroquine and chronic erythema nodosum. *Br J Dermatol* 1996; **134:** 373.

Systemic lupus erythematosus. For reference to the use of chloroquine in cutaneous and systemic lupus erythematosus, see Hydroxychloroquine, p.605.

Preparations

BP 2008: Chloroquine Phosphate Tablets; Chloroquine Sulphate Injection; Chloroquine Sulphate Tablets;
USP 31: Chloroquine Hydrochloride Injection; Chloroquine Phosphate Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Nivaquine; ***Austral.:*** Chlorquin; ***Austria:*** Resochin; ***Belg.:*** Nivaquine; ***Braz.:*** Clopirim†; Diclokin; Quinacris; ***Canad.:*** Aralen†; ***Cz.:*** Delagil; ***Denm.:*** Malarex; ***Fin.:*** Heliopar; ***Fr.:*** Nivaquine; ***Ger.:*** Resochin; Weimerquin; ***Hong Kong:*** Syncoquin; ***Hung.:*** Delagil; ***India:*** Clo-Kit; Emquin; Lariago; Maliago; Melubrin; Nivaquine-P; Resochin; ***Indon.:*** Avloclor; Malarex; Mexaquin; Resochin; Riboquin; ***Irl.:*** Avloclor; ***Israel:*** Avloclor; ***Mex.:*** Aralen; Maclorex; Paluken†; ***Neth.:*** Nivaquine; ***NZ:*** Chlorquin; Nivaquine; ***Philipp.:*** Aralen; Chlorofoz; ***Pol.:*** Arechin; ***Port.:*** Resochina; ***Rus.:*** Delagil (Делагил); ***S.Afr.:*** Daramal; Mirquin; Nivaquine; Plasmoquine; ***Spain:*** Resochin; ***Switz.:*** Chlorochin; Nivaquine; ***Thai.:*** Diroquine; Genocin; Maliaquine; P-Roquine†; ***UK:*** Avloclor; Malarivon; Malaviron; Nivaquine; ***USA:*** Aralen.

Multi-ingredient: ***Arg.:*** Tri-Emcortina†; ***Fr.:*** Savarine; ***S.Afr.:*** Daramal-Paludrine†.

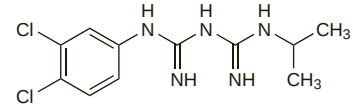
Chlorproguanil Hydrochloride *(BANM, rINNM)*

Chlorproguanil, Chlorhydrate de; Chlorproguanili Hydrochloridum; Hidrocloruro de clorproguanil; M-5943. 1-(3,4-Dichlorophenyl)-5-isopropylbiguanide hydrochloride.

Хлорпрогуанила Гидрохлорид

$C_{11}H_{15}Cl_2N_5,HCl$ = 324.6.

CAS — 537-21-3 (chlorproguanil); 15537-76-5 (chlorproguanil hydrochloride).



(chlorproguanil)

Profile

Chlorproguanil is a biguanide antimalarial used for malaria prophylaxis similarly to proguanil (p.609). It is sometimes given with dapsone. Combination with both dapsone and artesunate is also being investigated for malaria treatment.

◊ Reviews.

1. Bukirwa H, *et al.* Chlorproguanil-dapsone for treating uncomplicated malaria. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2004 (accessed 17/05/05).

Halofantrine Hydrochloride *(BANM, USAN, rINNM)*

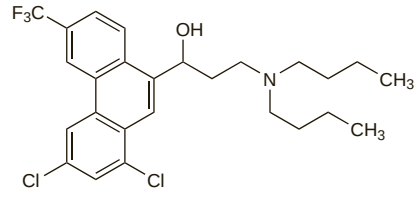
Halofantriinihydrokloridi; Halofantrin hydrochlorid; Halofantrine, Chlorhydrate d'; Halofantrine, chlorhydrate de; Halofantrin-hidroklorid; Halofantrinhydroklorid; Halofantrini hydrochloridum; Halofantrino hidrochloridas; Hidrocloruro de halofantrina; WR-171669. (*RS*)-3-Dibutylamino-1-(1,3-dichloro-6-trifluoromethyl-9-phenanthryl)propan-1-ol hydrochloride; 1,3-Dichloro-α-[2-(dibutylamino)ethyl]-6-trifluoromethyl-9-phenanthrene-methanol hydrochloride.

Галофантрина Гидрохлорид

$C_{26}H_{30}Cl_2F_3NO,HCl$ = 536.9.

CAS — 69756-53-2 (halofantrine); 36167-63-2 (halofantrine hydrochloride); 66051-63-6 (±-halofantrine).

ATC — P01BX01.



(halofantrine)

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Halofantrine Hydrochloride). A white or almost white powder. It exhibits polymorphism. Practically insoluble in water; sparingly soluble in alcohol; freely soluble in methyl alcohol. Protect from light.

Adverse Effects and Precautions

Adverse effects associated with halofantrine include diarrhoea, abdominal pain, nausea, vomiting, pruritus, and skin rash. Transient elevation of serum transaminases, intravascular haemolysis, and hypersensitivity reactions have also been reported.

Halofantrine can adversely affect the heart particularly by prolonging QT interval. Serious ventricular arrhythmias have been reported and fatalities have occurred. As a result it is contra-indicated in patients known to have a prolonged QT interval or those with cardiac disease or a family history of congenital QT prolongation, and also in those with unexplained syncopal attacks, thiamine deficiency, or electrolyte disturbances, or taking other arrhythmogenic drugs (see also Effects on the Heart, below, and Interactions, below).

Halofantrine is not recommended during pregnancy or breast feeding. It should not be taken on a full stomach since this increases its bioavailability and thus the risk of toxicity; after taking halofantrine, fatty food should be avoided for 24 hours.

Effects on the blood. Halofantrine has been associated with acute intravascular haemolysis.[1,2]

1. Vachon F, *et al.* Halofantrine and acute intravascular haemolysis. *Lancet* 1992; **340:** 909–10.
2. Mojon M, *et al.* Intravascular haemolysis following halofantrine intake. *Trans R Soc Trop Med Hyg* 1994; **88:** 91.

Effects on the heart. Prolonged PR[1,2] and QT[1-5] intervals have been reported in patients given halofantrine and there are individual reports of fatal cardiac arrest[1,5] and of torsade de pointes.[4] In 1994, the UK CSM[6] noted that QT interval prolongation occurred at recommended doses of halofantrine in the ma-