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**ANTIMALARIAL MEDICATIONS
AND THEIR MECHANISM OF
ACTION.**

Antimalarial medications or simply **antimalarials** are a type of antiparasitic chemical agent, often naturally derived, that can be used to treat or to prevent malaria, in the latter case, most often aiming at two susceptible target groups, young children and pregnant women.

Specifically, antimalarial drugs may be used to treat malaria in three categories of individuals, (i) those with suspected or confirmed infection, (ii) those visiting a malaria-endemic regions who have no immunity, to prevent infection via malaria prophylaxis, and (iii) or in broader groups of individuals, in routine but intermittent preventative

treatment in regions where malaria is endemic via intermittent preventive therapy.

Anti malarial Agents

1. QUININE : it has a long history stretching from Peru, and the discovery of the cinchona tree, and the potential uses of its bark, to the current day [when?] and a collection of derivatives that are still frequently used in the prevention and treatment of malaria. Quinine is an alkaloid that acts as a blood schizonticidal and weak gametocide against *Plasmodium vivax* and *Plasmodium malariae*. As an alkaloid, it is accumulated in the food vacuoles of *Plasmodium* species, especially *Plasmodium falciparum*. It acts by inhibiting the hemozoin biocrystallization, thus facilitating an aggregation of

cytotoxic heme. Quinine is less effective and more toxic as a blood schizonticidal agent than chloroquine; however, it is still very effective and widely used in the treatment of acute cases of severe *P. falciparum*. It is especially useful in areas where there is known to be a high level of resistance to chloroquine, mefloquine, and sulfa drug combinations with pyrimethamine. Quinine is also used in post-exposure treatment of individuals returning from an area where malaria is endemic. Use of quinine is characterised by a frequently experienced syndrome called cinchonism. Tinnitus (a hearing impairment), rashes, vertigo, nausea, vomiting and abdominal pain are the most common symptoms. Neurological effects are

experienced in some cases due to the drug's [neurotoxic](#) properties. These actions are mediated through the interactions of quinine causing a decrease in the excitability of the [motor neuron end plates](#). This often results in functional impairment of the [eighth cranial nerve](#), resulting in confusion, [delirium](#) and coma. Quinine can cause [hypoglycaemia](#) through its action of stimulating [insulin](#) secretion; this occurs in therapeutic doses and therefore it is advised that glucose levels are monitored in all patients every 4–6 hours. This effect can be exaggerated in pregnancy and therefore additional care in administering and monitoring the dosage is essential. Repeated or over-dosage can result in [kidney failure](#) and death through

depression of the [respiratory system](#).

2. CHLOROQUINE: was, until recently, the most widely used anti-malarial. It was the original prototype from which most methods of treatment are derived. It is also the least expensive, best tested and safest of all available drugs. The emergence of drug-resistant parasitic strains is rapidly decreasing its effectiveness; however, it is still the first-line drug of choice in most [sub-Saharan African](#) countries. It is now suggested that it is used in combination with other antimalarial drugs to extend its effective usage. Popular drugs based on chloroquine phosphate (also called nivaquine) are Chloroquine FNA, Resochin and Dawaquin. Chloroquine is a

4-aminoquinolone

compound with a complicated and still unclear mechanism of action. It is believed to reach high concentrations in the vacuoles of the parasite, which, due to its alkaline nature, raises the internal pH. It controls the conversion of toxic heme to hemozoin by inhibiting the biocrystallization of hemozoin, thus poisoning the parasite through excess levels of toxicity. Other potential mechanisms through which it may act include interfering with the biosynthesis of parasitic nucleic acids and the formation of a chloroquine-haem or chloroquine-DNA complex. The most significant level of activity found is against all forms of the schizonts (with the obvious exception of

chloroquine-resistant *P. falciparum* and *P. vivax* strains) and the [gametocytes](#) of *P. vivax*, *P. malariae*, [P. ovale](#) as well as the immature gametocytes of *P. falciparum*. Chloroquine also has a significant [anti-pyretic](#) and [anti-inflammatory](#) effect when used to treat *P. vivax* infections, and thus it may still remain useful even when resistance is more widespread. According to a report on the Science and Development Network website's sub-Saharan Africa section, there is very little drug resistance among children infected with malaria on the island of Madagascar, but what drug resistance there is exists against chloroquine. Children and adults should receive 25 mg of chloroquine per kg given

over three days. A [pharmacokinetically](#) superior regime, recommended by the WHO, involves giving an initial dose of 10 mg/kg followed 6–8 hours later by 5 mg/kg, then 5 mg/kg on the following two days. For [chemoprophylaxis](#): 5 mg/kg/week (single dose) or 10 mg/kg/week divided into six daily doses is advised.

Chloroquine is only recommended as a [prophylactic drug](#) in regions only affected by *P. vivax* and sensitive *P. falciparum* strains. Chloroquine has been used in the treatment of malaria for many years and no [abortifacient](#) or [teratogenic](#) effects have been reported during this time; therefore, it is considered very safe to use during pregnancy. However, [itching](#) can occur at intolerable level and

Chloroquine can be a provocation factor of [psoriasis](#).

3. AMODIAQUINE: a 4-aminoquinolone anti-malarial drug similar in structure and mechanism of action to chloroquine. Amodiaquine has tended to be administered in areas of chloroquine resistance while some patients prefer its tendency to cause less itching than chloroquine. Amodiaquine is now available in a combined formulation with artesunate ([ASAQ](#)) and is among the artemisinin-combination therapies recommended by the World Health Organization. Combination with sulfadoxine=pyrimethamine is not recommended. The drug should be given in doses between 25 mg/kg and 35 mg/kg over three

days in a similar method to that used in chloroquine administration. Adverse reactions are generally similar in severity and type to that seen in chloroquine treatment. In addition, [bradycardia](#), itching, nausea, vomiting and some abdominal pain have been recorded. Some blood and [hepatic](#) disorders have also been seen in a small number of patients

4. PYRIMETHAMINE: is used in the treatment of uncomplicated malaria. It is particularly useful in cases of chloroquine-resistant *P. falciparum* strains when combined with [sulfadoxine](#). It acts by inhibiting [dihydrofolate reductase](#) in the parasite thus preventing the biosynthesis of [purines](#) and [pyrimidines](#), thereby halting the processes of [DNA replication](#), [cell division](#)

and reproduction. It acts primarily on the schizonts during the erythrocytic phase, and nowadays is only used in concert with a [sulfonamide](#).

5. PROGUANIL: [biguanide](#); a synthetic derivative of pyrimidine. It was developed in 1945 by a British Antimalarial research group. It has many mechanisms of action but primarily is mediated through conversion to the active [metabolite cycloguanil](#). This inhibits the malarial dihydrofolate reductase enzyme. Its most prominent effect is on the primary tissue stages of *P. falciparum*, *P. vivax* and *P. ovale*. It has no known effect against [hypnozoites](#) therefore is not used in the prevention of relapse. It has a weak blood schizonticidal activity and is not

recommended for therapy of acute infection. However it is useful in [prophylaxis](#) when combined with [atovaquone](#) or [chloroquine](#) (in areas where there is no chloroquine resistance).

3 mg/kg is the advised dosage per day, (hence approximate adult dosage is 200 mg). The

pharmacokinetic profile of the drugs indicates that a half dose, twice daily maintains the [plasma](#) levels with a greater level of consistency, thus giving a greater level of protection.

6. The proguanil- chloroquine combination does not provide effective protection against resistant strains of *P. falciparum*. There are very few side effects to proguanil, with slight hair loss and mouth ulcers being occasionally reported following prophylactic use.

Proguanil hydrochloride is marketed as **Paludrine** by [AstraZeneca](#).

7. [Artemether](#) is a [methyl ether](#) derivative of dihydroartemesinin. It is similar to artemesinin in mode of action but demonstrates a reduced ability as a hypnozoitocidal compound, instead acting more significantly to decrease gametocyte carriage. Similar restrictions are in place, as with artemesinin, to prevent the development of resistance, therefore it is only used in combination therapy for severe acute cases of drug-resistant *P. falciparum*. It should be administered in a 7-day course with 4 mg/kg given per day for three days, followed by 1.6 mg/kg for three days. Side effects of the drug are few but include potential neurotoxicity

developing if high doses are given. [[citation needed](#)]

8. [Artesunate](#) is a [hemisuccinate](#) derivative of the active metabolite dihydroartemisin. Currently [[when?](#)] it is the most frequently used of all the artemisinin-type drugs. Its only effect is mediated through a reduction in the gametocyte transmission. It is used in combination therapy and is effective in cases of uncomplicated *P. falciparum*. The dosage recommended by the WHO is a five or seven day course (depending on the predicted adherence level) of 4 mg/kg for three days (usually given in combination with mefloquine) followed by 2 mg/kg for the remaining two or four days. In large studies carried out on over 10,000 patients in Thailand no adverse effects have

been shown.

9. LUMERFAMTRINE is a relative of halofantrine that is used in some combination antimalarial regimens. It is mostly used with arthemeter.