Guidelines for the treatment of malaria

World Health Organization

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GLOSSARY

ACT A combination of artemisinin or one if its derivatives with an antimalarial or antimalarials of a different class.

Asexual stage The life-cycle of the malaria parasite in host red blood cells (intra-erythrocytic development) from merozoite invasion to schizont rupture (merozoite → ring stage → trophozoite → schizont → merozoites). Duration approximately 48 h in *Plasmodium falciparum*, *P. ovale* and *P. vivax*; 72 h in *P. malariae*.

Asexual parasitaemia The presence in host red blood cells of asexual parasites. The level of asexual parasitaemia can be expressed in several different ways: the percentage of infected red blood cells, the number of infected cells per unit volume of blood, the number of parasites seen in one microscopic field in a high-power examination of a thick blood film, or the number of parasites seen per 200–1000 white blood cells in a high-power examination of a thick blood film.

Cerebral malaria Severe falciparum malaria with coma (Glasgow coma scale <11, Blantyre coma scale <3). Malaria with coma persisting for >30 min after a seizure is considered to be cerebral malaria.

Combination therapy A combination of two or more different classes of antimalarial medicines with unrelated mechanisms of action.

Clinical cure Elimination of the symptoms and asexual blood stages of the malaria parasite that caused the patient or carer to seek treatment.

Drug resistance Reduced susceptibility of the causal agent to a drug. WHO defines resistance to antimalarials as the ability of a parasite strain to survive and/or multiply despite the administration and absorption of a medicine given in doses equal to – or higher than – those usually recommended but within the tolerance of the subject, with the caveat that the form of the drug active against the parasite must be able to gain access to the parasite or the infected red blood cell for the duration of the time necessary for its normal action. Resistance to antimalarials arises because of the selection of parasites with genetic mutations or gene amplifications that confer reduced susceptibility.

Gametocyte Sexual stages of malaria parasites present in the host red blood cells, which are infective to the anopheline mosquito.

Persistent liver stages of *P. vivax* and *P. ovale* malaria that remain dormant in host hepatocytes for a fixed interval (3–45 weeks) before maturing to hepatic schizonts. These then burst and release merozoites, which infect red blood cells. Hypnozoites are the source of relapses.

A dark brown granular pigment formed by malaria parasites as a by-product of haemoglobin catabolism. The pigment is evident in mature trophozoites and schizonts.

Parasites released into the host bloodstream when a hepatic or erythrocytic schizont bursts. These then invade the red blood cells.

Antimalarial treatment with a single medicine (either a single active compound or a synergistic combination of two compounds with related mechanism of action).

Plasmodium. A genus of protozoan vertebrate blood parasites that includes the causal agents of malaria. *Plasmodium falciparum*, *P. malariae*, *P. ovale* and *P. vivax* cause malaria in humans.

The life-cycle of the malaria parasite when it first enters the host. Following inoculation into a human by the female anopheline mosquito, sporozoites invade parenchyma cells in the host liver and multiply within the hepatocytes for 5–12 days, forming hepatic schizonts. These then burst liberating merozoites into the bloodstream, which subsequently invade red blood cells.

In *P. vivax* and *P. ovale* infections only, this comprises cure as defined above plus prevention of relapses.

An antigen-based stick, cassette or card test for malaria in which a coloured line indicates that plasmodial antigens have been detected.

The recurrence of asexual parasitaemia after treatment of the infection with the same infection that caused the original illness (in endemic areas now defined by molecular genotyping). This results from incomplete clearance of parasitaemia by treatment and is therefore different to a relapse in *P. vivax* and *P. ovale* infections.

The recurrence of asexual parasitaemia following treatment. This can be caused by a recrudescence, a relapse (in *P. vivax* and *P. ovale* infections only) or a new infection.

The recurrence of asexual parasitaemia in *P. vivax* and *P. ovale* malaria deriving from persisting liver stages. Relapse occurs when the blood stage infection has been eliminated but hypnozoites persist in the liver and mature to form hepatic schizonts. After a variable interval of weeks (tropical strains) or months (temperate strains) the hepatic schizonts burst and liberate merozoites into the bloodstream.

Young usually ring-shaped intra-erythrocytic malaria parasites, before malaria pigment is evident under microscopy.

Mature malaria parasites in host liver cells (hepatic schizonts) or red blood cells (erythrocytic schizonts) that are undergoing nuclear division. This process is called schizogony.

Resistance to antimalarials emerges and spreads because of the selective survival advantage that resistant parasites have in the presence of antimalarials that they are resistant to. Selection pressure describes the intensity and magnitude of the selection process; the greater the proportion of parasites in a given parasite population exposed to concentrations of an antimalarial that allow proliferation of resistant, but not sensitive parasites, the greater is the selection pressure.

Haemoglobin concentration of <5 g/100 ml.

Acute falciparum malaria with signs of severity and/or evidence of vital organ dysfunction.

Motile malaria parasites that are infective to humans, inoculated by a feeding female anopheline mosquito. The sporozoites invade hepatocytes.

The intensity of malaria transmission measured by the frequency with which people living in an area are bitten by anopheline mosquitoes carrying sporozoites. This is often expressed as the annual entomological inoculation rate (EIR), which is the number of inoculations of malaria parasites received by one person in one year.

Stage of development of the malaria parasites within host red blood cells from the ring stage and before nuclear division. Mature trophozoites contain visible malaria pigment.

. Symptomatic infection with malaria parasitaemia without signs of severity and/or evidence of vital organ dysfunction.

ABBREVIATIONS

ACT	artemisinin-based combination therapy
AL	artemether-lumefantrine combination
AQ	amodiaquine
AS	artesunate
AS+AQ	artesunate + amodiaquine combination
AS+MQ	artesunate + mefloquine combination
AS+SP	artesunate + sulfadoxine-pyrimethamine combination
CI	confidence interval
CQ	chloroquine
EIR	entomological inoculation rate
HIV/AIDS	human immunodeficiency virus/ acquired immunodeficiency syndrome
HRP2	histidine-rich protein 2
IC_{50}	concentration providing 50% inhibition
MIC	minimum inhibitory concentration
MQ	mefloquine
OR	odds ratio
PCR	polymerase chain reaction
*p*LDH	*parasite*-lactate dehydrogenase
RCT	randomized controlled trial
RDT	rapid diagnostic test
RR	relative risk
SP	sulfadoxine–pyrimethamine
WHO	World Health Organization
WMD	weighted mean difference