[Template:Pp-semi-indef](/wiki/Template:Pp-semi-indef" \o "Template:Pp-semi-indef) [Template:Pp-move-indef](/wiki/Template:Pp-move-indef) [Template:Infobox medical condition](/wiki/Template:Infobox_medical_condition) **Malaria** is a [mosquito-borne infectious disease](/wiki/Mosquito-borne_disease) of humans and other animals caused by parasitic [protozoans](/wiki/Protozoa) (a group of single-celled [microorganisms](/wiki/Microorganism)) belonging to the [*Plasmodium*](/wiki/Plasmodium) [type](/wiki/Genus).[[1]](#cite_note-1) Malaria causes symptoms that typically include [fever](/wiki/Fever), [fatigue](/wiki/Malaise), [vomiting](/wiki/Vomiting), and [headaches](/wiki/Headache). In severe cases it can cause [yellow skin](/wiki/Jaundice), [seizures](/wiki/Epileptic_seizure), [coma](/wiki/Coma), or [death](/wiki/Death).[[2]](#cite_note-2) Symptoms usually begin ten to fifteen days after being bitten. If not properly treated, people may have recurrences of the disease months later.<ref name=WHO2014/> In those who have recently survived an infection, reinfection usually causes milder symptoms. This partial [resistance](/wiki/Immunity_(medical)) disappears over months to years if the person has no continuing exposure to malaria.[[2]](#cite_note-2) The disease is most commonly transmitted by an infected female [*Anopheles*](/wiki/Anopheles) mosquito. The mosquito bite introduces the [parasites](/wiki/Parasite) from the mosquito's [saliva](/wiki/Saliva) into a person's [blood](/wiki/Circulatory_system).<ref name=WHO2014/> The parasites travel to the liver where they mature and reproduce. Five species of *Plasmodium* can infect and be spread by humans.[[2]](#cite_note-2) Most deaths are caused by [*P. falciparum*](/wiki/Plasmodium_falciparum) because [*P. vivax*](/wiki/Plasmodium_vivax), [*P. ovale*](/wiki/Plasmodium_ovale), and [*P. malariae*](/wiki/Plasmodium_malariae) generally cause a milder form of malaria.[[2]](#cite_note-2) The species [*P. knowlesi*](/wiki/Plasmodium_knowlesi) rarely causes disease in humans.<ref name=WHO2014/> Malaria is typically diagnosed by the microscopic examination of blood using [blood films](/wiki/Blood_film), or with [antigen](/wiki/Antigen)-based [rapid diagnostic tests](/wiki/Malaria_antigen_detection_tests).[[2]](#cite_note-2) Methods that use the [polymerase chain reaction](/wiki/Polymerase_chain_reaction) to detect the parasite's [DNA](/wiki/DNA) have been developed, but are not widely used in areas where malaria is [common](/wiki/Endemic_(epidemiology)) due to their cost and complexity.[[3]](#cite_note-3) The risk of disease can be reduced by preventing mosquito bites by using [mosquito nets](/wiki/Mosquito_net) and [insect repellents](/wiki/Insect_repellent), or with mosquito-control measures such as spraying [insecticides](/wiki/Insecticide) and draining standing water.[[2]](#cite_note-2) Several medications are available to [prevent malaria](/wiki/Malaria_prophylaxis) in travellers to areas where the disease is common. Occasional doses of the medication [sulfadoxine/pyrimethamine](/wiki/Sulfadoxine/pyrimethamine) are recommended in [infants](/wiki/Infant) and after the [first trimester](/wiki/First_trimester) of [pregnancy](/wiki/Pregnancy) in areas with high rates of malaria. Despite a need, no effective [vaccine](/wiki/Vaccine) exists, although efforts to develop one are ongoing.<ref name=WHO2014/> The recommended treatment for malaria is a combination of [antimalarial medications](/wiki/Antimalarial_medication) that includes an [artemisinin](/wiki/Artemisinin).[[2]](#cite_note-2) The second medication may be either [mefloquine](/wiki/Mefloquine), [lumefantrine](/wiki/Lumefantrine), or sulfadoxine/pyrimethamine.<ref name=WHO2010>[Template:Cite book](/wiki/Template:Cite_book)</ref> [Quinine](/wiki/Quinine) along with [doxycycline](/wiki/Doxycycline) may be used if an artemisinin is not available.<ref name=WHO2010/> It is recommended that in areas where the disease is common, malaria is confirmed if possible before treatment is started due to concerns of increasing [drug resistance](/wiki/Drug_resistance). Resistance among the parasites has developed to several antimalarial medications; for example, [chloroquine](/wiki/Chloroquine)-resistant *P. falciparum* has spread to most malarial areas, and resistance to artemisinin has become a problem in some parts of Southeast Asia.<ref name=WHO2014>[Template:Cite web](/wiki/Template:Cite_web)</ref>

The disease is widespread in the [tropical](/wiki/Tropics) and [subtropical](/wiki/Subtropical) regions that exist in a broad band around the [equator](/wiki/Equator).[[2]](#cite_note-2) This includes much of [Sub-Saharan Africa](/wiki/Sub-Saharan_Africa), [Asia](/wiki/Asia), and [Latin America](/wiki/Latin_America). In 2015, there were 214 million cases of malaria worldwide.<ref name=WHO15>[Template:Cite web](/wiki/Template:Cite_web)</ref> This resulted in an estimated 438,000 deaths, 90% of which occurred in Africa.<ref name=WHO15/> Rates of disease have decreased from 2000 to 2015 by 37%,<ref name=WHO15/> but increased from 2014 during which there were 198 million cases.<ref name=WHO2014Book>[Template:Cite book](/wiki/Template:Cite_book)</ref> Malaria is commonly associated with poverty and has a major negative effect on [economic development](/wiki/Economic_development).[[4]](#cite_note-4)[[5]](#cite_note-5) In Africa, it is estimated to result in losses of US$12 billion a year due to increased healthcare costs, lost ability to work, and negative effects on tourism.[[6]](#cite_note-6)

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## Signs and symptoms[[edit](/index.php?title=(none)&action=edit&section=1)]

[thumb|250px|Main symptoms of malaria](/wiki/File:Symptoms_of_Malaria.png)[[7]](#cite_note-7) The signs and symptoms of malaria typically begin 8–25 days following infection;[[7]](#cite_note-7) however, symptoms may occur later in those who have taken antimalarial medications as prevention.[[3]](#cite_note-3) Initial manifestations of the disease—common to all malaria species—are similar to [flu](/wiki/Flu)-like symptoms,[[8]](#cite_note-8) and can resemble other conditions such as [sepsis](/wiki/Sepsis), [gastroenteritis](/wiki/Gastroenteritis), and [viral diseases](/wiki/Viral_disease).[[3]](#cite_note-3) The presentation may include [headache](/wiki/Headache), [fever](/wiki/Fever), [shivering](/wiki/Shivering), [joint pain](/wiki/Arthralgia), [vomiting](/wiki/Vomiting), [hemolytic anemia](/wiki/Hemolytic_anemia), [jaundice](/wiki/Jaundice), [hemoglobin in the urine](/wiki/Hemoglobinuria), [retinal damage](/wiki/Retinopathy), and [convulsions](/wiki/Convulsion).[[9]](#cite_note-9) The classic symptom of malaria is [paroxysm](/wiki/Paroxysmal_attacks)—a cyclical occurrence of sudden coldness followed by shivering and then fever and sweating, occurring every two days ([tertian fever](/wiki/Fever#Types)) in *P. vivax* and *P. ovale* infections, and every three days ([quartan fever](/wiki/Fever#Types)) for *P. malariae*. *P. falciparum* infection can cause recurrent fever every 36–48 hours, or a less pronounced and almost continuous fever.[[10]](#cite_note-10) Severe malaria is usually caused by *P. falciparum* (often referred to as falciparum malaria). Symptoms of falciparum malaria arise 9–30 days after infection.[[8]](#cite_note-8) Individuals with cerebral malaria frequently exhibit [neurological](/wiki/Neurological_disorder) symptoms, including [abnormal posturing](/wiki/Abnormal_posturing), [nystagmus](/wiki/Nystagmus), [conjugate gaze palsy](/wiki/Conjugate_gaze_palsy) (failure of the eyes to turn together in the same direction), [opisthotonus](/wiki/Opisthotonus), [seizures](/wiki/Seizure), or [coma](/wiki/Coma).[[8]](#cite_note-8)

### Complications[[edit](/index.php?title=(none)&action=edit&section=2)]

Malaria has several serious [complications](/wiki/Complication_(medicine)). Among these is the development of [respiratory distress](/wiki/Respiratory_distress), which occurs in up to 25% of adults and 40% of children with severe *P. falciparum* malaria. Possible causes include respiratory compensation of [metabolic acidosis](/wiki/Metabolic_acidosis), noncardiogenic [pulmonary oedema](/wiki/Pulmonary_oedema), concomitant [pneumonia](/wiki/Pneumonia), and severe [anaemia](/wiki/Anaemia). Although rare in young children with severe malaria, [acute respiratory distress syndrome](/wiki/Acute_respiratory_distress_syndrome) occurs in 5–25% of adults and up to 29% of pregnant women.[[11]](#cite_note-11) [Coinfection](/wiki/Coinfection) of [HIV](/wiki/HIV) with malaria increases mortality.[[12]](#cite_note-12) Renal failure is a feature of [blackwater fever](/wiki/Blackwater_fever), where hemoglobin from [lysed](/wiki/Lysis) red blood cells leaks into the urine.[[8]](#cite_note-8) Infection with *P. falciparum* may result in cerebral malaria, a form of severe malaria that involves [encephalopathy](/wiki/Encephalopathy). It is associated with retinal whitening, which may be a useful clinical sign in distinguishing malaria from other causes of fever.[[13]](#cite_note-13) [Enlarged spleen](/wiki/Splenomegaly), [enlarged liver](/wiki/Hepatomegaly) or [both of these](/wiki/Hepatosplenomegaly), severe headache, [low blood sugar](/wiki/Hypoglycemia), and [hemoglobin in the urine](/wiki/Hemoglobinuria) with [renal failure](/wiki/Renal_failure) may occur.[[8]](#cite_note-8) Complications may include spontaneous bleeding, [coagulopathy](/wiki/Coagulopathy), and [shock](/wiki/Circulatory_shock).[[14]](#cite_note-14) [Malaria in pregnant women](/wiki/Pregnancy-associated_malaria) is an important cause of [stillbirths](/wiki/Stillbirth), [infant mortality](/wiki/Infant_mortality), [abortion](/wiki/Abortion) and [low birth weight](/wiki/Low_birth_weight),[[15]](#cite_note-15) particularly in *P. falciparum* infection, but also with *P. vivax*.[[16]](#cite_note-16)

## Cause[[edit](/index.php?title=(none)&action=edit&section=3)]

[Template:Main](/wiki/Template:Main)

Malaria [parasites](/wiki/Parasite) belong to the genus [*Plasmodium*](/wiki/Plasmodium) (phylum [Apicomplexa](/wiki/Apicomplexa)). In humans, malaria is caused by [*P. falciparum*](/wiki/Plasmodium_falciparum), [*P. malariae*](/wiki/Plasmodium_malariae), [*P. ovale*](/wiki/Plasmodium_ovale), [*P. vivax*](/wiki/Plasmodium_vivax) and [*P. knowlesi*](/wiki/Plasmodium_knowlesi).[[17]](#cite_note-17)[[18]](#cite_note-18) Among those infected, *P. falciparum* is the most common species identified (~75%) followed by *P. vivax* (~20%).[[3]](#cite_note-3) Although *P. falciparum* traditionally accounts for the majority of deaths,[[19]](#cite_note-19) recent evidence suggests that *P. vivax* malaria is associated with potentially life-threatening conditions about as often as with a diagnosis of *P. falciparum* infection.[[20]](#cite_note-20) *P. vivax* proportionally is more common outside Africa.[[21]](#cite_note-21) There have been documented human infections with several species of *Plasmodium* from [higher apes](/wiki/Simian); however, except for *P. knowlesi*—a [zoonotic](/wiki/Zoonosis) species that causes malaria in [macaques](/wiki/Macaques)[[18]](#cite_note-18)—these are mostly of limited public health importance.[[22]](#cite_note-22) [Global warming](/wiki/Effects_of_global_warming_on_human_health#Malaria) is likely to affect malaria transmission, but the severity and geographic distribution of such effects is uncertain.[[23]](#cite_note-23)<ref name=who-chap6>[Template:Cite web](/wiki/Template:Cite_web)</ref>

### Life cycle[[edit](/index.php?title=(none)&action=edit&section=4)]

[thumb|350px|The life cycle of malaria parasites. A mosquito causes an infection by a bite. First, sporozoites enter the bloodstream, and migrate to the liver. They infect](/wiki/File:Life_Cycle_of_the_Malaria_Parasite.jpg) [liver cells](/wiki/Liver_cells), where they multiply into merozoites, rupture the liver cells, and return to the bloodstream. The merozoites infect red blood cells, where they develop into ring forms, trophozoites and schizonts that in turn produce further merozoites. [Sexual forms](/wiki/Gametocytes) are also produced, which, if taken up by a mosquito, will infect the insect and continue the life cycle.

In the [life cycle](/wiki/Plasmodium#¬if_cycle) of *Plasmodium*, a female [*Anopheles*](/wiki/Anopheles) mosquito (the [definitive host](/wiki/Host_(biology))) transmits a motile infective form (called the [sporozoite](/wiki/Sporozoite)) to a vertebrate host such as a human (the secondary host), thus acting as a transmission [vector](/wiki/Vector_(epidemiology)). A sporozoite travels through the blood vessels to liver cells ([hepatocytes](/wiki/Hepatocyte)), where it reproduces [asexually](/wiki/Asexual_reproduction) (tissue [schizogony](/wiki/Schizogony)), producing thousands of [merozoites](/wiki/Merozoite). These infect new red blood cells and initiate a series of asexual multiplication cycles (blood schizogony) that produce 8 to 24 new infective merozoites, at which point the cells burst and the infective cycle begins anew.[[24]](#cite_note-24) Other merozoites develop into immature [gametocytes](/wiki/Gametocyte#Gametocytes_and_malaria), which are the precursors of male and female [gametes](/wiki/Gamete). When a fertilised mosquito bites an infected person, gametocytes are taken up with the blood and mature in the mosquito gut. The male and female gametocytes fuse and form an [ookinete](/wiki/Ookinete)—a fertilized, motile [zygote](/wiki/Zygote). Ookinetes develop into new sporozoites that migrate to the insect's [salivary glands](/wiki/Salivary_gland), ready to infect a new vertebrate host. The sporozoites are injected into the skin, in the saliva, when the mosquito takes a subsequent blood meal.[[25]](#cite_note-25) Only female mosquitoes feed on blood; male mosquitoes feed on plant nectar, and do not transmit the disease. The females of the *Anopheles* genus of mosquito prefer to feed at night. They usually start searching for a meal at dusk, and will continue throughout the night until taking a meal.[[26]](#cite_note-26) Malaria parasites can also be transmitted by [blood transfusions](/wiki/Blood_transfusion), although this is rare.[[27]](#cite_note-27)

### Recurrent malaria[[edit](/index.php?title=(none)&action=edit&section=5)]

Symptoms of malaria can recur after varying symptom-free periods. Depending upon the cause, recurrence can be classified as either [recrudescence](/wiki/Recrudescence), [relapse](/wiki/Relapse), or reinfection. Recrudescence is when symptoms return after a symptom-free period. It is caused by parasites surviving in the blood as a result of inadequate or ineffective treatment.[[28]](#cite_note-28) Relapse is when symptoms reappear after the parasites have been eliminated from blood but persist as dormant [hypnozoites](/wiki/Plasmodium#Life_cycle) in liver cells. Relapse commonly occurs between 8–24 weeks and is commonly seen with *P. vivax* and *P. ovale* infections.[[3]](#cite_note-3) *P. vivax* malaria cases in [temperate](/wiki/Temperate) areas often involve [overwintering](/wiki/Overwintering) by hypnozoites, with relapses beginning the year after the mosquito bite.[[29]](#cite_note-29) Reinfection means the parasite that caused the past infection was eliminated from the body but a new parasite was introduced. Reinfection cannot readily be distinguished from recrudescence, although recurrence of infection within two weeks of treatment for the initial infection is typically attributed to treatment failure.[[30]](#cite_note-30) People may develop some [immunity](/wiki/Premunity) when exposed to frequent infections.[[31]](#cite_note-31)

## Pathophysiology[[edit](/index.php?title=(none)&action=edit&section=6)]

[Template:Further2](/wiki/Template:Further2) [thumb|right|](/wiki/File:Maternal_malaria_placenta_-_cropped_-_very_high_mag.jpg)[Micrograph](/wiki/Micrograph) of a [placenta](/wiki/Placenta) from a [stillbirth](/wiki/Stillbirth) due to maternal malaria. [H&E stain](/wiki/H&E_stain). Red blood cells are anuclear; blue/black staining in bright red structures (red blood cells) indicate foreign nuclei from the parasites. [thumb|Electron micrograph of a *Plasmodium falciparum*-infected red blood cell (center), illustrating adhesion protein "knobs"](/wiki/File:Red_blood_cells_infected_with_malaria.jpg)

Malaria infection develops via two phases: one that involves the [liver](/wiki/Liver) (exoerythrocytic phase), and one that involves red blood cells, or [erythrocytes](/wiki/Erythrocyte) (erythrocytic phase). When an infected mosquito pierces a person's skin to take a blood meal, sporozoites in the mosquito's saliva enter the bloodstream and migrate to the liver where they infect hepatocytes, multiplying asexually and asymptomatically for a period of 8–30 days.[[32]](#cite_note-32) After a potential dormant period in the liver, these organisms [differentiate](/wiki/Cellular_differentiation) to yield thousands of merozoites, which, following rupture of their host cells, escape into the blood and infect red blood cells to begin the erythrocytic stage of the life cycle.[[32]](#cite_note-32) The parasite escapes from the liver undetected by wrapping itself in the [cell membrane](/wiki/Cell_membrane) of the infected host liver cell.[[33]](#cite_note-33) Within the red blood cells, the parasites multiply further, again asexually, periodically breaking out of their host cells to invade fresh red blood cells. Several such amplification cycles occur. Thus, classical descriptions of waves of fever arise from simultaneous waves of merozoites escaping and infecting red blood cells.[[32]](#cite_note-32) Some *P. vivax* sporozoites do not immediately develop into exoerythrocytic-phase merozoites, but instead produce hypnozoites that remain dormant for periods ranging from several months (7–10 months is typical) to several years. After a period of dormancy, they reactivate and produce merozoites. Hypnozoites are responsible for long incubation and late relapses in *P. vivax* infections,[[29]](#cite_note-29) although their existence in *P. ovale* is uncertain.[[34]](#cite_note-34) The parasite is relatively protected from attack by the body's [immune system](/wiki/Immune_system) because for most of its human life cycle it resides within the liver and blood cells and is relatively invisible to immune surveillance. However, circulating infected blood cells are destroyed in the [spleen](/wiki/Spleen). To avoid this fate, the *P. falciparum* parasite displays adhesive [proteins](/wiki/Protein) on the surface of the infected blood cells, causing the blood cells to stick to the walls of small blood vessels, thereby sequestering the parasite from passage through the general circulation and the spleen.[[35]](#cite_note-35) The blockage of the microvasculature causes symptoms such as in placental malaria.[[36]](#cite_note-36) Sequestered red blood cells can breach the [blood–brain barrier](/wiki/Blood–brain_barrier) and cause cerebral malaria.[[37]](#cite_note-37)

### Genetic resistance[[edit](/index.php?title=(none)&action=edit&section=7)]

[Template:Main](/wiki/Template:Main) According to a 2005 review, due to the high levels of [mortality](/wiki/Death) and [morbidity](/wiki/Morbidity) caused by malaria—especially the *P. falciparum* species—it has placed the greatest [selective pressure](/wiki/Selection_(biology)) on the [human genome](/wiki/Human_genome) in recent history. Several genetic factors provide some resistance to it including [sickle cell trait](/wiki/Sickle_cell_trait), [thalassaemia](/wiki/Thalassaemia) traits, [glucose-6-phosphate dehydrogenase deficiency](/wiki/Glucose-6-phosphate_dehydrogenase_deficiency), and the absence of [Duffy antigens](/wiki/Duffy_antigen) on red blood cells.[[38]](#cite_note-38)[[39]](#cite_note-39) The impact of sickle cell trait on malaria immunity illustrates some evolutionary trade-offs that have occurred because of endemic malaria. Sickle cell trait causes a change in the hemoglobin molecule in the blood. Normally, red blood cells have a very flexible, biconcave shape that allows them to move through narrow [capillaries](/wiki/Capillaries); however, when the modified [hemoglobin S](/wiki/Hemoglobin_S) molecules are exposed to low amounts of oxygen, or crowd together due to dehydration, they can stick together forming strands that cause the cell to sickle or distort into a curved shape. In these strands the molecule is not as effective in taking or releasing oxygen, and the cell is not flexible enough to circulate freely. In the early stages of malaria, the parasite can cause infected red cells to sickle, and so they are removed from circulation sooner. This reduces the frequency with which malaria parasites complete their life cycle in the cell. Individuals who are [homozygous](/wiki/Homozygous) (with two copies of the abnormal hemoglobin beta [allele](/wiki/Allele)) have [sickle-cell anaemia](/wiki/Sickle-cell_anaemia), while those who are heterozygous (with one abnormal allele and one normal allele) experience resistance to malaria without severe anemia. Although the shorter life expectancy for those with the homozygous condition would tend to disfavor the trait's survival, the trait is preserved in malaria-prone regions because of the [benefits](/wiki/Heterozygote_advantage) provided by the heterozygous form.[[39]](#cite_note-39)[[40]](#cite_note-40)

### Liver dysfunction[[edit](/index.php?title=(none)&action=edit&section=8)]

Liver dysfunction as a result of malaria is uncommon and usually only occurs in those with another liver condition such as [viral hepatitis](/wiki/Viral_hepatitis) or [chronic liver disease](/wiki/Chronic_liver_disease). The syndrome is sometimes called *malarial hepatitis*.[[41]](#cite_note-41) While it has been considered a rare occurrence, malarial hepatopathy has seen an increase, particularly in Southeast Asia and India. Liver compromise in people with malaria correlates with a greater likelihood of complications and death.[[41]](#cite_note-41)

## Diagnosis[[edit](/index.php?title=(none)&action=edit&section=9)]

[Template:Main](/wiki/Template:Main) [thumb|The blood film is the](/wiki/File:5901_lores.jpg) [gold standard](/wiki/Gold_standard_(test)) for malaria diagnosis. [thumb|Ring-forms and](/wiki/File:Plasmodium.jpg) [gametocytes](/wiki/Gametocyte) of *Plasmodium falciparum* in human blood Owing to the non-specific nature of the presentation of symptoms, diagnosis of malaria in non-endemic areas requires a high degree of suspicion, which might be elicited by any of the following: recent travel history, [enlarged spleen](/wiki/Splenomegaly), fever, [low number of platelets](/wiki/Thrombocytopenia) in the blood, and [higher-than-normal levels of bilirubin](/wiki/Hyperbilirubinemia) in the blood combined with a normal level of [white blood cells](/wiki/White_blood_cells).[[3]](#cite_note-3) Malaria is usually confirmed by the microscopic examination of [blood films](/wiki/Blood_film) or by [antigen](/wiki/Antigen)-based [rapid diagnostic tests](/wiki/Malaria_antigen_detection_tests) (RDT).[[42]](#cite_note-42)[[43]](#cite_note-43) In some areas, RDTs need to be able to distinguish whether the malaria symptoms are caused by Plasmodium falciparum or by other species of parasites since treatment strategies could differ for non-falciparum infections.[[44]](#cite_note-44) Microscopy is the most commonly used method to detect the malarial parasite—about 165 million blood films were examined for malaria in 2010.[[45]](#cite_note-45) Despite its widespread usage, diagnosis by microscopy suffers from two main drawbacks: many settings (especially rural) are not equipped to perform the test, and the accuracy of the results depends on both the skill of the person examining the blood film and the levels of the parasite in the blood. The [sensitivity](/wiki/Sensitivity_and_specificity) of blood films ranges from 75–90% in optimum conditions, to as low as 50%. Commercially available RDTs are often more accurate than blood films at predicting the presence of malaria parasites, but they are widely variable in diagnostic sensitivity and specificity depending on manufacturer, and are unable to tell how many parasites are present.[[45]](#cite_note-45) In regions where laboratory tests are readily available, malaria should be suspected, and tested for, in any unwell person who has been in an area where malaria is endemic. In areas that cannot afford laboratory diagnostic tests, it has become common to use only a history of fever as the indication to treat for malaria—thus the common teaching "fever equals malaria unless proven otherwise". A drawback of this practice is [overdiagnosis](/wiki/Overdiagnosis) of malaria and mismanagement of non-malarial fever, which wastes limited resources, erodes confidence in the health care system, and contributes to drug resistance.[[46]](#cite_note-46) Although [polymerase chain reaction](/wiki/Polymerase_chain_reaction)-based tests have been developed, they are not widely used in areas where malaria is common as of 2012, due to their complexity.[[3]](#cite_note-3)

### Classification[[edit](/index.php?title=(none)&action=edit&section=10)]

Malaria is classified into either "severe" or "uncomplicated" by the [World Health Organization](/wiki/World_Health_Organization) (WHO).[[3]](#cite_note-3) It is deemed severe when *any* of the following criteria are present, otherwise it is considered uncomplicated.[[47]](#cite_note-47)\* Decreased consciousness

* Significant weakness such that the person is unable to walk
* Inability to feed
* Two or more [convulsions](/wiki/Convulsions)
* [Low blood pressure](/wiki/Low_blood_pressure) (less than 70 [mmHg](/wiki/MmHg) in adults and 50 mmHg in children)
* [Breathing problems](/wiki/Respiratory_distress)
* [Circulatory shock](/wiki/Circulatory_shock)
* [Kidney failure](/wiki/Kidney_failure) or [hemoglobin](/wiki/Hemoglobin) in the urine
* Bleeding problems, or hemoglobin less than 50 g/L (5 g/dL)
* [Pulmonary oedema](/wiki/Pulmonary_oedema)
* [Blood glucose](/wiki/Blood_glucose) less than 2.2 mmol/L (40 mg/dL)
* [Acidosis](/wiki/Acidosis) or [lactate](/wiki/Lactic_acid) levels of greater than 5 mmol/L
* A parasite level in the blood of greater than 100,000 per [microlitre](/wiki/Microlitre) (µL) in low-intensity transmission areas, or 250,000 per µL in high-intensity transmission areas

Cerebral malaria is defined as a severe *P. falciparum*-malaria presenting with neurological symptoms, including coma (with a [Glasgow coma scale](/wiki/Glasgow_coma_scale) less than 11, or a [Blantyre coma scale](/wiki/Blantyre_coma_scale) greater than 3), or with a coma that lasts longer than 30 minutes after a seizure.[[48]](#cite_note-48) Various types of malaria have been called by the names below:[[49]](#cite_note-49)

|  |  |  |
| --- | --- | --- |
| **Name** | **Pathogen** | **Notes** |
| algid malaria | [*Plasmodium falciparum*](/wiki/Plasmodium_falciparum) | severe malaria affecting the [cardiovascular system](/wiki/Cardiovascular_system) and causing [chills](/wiki/Chills) and [circulatory shock](/wiki/Circulatory_shock) |
| bilious malaria | [*Plasmodium falciparum*](/wiki/Plasmodium_falciparum) | severe malaria affecting the [liver](/wiki/Liver) and causing [vomiting](/wiki/Vomiting) and [jaundice](/wiki/Jaundice) |
| cerebral malaria | [*Plasmodium falciparum*](/wiki/Plasmodium_falciparum) | severe malaria affecting the [cerebrum](/wiki/Cerebrum) |
| congenital malaria | various [plasmodia](/wiki/Plasmodium) | plasmodium introduced from the mother via the [fetal circulation](/wiki/Fetal_circulation) |
| falciparum malaria, *Plasmodium falciparum* malaria, pernicious malaria | [*Plasmodium falciparum*](/wiki/Plasmodium_falciparum) |  |
| ovale malaria, *Plasmodium ovale* malaria | [*Plasmodium ovale*](/wiki/Plasmodium_ovale) |  |
| quartan malaria, malariae malaria, *Plasmodium malariae* malaria | [*Plasmodium malariae*](/wiki/Plasmodium_malariae) | paroxysms every fourth day ([quartan](/wiki/Wikt:quartan#Adjective)), counting the day of occurrence as the first day |
| quotidian malaria | [*Plasmodium falciparum*](/wiki/Plasmodium_falciparum), [*Plasmodium vivax*](/wiki/Plasmodium_vivax) | paroxysms daily ([quotidian](/wiki/Wikt:quotidian#Adjective)) |
| tertian malaria | [*Plasmodium falciparum*](/wiki/Plasmodium_falciparum), [*Plasmodium ovale*](/wiki/Plasmodium_ovale), [*Plasmodium vivax*](/wiki/Plasmodium_vivax) | paroxysms every third day ([tertian](/wiki/Wikt:tertian#Adjective)), counting the day of occurrence as the first |
| transfusion malaria | various [plasmodia](/wiki/Plasmodium) | plasmodium introduced by [blood transfusion](/wiki/Blood_transfusion), [needle sharing](/wiki/Needle_sharing), or [needlestick injury](/wiki/Needlestick_injury) |
| vivax malaria, *Plasmodium vivax* malaria | [*Plasmodium vivax*](/wiki/Plasmodium_vivax) |  |
|  |  |  |

## Prevention[[edit](/index.php?title=(none)&action=edit&section=11)]

[thumb|An](/wiki/File:Anopheles_stephensi.jpeg) [*Anopheles stephensi*](/wiki/Anopheles_stephensi) mosquito shortly after obtaining blood from a human (the droplet of blood is expelled as a surplus). This mosquito is a vector of malaria, and mosquito control is an effective way of reducing its incidence.

Methods used to prevent malaria include medications, mosquito elimination and the prevention of bites. There is no [vaccine for malaria](/wiki/Malaria_vaccine). The presence of malaria in an area requires a combination of high human population density, high anopheles mosquito population density and high rates of transmission from humans to mosquitoes and from mosquitoes to humans. If any of these is lowered sufficiently, the parasite will eventually disappear from that area, as happened in North America, Europe and parts of the Middle East. However, unless the parasite is eliminated from the whole world, it could become re-established if conditions revert to a combination that favours the parasite's reproduction. Furthermore, the cost per person of eliminating anopheles mosquitoes rises with decreasing population density, making it economically unfeasible in some areas.[[50]](#cite_note-50) Prevention of malaria may be more cost-effective than treatment of the disease in the long run, but the [initial costs](/wiki/Capital_cost) required are out of reach of many of the world's poorest people. There is a wide difference in the costs of control (i.e. maintenance of low endemicity) and elimination programs between countries. For example, in China—whose government in 2010 announced a strategy to pursue malaria elimination in the [Chinese provinces](/wiki/Chinese_province)—the required investment is a small proportion of public expenditure on health. In contrast, a similar program in Tanzania would cost an estimated one-fifth of the public health budget.[[51]](#cite_note-51) In areas where malaria is common, children under five years old often have [anemia](/wiki/Anemia) which is sometimes due to malaria. Giving children with anemia in these areas preventive antimalarial medication improves red blood cell levels slightly but did not affect the risk of death or need for hospitalization.[[52]](#cite_note-52)

### Mosquito control[[edit](/index.php?title=(none)&action=edit&section=12)]

[Template:Further2](/wiki/Template:Further2) [thumb|left|Man spraying kerosene oil in standing water,](/wiki/File:Mansprayingkeroseneoil.jpg) [Panama Canal Zone](/wiki/Panama_Canal_Zone) 1912 [Vector control](/wiki/Vector_control) refers to methods used to decrease malaria by reducing the levels of transmission by mosquitoes. For individual protection, the most effective [insect repellents](/wiki/Insect_repellent) are based on [DEET](/wiki/DEET) or [picaridin](/wiki/Picaridin).[[53]](#cite_note-53) Insecticide-treated [mosquito nets](/wiki/Mosquito_net) (ITNs) and [indoor residual spraying](/wiki/Indoor_residual_spraying) (IRS) have been shown to be highly effective in preventing malaria among children in areas where malaria is common.[[54]](#cite_note-54)[[55]](#cite_note-55) Prompt treatment of confirmed cases with artemisinin-based combination therapies (ACTs) may also reduce transmission.[[56]](#cite_note-56)[thumb|right|Walls where indoor residual spraying of DDT has been applied. The mosquitoes remain on the wall until they fall down dead on the floor.](/wiki/File:Mosquitoes-Killedy-By-DDT-Lake-Victoria.JPG)

[thumb|A mosquito net in use.](/wiki/File:Mosquitonet149.jpg) Mosquito nets help keep mosquitoes away from people and reduce infection rates and transmission of malaria. Nets are not a perfect barrier and are often treated with an insecticide designed to kill the mosquito before it has time to find a way past the net. Insecticide-treated nets are estimated to be twice as effective as untreated nets and offer greater than 70% protection compared with no net.[[57]](#cite_note-57) Between 2000 and 2008, the use of ITNs saved the lives of an estimated 250,000 infants in Sub-Saharan Africa.[[58]](#cite_note-58) About 13% of households in Sub-Saharan countries owned ITNs in 2007[[59]](#cite_note-59) and 31% of African households were estimated to own at least one ITN in 2008. In 2000, 1.7 million (1.8%) African children living in areas of the world where malaria is common were protected by an ITN. That number increased to 20.3 million (18.5%) African children using ITNs in 2007, leaving 89.6 million children unprotected[[60]](#cite_note-60) and to 68% African children using mosquito nets in 2015.<ref name = UNICEF2015/> Most nets are impregnated with [pyrethroids](/wiki/Pyrethroid), a class of insecticides with low [toxicity](/wiki/Toxicity). They are most effective when used from dusk to dawn.[[61]](#cite_note-61) It is recommended to hang a large "bed net" above the center of a bed and either tuck the edges under the mattress or make sure it is large enough such that it touches the ground.[[62]](#cite_note-62) Indoor residual spraying is the spraying of insecticides on the walls inside a home. After feeding, many mosquitoes rest on a nearby surface while digesting the bloodmeal, so if the walls of houses have been coated with insecticides, the resting mosquitoes can be killed before they can bite another person and transfer the malaria parasite.[[63]](#cite_note-63) As of 2006, the [World Health Organization](/wiki/World_Health_Organization) recommends 12 insecticides in IRS operations, including [DDT](/wiki/DDT#Use_against_malaria) and the pyrethroids [cyfluthrin](/wiki/Cyfluthrin) and [deltamethrin](/wiki/Deltamethrin).[[64]](#cite_note-64) This public health use of small amounts of DDT is permitted under the [Stockholm Convention](/wiki/Stockholm_Convention), which prohibits its agricultural use.[[65]](#cite_note-65) One problem with all forms of IRS is [insecticide resistance](/wiki/Insecticide_resistance). Mosquitoes affected by IRS tend to rest and live indoors, and due to the irritation caused by spraying, their descendants tend to rest and live outdoors, meaning that they are less affected by the IRS.[[66]](#cite_note-66) There are a number of other methods to reduce mosquito bites and slow the spread of malaria. Efforts to decrease mosquito larva by decreasing the availability of open water in which they develop or by adding substances to decrease their development is effective in some locations.[[67]](#cite_note-67) Electronic mosquito repellent devices which make very high frequency sounds that are supposed to keep female mosquitoes away, do not have supporting evidence.[[68]](#cite_note-68)

### Other methods[[edit](/index.php?title=(none)&action=edit&section=13)]

Community participation and [health education](/wiki/Health_education) strategies promoting awareness of malaria and the importance of control measures have been successfully used to reduce the incidence of malaria in some areas of the developing world.[[69]](#cite_note-69) Recognizing the disease in the early stages can stop the disease from becoming fatal. Education can also inform people to cover over areas of stagnant, still water, such as water tanks that are ideal breeding grounds for the parasite and mosquito, thus cutting down the risk of the transmission between people. This is generally used in urban areas where there are large centers of population in a confined space and transmission would be most likely in these areas.[[70]](#cite_note-70) [Intermittent preventive therapy](/wiki/Intermittent_preventive_therapy) is another intervention that has been used successfully to control malaria in pregnant women and infants,[[71]](#cite_note-71) and in preschool children where transmission is seasonal.[[72]](#cite_note-72)

### Medications[[edit](/index.php?title=(none)&action=edit&section=14)]

[Template:Main](/wiki/Template:Main) There are a number of drugs that can help prevent or interrupt malaria in travelers to places where infection is common. Many of these drugs are also used in treatment. [Chloroquine](/wiki/Chloroquine) may be used where chloroquine-resistant parasites are not common.[[73]](#cite_note-73) In places where *Plasmodium* is resistant to one or more medications, three medications—[mefloquine](/wiki/Mefloquine) (*Lariam*), [doxycycline](/wiki/Doxycycline) (available generically), or the combination of [atovaquone](/wiki/Atovaquone) and [proguanil](/wiki/Proguanil) hydrochloride (*Malarone*)—are frequently used when prophylaxis is needed.[[73]](#cite_note-73) Doxycycline and the atovaquone plus proguanil combination are the best tolerated; mefloquine is associated with death, suicide, and neurological and psychiatric symptoms.[[73]](#cite_note-73) The protective effect does not begin immediately, and people visiting areas where malaria exists usually start taking the drugs one to two weeks before arriving and continue taking them for four weeks after leaving (except for atovaquone/proguanil, which only needs to be started two days before and continued for seven days afterward).[[74]](#cite_note-74) The use of preventative drugs is often not practical for those who live in areas where malaria exists, and their use is usually only in pregnant women and short-term visitors. This is due to the cost of the drugs, [side effects](/wiki/Adverse_effect_(medicine)) from long-term use, and the difficulty in obtaining anti-malarial drugs outside of wealthy nations.[[75]](#cite_note-75) During pregnancy, medication to prevent malaria has been found to improve the weight of the baby at birth and decrease the risk of [anemia](/wiki/Anemia) in the mother.[[76]](#cite_note-76) The use of preventative drugs where malaria-bearing mosquitoes are present may encourage the development of partial resistance.[[77]](#cite_note-77)

## Treatment[[edit](/index.php?title=(none)&action=edit&section=15)]

[alt=Advertisement entitled "The Mosquito Danger". Includes 6 panel cartoon: #1 breadwinner has malaria, family starving; #2 wife selling ornaments; #3 doctor administers quinine; #4 patient recovers; #5 doctor indicating that quinine can be obtained from post office if needed again; #6 man who refused quinine, dead on stretcher.|thumb|An advertisement for](/wiki/File:%22British_India%22,_six_stages_of_malaria._Wellcome_L0022443.jpg) [quinine](/wiki/Quinine) as a malaria treatment from 1927.

Malaria is treated with [antimalarial medications](/wiki/Antimalarial_medication); the ones used depends on the type and severity of the disease. While [medications against fever](/wiki/Antipyretics) are commonly used, their effects on outcomes are not clear.[[78]](#cite_note-78) Simple or uncomplicated malaria may be treated with oral medications. The most effective treatment for *P. falciparum* infection is the use of [artemisinins](/wiki/Artemisinin) in combination with other antimalarials (known as [artemisinin-combination therapy](/wiki/Artemisinin-combination_therapy), or ACT), which decreases resistance to any single drug component.[[79]](#cite_note-79) These additional antimalarials include: [amodiaquine](/wiki/Amodiaquine), [lumefantrine](/wiki/Lumefantrine), mefloquine or [sulfadoxine/pyrimethamine](/wiki/Sulfadoxine/pyrimethamine).[[80]](#cite_note-80) Another recommended combination is [dihydroartemisinin](/wiki/Dihydroartemisinin) and [piperaquine](/wiki/Piperaquine).[[81]](#cite_note-81)[[82]](#cite_note-82) ACT is about 90% effective when used to treat uncomplicated malaria.[[58]](#cite_note-58) To treat malaria during pregnancy, the WHO recommends the use of quinine plus [clindamycin](/wiki/Clindamycin) early in the pregnancy (1st trimester), and ACT in later stages (2nd and 3rd trimesters).[[83]](#cite_note-83) In the 2000s (decade), malaria with partial resistance to artemisins emerged in Southeast Asia.[[84]](#cite_note-84)[[85]](#cite_note-85) Infection with *P. vivax*, *P. ovale* or *P. malariae* usually do not require hospitalization. Treatment of *P. vivax* requires both treatment of blood stages (with chloroquine or ACT) and clearance of liver forms with [primaquine](/wiki/Primaquine).[[86]](#cite_note-86) Treatment with [tafenoquine](/wiki/Tafenoquine) prevents relapses after confirmed *P. vivax* malaria.[[87]](#cite_note-87) Severe and complicated malaria are almost always caused by infection with *P. falciparum*. The other species usually cause only febrile disease.[[88]](#cite_note-88) Severe and complicated malaria are medical emergencies since mortality rates are high (10% to 50%).[[89]](#cite_note-89) Cerebral malaria is the form of severe and complicated malaria with the worst neurological symptoms.[[90]](#cite_note-90)Recommended treatment for severe malaria is the [intravenous](/wiki/Parenteral_administration) use of antimalarial drugs. For severe malaria, [parenteral](/wiki/Parenteral) artesunate was superior to quinine in both children and adults.[[91]](#cite_note-91) In another systematic review, artemisinin derivatives (artemether and arteether) were as efficacious as quinine in the treatment of cerebral malaria in children.[[92]](#cite_note-92) Treatment of severe malaria involves supportive measures that are best done in a [critical care unit](/wiki/Critical_care_unit). This includes the management of [high fevers](/wiki/Hyperpyrexia) and the seizures that may result from it. It also includes monitoring for [poor breathing effort](/wiki/Respiratory_depression), low blood sugar, and [low blood potassium](/wiki/Hypokalemia).[[19]](#cite_note-19)

### Resistance[[edit](/index.php?title=(none)&action=edit&section=16)]

[Drug resistance](/wiki/Drug_resistance) poses a growing problem in 21st-century malaria treatment.[[93]](#cite_note-93) Resistance is now common against all classes of antimalarial drugs apart from [artemisinins](/wiki/Artemisinin). Treatment of resistant strains became increasingly dependent on this class of drugs. The cost of artemisinins limits their use in the developing world.[[94]](#cite_note-94) Malaria strains found on the Cambodia–Thailand border are resistant to combination therapies that include artemisinins, and may therefore be untreatable.[[95]](#cite_note-95) Exposure of the parasite population to artemisinin monotherapies in subtherapeutic doses for over 30 years and the availability of substandard artemisinins likely drove the selection of the resistant phenotype.[[96]](#cite_note-96) Resistance to artemisinin has been detected in Cambodia, Myanmar, Thailand, and Vietnam,[[97]](#cite_note-97) and there has been emerging resistance in Laos.<ref name = Briggs>Briggs, Helen (30 July 2014) [Call for 'radical action' on drug-resistant malaria](http://www.bbc.co.uk/news/health-28569966) BBC News, health, Retrieved 30 July 2013</ref>[[98]](#cite_note-98)

## Prognosis[[edit](/index.php?title=(none)&action=edit&section=17)]

[thumb|upright=1.2|](/wiki/File:Malaria_world_map_-_DALY_-_WHO2004.svg)[Disability-adjusted life year](/wiki/Disability-adjusted_life_year) for malaria per 100,000 inhabitants in 2004[Template:Multicol](/wiki/Template:Multicol) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Multicol-break](/wiki/Template:Multicol-break) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Multicol-end](/wiki/Template:Multicol-end) When properly treated, people with malaria can usually expect a complete recovery.[[99]](#cite_note-99) However, severe malaria can progress extremely rapidly and cause death within hours or days.[[100]](#cite_note-100) In the most severe cases of the disease, [fatality rates](/wiki/Fatality_rate) can reach 20%, even with intensive care and treatment.[[3]](#cite_note-3) Over the longer term, developmental impairments have been documented in children who have suffered episodes of severe malaria.[[101]](#cite_note-101) [Chronic](/wiki/Chronic_(medicine)) infection without severe disease can occur in an immune-deficiency syndrome associated with a decreased responsiveness to [*Salmonella*](/wiki/Salmonella) bacteria and the [Epstein–Barr virus](/wiki/Epstein–Barr_virus).[[102]](#cite_note-102) During childhood, malaria causes anemia during a period of rapid brain development, and also direct brain damage resulting from cerebral malaria.[[101]](#cite_note-101) Some survivors of cerebral malaria have an increased risk of neurological and cognitive deficits, [behavioural disorders](/wiki/Emotional_and_behavioral_disorders), and [epilepsy](/wiki/Epilepsy).[[103]](#cite_note-103) Malaria prophylaxis was shown to improve cognitive function and school performance in [clinical trials](/wiki/Clinical_trial) when compared to [placebo](/wiki/Placebo) groups.[[101]](#cite_note-101)

## Epidemiology[[edit](/index.php?title=(none)&action=edit&section=18)]

[[File:Paludisme.png|thumb|left|Distribution of malaria in the world:[[104]](#cite_note-104) ♦ Elevated occurrence of chloroquine- or multi-resistant malaria   
♦ Occurrence of chloroquine-resistant malaria   
♦ No *Plasmodium falciparum* or chloroquine-resistance   
♦ No malaria ]] The WHO estimates that in 2010 there were 219 million cases of malaria resulting in 660,000 deaths.[[3]](#cite_note-3)[[105]](#cite_note-105) Others have estimated the number of cases at between 350 and 550 million for falciparum malaria[[106]](#cite_note-106) and deaths in 2010 at 1.24 million[[107]](#cite_note-107) up from 1.0 million deaths in 1990.[[108]](#cite_note-108) The majority of cases (65%) occur in children under 15 years old.[[107]](#cite_note-107) About 125 million pregnant women are at risk of infection each year; in [Sub-Saharan Africa](/wiki/Sub-Saharan_Africa), maternal malaria is associated with up to 200,000 estimated infant deaths yearly.[[15]](#cite_note-15) There are about 10,000 malaria cases per year in Western Europe, and 1300–1500 in the United States.[[11]](#cite_note-11) About 900 people died from the disease in Europe between 1993 and 2003.[[53]](#cite_note-53) Both the global incidence of disease and resulting mortality have declined in recent years. According to the WHO and UNICEF, deaths attributable to malaria in 2015 were reduced by 60%<ref name=UNICEF2015>[Template:Cite web](/wiki/Template:Cite_web)</ref> from a 2000 estimate of 985,000, largely due to the widespread use of insecticide-treated nets and artemisinin-based combination therapies.[[58]](#cite_note-58) In 2012, there were 207 million cases of malaria. That year, the disease is estimated to have killed between 473,000 and 789,000 people, many of whom were children in Africa.[[1]](#cite_note-1) Efforts at decreasing the disease in Africa since the turn of millennium have been partially effective, with rates of the disease dropping by an estimated forty percent on the continent.[[109]](#cite_note-109) Malaria is presently endemic in a broad band around the equator, in areas of the Americas, many parts of Asia, and much of Africa; in Sub-Saharan Africa, 85–90% of malaria fatalities occur.[[110]](#cite_note-110) An estimate for 2009 reported that countries with the highest death rate per 100,000 of population were [Ivory Coast](/wiki/Ivory_Coast) (86.15), [Angola](/wiki/Angola) (56.93) and [Burkina Faso](/wiki/Burkina_Faso) (50.66).[[111]](#cite_note-111) A 2010 estimate indicated the deadliest countries per population were Burkina Faso, [Mozambique](/wiki/Mozambique) and [Mali](/wiki/Mali).[[107]](#cite_note-107) The [Malaria Atlas Project](/wiki/Malaria_Atlas_Project) aims to map global [endemic](/wiki/Endemic_(epidemiology)) levels of malaria, providing a means with which to determine the global spatial limits of the disease and to assess [disease burden](/wiki/Disease_burden).[[112]](#cite_note-112)[[113]](#cite_note-113) This effort led to the publication of a map of *P. falciparum* endemicity in 2010.[[114]](#cite_note-114) As of 2010, about 100 countries have endemic malaria.[[105]](#cite_note-105)[[115]](#cite_note-115) Every year, 125 million international travellers visit these countries, and more than 30,000 contract the disease.[[53]](#cite_note-53) The geographic distribution of malaria within large regions is complex, and malaria-afflicted and malaria-free areas are often found close to each other.[[116]](#cite_note-116) Malaria is prevalent in tropical and subtropical regions because of rainfall, consistent high temperatures and high humidity, along with stagnant waters in which mosquito larvae readily mature, providing them with the environment they need for continuous breeding.[[117]](#cite_note-117) In drier areas, outbreaks of malaria have been predicted with reasonable accuracy by mapping rainfall.[[118]](#cite_note-118) Malaria is more common in rural areas than in cities. For example, several cities in the [Greater Mekong Subregion](/wiki/Greater_Mekong_Subregion) of Southeast Asia are essentially malaria-free, but the disease is prevalent in many rural regions, including along international borders and forest fringes.[[119]](#cite_note-119) In contrast, malaria in Africa is present in both rural and urban areas, though the risk is lower in the larger cities.[[120]](#cite_note-120)

## History[[edit](/index.php?title=(none)&action=edit&section=19)]

[Template:Main](/wiki/Template:Main) [thumb|upright|Ancient malaria oocysts preserved in](/wiki/File:Malaria_pathogens.jpg) [Dominican amber](/wiki/Dominican_amber) Although the parasite responsible for *P. falciparum* malaria has been in existence for 50,000–100,000 years, the population size of the parasite did not increase until about 10,000 years ago, concurrently with advances in agriculture[[121]](#cite_note-121) and the development of human settlements. Close relatives of the human malaria parasites remain common in chimpanzees. Some evidence suggests that the *P. falciparum* malaria may have originated in gorillas.[[122]](#cite_note-122) References to the unique periodic fevers of malaria are found throughout recorded history.[[123]](#cite_note-123) Hippocrates described periodic fevers, labelling them tertian, quartan, subtertian and quotidian.[[124]](#cite_note-124) The Roman [Columella](/wiki/Columella) associated the disease with insects from swamps.[[124]](#cite_note-124) Malaria may have contributed to the decline of the [Roman Empire](/wiki/Roman_Empire),[[125]](#cite_note-125) and was so pervasive in Rome that it was known as the "[Roman fever](/wiki/Roman_Fever_(disease))".[[126]](#cite_note-126) Several regions in ancient Rome were considered at-risk for the disease because of the favourable conditions present for malaria vectors. This included areas such as southern Italy, the island of [Sardinia](/wiki/Sardinia), the [Pontine Marshes](/wiki/Pontine_Marshes), the lower regions of coastal [Etruria](/wiki/Etruria) and the city of [Rome](/wiki/Rome) along the [Tiber River](/wiki/Tiber_River). The presence of stagnant water in these places was preferred by mosquitoes for breeding grounds. Irrigated gardens, swamp-like grounds, runoff from agriculture, and drainage problems from road construction led to the increase of standing water.[[127]](#cite_note-127)[thumb|left|British doctor](/wiki/File:Ronald_Ross.jpg) [Ronald Ross](/wiki/Ronald_Ross) received the [Nobel Prize for Physiology or Medicine](/wiki/Nobel_Prize_for_Physiology_or_Medicine) in 1902 for his work on malaria.

The term malaria originates from [Medieval](/wiki/Middle_Ages) [Template:Lang-it](/wiki/Template:Lang-it)—"[bad air](/wiki/Miasma_theory_of_disease)"; the disease was formerly called *ague* or *marsh fever* due to its association with swamps and marshland.[[128]](#cite_note-128) The term first appeared in the English literature about 1829.[[124]](#cite_note-124) Malaria was once common in most of Europe and North America,[[129]](#cite_note-129) where it is no longer endemic,[[130]](#cite_note-130) though imported cases do occur.[[131]](#cite_note-131) Scientific studies on malaria made their first significant advance in 1880, when [Charles Louis Alphonse Laveran](/wiki/Charles_Louis_Alphonse_Laveran)—a French army doctor working in the military hospital of [Constantine](/wiki/Constantine,_Algeria) in [Algeria](/wiki/Algeria)—observed parasites inside the red blood cells of infected people for the first time. He therefore proposed that malaria is caused by this organism, the first time a [protist](/wiki/Protist) was identified as causing disease.[[132]](#cite_note-132) For this and later discoveries, he was awarded the 1907 [Nobel Prize for Physiology or Medicine](/wiki/Nobel_Prize_for_Physiology_or_Medicine). A year later, [Carlos Finlay](/wiki/Carlos_Finlay), a Cuban doctor treating people with [yellow fever](/wiki/Yellow_fever) in [Havana](/wiki/Havana), provided strong evidence that mosquitoes were transmitting disease to and from humans.[[133]](#cite_note-133) This work followed earlier suggestions by [Josiah C. Nott](/wiki/Josiah_C._Nott),[[134]](#cite_note-134) and work by [Sir Patrick Manson](/wiki/Sir_Patrick_Manson), the "father of tropical medicine", on the transmission of [filariasis](/wiki/Filariasis).[[135]](#cite_note-135) [thumb|left|Chinese](/wiki/File:Tu_Youyou_5012-1-2015.jpg) [traditional Chinese medicine](/wiki/Traditional_Chinese_medicine) researcher [Tu Youyou](/wiki/Tu_Youyou) received the [Nobel Prize for Physiology or Medicine](/wiki/Nobel_Prize_for_Physiology_or_Medicine) in 2015 for her work on antimalarial drug [artemisin](/wiki/Artemisin). In April 1894, a Scottish physician [Sir Ronald Ross](/wiki/Ronald_Ross) visited Sir Patrick Manson at his house on Queen Anne Street, London. This visit was the start of four years of collaboration and fervent research that culminated in 1898 when Ross, who was working in the [Presidency General Hospital](/wiki/Presidency_General_Hospital) in [Calcutta](/wiki/Kolkata), proved the complete life-cycle of the malaria parasite in mosquitoes. He thus proved that the mosquito was the vector for malaria in humans by showing that certain mosquito species transmit malaria to birds. He isolated malaria parasites from the salivary glands of mosquitoes that had fed on infected birds.[[136]](#cite_note-136) For this work, Ross received the 1902 Nobel Prize in Medicine. After resigning from the Indian Medical Service, Ross worked at the newly established [Liverpool School of Tropical Medicine](/wiki/Liverpool_School_of_Tropical_Medicine) and directed malaria-control efforts in [Egypt](/wiki/Egypt), [Panama](/wiki/Panama), [Greece](/wiki/Greece) and [Mauritius](/wiki/Mauritius).[[137]](#cite_note-137) The findings of Finlay and Ross were later confirmed by a medical board headed by [Walter Reed](/wiki/Walter_Reed) in 1900. Its recommendations were implemented by [William C. Gorgas](/wiki/William_C._Gorgas) in [the health measures undertaken](/wiki/Health_measures_during_the_construction_of_the_Panama_Canal) during construction of the [Panama Canal](/wiki/Panama_Canal). This public-health work saved the lives of thousands of workers and helped develop the methods used in future public-health campaigns against the disease.[[138]](#cite_note-138) [thumb|right|*Artemisia annua*, source of the antimalarial drug artemisin](/wiki/File:Artemisia_annua_West_Virginia.jpg)

The first effective treatment for malaria came from the bark of [cinchona tree](/wiki/Cinchona), which contains [quinine](/wiki/Quinine). This tree grows on the slopes of the [Andes](/wiki/Andes), mainly in [Peru](/wiki/Peru). The [indigenous peoples of Peru](/wiki/Indigenous_peoples_of_Peru) made a [tincture](/wiki/Tincture) of cinchona to control fever. Its effectiveness against malaria was found and the [Jesuits](/wiki/Jesuit) introduced the treatment to Europe around 1640; by 1677, it was included in the [London Pharmacopoeia](/wiki/London_Pharmacopoeia) as an antimalarial treatment.[[139]](#cite_note-139) It was not until 1820 that the active ingredient, quinine, was extracted from the bark, isolated and named by the French chemists [Pierre Joseph Pelletier](/wiki/Pierre_Joseph_Pelletier) and [Joseph Bienaimé Caventou](/wiki/Joseph_Bienaimé_Caventou).[[140]](#cite_note-140)[[141]](#cite_note-141) Quinine became the predominant malarial medication until the 1920s, when other medications began to be developed. In the 1940s, chloroquine replaced quinine as the treatment of both uncomplicated and severe malaria until resistance supervened, first in Southeast Asia and South America in the 1950s and then globally in the 1980s.[[142]](#cite_note-142) The medicinal value of [Artemisia annua](/wiki/Artemisia_annua) has been used by Chinese herbalists in [traditional Chinese medicines](/wiki/Traditional_Chinese_medicines) for 2,000 years. In 1596, Li Shizhen recommended tea made from qinghao specifically to treat malaria symptoms in his "[Compendium of Materia Medica](/wiki/Compendium_of_Materia_Medica)". Artemisinins, discovered by Chinese scientist [Tu Youyou](/wiki/Tu_Youyou) and colleagues in the 1970s from the plant [*Artemisia annua*](/wiki/Artemisia_annua), became the recommended treatment for *P. falciparum* malaria, administered in combination with other antimalarials as well as in severe disease.[[143]](#cite_note-143) Tu says she was influenced by a [traditional Chinese herbal medicine](/wiki/Chinese_herbology) source, *The Handbook of Prescriptions for Emergency Treatments*, written in 340 by [Ge Hong](/wiki/Ge_Hong)[[144]](#cite_note-144) For her work on malaria, [Tu Youyou](/wiki/Tu_Youyou) received the 2015 [Nobel Prize in Physiology or Medicine](/wiki/Nobel_Prize_in_Physiology_or_Medicine)<ref name=Nobel>[Template:Cite web](/wiki/Template:Cite_web)</ref>

*Plasmodium vivax* was used between 1917 and the 1940s for [malariotherapy](/wiki/Malariotherapy)—deliberate injection of malaria parasites to induce fever to combat certain diseases such as tertiary [syphilis](/wiki/Syphilis). In 1927, the inventor of this technique, [Julius Wagner-Jauregg](/wiki/Julius_Wagner-Jauregg), received the Nobel Prize in Physiology or Medicine for his discoveries. The technique was dangerous, killing about 15% of patients, so it is no longer in use.[[145]](#cite_note-145) [thumb|U.S. Marines with malaria in a rough field hospital on](/wiki/File:GuadMarinesMalaria.gif) [Guadalcanal](/wiki/Guadalcanal), October 1942

The first pesticide used for indoor residual spraying was [DDT](/wiki/DDT).[[146]](#cite_note-146) Although it was initially used exclusively to combat malaria, its use quickly spread to [agriculture](/wiki/Agriculture). In time, pest control, rather than disease control, came to dominate DDT use, and this large-scale agricultural use led to the evolution of [resistant](/wiki/Pesticide_resistance) mosquitoes in many regions. The DDT resistance shown by *Anopheles* mosquitoes can be compared to [antibiotic resistance](/wiki/Antibiotic_resistance) shown by bacteria. During the 1960s, awareness of the negative consequences of its indiscriminate use increased, ultimately leading to bans on agricultural applications of DDT in many countries in the 1970s.[[65]](#cite_note-65) Before DDT, malaria was successfully eliminated or controlled in tropical areas like Brazil and Egypt by removing or poisoning the breeding grounds of the mosquitoes or the aquatic habitats of the larva stages, for example by applying the highly toxic arsenic compound [Paris Green](/wiki/Paris_Green) to places with standing water.[[147]](#cite_note-147) [Malaria vaccines](/wiki/Malaria_vaccine) have been an elusive goal of research. The first promising studies demonstrating the potential for a malaria vaccine were performed in 1967 by immunizing mice with live, radiation-[attenuated](/wiki/Attenuator_(genetics)) sporozoites, which provided significant protection to the mice upon subsequent injection with normal, viable sporozoites. Since the 1970s, there has been a considerable effort to develop similar vaccination strategies for humans.[[148]](#cite_note-148)

## Society and culture[[edit](/index.php?title=(none)&action=edit&section=20)]

[Template:See also](/wiki/Template:See_also)

### Economic impact[[edit](/index.php?title=(none)&action=edit&section=21)]

[thumb|right|Malaria clinic in Tanzania](/wiki/File:Saving_Lives_with_SMS_for_Life.jpg)

Malaria is not just a disease commonly associated with poverty: some evidence suggests that it is also a cause of poverty and a major hindrance to [economic development](/wiki/Economic_development).[[4]](#cite_note-4)[[5]](#cite_note-5) Although tropical regions are most affected, malaria's furthest influence reaches into some temperate zones that have extreme seasonal changes. The disease has been associated with major negative economic effects on regions where it is widespread. During the late 19th and early 20th centuries, it was a major factor in the slow economic development of the American southern states.[[149]](#cite_note-149) A comparison of average per capita [GDP](/wiki/GDP) in 1995, adjusted for [parity of purchasing power](/wiki/Purchasing_power_parity), between countries with malaria and countries without malaria gives a fivefold difference ($1,526 USD versus $8,268 USD). In the period 1965 to 1990, countries where malaria was common had an average per capita GDP that increased only 0.4% per year, compared to 2.4% per year in other countries.[[150]](#cite_note-150) Poverty can increase the risk of malaria, since those in poverty do not have the financial capacities to prevent or treat the disease. In its entirety, the economic impact of malaria has been estimated to cost Africa US$12 billion every year. The economic impact includes costs of health care, working days lost due to sickness, days lost in education, decreased productivity due to brain damage from cerebral malaria, and loss of investment and tourism.[[6]](#cite_note-6) The disease has a heavy burden in some countries, where it may be responsible for 30–50% of hospital admissions, up to 50% of [outpatient](/wiki/Outpatient) visits, and up to 40% of public health spending.[[151]](#cite_note-151) [thumb|Child with malaria in](/wiki/File:Malaria_Patient,_Nyangaton,_Ethiopia_(15151075077).jpg) [Ethiopia](/wiki/Ethiopia) Cerebral malaria is one of the leading causes of neurological disabilities in African children.[[103]](#cite_note-103) Studies comparing cognitive functions before and after treatment for severe malarial illness continued to show significantly impaired school performance and cognitive abilities even after recovery.[[101]](#cite_note-101) Consequently, severe and cerebral malaria have far-reaching [socioeconomic](/wiki/Socioeconomic) consequences that extend beyond the immediate effects of the disease.[[152]](#cite_note-152)

### Counterfeit and substandard drugs[[edit](/index.php?title=(none)&action=edit&section=22)]

Sophisticated [counterfeits](/wiki/Counterfeit_drugs) have been found in several Asian countries such as [Cambodia](/wiki/Cambodia),[[153]](#cite_note-153) [China](/wiki/People's_Republic_of_China),[[154]](#cite_note-154) [Indonesia](/wiki/Indonesia), [Laos](/wiki/Laos), [Thailand](/wiki/Thailand), and [Vietnam](/wiki/Vietnam), and are an important cause of avoidable death in those countries.[[155]](#cite_note-155) The WHO said that studies indicate that up to 40% of artesunate-based malaria medications are counterfeit, especially in the Greater [Mekong](/wiki/Mekong) region and have established a rapid alert system to enable information about counterfeit drugs to be rapidly reported to the relevant authorities in participating countries.[[156]](#cite_note-156) There is no reliable way for doctors or lay people to detect counterfeit drugs without help from a laboratory. Companies are attempting to combat the persistence of counterfeit drugs by using new technology to provide security from source to distribution.[[157]](#cite_note-157) Another clinical and public health concern is the proliferation of substandard antimalarial medicines resulting from inappropriate concentration of ingredients, contamination with other drugs or toxic impurities, poor quality ingredients, poor stability and inadequate packaging.[[158]](#cite_note-158) A 2012 study demonstrated that roughly one-third of antimalarial medications in Southeast Asia and Sub-Saharan Africa failed chemical analysis, packaging analysis, or were falsified.[[159]](#cite_note-159)

### War[[edit](/index.php?title=(none)&action=edit&section=23)]

[thumb|right|World War II poster](/wiki/File:%22Don't_go_to_Bed_with_Malaria_Mosquito%22_-_NARA_-_514146.tif) Throughout history, the contraction of malaria has played a prominent role in the fates of government rulers, nation-states, military personnel, and military actions.[[160]](#cite_note-160) In 1910, [Nobel Prize in Medicine](/wiki/Nobel_Prize_in_Medicine)-winner Ronald Ross (himself a malaria survivor), published a book titled *The Prevention of Malaria* that included a chapter titled "The Prevention of Malaria in War." The chapter's author, Colonel C. H. Melville, Professor of Hygiene at [Royal Army Medical College](/wiki/Royal_Army_Medical_College) in London, addressed the prominent role that malaria has historically played during wars: "The history of malaria in war might almost be taken to be the history of war itself, certainly the history of war in the Christian era. ... It is probably the case that many of the so-called camp fevers, and probably also a considerable proportion of the camp dysentery, of the wars of the sixteenth, seventeenth and eighteenth centuries were malarial in origin."[[161]](#cite_note-161) Malaria was the most important health hazard encountered by U.S. troops in the South Pacific during [World War II](/wiki/World_War_II), where about 500,000 men were infected.[[162]](#cite_note-162) According to Joseph Patrick Byrne, "Sixty thousand American soldiers died of malaria during the African and South Pacific campaigns."[[163]](#cite_note-163) Significant financial investments have been made to procure existing and create new anti-malarial agents. During [World War I](/wiki/World_War_I) and World War II, inconsistent supplies of the natural anti-malaria drugs [cinchona bark](/wiki/Cinchona_bark) and quinine prompted substantial funding into [research and development](/wiki/Research_and_development) of other drugs and vaccines. American military organizations conducting such research initiatives include the Navy Medical Research Center, [Walter Reed Army Institute of Research](/wiki/Walter_Reed_Army_Institute_of_Research), and the [U.S. Army Medical Research Institute of Infectious Diseases](/wiki/U.S._Army_Medical_Research_Institute_of_Infectious_Diseases) of the US Armed Forces.[[164]](#cite_note-164) Additionally, initiatives have been founded such as Malaria Control in War Areas (MCWA), established in 1942, and its successor, the Communicable Disease Center (now known as the [Centers for Disease Control and Prevention](/wiki/Centers_for_Disease_Control_and_Prevention), or CDC) established in 1946. According to the CDC, MCWA "was established to control malaria around military training bases in the southern United States and its territories, where malaria was still problematic".[[165]](#cite_note-165)

### Eradication efforts[[edit](/index.php?title=(none)&action=edit&section=24)]

[thumb|Members of the Malaria Commission of the](/wiki/File:Members_of_the_Malaria_Commission_on_the_Danube_delta,_1929_Wellcome_L0011626.jpg) [League of Nations](/wiki/League_of_Nations) collecting larvae on the [Danube delta](/wiki/Danube_delta), 1929 Several notable attempts are being made to eliminate the parasite from sections of the world, or to [eradicate it worldwide](/wiki/Eradication_of_infectious_diseases). In 2006, the organization [Malaria No More](/wiki/Malaria_No_More) set a public goal of eliminating malaria from Africa by 2015, and the organization plans to dissolve if that goal is accomplished.[[166]](#cite_note-166) Several malaria vaccines are in clinical trials, which are intended to provide protection for children in endemic areas and reduce the speed of transmission of the disease. [Template:As of](/wiki/Template:As_of), [The Global Fund to Fight AIDS, Tuberculosis and Malaria](/wiki/The_Global_Fund_to_Fight_AIDS,_Tuberculosis_and_Malaria) has distributed 230 million insecticide-treated nets intended to stop mosquito-borne transmission of malaria.[[167]](#cite_note-167) The U.S.-based [Clinton Foundation](/wiki/Clinton_Foundation) has worked to manage demand and stabilize prices in the artemisinin market.[[168]](#cite_note-168) Other efforts, such as the Malaria Atlas Project, focus on analysing climate and weather information required to accurately predict the spread of malaria based on the availability of habitat of malaria-carrying parasites.[[112]](#cite_note-112) The [Malaria Policy Advisory Committee](/wiki/Malaria_Policy_Advisory_Committee) (MPAC) of the [World Health Organization](/wiki/World_Health_Organization) (WHO) was formed in 2012, "to provide strategic advice and technical input to WHO on all aspects of malaria control and elimination".[[169]](#cite_note-169) In November 2013, WHO and the malaria vaccine funders group set a goal to develop vaccines designed to interrupt malaria transmission with the long-term goal of malaria eradication.[[170]](#cite_note-170) Malaria has been successfully eliminated or greatly reduced in certain areas. Malaria was once common in the United States and southern Europe, but vector control programs, in conjunction with the monitoring and treatment of infected humans, eliminated it from those regions. Several factors contributed, such as the draining of wetland breeding grounds for agriculture and other changes in [water management](/wiki/Water_management) practices, and advances in sanitation, including greater use of glass windows and screens in dwellings.[[171]](#cite_note-171) Malaria was eliminated from most parts of the USA in the early 20th century by such methods, and the use of the [pesticide](/wiki/Pesticide) DDT and other means eliminated it from the remaining pockets in the South in the 1950s.[[172]](#cite_note-172) (see [National Malaria Eradication Program](/wiki/National_Malaria_Eradication_Program)) In [Suriname](/wiki/Suriname), the disease has been cleared from its capital city and coastal areas through a three-pronged approach initiated by the [Global Malaria Eradication program](/wiki/Global_Malaria_Eradication_program) in 1955, involving: vector control through the use of DDT and IRS; regular collection of blood smears from the population to identify existing malaria cases; and providing chemotherapy to all affected individuals.[[173]](#cite_note-173) [Bhutan](/wiki/Bhutan) is pursuing an aggressive malaria elimination strategy, and has achieved a 98.7% decline in microscopy-confirmed cases from 1994 to 2010. In addition to vector control techniques such as IRS in high-risk areas and thorough distribution of long-lasting ITNs, factors such as economic development and increasing access to health services have contributed to Bhutan's successes in reducing malaria incidence.[[174]](#cite_note-174) The UK's [Department for International Development](/wiki/Department_for_International_Development) and the [Bill and Melinda Gates Foundation](/wiki/Bill_and_Melinda_Gates_Foundation) will spend $4.5bn over five years from 2016 in an effort to end deaths caused by the disease.[[175]](#cite_note-175)

## Research[[edit](/index.php?title=(none)&action=edit&section=25)]

The Malaria Eradication Research Agenda (malERA) initiative was a consultative process to identify which areas of research and development (R&D) needed to be addressed for the worldwide eradication of malaria.[[176]](#cite_note-176)[[177]](#cite_note-177)

### Vaccine[[edit](/index.php?title=(none)&action=edit&section=26)]

[Template:See also](/wiki/Template:See_also) Immunity (or, more accurately, [tolerance](/wiki/Immune_tolerance)) to *P. falciparum* malaria does occur naturally, but only in response to years of repeated infection.[[31]](#cite_note-31) An individual can be protected from a *P. falciparum* infection if they receive about a thousand bites from mosquitoes that carry a version of the parasite rendered non-infective by a dose of [X-ray](/wiki/X-ray) [irradiation](/wiki/Irradiation).[[178]](#cite_note-178) An effective [vaccine](/wiki/Vaccination) is not yet available for malaria, although several are under development.[[179]](#cite_note-179) The highly [polymorphic](/wiki/Polymorphism_(biology)) nature of many *P. falciparum* proteins results in significant challenges to vaccine design. Vaccine candidates that target antigens on gametes, zygotes, or ookinetes in the mosquito midgut aim to block the transmission of malaria. These transmission-blocking vaccines induce antibodies in the human blood; when a mosquito takes a blood meal from a protected individual, these antibodies prevent the parasite from completing its development in the mosquito.[[180]](#cite_note-180) Other vaccine candidates, targeting the blood-stage of the parasite's life cycle, have been inadequate on their own.[[181]](#cite_note-181) For example, [SPf66](/wiki/SPf66) was tested extensively in areas where the disease is common in the 1990s, but trials showed it to be insufficiently effective.[[182]](#cite_note-182) Several potential vaccines targeting the pre-erythrocytic stage of the parasite's life cycle are being developed, with [RTS,S](/wiki/RTS,S) as a leading candidate;[[178]](#cite_note-178) it is expected to be licensed in 2015.[[102]](#cite_note-102) A US biotech company, [Sanaria](/wiki/Sanaria), is developing a pre-erythrocytic [attenuated vaccine](/wiki/Attenuated_vaccine) called PfSPZ that uses whole sporozoites to induce an immune response.[[183]](#cite_note-183) In 2006, the [Malaria Vaccine Advisory Committee](/wiki/Malaria_Vaccine_Advisory_Committee) to the WHO outlined a "Malaria Vaccine Technology Roadmap" that has as one of its landmark objectives to "develop and license a first-generation malaria vaccine that has a protective efficacy of more than 50% against severe disease and death and lasts longer than one year" by 2015.[[184]](#cite_note-184)

### Medications[[edit](/index.php?title=(none)&action=edit&section=27)]

Malaria parasites contain [apicoplasts](/wiki/Apicoplast), organelles usually found in plants, complete with their own [genomes](/wiki/Genome). These apicoplasts are thought to have originated through the [endosymbiosis](/wiki/Endosymbiont) of algae and play a crucial role in various aspects of parasite metabolism, such as [fatty acid biosynthesis](/wiki/Fatty_acid_biosynthesis). Over 400 proteins have been found to be produced by apicoplasts and these are now being investigated as possible targets for novel anti-malarial drugs.[[185]](#cite_note-185) With the onset of drug-resistant *Plasmodium* parasites, new strategies are being developed to combat the widespread disease. One such approach lies in the introduction of synthetic [pyridoxal](/wiki/Pyridoxal)-amino acid [adducts](/wiki/Adduct), which are taken up by the parasite and ultimately interfere with its ability to create several essential [B vitamins](/wiki/B_vitamin).[[186]](#cite_note-186)[[187]](#cite_note-187) Antimalarial drugs using [synthetic metal-based](/wiki/Organometallic_chemistry) [complexes](/wiki/Coordination_complex) are attracting research interest.[[188]](#cite_note-188)[[189]](#cite_note-189)

* (+)-SJ733: Part of a wider class of experimental drugs called [spiroindolone](/wiki/Spiroindolone). It inhibits the ATP4 protein of infected red blood cells that cause the cells to shrink and become rigid like the aging cells. This triggers the immune system to eliminate the infected cells from the system as demonstrated in a mouse model. As of 2014, a [Phase 1 clinical trial](/wiki/Phases_of_clinical_research#Phase_1) to assess the safety profile in human is planned by the [Howard Hughes Medical Institute](/wiki/Howard_Hughes_Medical_Institute).<ref name=atp4>[Template:Cite web](/wiki/Template:Cite_web)</ref>
* NITD246 and [NITD609](/wiki/NITD609): Also belonged to the class of spiroindolone and target the ATP4 protein.<ref name=atp4/>

### Other[[edit](/index.php?title=(none)&action=edit&section=28)]

A non-chemical vector control strategy involves genetic manipulation of malaria mosquitoes. Advances in [genetic engineering](/wiki/Genetic_engineering) technologies make it possible to introduce foreign DNA into the mosquito genome and either decrease the lifespan of the mosquito, or make it more resistant to the malaria parasite. [Sterile insect technique](/wiki/Sterile_insect_technique) is a genetic control method whereby large numbers of sterile male mosquitoes are reared and released. Mating with wild females reduces the wild population in the subsequent generation; repeated releases eventually eliminate the target population.[[57]](#cite_note-57) [Genomics](/wiki/Genomics) is central to malaria research. With the [sequencing](/wiki/Whole_genome_sequencing) of *P. falciparum*, one of its vectors *Anopheles gambiae*, and the [human genome](/wiki/Human_genome), the genetics of all three organisms in the malaria lifecycle can be studied.[[190]](#cite_note-190) Another new application of genetic technology is the ability to produce [genetically modified](/wiki/Genetically_modified_organism) mosquitoes that do not transmit malaria, potentially allowing [biological control](/wiki/Biological_control) of malaria transmission.[[191]](#cite_note-191) In one study, a genetically-modified strain of [*Anopheles stephensi*](/wiki/Anopheles_stephensi) was created that no longer supported malaria transmission, and this resistance was passed down to mosquito offspring.[[192]](#cite_note-192) [Gene drive](/wiki/Gene_drive) is a technique for changing wild populations, for instance to combat insects so they cannot transmit diseases (in particular mosquitoes in the cases of malaria and [zika](/wiki/Zika_virus)).[[193]](#cite_note-193)

## Other animals[[edit](/index.php?title=(none)&action=edit&section=29)]

Nearly 200 parasitic *Plasmodium* species have been identified that infect [birds](/wiki/Plasmodium_species_infecting_birds), [reptiles](/wiki/Plasmodium_species_infecting_reptiles), and [other mammals](/wiki/Plasmodium_species_infecting_mammals_other_than_primates),[[194]](#cite_note-194) and about 30 species naturally infect non-human primates.[[195]](#cite_note-195) Some malaria parasites that affect non-human primates (NHP) serve as [model organisms](/wiki/Model_organism) for human malarial parasites, such as [*P. coatneyi*](/wiki/Plasmodium_coatneyi) (a model for *P. falciparum*) and [*P. cynomolgi*](/wiki/Plasmodium_cynomolgi) (*P. vivax*). Diagnostic techniques used to detect parasites in NHP are similar to those employed for humans.[[196]](#cite_note-196) Malaria parasites that infect rodents are widely used as models in research, such as [*P. berghei*](/wiki/Plasmodium_berghei).[[197]](#cite_note-197) [Avian malaria](/wiki/Avian_malaria) primarily affects species of the order [Passeriformes](/wiki/Passeriformes), and poses a substantial threat to birds of [Hawaii](/wiki/Hawaii), the [Galapagos](/wiki/Galapagos), and other [archipelagoes](/wiki/Archipelago). The parasite [*P. relictum*](/wiki/Plasmodium_relictum) is known to play a role in limiting the distribution and abundance of [endemic Hawaiian birds](/wiki/Endemic_birds_of_Hawaii). [Global warming](/wiki/Global_warming) is expected to increase the prevalence and global distribution of avian malaria, as elevated temperatures provide optimal conditions for parasite reproduction.[[198]](#cite_note-198)

## References[[edit](/index.php?title=(none)&action=edit&section=30)]

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Cited literature

* [Template:Cite report](/wiki/Template:Cite_report)
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## Further reading[[edit](/index.php?title=(none)&action=edit&section=31)]

* [Template:Cite book](/wiki/Template:Cite_book)
* [Template:Cite book](/wiki/Template:Cite_book)

## External links[[edit](/index.php?title=(none)&action=edit&section=32)]

[Template:Sister project links](/wiki/Template:Sister_project_links)

* [Template:Dmoz](/wiki/Template:Dmoz)
* [WHO site on malaria](http://www.emro.who.int/entity/malaria-control-and-elimination/)
* [UNHCO site on malaria](http://www.unhco.org/malaria/)
* [Global Malaria Action Plan](http://www.rollbackmalaria.org/gmap/) (2008)
* [Doctors Without Borders/Médecins Sans Frontières – *Malaria*](http://doctorswithoutborders.org/news/issue.cfm?id=2395) information pages
* [WHO/TDR Malaria Database](https://web.archive.org/web/20130520072620/http://www.wehi.edu.au/other_domains/MalDB/who.html) via the [Wayback Machine](/wiki/Wayback_Machine)
* [Anti-malaria and sustainable development](http://www.antimalariaomd.org/en/index.php)
* [Worldwide Antimalarial Resistance Network (WWARN)](http://www.wwarn.org)

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