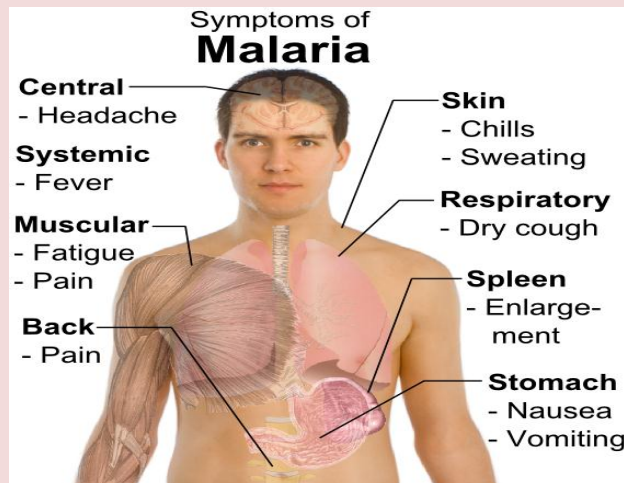


Malaria

(A mosquito-borne infectious disease of humans and other animals caused by eukaryotic protists of the genus Plasmodium.)

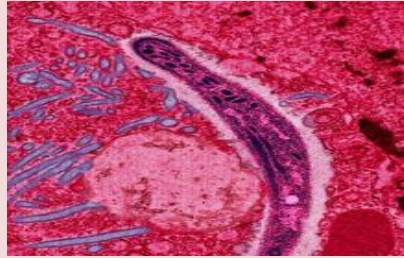
The disease results from the multiplication of Plasmodium parasites within red blood cells, causing symptoms that typically include fever and headache, in severe cases progressing to coma or death. It is widespread in tropical and subtropical regions, including much of Sub-Saharan Africa, Asia, and the Americas.

Signs and symptoms



- ✚ fever, shivering, arthralgia (joint pain),
- ✚ vomiting,
- ✚ anemia (caused by hemolysis),
- ✚ jaundice, hemoglobinuria, retinal damage, and convulsions
- ✚ . **The classic symptom of malaria**--- cyclical occurrence of sudden coldness followed by rigor and then fever and sweating lasting four to six hours, occurring every two days in *P. vivax* and *P. ovale* infections, and every three days for *P. Malariae*; *P. falciparum* can have recurrent fever every 36–48 hours or a less pronounced and almost continuous fever.
- ✚ malaria in pregnant women is an important cause of stillbirths, infant mortality and low birth weight esp in *P. falciparum* infection
- ✚
- ✚ high intracranial pressure, & abnormal posturing,
- ✚ Cerebral malaria is associated with retinal whitening,
- ✚ severe malaria -- coma
- ✚ . Splenomegaly severe headache, cerebral ischemia, hepatomegaly hypoglycemia, and hemoglobinuria with renal failure. (in blackwater fever)

Cause



Malaria parasites are members of the genus Plasmodium

In humans malaria is caused by P. falciparum, P. malariae, P. ovale, P. vivax and P. knowlesi.

- P. vivax is responsible for the largest number of malaria infections worldwide,
- P. falciparum account for about 90% of the deaths from malaria
- Plasmodium species also infect birds, reptiles, monkeys, chimpanzees and rodents.

Life cycle

Definitive hosts /transmission vectors-- Female mosquitoes of the Anopheles genus

Secondary hosts --humans and other vertebrates.

- ✚ Young mosquitoes first ingest the malaria parasite by feeding on an infected human carrier and the infected Anopheles mosquitoes carry Plasmodium sporozoites in their salivary glands
- ✚ Once ingested, the parasite gametocytes taken up in the blood will further differentiate into male or female gametes and then fuse in the mosquito's gut.
- ✚ This produces an ookinete that penetrates the gut lining and produces an oocyst in the gut wall.
- ✚ When the oocyst ruptures, it releases sporozoites that migrate through the mosquito's body to the salivary glands, where they are then ready to infect a new human host. (Anterior station transfer).
- ✚ The sporozoites are injected into the skin, alongside saliva, when the mosquito takes a subsequent blood meal.
- ✚ Only female mosquitoes feed on blood while male mosquitoes feed on plant nectar thus males do not transmit the disease.

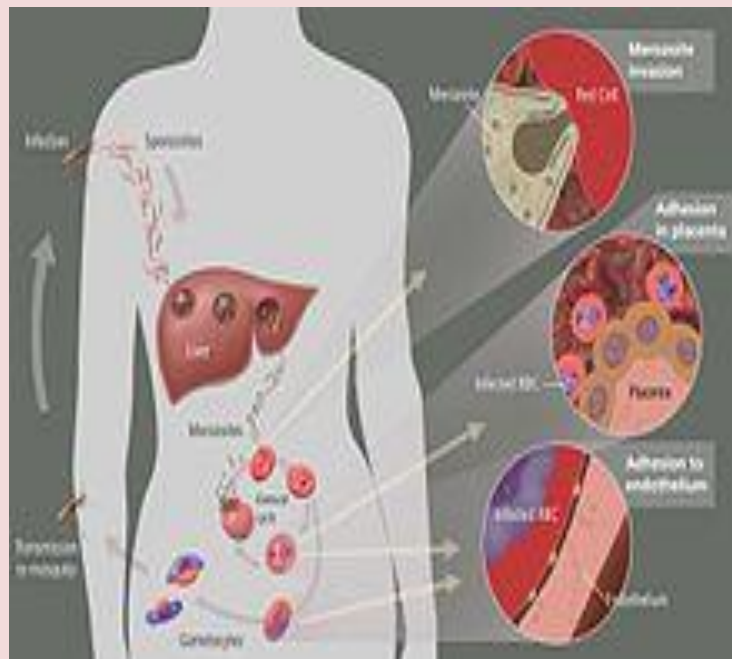
Malaria parasites can also be transmitted by blood transfusions, although this is rare.

Recurrent malaria

Malaria recurs after treatment for three reasons.

- ✚ Recrudescence occurs when parasites are not cleared by treatment,
- ✚ reinfection indicates complete clearance with new infection established from a separate infective mosquito bite
- ✚ Relapse is specific to *P. vivax* and *P. ovale* and involves re-emergence of blood-stage parasites from latent parasites (hypnozoites) in the liver. (The longest incubation period reported for a *P. vivax* infection is 30 years).

Pathogenesis



The life cycle of malaria parasites

In Mosquito

- ✚ When a mosquito pierces the skin of an infected person, it potentially picks up gametocytes within the blood.
- ✚ Fertilization and sexual recombination of the parasite occurs in the mosquito's gut.

In the human body (Exoerythrocytic and an erythrocytic phase)

Exoerythrocytic Phase (In Liver).

- ✚ A mosquito infects a person by taking a blood meal.
- ✚ Sporozoites enter the bloodstream, and migrate to the liver.
- ✚ They infect liver cells (hepatocytes), where they multiply into merozoites, rupture the liver cells, and escape back into the bloodstream.

Erythrocytic phase (In Rbc)

- ✚ Then, the merozoites infect red blood cells, where they develop into ring forms, trophozoites and schizonts which in turn produce further merozoites.
- ✚ Periodically break out of their hosts to invade fresh red blood cells leads to waves of fever (intermittent).
- ✚ Sexual forms (gametocytes) are also produced, which, if taken up by a mosquito, will infect the insect and continue the life cycle.

Dormancy state

- ✚ Some *P. vivax* and *P. ovale* sporozoites do not immediately develop into exoerythrocytic-phase merozoites, but instead produce hypnozoites that remain dormant for periods (several months to years)
- ✚ Hypnozoites are responsible for long incubation and late relapses in these two species of malaria.
- ✚ After a period of dormancy, they reactivate and produce merozoites.

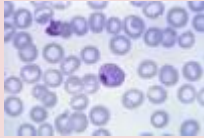

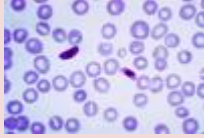
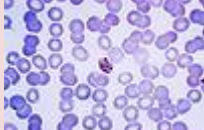
*The parasite is relatively protected from attack by the body's immune system because for most of its human life cycle it resides within the liver and blood cells and is relatively invisible to immune surveillance. However, circulating infected blood cells are destroyed in the spleen. To avoid this fate, the *P. falciparum* parasite displays adhesive proteins (PfEMP1) 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. This "stickiness" is the main factor giving rise to hemorrhagic complications of malaria. High endothelial venules (the smallest branches of the circulatory system) can be blocked by the attachment of masses of these infected red blood cells. The blockage of these vessels causes symptoms such as in placental and cerebral malaria. In cerebral malaria the sequestered red blood cells can breach the blood brain barrier possibly leading to coma.*



Diagnosis

1 Blood films

- Thin films are ---allow species identification.
- Thick film---- detect parasite levels (or parasitemia) as few as 5 parasites/μL blood.

| Species | Appearance | Periodicity | Liver persistent |
|-------------------------------------|---|-------------|------------------|
| <u><i>Plasmodium vivax</i></u> |  | tertian | yes |
| <u><i>Plasmodium ovale</i></u> |  | tertian | yes |
| <u><i>Plasmodium falciparum</i></u> |  | tertian | no |
| <u><i>Plasmodium malariae</i></u> |  | quartan | no |

2 Antigen tests ("Dipsticks")—used for field tests.

- read visually as the presence or absence of colored stripes on the dipstick
- Can determine if parasites are present in the blood, but not how many.

3 Molecular methods/PCR

- more accurate than microscopy

4 Subjective Diagnoses

- history of subjective fever, rectal temperature, nailbed pallor, and splenomegaly were used as treatment indications

- 5 Differential

- Recent investigations suggest that malarial retinopathy is better (collective sensitivity of 95% and specificity of 90%) than any other clinical or laboratory feature in distinguishing malarial from non-malarial coma.

Prevention



- ☞ prophylactic drugs/ Malaria prophylaxis
- mosquito eradication/ Mosquito control and
- The prevention of mosquito bites.

Malaria prophylaxis

- ✚ drugs, most of which are also used for treatment of malaria, can be taken preventively (Chloroquine, Doxycycline and the atovaquone and proguanil combination etc)
- ✚ The prophylactic effect does not begin immediately upon starting the drugs, so take the drugs one to two weeks before arriving and must continue taking them for 4 weeks after leaving (with the exception of atovaquone proguanil that only needs be started 2 days prior and continued for 7 days afterwards).
- ✚ Drugs are taken daily or weekly, at a lower dose than would be used for treatment of a person who had actually contracted the disease.
- ✚ Use of prophylactic drugs is seldom practical for full-time residents of malaria-endemic areas.

Vector control

1 General methods

- Monitoring mosquito populations via landing rate counts, or mechanical traps
-
- Source reduction by
 - emptying standing water
 - Open water marsh management (OWMM) --- The network of ditches drains the mosquito habitat and lets in fish which will feed on mosquito larvae.

- Biocontrol

(Use of natural enemies to manage mosquito populations).

- Direct introduction of parasites, pathogens and predators to target mosquitoes. (Effective biocontrol agents include predatory fish that feed on mosquito larvae such as mosquitofish and some cyprinids, killifish and Tilapia.
- Dragonfly naiads, which consume mosquito larvae in the breeding waters, and adult dragonflies, which eat adult mosquitoes.
- Birds, bats, lizards and frogs, but evidence of effectiveness of these agents is only anecdotal.
- Mosquitoes have their own set of diseases (some of them can be utilized for mosquito management---. Microbial pathogens include viruses, bacteria, fungi, protozoa, nematodes, and microsporidia)
- Dead spores of varieties of the natural soil bacterium *Bacillus thuringiensis*, especially *Bt israelensis* (BTI). BTI is used to interfere in the digestion systems of larvae. It can be dispersed by hand or dropped by helicopter in large areas. BTI is no longer effective after the larvae turn into pupae, because they stop eating.
- Integrated pest management (IPM) is the use of the most environmentally appropriate method or combination of methods to control pest populations.

- Larviciding

- Accomplished through use of contact poisons, growth regulators, surface films, stomach poisons (including bacterial agents), and biological agents such as fungi, nematodes, copepods, and fish.
- Methoprene, considered slightly toxic to larger animals, which mimics and interferes with natural growth hormones in mosquito larvae, preventing development.
- Larvae of *Anopheles gambiae* can survive for several days on moist mud, and that treatments should therefore include mud and soil several meters from puddles.

- Adulticiding

- ✚ Accomplished by ground-based applications or via aerial application of chemical pesticides.
- ✚ Low-volume applications of pesticides or use of thermal fogging.

Use of DDT

- ✚ DDT was formerly used throughout the world for large area mosquito control, but it is now banned in most developed countries.

- ✚ DDT remains in common use in many developing countries. It is sometimes approved for use only in specific, limited circumstances where it is most effective, such as application to walls.

Other methods

- A newer approach to killing mosquitoes in a non-toxic way is to use a device that burns propane, thus generating carbon dioxide, warmth, and water vapor. (Draws the mosquitoes toward the propane flame, where they are then sucked into a net or holder where they collect).
- Some newer mosquito traps or known mosquito attractants emit a plume of carbon dioxide together with other mosquito attractants such as sugary scents, lactic acid, octenol, warmth, water vapor and sounds.
- A traditional approach is the use of lethal Ovitrap by providing artificial breeding spots for the mosquitoes but destroying the developing larvae
- The latest approach is the automatic lethal ovitrap which works like a traditional ovitrap but automates all steps needed to provide the breeding spots and to destroy the developing larvae
- Scientists have created male mosquitoes which were spermless and are experimenting with methods of introducing the sterile males into the environment in the hope of reducing overall mosquito numbers

Prevention of mosquito bites

- Mosquito nets and bedclothes.
- Application of mosquito repellent body creams /lotions

Immunization

- Malaria vaccine

Treatment

- Antimalarial drugs

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