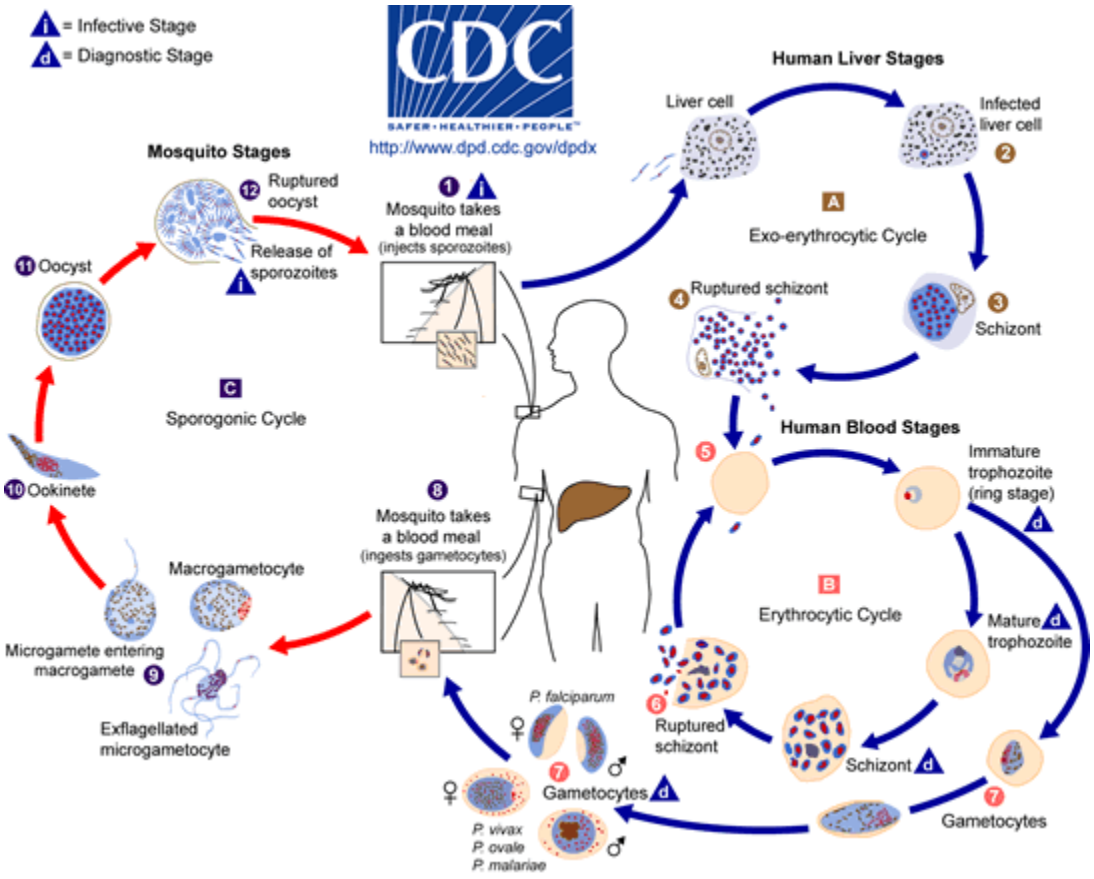
Malaria

Causal Agents:

Blood parasites of the genus *Plasmodium*. There are approximately 156 named species of *Plasmodium* which infect various species of vertebrates. Four are known to infect humans: *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*.

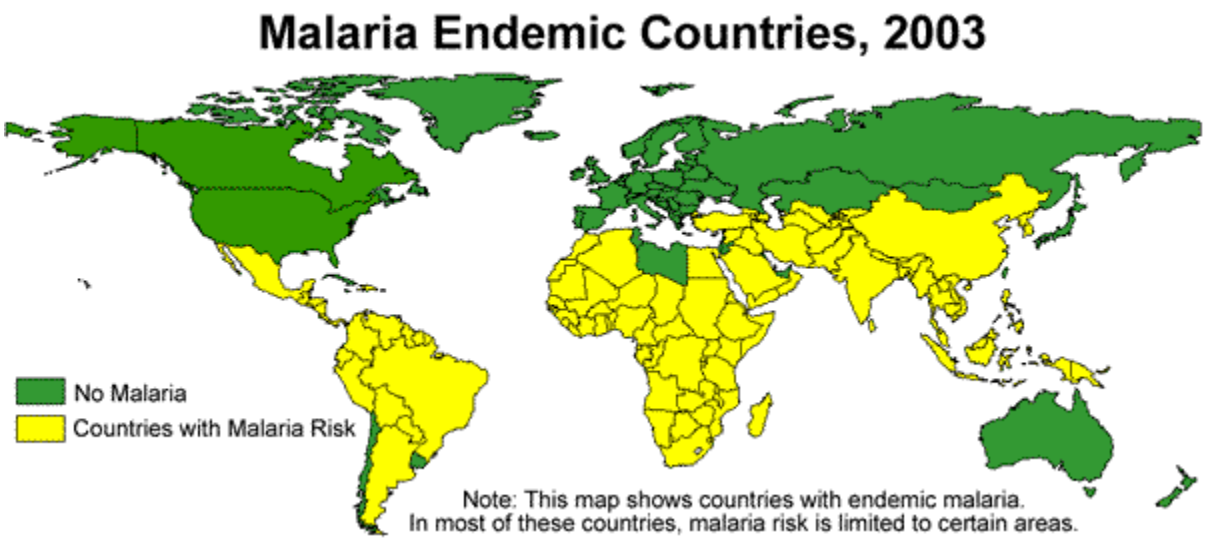
Life Cycle:



The malaria parasite life cycle involves two hosts. During a blood meal, a malaria-infected female *Anopheles* mosquito inoculates sporozoites into the human host ❶. Sporozoites infect liver cells ❷ and mature into schizonts ❸, which rupture and release merozoites ❹. (Of note, in *P. vivax* and *P. ovale* a dormant stage [hypnozoites] can persist in the liver and cause relapses by invading the bloodstream weeks, or even years later.) After this initial replication in the liver (exo-erythrocytic schizogony Ⓐ), the parasites undergo asexual multiplication in the erythrocytes (erythrocytic schizogony Ⓑ). Merozoites infect red blood cells ❺. The ring stage trophozoites mature into schizonts, which rupture releasing merozoites ❻. Some parasites differentiate into sexual erythrocytic stages (gametocytes) ❼. Blood stage parasites are responsible for the clinical manifestations of the disease.

The gametocytes, male (microgametocytes) and female (macrogametocytes), are ingested by an *Anopheles* mosquito during a blood meal 8. The parasites' multiplication in the mosquito is known as the sporogonic cycle C. While in the mosquito's stomach, the microgametes penetrate the macrogametes generating zygotes 9. The zygotes in turn become motile and elongated (ookinetes) 10which invade the midgut wall of the mosquito where they develop into oocysts 11. The oocysts grow, rupture, and release sporozoites 12, which make their way to the mosquito's salivary glands. Inoculation of the sporozoites into a new human host perpetuates the malaria life cycle 1.

Geographic Distribution:



Malaria generally occurs in areas where environmental conditions allow parasite multiplication in the vector. Thus, malaria is usually restricted to tropical and subtropical areas (see map) and altitudes below 1,500 m. However, this distribution might be affected by climatic changes, especially global warming, and population movements. Both *Plasmodium falciparum* and *P. malariae* are encountered in all shaded areas of the map (with *P. falciparum* by far the most prevalent). *Plasmodium vivax* and *P. ovale* are traditionally thought to occupy complementary niches, with *P. ovale* predominating in Sub-Saharan Africa and *P. vivax* in the other areas; however these two species are not always distinguishable on the basis of morphologic characteristics alone; the use of molecular tools will help clarify their exact distribution.

Clinical features:

The symptoms of uncomplicated malaria can be rather non-specific and the diagnosis can be missed if health providers are not alert to the possibility of this disease. Since untreated malaria can progress to severe forms that may be rapidly (<24 hours) fatal, malaria should always be considered in patients who have a history of exposure (mostly: past travel or residence in disease-endemic areas). The most frequent symptoms include fever and chills, which can be accompanied by headache, myalgias, arthralgias, weakness, vomiting, and diarrhea. Other clinical features include splenomegaly, anemia, thrombocytopenia, hypoglycemia, pulmonary or renal dysfunction, and neurologic changes. The clinical presentation can vary substantially depending on the infecting species, the level of parasitemia, and the immune status of the patient. Infections caused by *P.*

falciparum can progress to severe, potentially fatal forms with central nervous system involvement (cerebral malaria), acute renal failure, severe anemia, or adult respiratory distress syndrome. Complications of *P. vivax* malaria include splenomegaly (with, rarely, splenic rupture), and those of *P. malariae* include nephrotic syndrome.

Laboratory Diagnosis:

The first step toward diagnosis (and treatment) of malaria is to consider malaria in the differential diagnosis!

Diagnostic findings

Microscopic identification is the method most frequently used to demonstrate an active infection.

- Microscopy
- Comparison of *Plasmodium* species
- Molecular diagnosis techniques can complement microscopy, especially in species identification.
- Antibody Detection can detect past (not necessarily active) infections.
- Immunologic/Biochemical detection of malaria parasite products are available and under evaluation.
- Bench aids for Malaria

Treatment:

Treatment varies according to the infecting species, the geographic area where the infection was acquired, and the severity of the disease.