

# MALARIA

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Malaria is a disease affecting 100 million people annually with a mortality rate of 1%. It is caused by a parasite *Plasmodium* which lives in blood and other tissues.

Malaria means "bad air", was so named because of association of the disease with the odorous air of swamps. Parasite was discovered in the blood by Laveran in 1880. In 1898 Ross experimentally proved the mosquito transmission of the disease. Afterwards Grassia and his pupils worked independently and described the cycle of human malaria in *Anopheles*.

Endemic and epidemic malaria are found in all countries between the 30° South and 40° North lines of latitude. Malaria is primarily a disease of hot humid countries at altitudes less than 2200m above mean sea level, where conditions

are ideal for prolific breeding of mosquito vector *Anopheles*. It is endemic in South Asian countries, in parts of Africa and in parts of South and Central America. Other than the mosquito, malaria also can be transmitted by blood transfusion.

At present malaria is the most important communicable disease in Sri Lanka, which has devastating results both economically and socially. During the year 1998, 1.3 million blood samples of fever patients were screened and 15.8%, were positive, compared to 16.4% positive in 1997. Of which 80%, were due to *Plasmodium vivax*. The rest was due to *Plasmodium falciparum*. Sixty two percent (62%) of total malaria cases were reported from the North-Eastern Province.

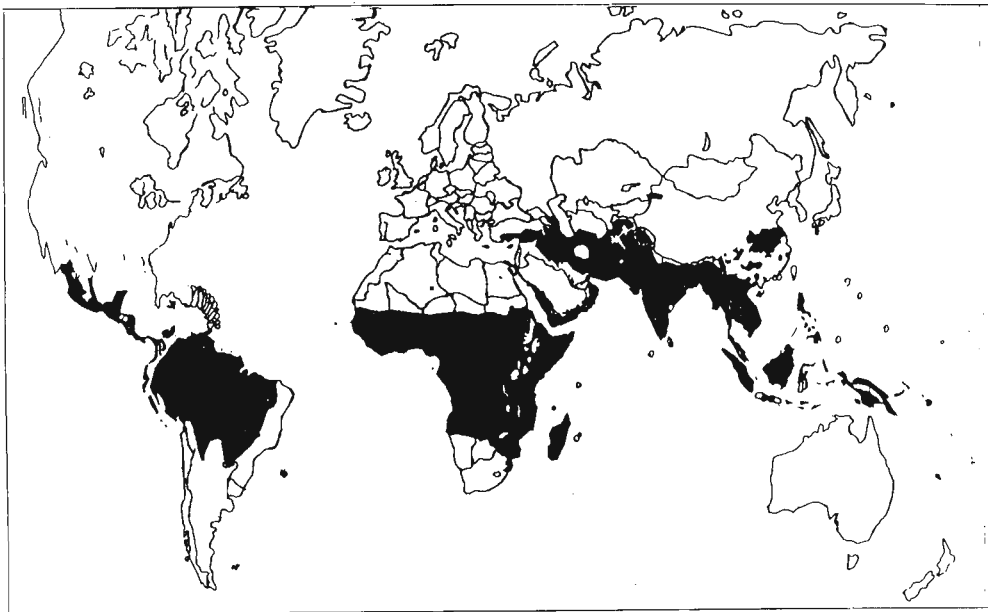


Figure 1: Distribution of Malaria in the world

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During 1998, 115 deaths were due to malaria. Of which 106 (92%) were from North Eastern Province.

The main reason for the increase in mortality and morbidity due to malaria in these areas was the practical difficulties encountered in case detection and treatment of malaria patients. Still the predominant parasite species continues to be *Plasmodium vivax*. The principal vector continues to be *Anopheles culicifacies*. Secondary vectors are *Anopheles subpictus* and *Anopheles annularis*.

Four species of *Plasmodium* are capable of causing malaria in man.

*Plasmodium vivax*

*Plasmodium falciparum*

*Plasmodium malariae*

*Plasmodium ovalae*

*P.vivax* is the commonest and most widely distributed species being prevalent in both tropical and temperate zones. *P.vivax* causes "tertian" or "benign tertian" malaria which is likely to cause relapses. *P.falciparum* is prevalent in the tropics but does not thrive as *P.vivax* in temperate countries. It causes "malignant tertian" malaria which is dangerous than other types. There is no animal reservoir for any of these human parasite diseases except possibly Chimpanzees for *P.malariae*. In Sri Lanka only *P.vivax* and *P.falciparum* malarial parasites are found.

## Life Cycle

General nature of the life cycle of all species of *Plasmodium* is similar.

- In human
- Exo-erythrocytic stage
  - Erythrocytic stage

## Mosquito cycle

### *Exo-erythrocytic stage*

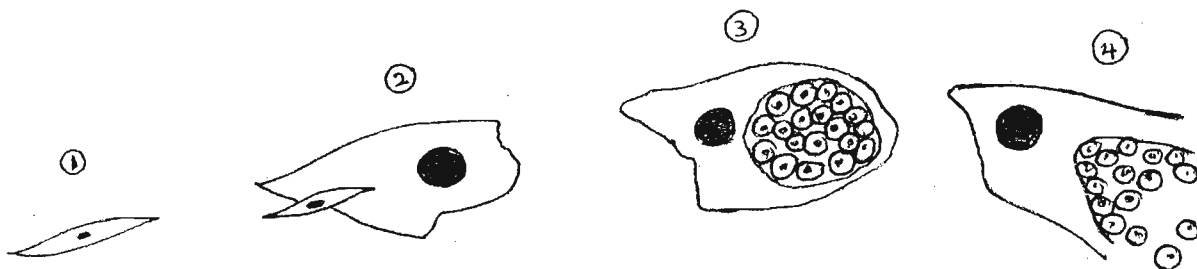
When a mosquito bites a human it introduces sporozoites (stage which is infective to human). The parasite does not enter red blood cells at once. Parasites leave the circulation and enter into the liver. Those sporozoites that are not removed by the body's defence mechanism undergo development within the liver cells. They go through development (at least two schizogonic cycles) within the liver cells before invading blood. Then parasites rupture the liver cells and invade the blood stream and enter into red blood cells. At this stage parasites are called micro merozoites.

### *Erythrocytic stage*

About a week or ten days after introducing sporozoites the parasites (micro merozoites) invade red blood cells and pass through several stages of development. The earliest form is the "ring stage". Later it is developed and become trophozoites, shizonts and finally merozoites. These parasitic forms are found in peripheral blood about 12 days after inoculation of the sporozoites in *P.vivax* infections and 9 days in *P.falciparum* infections.

*Gametogeny* (the process of development of sexual stages)

Within red blood cells the process may continue for a considerable period of time and stage of gametogeny occurs. At this stage few merozoites develop into sexual form of the parasite known as gametocytes. Mature forms are found in peripheral blood and now the patient is infective. When an *Anopheles* mosquito bites the patient this stage of parasite enter the mosquito stomach and the life cycle continues.



**Figure 2: Exo-Erythrocytic stage**

1. Sporozoite
2. Sporozoite enters into liver cells
3. Development and multiplication within the liver cells
4. The liver cells rupture and micromerozoites liberate into blood

### Mosquito cycle

The gametocytes are of two types. Micro-gametocyte (male form) and Macro-gametocyte (female form). Both forms are found in mosquito stomach. Male gametocytes form flagella like structures and swim actively and unite with the inactive female gametocytes. Later an oocyst results and finally sporozoites break loose from the oocyst. Such an oocyst may contain more than 10,000 sporozoites and there may be about 50 oocysts on one mosquito stomach. Sporozoites make their way to salivary glands and assemble in the cell lining of the salivary glands. There may be up to 200,000 sporozoites in one mosquito. They enter the lumen of the ducts and discharge with saliva when the mosquito bites. It may take 20 or more bites to discharge them all.

### Clinical features

Malaria clinical features usually precede by various premonitory symptoms and comprise of three stages.

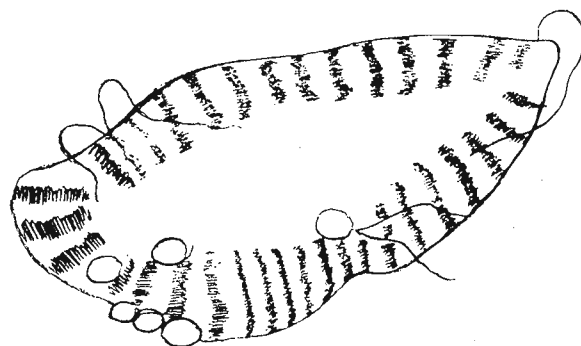
Cold stage: Starts with shivering and a feeling of intense cold. Teeth chatter and patient covers himself with any available clothing and blankets. Skin becomes dry and pale with high pulse rate. Vomiting occurs and children often have convulsive seizures. This stage lasts for 15 minutes to one hour.

Hot stage: Feeling of intense cold gives way to one of the distressing heat. The face is flush and skin becomes dry and burning, headache becomes intense, nausea and vomiting are common. The pulse rate is high. There is often intense thirst while the temperature may rise to 41°C (106°F) or more. This stage lasts for two to six hours.

Sweating stage: The patient breaks out in profuse sweat. So that his bedding become drenched. The temperature falls rapidly, often below the normal level. He usually falls into a deep sleep and on waking feels weak but other wise normal. This stage lasts for two to four hours.

In all types of infections the periodic febrile response is related to the time of rupture of a sufficient number of mature schizonts and consequent discharge of merozoites into the blood stream.

The incubation period in malaria covers the time between the infection and the first appearance of clinical signs of which fever is the most common. In *Plasmodium vivax* infections it is 13-17 days, (may go up to 9 months) whereas in *Plasmodium falciparum* infections it varies between 9-14 days.



**Figure 4: An oocyst of the parasite developing in mosquito stomach**

*Plasmodium falciparum* is potentially the most severe form of malaria, with high levels of parasites in the blood. It affects kidneys, liver, brain and gastro intestinal tract. The fever has no particular pattern. If the amount of parasites in the blood exceeds more than 5% of red blood cells severe form of malaria may develop.

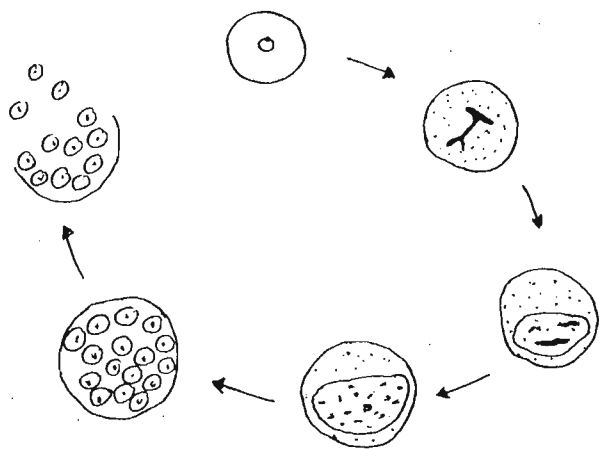
Cerebral malaria with elevation in body temperature and rapid deterioration in consciousness, convulsion coma and death may result.

Gastro intestinal symptoms with stools containing blood, mucus and pus together with abdominal pain.

Renal complications with blood in the urine and renal failure.

### **Treatment**

General treatment: to control fever antipyretic as Asprin and Paracetamol can be given. Intravenous fluid may be required.



**Figure 3: Erythrocytic stage**

**From ring stage to merozoites**

**Ring stage, development of the parasite within the RBC, release of merozoites in the blood**

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Drug treatment - Chloroquine is the drug of choice, some species especially *P.falciparum* has shown resistant to Chloroquine. They are treated with a combination of sulphurdioxine and pyrimethamine.

## Control of Malaria

Control of Malaria started in Sri Lanka way back in 1946 by introducing DDT spraying. The spraying programme covers all houses in Malaria endemic areas. It was so effective; subsequently the malaria eradication programme was launched in 1958. Resulted near eradication in 1963 when only 17 cases were recorded within the country. But due to multitude of factors resurgence of the disease occurred often for a few years, which led to an epidemic situation in 1968-1969. The significant technical problem was the emergence of DDT resistance in the vector mosquito, which later resulted in the change of insecticide spraying to Malathion in August 1977. At first there was a significant drop in incidence, but in 1982 there was again a sharp rise in incidence.

So now the control of malaria would be a multi disciplinary approach. The major constraint in malaria control is that even when carried out efficiently and cost effectively, it is relatively expensive.

### Control through treatment

The provision of easy access to treatment is the main approach in malaria control. In areas of malaria endemicity, radical treatment of cases of clinical malaria with appropriate drugs is often used to reduce transmission.

## Chemoprophylaxis as a control tool

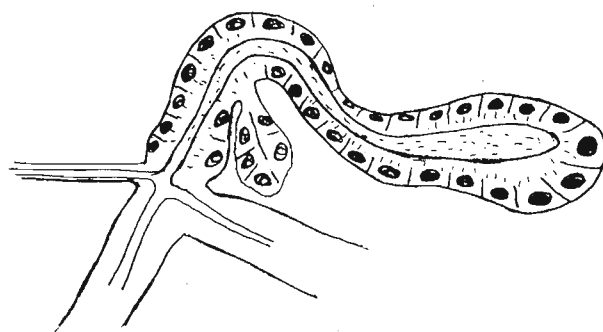
People living in the endemic areas primarily young children and pregnant women are given medicine even without the disease to protect from the disease.

## Malaria Vaccines

Malaria vaccines are being developed against three stages of the parasite's life cycle with particular focus on *P.falciparum* malaria, due to its severity and high prevalence. Vaccines that destroy the initial stages of the parasite after entering the body. Such vaccines would prevent sporozoites from developing after being inoculated into human host, blocking infection and preventing clinical disease and transmission.

Another vaccine is targeting the blood stages blocking invasion, development and spread of merozoites in red blood cells.

Also, vaccines are being developed to prevent transmission by destroying sexual forms.



**Figure 5: Salivary gland of the mosquito with merozoites within the cells and lumen**

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### Prevention of Human-vector contact

Several self protective techniques exist which if used consistently can greatly reduce human vector contact and in some cases destroy the vector. *Anopheles* mosquitoes are usually found from dusk to dawn. Bed nets to protect against mosquito bites, while sleeping is very helpful. In recent years it has been shown that using bed nets in malaria endemic areas particularly nets impregnated with pyrethroid (insecticide) such as permethrin can be safe and an effective barrier between human and mosquito.

In addition, individual measures to prevent human vector contact and reduce vector population include impregnating curtains and small fumigation mats with pyrethroid, burning coils, applying repellents and spraying living places.

Installing windows and door screening and wearing protective clothing particularly after sunset also reduces contact with the mosquito. When selecting a site for new housing, temporary or permanent, should avoid places adjacent to mosquito breeding sites. Improving housing construction may protect humans against contact with mosquitoes.

### Reducing Breeding sites

Draining or filling places around human dwellings where water collects, such as potholes, small ponds and old cans and covering wells or water tanks will reduce mosquito breeding sites.

Also careful planning of rural and urban development projects such as construction, road building, irrigation system and well digging is critical.

### **Destruction of Mosquito Vector**

There are several techniques used to destroy the mosquito in both its larval and adult stages. eg: biological control methods involving introducing mosquito pathogens or predators such as bacteria and larvivorous (larvae-eating) fish.