
MALARIA

Malaria is a protozoan disease transmitted by the bite of infected *Anopheles* mosquitoes.

It is the most important of the parasitic diseases of humans, with transmission in 107 countries containing 3 billion people and causing 1–3 million deaths each year.

Malaria has now been eliminated from the United States, Canada, Europe, and Russia but, despite enormous control efforts, has resurged in many parts of the tropics.

Malaria is a long-lasting infectious disease caused by the simplest of the genus plasmodia, characterized by

periodic attacks of fever,

enlarged liver,

spleen

and progressive anemia.

The disease has been known since ancient times.

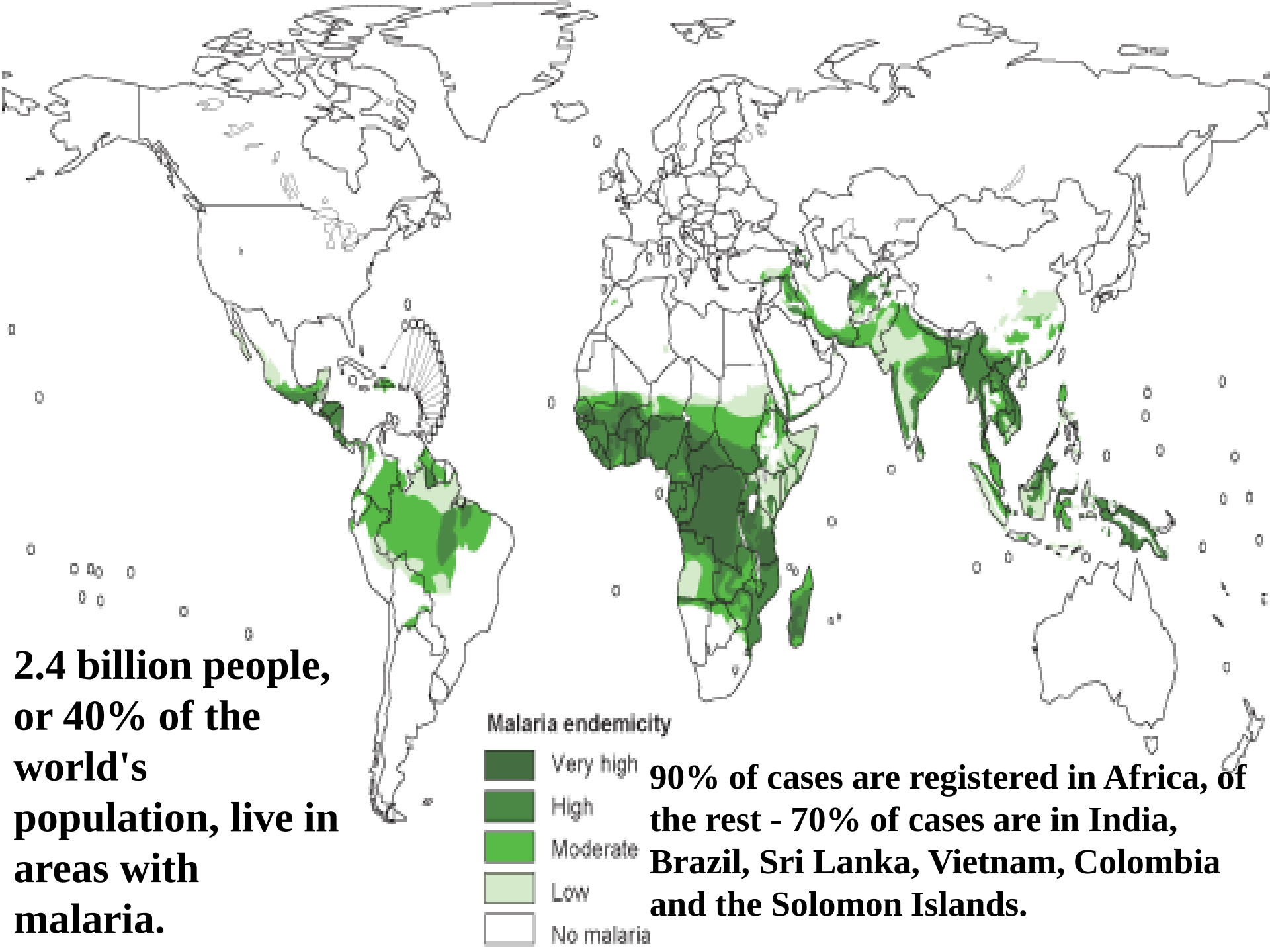
The term malaria itself was introduced by the Italian anatomist G.M. Lancisi in 1717, which linked the cause of the disease with the poisonous evaporation of marshes (from Italian. “Mala aria” - bad air).

Malaria has been and remains one of the most common infectious diseases on the globe. The global malaria eradication company worldwide (WHO resolution of 1955), which was held for several years, failed.

According to WHO

Every year, about 250 million people become sick with malaria as a result of living or traveling to endemic regions of malaria, of which 1.5-2.7 million die.

Most of the dead are children, the vast majority of children are infected under the age of 5 years.



2.4 billion people, or 40% of the world's population, live in areas with malaria.

90% of cases are registered in Africa, of the rest - 70% of cases are in India, Brazil, Sri Lanka, Vietnam, Colombia and the Solomon Islands.

According to the World Health Organization, currently

82 countries of the world are highly endemic and are in the process of fighting malaria,

12 countries - in the pre-elimination period,

16 countries have reached the elimination of malaria in their territories and 27 countries received the status of "free from malaria", confirmed by WHO certificate

Over the past decade, from the third place in the number of deaths in a year (after pneumonia and tuberculosis), malaria has reached the first among infectious diseases. Malaria kills 15 times more people every year than does AIDS.

Mortality is expected to double in the next 20 years.

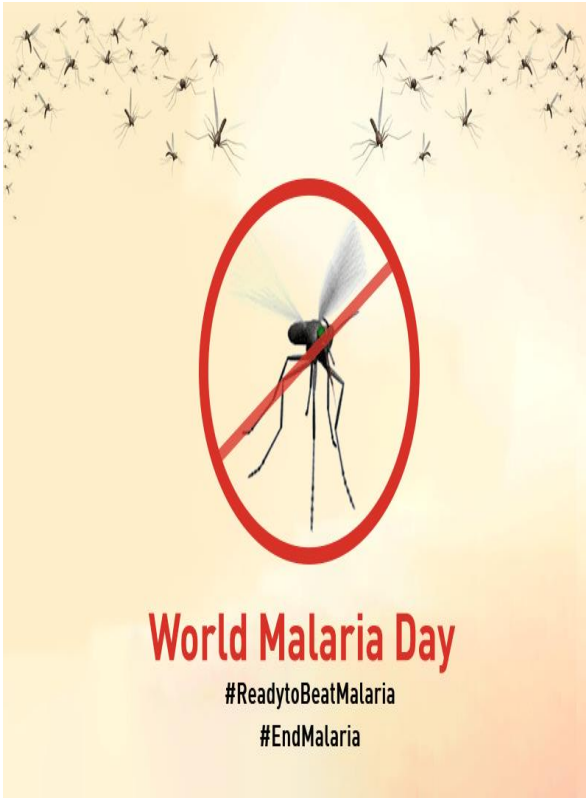
April 25 is the World Malaria Day

Since 2007, annually, on April 25, World Malaria Day has been celebrated.

This date was established by the World Health Assembly at its 60th session in May 2007.

Malaria Day is dedicated to promoting global efforts to ensure effective malaria control in all countries.

The purpose of the International Malaria Day is to explain that malaria is curable, to explain to the public the need for preventive measures, to draw the attention of both experts and research and training institutions, companies and foundations to the search for solutions to this problem.



The risk of spreading malaria (in the presence of mosquito vectors and the source of infection) is determined by the number of days per year with air temperatures above 15 degrees:

less than 30 - the spread of malaria is impossible

from 30 to 90 - low risk

from 90 to 120 - medium risk

120 to 150 days - high risk

more than 150 - an opportunity the spread of malaria very high

Etiology

The causative agents of malaria are the simplest genus Plasmodium (plasmodium).

Malaria in humans is caused by 4 types of pathogen:

- **Plasmodium falciparum - the causative agent of tropical malaria (daily attacks may occur); opened in 1890**

- **Plasmodium vivax - the causative agent of three-day malaria; opened in 1885**

- **Plasmodium ovale - the causative agent of three-day malaria; opened in 1922**

- **Plasmodium malariae - causative agent of four-day malaria; opened in 1885**

In 2004, it was found that malaria in humans can also be caused by a fifth species,
P. Knowlesi, which is common in Southeast Asia and causes malaria in long-tailed macaques (Macaca fascicularis).
These forms of malaria also differ in the duration of the incubation period, the duration of the various stages of the life
cycle of plasmodia,
the symptoms and course

Almost half of the Plasmodium falciparum strains are drug resistant to antimalarial drugs.

Therefore, tropical malaria is the most dangerous, it often takes a protracted (over 50%) and malignant (3-5%) course.

Tropical malaria is the cause of death in 98% of all fatal cases of malaria.

The tiny unicellular parasite is a great master of disguise.
By varying the proteins on its surface, Plasmodium can change its "appearance", over and over again avoiding recognition by our immune system.
And 5 thousand of its genes are constantly mutating, providing resistance to all the drugs that we create.
This is why malaria is considered a very powerful adversary.

Immunity

Children born to mothers who have had malaria have passive immunity that lasts 3-6 months. Acquired immunity is short-lived, occurs to a certain type of pathogen and is supported by repeated infections. The development of immunity explains the spontaneous cure.

The immunity in malaria is strictly species- and strain-specific. Immunity to P. vivax, P. malariae is more rapidly generated, and slower to P. falciparum.

Almost the entire population of the Earth is susceptible to malaria, only some groups of people have relative resistance to these parasites:
Many members of the Negroid race are resistant to Plasmodium vivax.

Patients suffering from hemoglobinopathies (e.g. sickle cell anemia), because malarial plasmodia cannot develop in morphologically altered red blood cells.
Persons with congenital deficiency of glucose-6-dehydrogenase, because parasites are also unable to reproduce in red blood cells under such conditions.

Epidemiology

The source of infection is a sick person or parasitic carrier, in the blood of which there are gametocytes (mature sexual forms of plasmodia).
Perhaps intrauterine infection of the fetus through the placenta and infection by blood transfusion, if the donor was a parasitic carrier.
In addicts who use shared syringes, group diseases of malaria are described.

In foci of malaria, children are more likely to be a source of infection than adults.
This is due to the fact that in adults, as a result of acquired immunity, the intensity of erythrocyte schizogony and the number of gametocytes formed, as well as the duration of carriage of gametocytes are less than in children.
The availability of children to mosquito bites also matters.

When infected with tropical malaria, a person becomes a source of infection 10-12 days after the onset of parasitemia and can remain after 1-2 weeks, sometimes up to 6 weeks, after asexual parasites disappear naturally or under the influence of treatment.

With other forms of malaria, the person remains source of infection from the onset of asexual forms until they disappear.

The pathogen is transmitted by a female mosquito of the genus Anopheles.

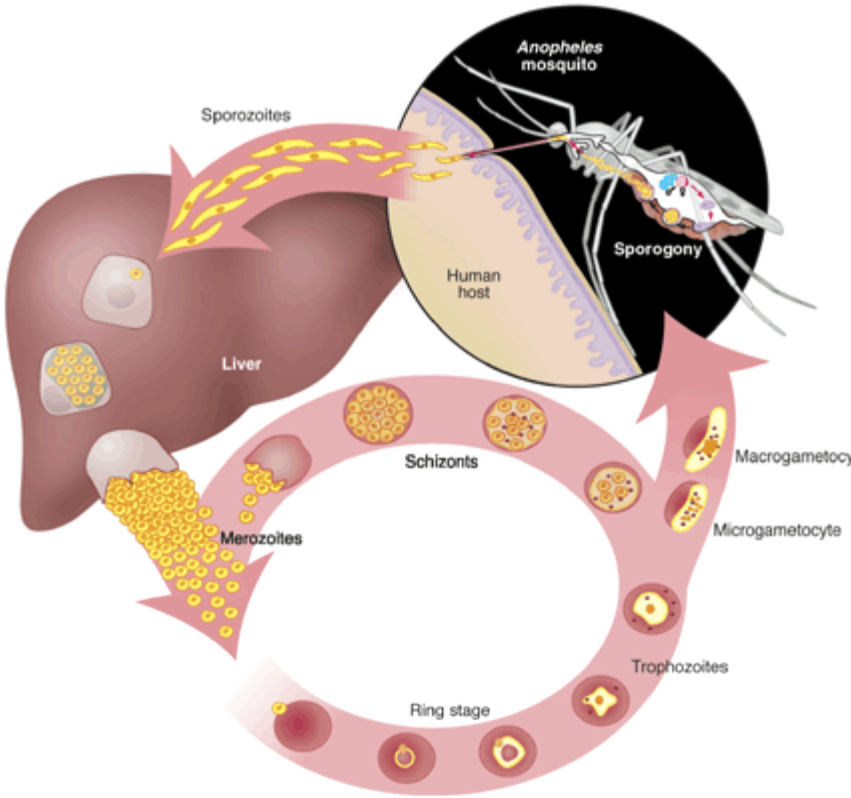
Mosquitoes of the genus Anopheles (dangerous, harmful, anathema) become infected during the bloodsucking of a person suffering from malaria or a parasitic carrier.

The incidence of malaria is characterized by pronounced seasonality, which is determined by the period of activity of mosquitoes.

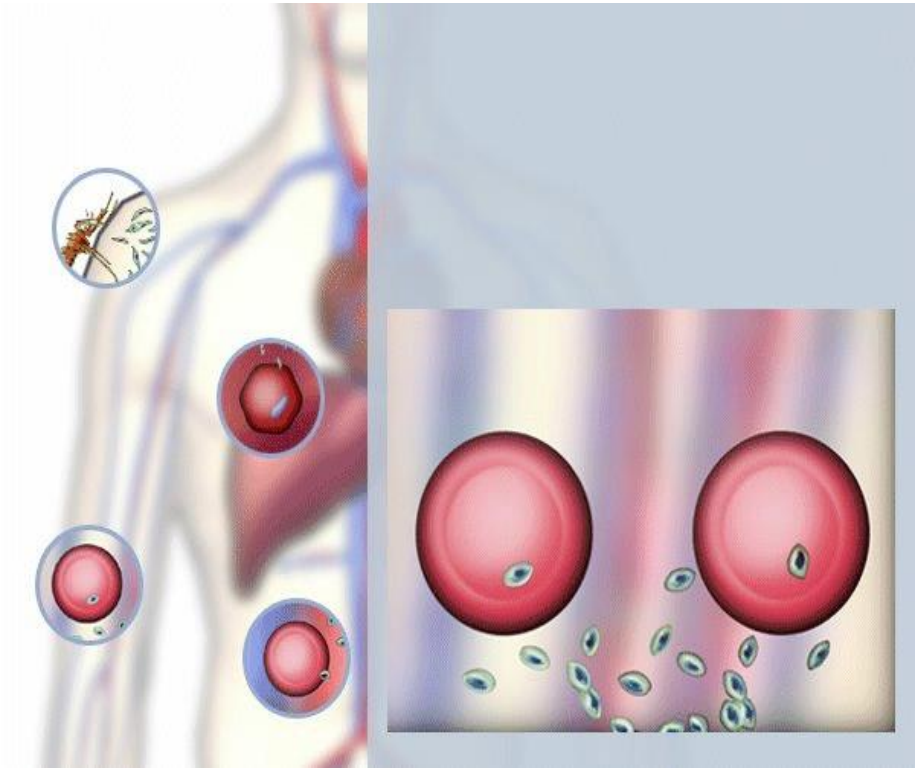
The largest number of diseases is recorded in the summer and autumn months.

In the winter months, the pathogen persists only in the human body.

The causative agent of malaria undergoes a complex development cycle in the human body (schizogony, asexual stage) and mosquito (sporogony, sexual stage).
Sporozoites enter the human body when they are bitten by an infected mosquito, which penetrate the liver cells, where they turn into tissue schizonts.
Tissue schizonts grow and divide many times.
The duration of tissue schizogony in different types of plasmodia takes from 6 to 18 days.



Then the parasites penetrate the red blood cells and the red blood cell cycle begins.
As a result of the division of erythrocyte schizonts, asexual (agamontas) and sexual (gamontas) forms of parasites are formed.
With the appearance of sexual forms in the blood, a person becomes infectious



The development of plasmodia in erythrocytes goes through four stages: rings (trophozoite), amoeba-shaped schizont, fragmentation (morula formation) and (for some parasites) gametocyte formation. With the destruction of the red blood cell, merozoites enter the blood plasma, and from there - into new red blood cells.

The cycle of red blood cell schizogony is repeated many times. The growth of trophozoite in an erythrocyte takes a constant time for each type of plasmodium.

Erythrocyte schizogony lasts 48 hours in the causative agents of three-day and tropical malaria, and 72 hours in four-day malaria. After that, the infected red blood cells are destroyed and the parasite enters the bloodstream.

At this point, a febrile seizure occurs as a response to the entry of a foreign protein into the blood.

The immediate cause of malaria fever attacks is the release of merozoites, a foreign protein, malaria pigment, hemoglobin, potassium salts, red blood cell residues, which alter the specific reactivity of the body and, when acting on a heat-regulating center, cause a temperature reaction.

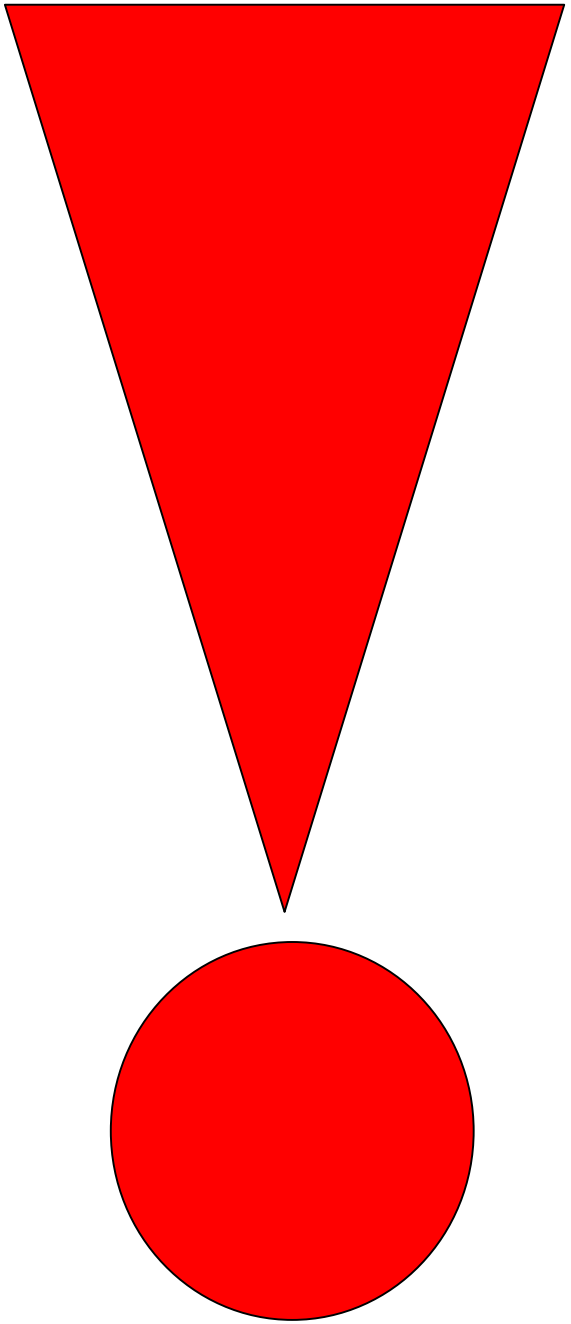
All clinical manifestations of malaria are associated only with erythrocyte schizogony.

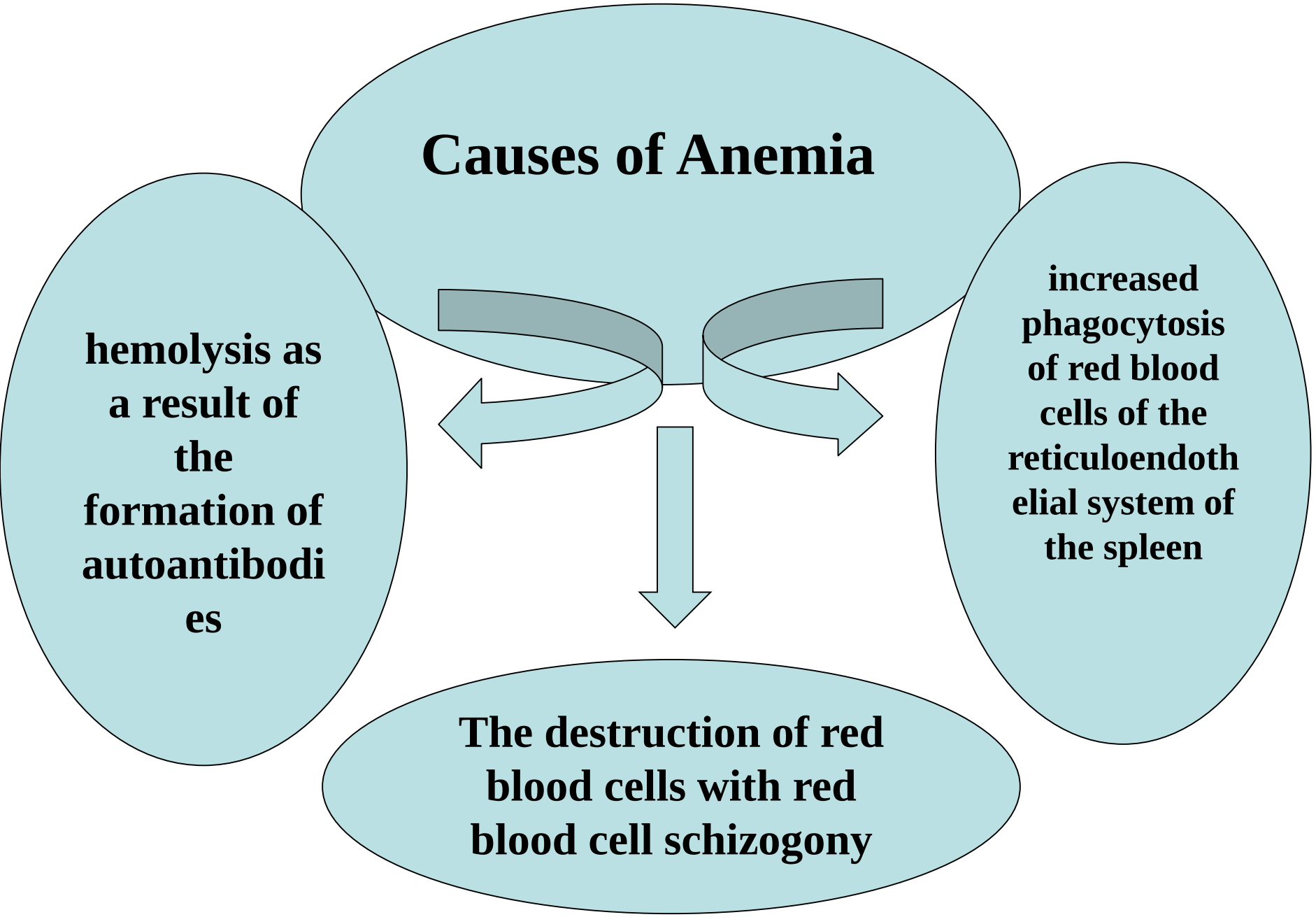
The most striking clinical manifestation of malaria is fever, which occurs only when the concentration of malaria parasites in the blood reaches a certain level. The minimum concentration of parasites that can cause fever is called the pyrogenic threshold, measured by the number of parasites in 1 µl of blood. The pyrogenic threshold depends on the individual properties of the organism and its immune state.

The pathogenesis of malignant forms is based on a systemic lesion of microvessels with thrombo hemorrhagic syndrome:

- **increased capillary permeability**
- **hemodynamic disturbances**
- **vasculitis**
- **shifts in the blood coagulation system**
- **hemorrhages (with tropical malaria)**

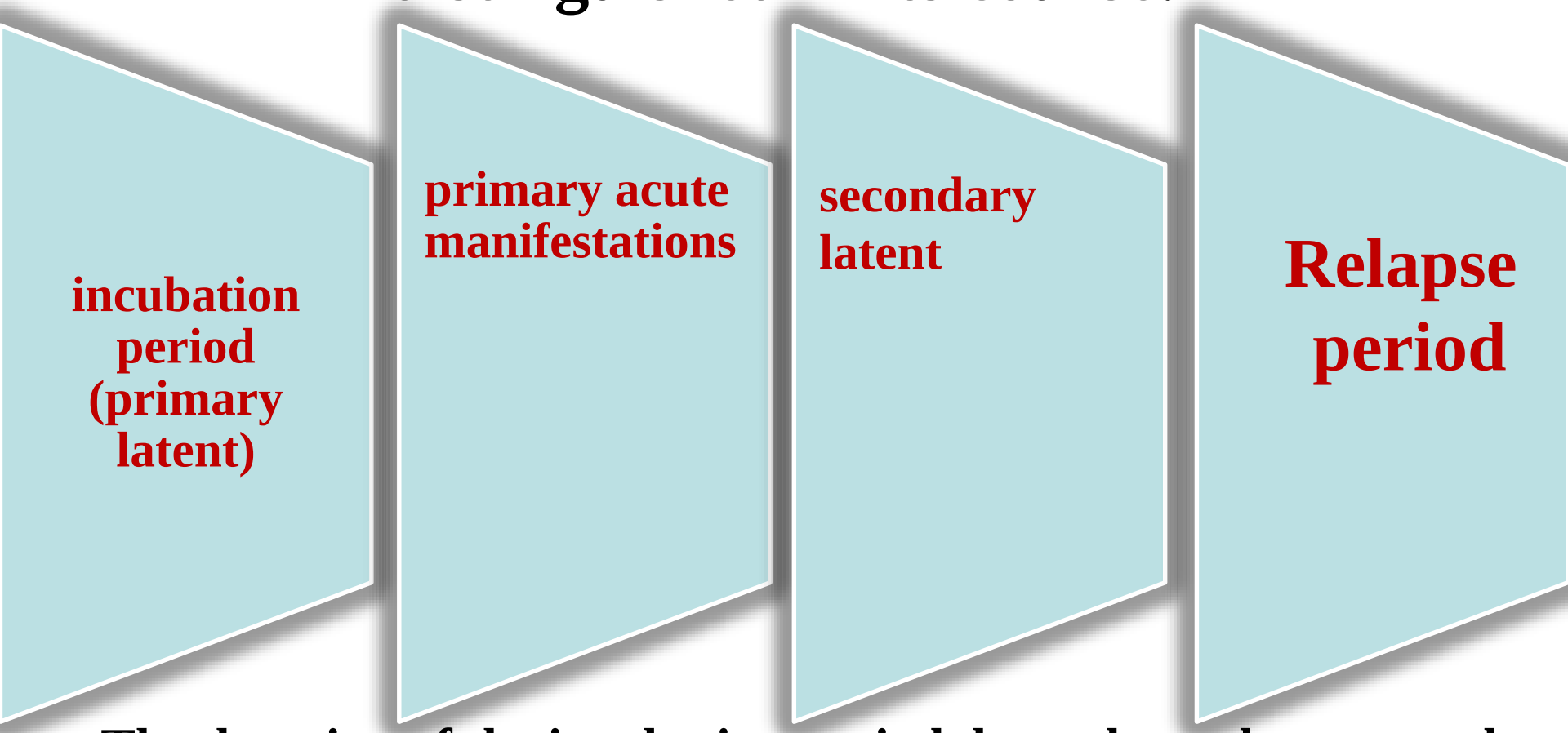
Of great importance in the pathogenesis of malaria is the sensitization of the body by a foreign protein and the development of autoimmunopathological reactions.




Causes of Anemia
hemolysis as a result of the formation of autoantibodies
increased phagocytosis of red blood cells of the reticuloendothelial system of the spleen
The destruction of red blood cells with red blood cell schizogony

CLINIC

Malaria is a polycyclic infection, 4 periods are distinguished in its course:



The duration of the incubation period depends on the type and strain of the pathogen.

Incubation period

With vivax malaria, it is 7–21 days with a short incubation and 6–20 months with a long incubation (in the northern latitudes), with ovale malaria - respectively 7 - 20 days or 7 - 10 months,

with four-day malaria - 14 - 42 days or more,

with tropical malaria - 6 - 31 days (usually 8 - 16).

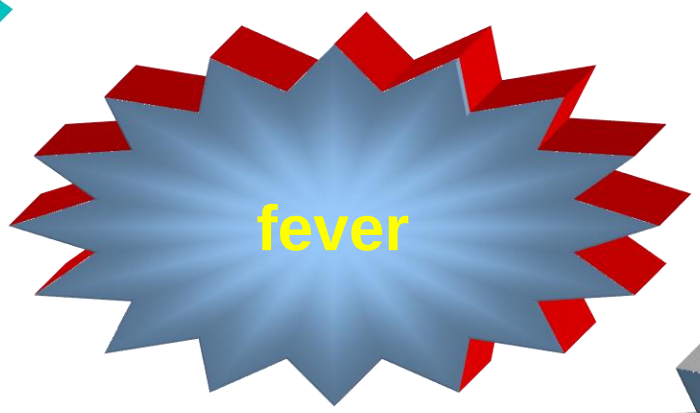
At the end of the incubation period, symptoms appear - precursors of the prodrome:

weakness

muscle,
headache,

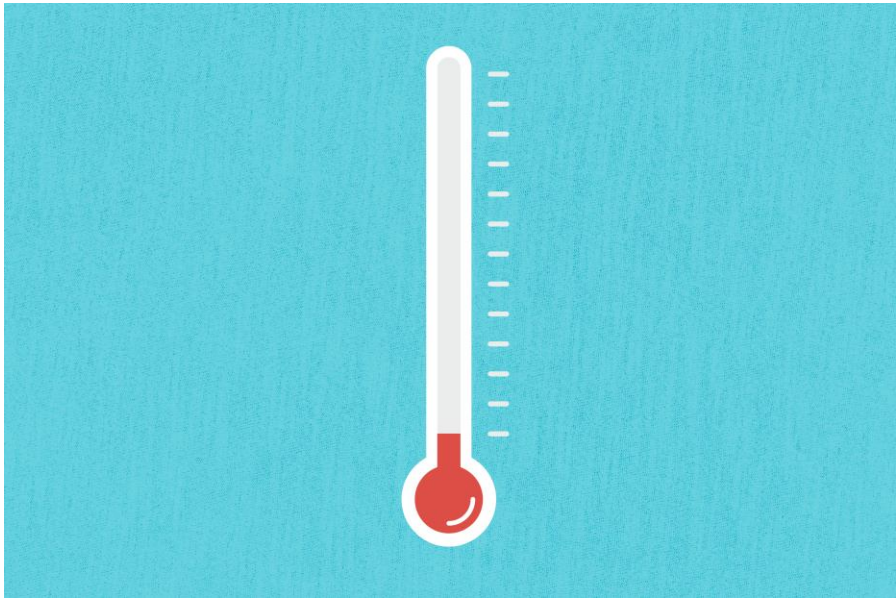
chilling, etc.

The second period is characterized by the most characteristic manifestation of malaria - repeated bouts of fever, for which a typical stage development

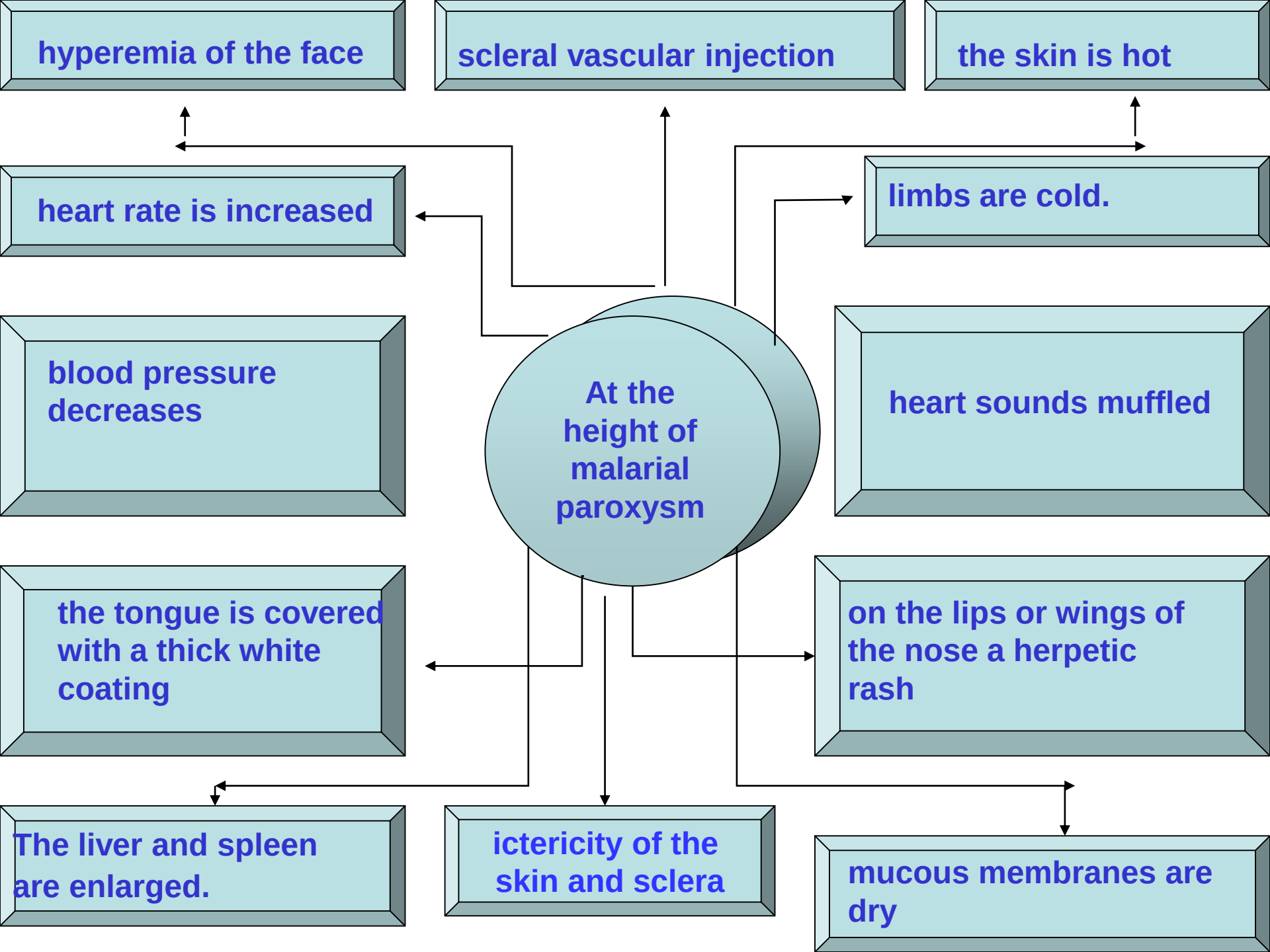


The attack occurs suddenly and begins with a chill. Chills with any fever occurs at the time of rapid restructuring of the hypothalamic thermostat to maintain a higher body temperature.
During a chill, which lasts from 30 min. up to 2 - 3 hours, body temperature rises, the patient cannot warm up, limbs are cyanotic and cold, pulse is quickened, breathing is shallow, blood pressure is increased

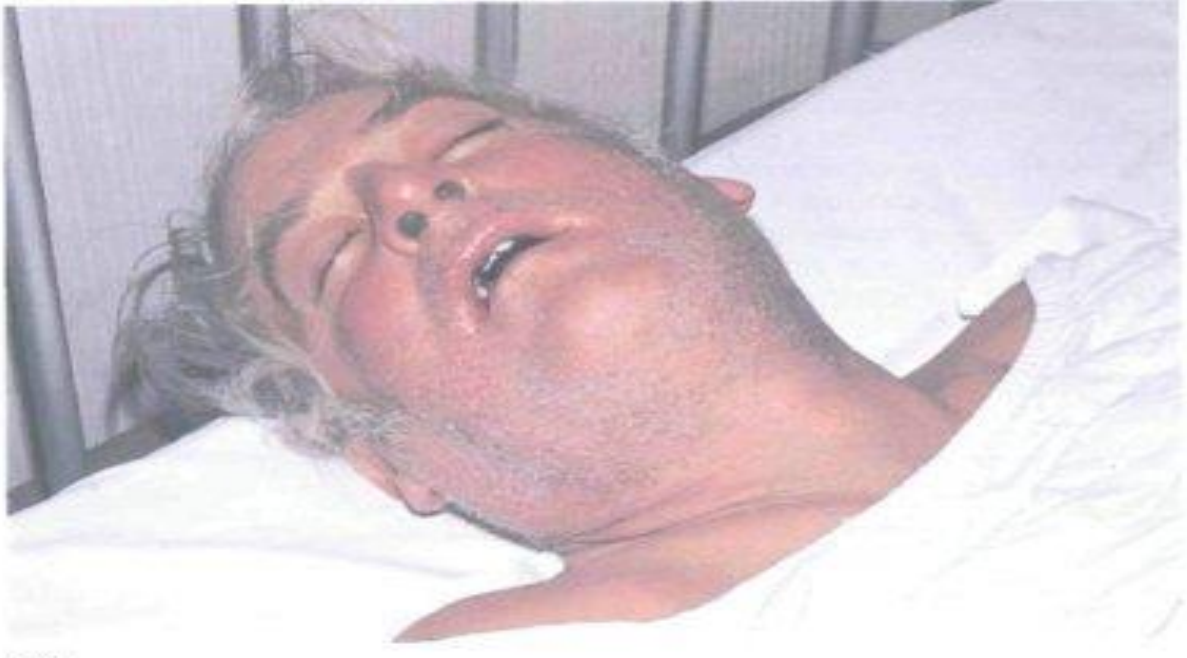
By the end of this period, the patient warms up, the temperature reaches 39 - 41 ° C, the heat period begins: the face turns red, the skin becomes hot and dry, the patient is excited, anxious, headache, delirium, confusion, sometimes convulsions are noted

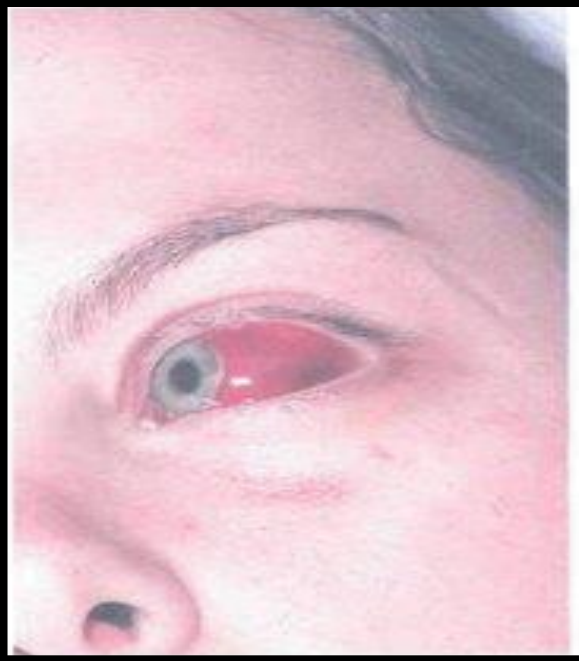


At the end of this period, the temperature drops rapidly, which is accompanied by profuse sweating. The patient calms down, falls asleep, a period of apyrexia sets in.
However, then the seizures are repeated with a certain cyclicity, depending on the type of pathogen.
In some cases, the initial (initial) fever is irregular or permanent.


hyperemia of the face
scleral vascular injection
the skin is hot
heart rate is increased
limbs are cold.
blood pressure decreases
At the height of malarial paroxysm
heart sounds muffled
the tongue is covered with a thick white coating
on the lips or wings of the nose a herpetic rash
The liver and spleen are enlarged.
ictericity of the skin and sclera
mucous membranes are dry

In general, malarial paroxysm lasts 6-12 hours, with tropical malaria - up to a day.
During the period of apyrexia, the patient's health is satisfactory, and his performance is not impaired.





Tropical malaria-
Maliqnat tertian malaria

Tropical malaria (P.falciparum) - is characterized by the severity of clinical manifestations and often has a malignant course.

The temperature curve is often of the wrong type with slight fluctuations, chills are not pronounced or even absent, sweating is not as significant as in other forms.

Attacks are manifested by

- **severe headache,**
- **frequent vomiting,**
- **diarrhea,**
- **lower back pain,**
- **rapid increase in size**
- **liver, spleen,**
- **jaundice often occurs,**
- **anemia quickly develops.**

The periods of apyrexia are short and not pronounced.

Lasts about a year

TERTIAN malaria (P.Vivax)

Tertian (Three-day) malaria - in severity, it occupies an intermediate position.

Attacks occur every other day or every day at strictly defined hours, usually in the first half of the day,

accompanied by

sudden coldness followed by shivering ,

fever,

sweating.

The course of the disease is about 1.5-2 years.

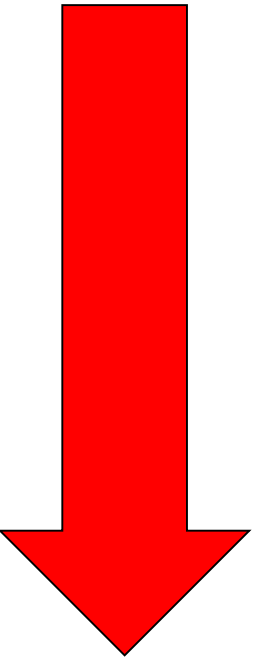
QUARTAN malaria (P.malaria)

Quartan (four –day) malaria is characterized
by a long, but relatively benign course.
Fever is intermittent from the very beginning.
Attacks are repeated after 2 days, often are long.
Parasitemia grows gradually and is not pronounced.
Duration about 3.5 years, sometimes many tens of years

Ovarian malaria

Ovarian malaria is the mildest form of malaria infection.
Attacks usually appear in the evening and night hours.
Fever is intermittent.
Chills and sweating are mild.
The course of the disease usually does not exceed 2 years.

In the first days of the disease, leukopenia with a neutrophilic shift to the left is usually detected, and in the following days

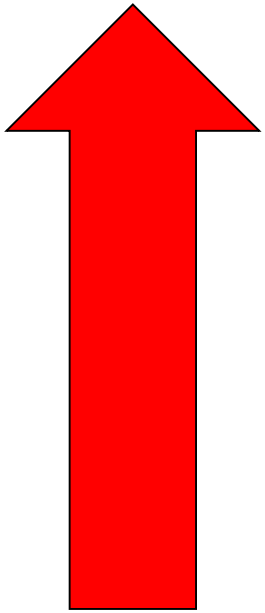


red blood cells

hemoglobin

white blood cells

platelet count



reticulocytes

ESR

lymphomonocytosis,

anisopoikilocytosis.

In the biochemical analysis of blood,
the content of indirect bilirubin increases
(a consequence of hemolysis of red blood cells),
AST and ALT;
cholesterol and albumin levels decrease;
the content of globulins increases.

Course of the disease

With timely treatment, the disease ends after 1-2 attacks.

Without treatment, seizures usually recur up to 10 or more times and can stop spontaneously, but the disease does not end there.

The period of apparent well-being (latent period) lasts from several weeks to a year or more (four-day malaria).

Course of the disease

EARLY RECIDIVES – appear in the first 2-3 months
Occurrence due to increased reproduction of red blood cell forms of the parasite

LATER RECIDIVES- - develop via 5-9 and more months
Occurrence associated with the release of blood from liver tissue forms of malarial plasmodia

Untreated, duration of illness:

With three-day malaria, about 2-3 years

With tropical malaria - 1-1.5 years,

With four-day malaria - may persist for years

COMPLICATIONS

CEREBRAL Edema
MALARIAN COMA
ACUTE KIDNEY FAILURE
MALARIAN ALGYD
MENTAL DISORDERS

MALARIAN COMA

It usually develops with tropical malaria in children 5-12 years old. It occurs in connection with severe cerebral hemodynamic disorders after filling almost the entire capillary network with red blood cells infected with schizonts.

STUNNING
CONDITION OF CONSCIOUSNESS
SHIPPERS
Meningeal Symptoms
CLONUS STOP
DISORDERS FROM THE CAS

Acute cerebral edema

One of the complications of malaria can be acute cerebral edema, which is more often observed with three-day malaria in children 4-15 years old. During the next attack of fever, severe headache, convulsions, loss of consciousness, vomiting, respiratory rhythm disturbance occur. Death occurs after 5-6 hours, if treatment is not started in a timely manner.

The appearance of the initial signs of this complication requires an immediate doctor's call and transfer of the patient to the intensive care unit for special treatment.

MALARIAN ALGYD

CHARACTERIZED BY THE COLLAPTOID STATE:

- **CONSCIOUSNESS SAVED, patient indifferent**
- **FACIAL FEATURES**
- **SKIN PALLETS**
- **COLD SWEAT**
- **PULSE THREADY**
- **ARTERIAL PRESSURE REDUCED**
- **DRY REFLEXES ARE NOT CAUSED**

MENTAL DISORDERS

CHARACTERIZED:

MOTOR EXCITATION

DIMMING CONSCIOUSNESS

By the appearance of hallucinations, etc.

DIAGNOSTICS

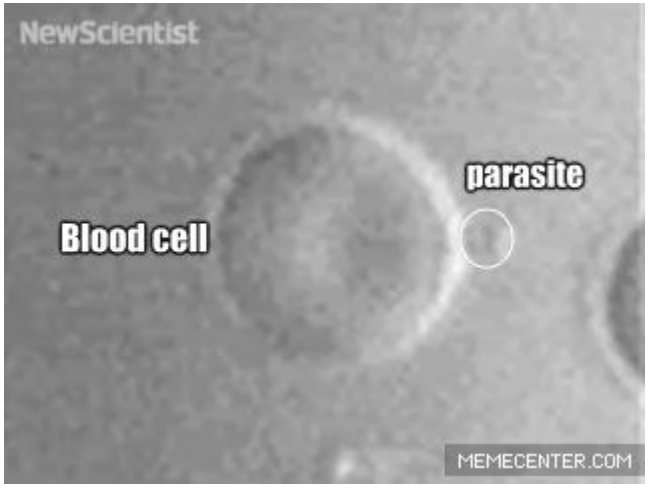
Epidemic anamnesis

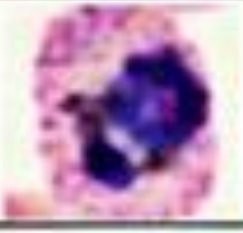
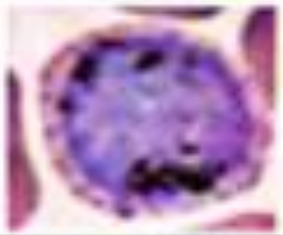
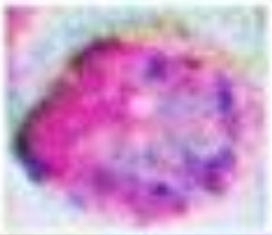
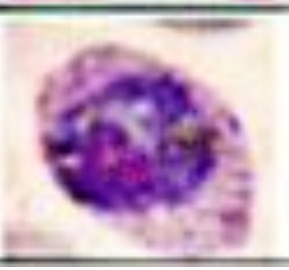
Clinic - typical febrile paroxysms with alternating seizures after 1 - 2 days, splenomegaly, anemia leukogram changes,

Laboratory data:

detection of parasites in a thick drop of blood (at least 3-4 glass slides with thick strokes) and in a normal smear (2-4 slides).

This means that the number of malaria parasites in the field of view when viewed significantly increased.
A thick drop corresponds to approximately 60-80 fields of view of a thin smear, thereby reducing viewing time.



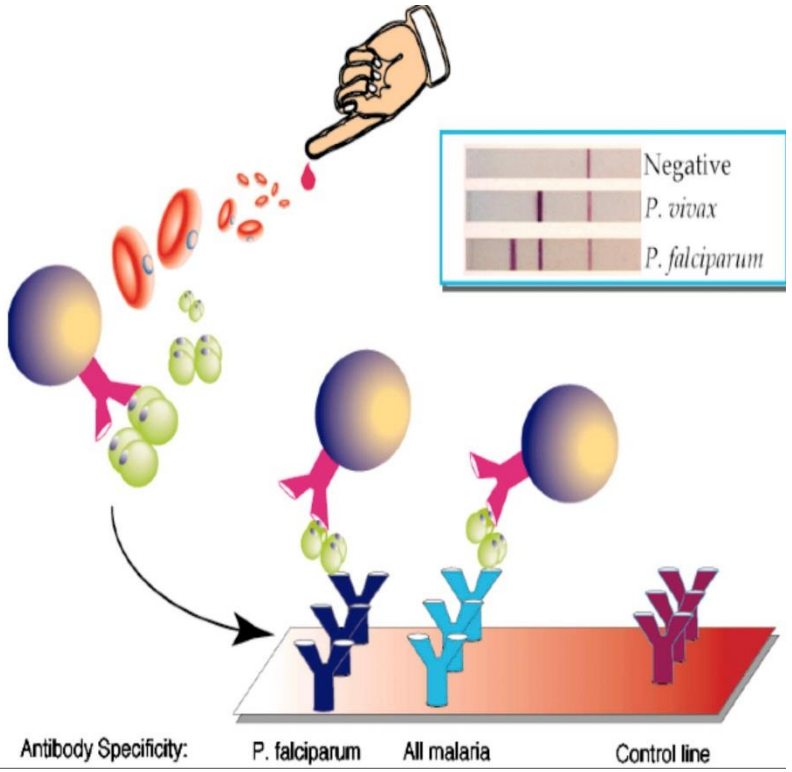
Species / Stages	P. Falciparum	P. Vivax	P. Malariae	P. Oval
Ring Stage				
Trophozoite				
Schizont				
Gametocyte				

Additionally determine:

the presence of malarial antibodies in dynamics in the reactions of indirect hemagglutination or enzyme-labeled antibodies.

In recent years, enzyme immunoassay has been develop to detect specific parasite proteins.

Malaria is also diagnosed using polymerase chain reaction (PCR) which is especially valuable with a low content of plasmodia in the blood.



DIFFERENTIAL DIAGNOSTICS

flu
typhoid-paratyphoid diseases
brucellosis
foodborne infection
leptospirosis
sepsis
phlebotomic fever
visceral leishmaniasis
in the presence of jaundice:
with viral hepatitis
yellow fever.
Malaria coma is differentiated from hepatic,
diabetic
uremic
cerebral.

All patients and parasitic carriers are subject to hospitalization.

They can be placed in any department, most often in a ward-type department, designed for examination and treatment of various patients, except acute infections (sorting department). Reconvalescents are discharged from the department after the disappearance of seizures, normalization of the peripheral blood picture and in the absence of malarial plasmodia in the blood.

Treatment

- Treatment for malaria depends on several factors: the species of malaria causing infection, severity of infection, the age of the infected individual…
- There are several families of drugs used to treat malaria:
  * *Chloroquine* (therapy and prophylaxis)
  * *Quinine* (Therapy only)
  * *Doxycycline* (Therapy and prophylaxis)

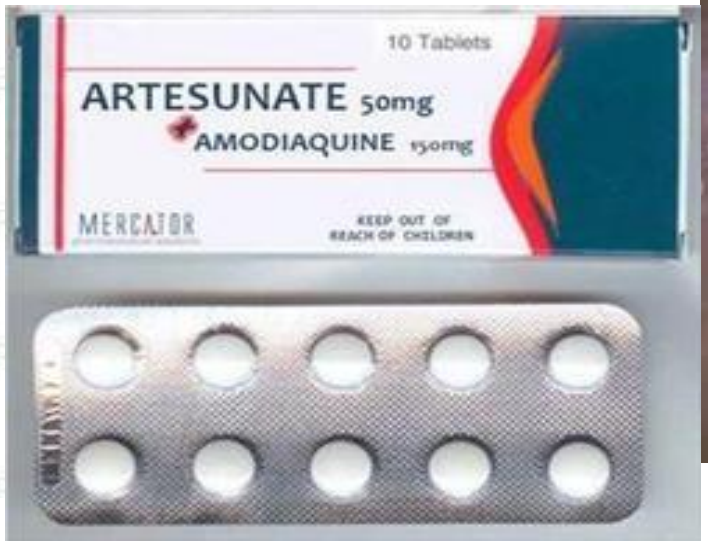
Treatment of MALARIA

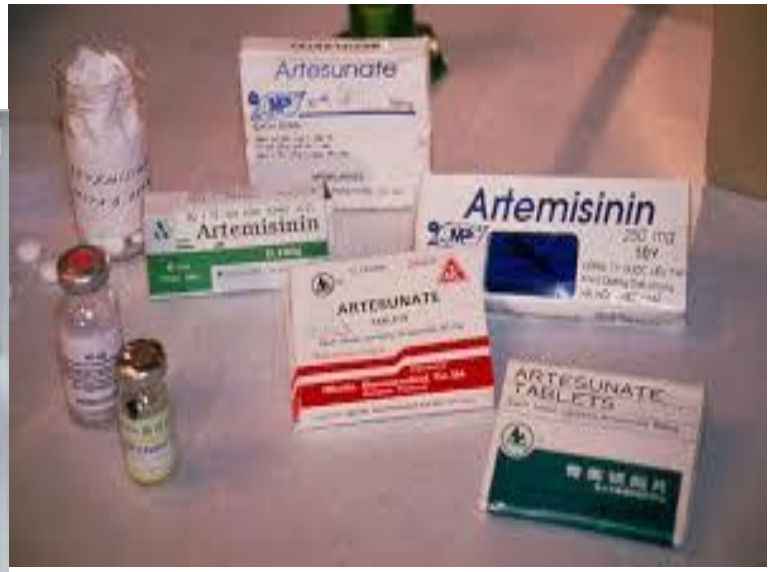
VIVAX	Chloroquine for 3days + Primaquine for 14days	
FALCIPARUM	Artemether for 3days + Lumefantine for 3days + Primaquine single dose on Day2	Artemether for 3days + Sulfadoxine 3d +Pyridoxine 3d + Primaquine single dose on Day2
MIXED INFECTION	Same as falciparum + Add primaquine for 14days	
SEVERE FALCIPARUM MALARIA	DOC: Artesunate i.v for 48hrs followed by oral ACT	In pregnancy : Quinine i.v for 48hrs followed by Quinine + Doxycycline/clindamycin


Lariam® 250 mg
Mefloquine
250 mg
8 Tablets
from 2015 The Guardian


Quinine Sulphate Tablets BP 300 mg
Quinestar
10 x 10 TABLETS


Fansidar®
(Sulfadoxine
+ Pyrimethamine)
500+25 mg
15ml
Syrup
Antimalarial
Martin Dow


10 Tablets
ARTESUNATE 50mg
AMODIAQUINE 150mg
MERCATOR
KEEP OUT OF REACH OF CHILDREN


Artesunate
Artemisinin
Artemisinin
ARTESUNATE
ARTESUNATE TABLETS

Quinine is a typical protoplasmic poison.
It blocks the enzymatic and biochemical processes of the cell.
Due to the effect on the thermal center, quinine has an antipyretic effect.
Quinine is used for atrial fibrillation and tachycardia.

In toxic doses, quinine depresses the cerebral cortex, causing dizziness, vomiting, etc. For the treatment of malaria and its prevention, quinine is prescribed mainly by mouth, with severe forms of malaria as an injection. Quinine has a specific effect on pathogens of malaria, affecting asexual forms of plasmodium, causing attacks of malaria; quinine does not affect and does not prevent relapse on the sexual and tissue stages of the parasite.

PREVENTION

Antimalarial measures may be targeted against the carrier and against the pathogen

The fight against the carrier is carried out by destruction adult mosquitoes and their larvae.

The most effective treatment of premises with persistent insecti

Hexachloran

Dieldrin

Malantion et al.

For individual prevention, the careful implementation of measures to protect housing from mosquito infestation and the use of individual protective equipment (ointments, creams, protective nets, etc.) are also important.

Prophylactic drugs

A number of drugs used to treat malaria can also be used for prevention. Typically, these medications are taken daily, or weekly, in a lower dose than for treatment. Preventive drugs are usually used by people visiting areas at risk of malaria and are almost never used by the local population due to the high cost and side effects of these drugs.

Modern medicines for prevention include mefloquine (Lariam®), doxycycline and atovaquone-proguanil hydrochloride (bigumal, Malaron®).

The choice of drug usually depends on the resistance of parasites in the area and side effects. The preventive effect does not start immediately, so you should start taking preventive drugs 1-2 weeks before arrival in the danger zone and 1-4 weeks after returning.