MALARIA

Core Course: Medical Microbiology
M.Sc., Microbiology
II Semester
Course Code: 24 MICCC5A

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WHAT IS MALARIA

- **Malaria is a serious and sometimes fatal disease caused by a parasite that commonly infects a certain type of mosquito which feeds on humans**

Malaria Definition

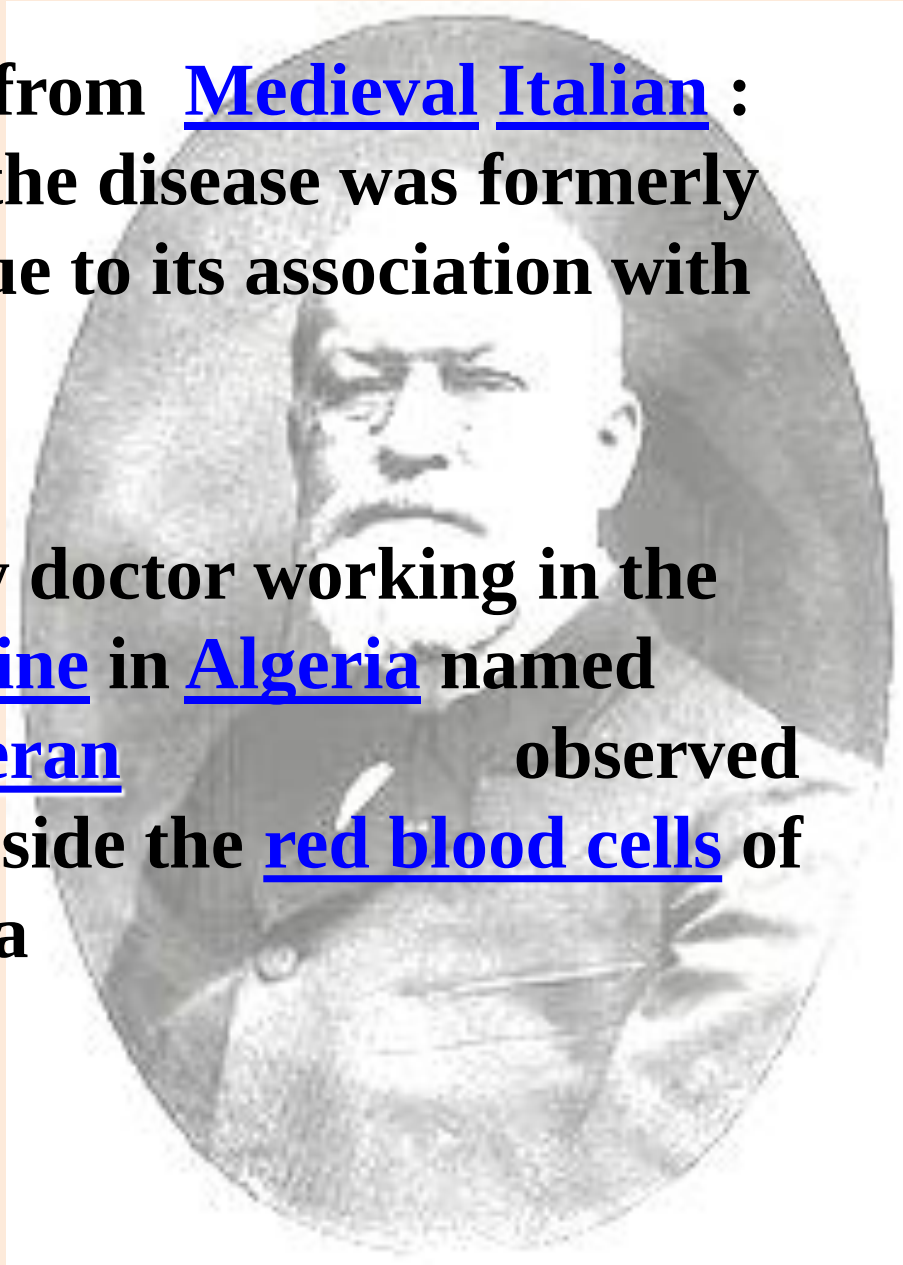
- **Malaria** is a **vector**-borne **infectious disease** caused by **protozoan parasites**

- **Malaria is caused by a parasite called Plasmodium, which is transmitted via the bites of infected mosquitoes.**
- **In the human body, the parasites multiply in the liver, and then Infect red blood cells.**

HISTORY

- **The term malaria originates from Medieval Italian : *mala aria* — "bad air"; and the disease was formerly called ague or marsh fever due to its association with swamps and marshland.**

- **In 1880, when a French army doctor working in the military hospital of Constantine in Algeria named Charles Louis Alphonse Laveran observed parasites for the first time, inside the red blood cells of people suffering from malaria**



- **Plasmodium falciparum causes Malignant tertian estivo – autumnal of Falciparum Malaria.**
- **Falciparum derived by Welch from**

"Falx " ***means*** **Sickle or Crescent and**

"Parere " means Bring forth

Habitat:

Parenchyma cells of liver, R.B.C.

Morphology

Stages in Human:

Liver: Liver stage Schizont

R.B.C: Trophozoite or ring form, Schizont and Gametocyte

Stages in Mosquito:

Ookinete

Oocyst

Sporozoite

CULTURE

- **Bass and Johns – First invitro cultivation.**
- **Trager and Jensen – Cultivate and Maintain in Human Blood Cells ,**
- **The culture medium consists of RPMI 1640 medium –**

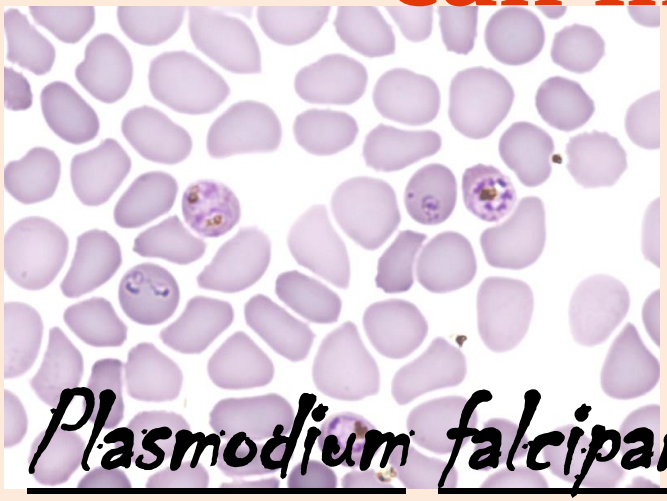
a thin layer of

Stationary human blood cells and

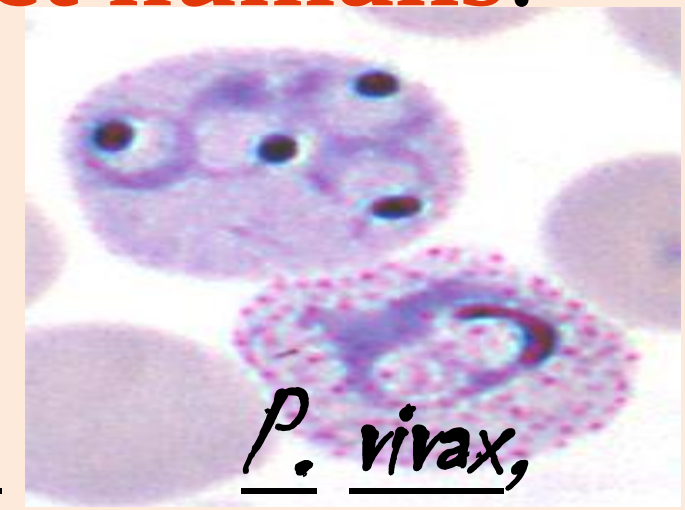
Over lay of Human Serum-

Maintained under 7% CO_2 and 1% O_2

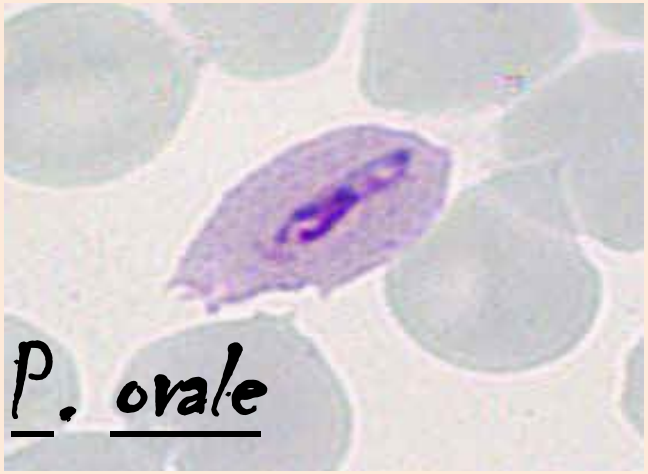
Four kinds of malaria parasites can infect humans:



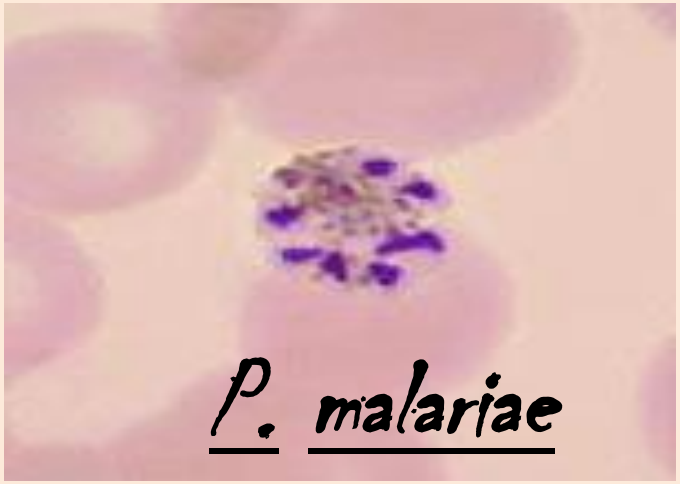
Plasmodium falciparum



P. vivax,



P. ovale



P. malariae

How is malaria transmitted?

- **Usually, people get malaria by being bitten by an infective female *Anopheles* mosquito.**
- **Only *Anopheles* mosquitoes can transmit malaria and they must have been infected through a previous blood meal taken on an infected person.**
- malaria can also be transmitted through blood transfusion, organ transplant, or the shared use of needles or syringes contaminated with blood.
- Malaria may also be transmitted from a mother to her unborn infant before or during delivery ("congenital" malaria). Because the malaria parasite is found in red blood cells of an infected person

Global distribution of MALARIA

- **It is widespread in tropical and subtropical regions, including parts of the Americas, Asia, and Africa.**
- **Each year, there are approximately 515 million cases of malaria, killing between one and three million people, the majority of whom are young children in Sub-Saharan Africa.**
- **Ninety percent of malaria-related deaths occur in Sub-Saharan Africa.**

Human Cycle

- **Exo- Erythrocytic Schizogony**
- **Erythrocytic Schizogony**
- **Gametocytogenisis**

Mosquito Cycle

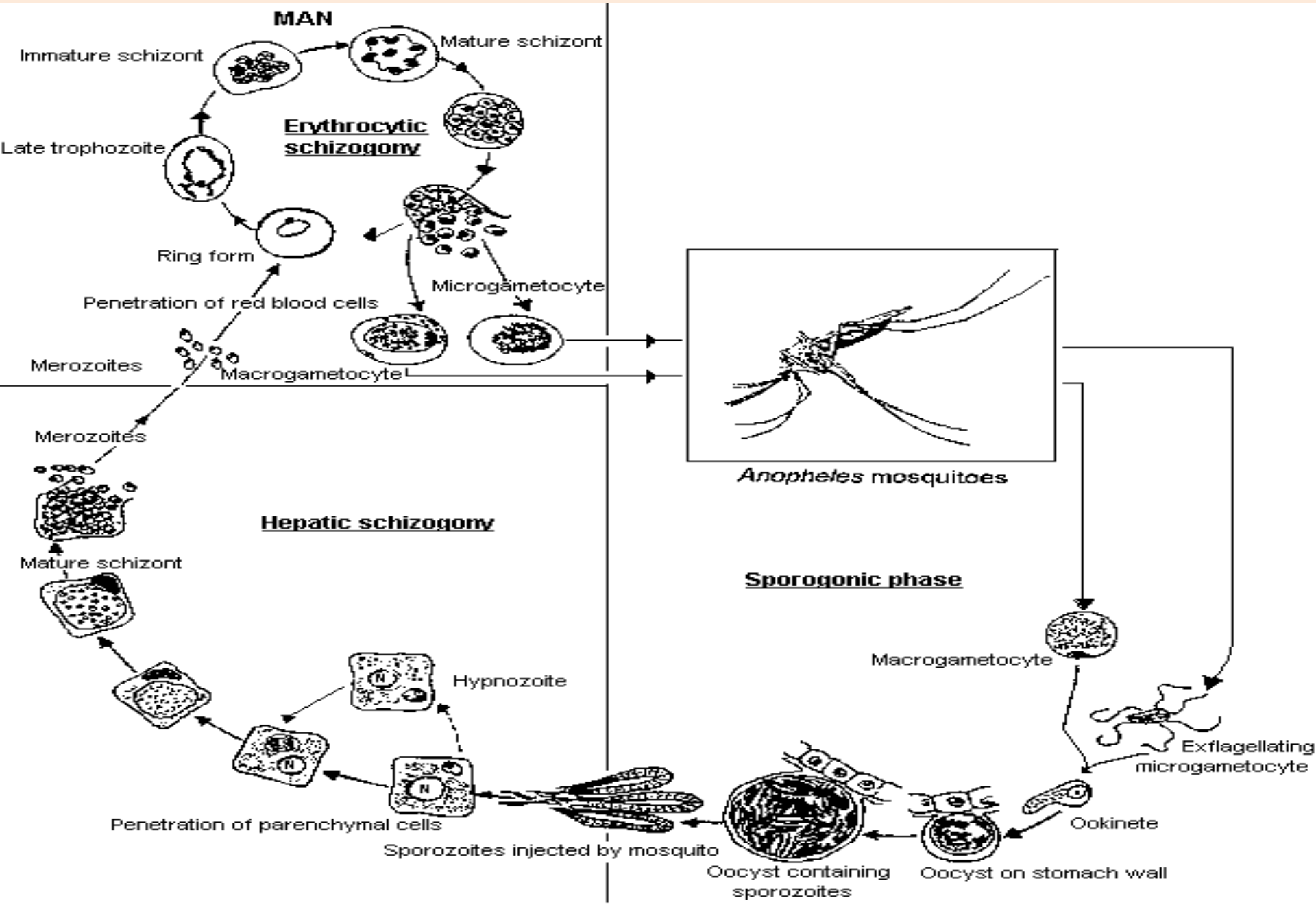
- Sporogony

Tissue schizogony (Pre- erythrocytic schizogony):

- Within half an hour, the sporozoites reach the liver and invade the liver cells. .
- Within the liver cells, the trophozoites start their intracellular asexual division. At the completion of this phase, thousands of extra erythrocytic merozoites are released from each liver cell.
- The time taken for the completion of the tissue phase is variable, depending on the infecting species

Pre-patent period.

- *8 - 25 days for P. falciparum,*
- *8 - 27 days for P. vivax,*
- *9 - 17 days for P. ovale,*
- *15 - 30 days for P. malariae)*
- *and this interval is called as pre-patent period.*



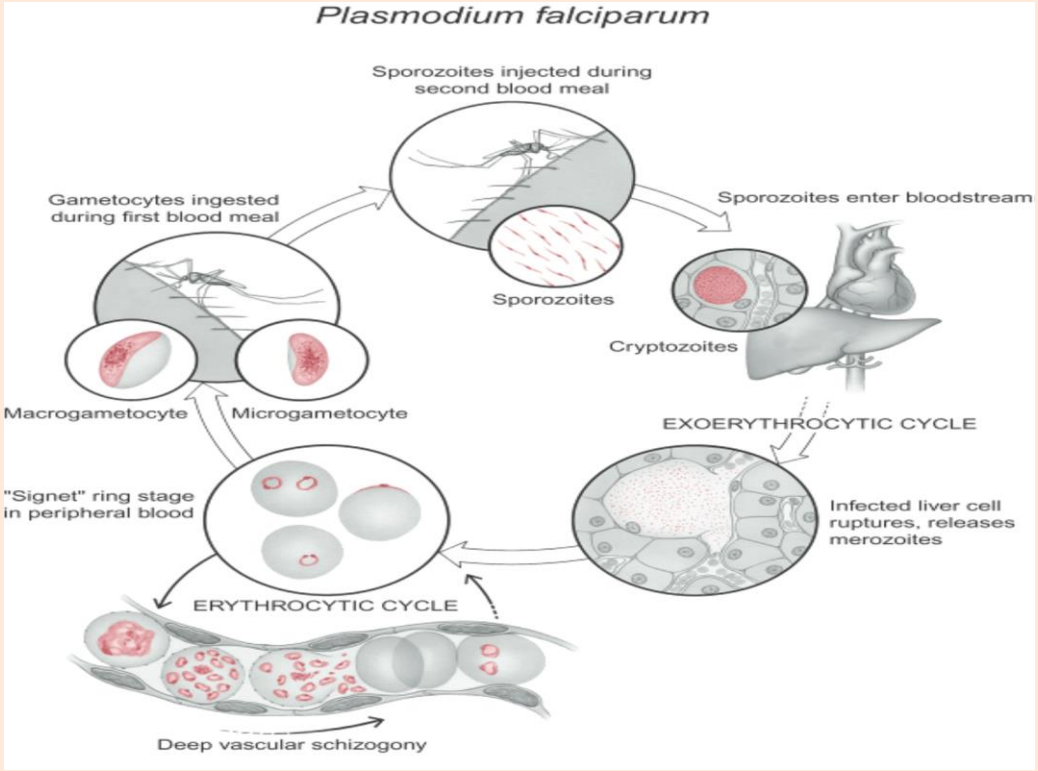
LIFE CYCLE of *PLASMODIUM* spp.

Adapted and redrawn from NCDC

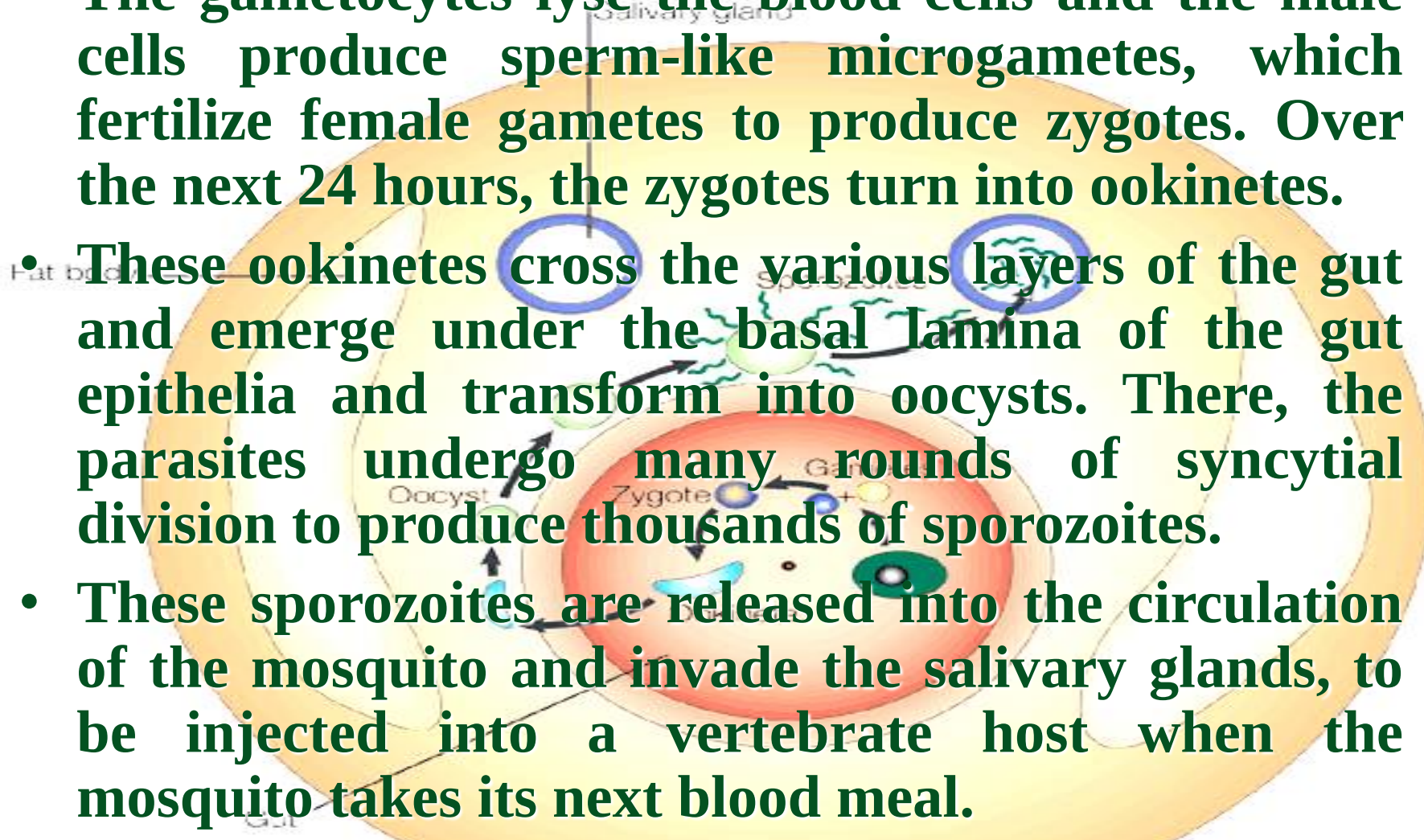
Sexual phase in the mosquito

Sporogony:

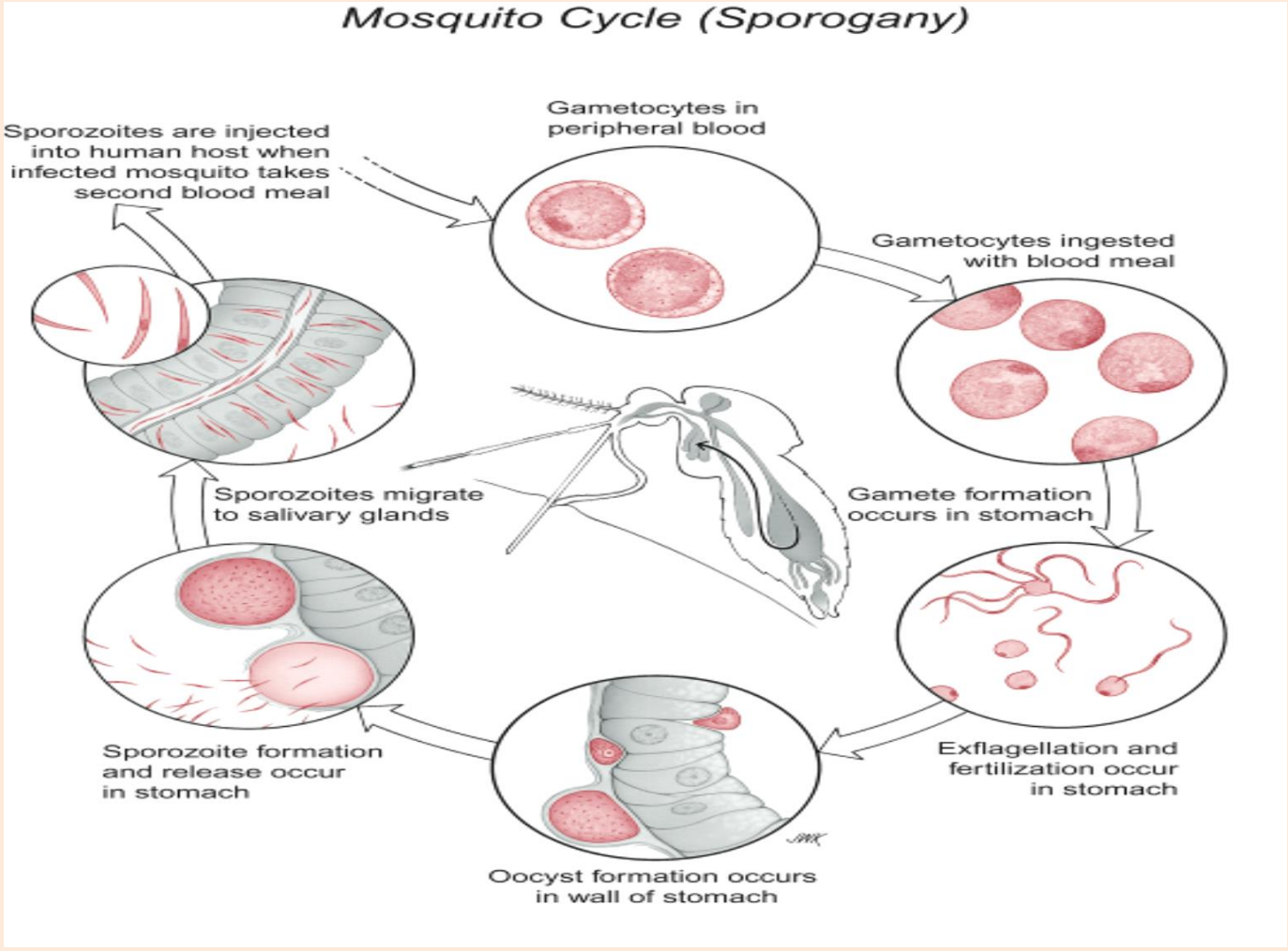
- **The gametocytes continue their development in the mosquito. The male and female gametes fuse and form into a zygote.**
- **This transforms into an ookinete which penetrates the gut wall and becomes an oocyst. The oocyst divides asexually into numerous sporozoites which reach the salivary gland of the mosquito.**
- **On biting a man, these sporozoites are inoculated into human blood stream.**
- **The sporogony in the mosquito takes about 10 - 20 days and thereafter the mosquito remains infective for 1 - 2 months.**


Plasmodium falciparum
Sporozoites injected during second blood meal
Sporozoites enter bloodstream
Sporozoites
Cryptozoites
Gametocytes ingested during first blood meal
Macrogametocyte
Microgametocyte
EXOERYTHROCYTIC CYCLE
"Signet" ring stage in peripheral blood
Infected liver cell ruptures, releases merozoites
ERYTHROCYTIC CYCLE
Deep vascular schizogony

- The gametocytes lyse the blood cells and the male cells produce sperm-like microgametes, which fertilize female gametes to produce zygotes. Over the next 24 hours, the zygotes turn into ookinetes.
- These ookinetes cross the various layers of the gut and emerge under the basal lamina of the gut epithelia and transform into oocysts. There, the parasites undergo many rounds of syncytial division to produce thousands of sporozoites.
- These sporozoites are released into the circulation of the mosquito and invade the salivary glands, to be injected into a vertebrate host when the mosquito takes its next blood meal.
- The development of the parasite in the mosquito is completed in about two weeks.

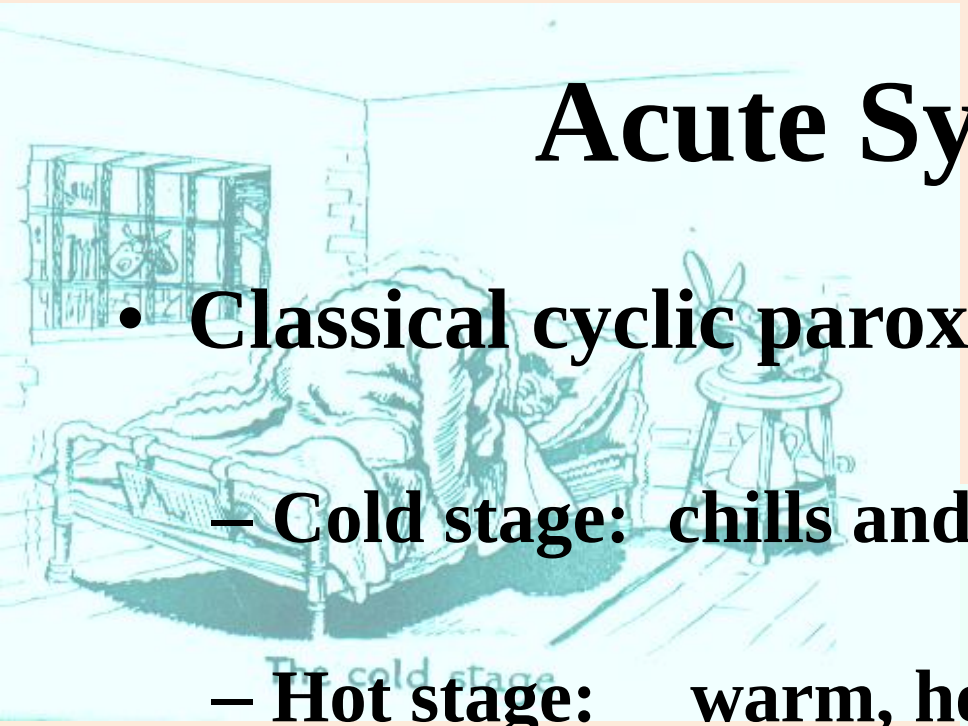


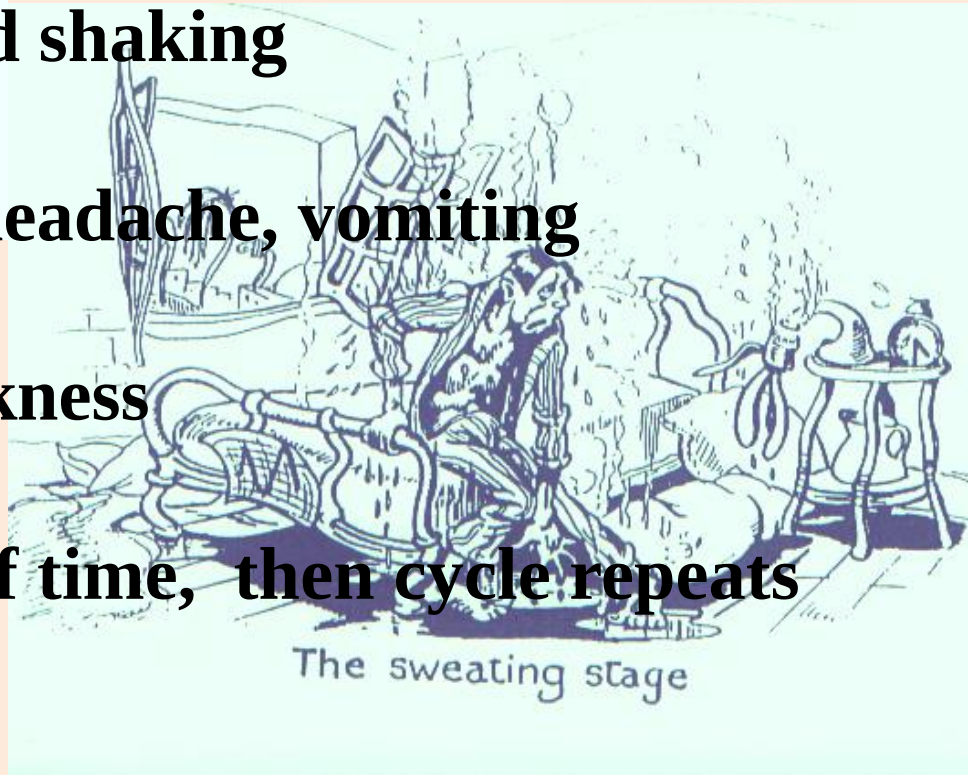
Nature Reviews | Genetics


Mosquito Cycle (Sporogany)
Gametocytes in peripheral blood
Sporozoites are injected into human host when infected mosquito takes second blood meal
Gametocytes ingested with blood meal
Sporozoites migrate to salivary glands
Gamete formation occurs in stomach
Sporozoite formation and release occur in stomach
Exflagellation and fertilization occur in stomach
Oocyst formation occurs in wall of stomach

Acute Symptoms

- **Classical cyclic paroxysm:**
  - **Cold stage: chills and shaking**
  - **Hot stage: warm, headache, vomiting**
  - **Sweating stage: weakness**
  - **Feel well for period of time, then cycle repeats itself**





Malaria Symptoms

- **Symptoms of malaria include fever and flu-like illness, including shaking chills, headache, muscle aches, and tiredness. Nausea, vomiting, and diarrhea may also occur.**
- **Malaria may cause anemia and jaundice (yellow coloring of the skin and eyes) because of the loss of red blood cells. Symptoms usually appear between 10 and 15 days after the mosquito bite. If not treated, malaria can quickly become life-threatening by disrupting the blood supply to vital organs.**
- **Infection with one type of malaria, *Plasmodium falciparum*, if not promptly treated, may cause kidney failure, seizures, mental confusion, coma, and death. In many parts of the world, the parasites have developed resistance to a number of malaria medicines.•**
- **Symptoms occur 6-14 days after infection**

- **Fever**
- **Rigors**
- **Headaches**
- **Sweating**
- **Tiredness**
- **Myalgia (limbs and back)**
- **Abdominal pain**
- **Diarrhea**
- **Loss of appetite**
- **Orthostatic hypotension**
- **Nausea**
- **Slight jaundice**
- **Cough**
- **Enlarged liver and spleen (sometimes not palpable)**
- **Vomiting**

Pathogenesis

- **Destruction of erythrocytes; anemia**
- **Liberation of parasite and erythrocyte material into circulation**
- **Host reaction to these events (multiple organ system disease, acidosis in acute disease)**
- ***P. falciparum* has unique sequestration in microcirculation of vital organs interfering with flow and tissue metabolism**
- **Long-term effects of repeated infections - learning**
- **deficit, spontaneous abortion, reduced growth rates; all may be due to prolonged acidosis**

Pathogenesis of various syndromes associated with MALARIA

- **Fever: The activated Macrophages produce Mono nuclear cell derived Cytokines, Interleukin I, and Tumor Necrosis Factor Which cause Fever, Chill and Sweat.**
- **Anaemia**
- **Blackwater Fever**
- **Cerebral Malaria, Pulmonary Odema, Acute Failure**
- **Hypoglycemia**

Pathological Changes in Various Organs.

- **Liver: Enlarged, in Chronic cases: Pigmented. Kuffer cells are increased and filled with Parasites, Parasite pigmentsand cellular debris**

- **Spleen: Enlarged, soft, Rupture may occur in rare. Ague Cake: Greyish, Dark Brown even in Black.**

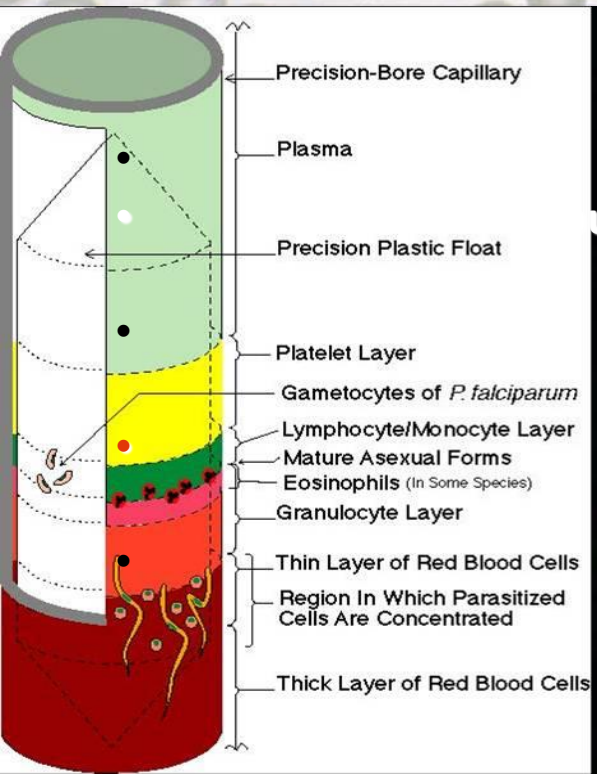
- **Kidney, Adrenal Gland, Bone Marrow, Lung, Stomach, Heart, Brain.**

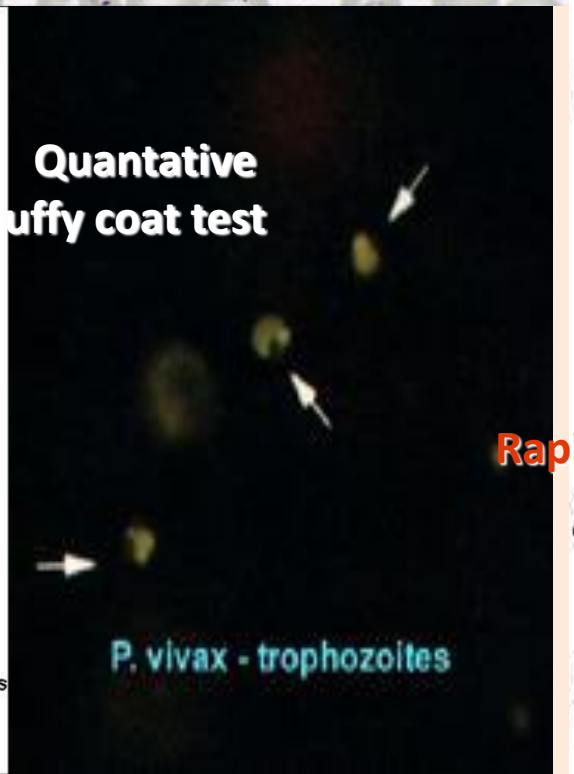
DIAGNOSIS

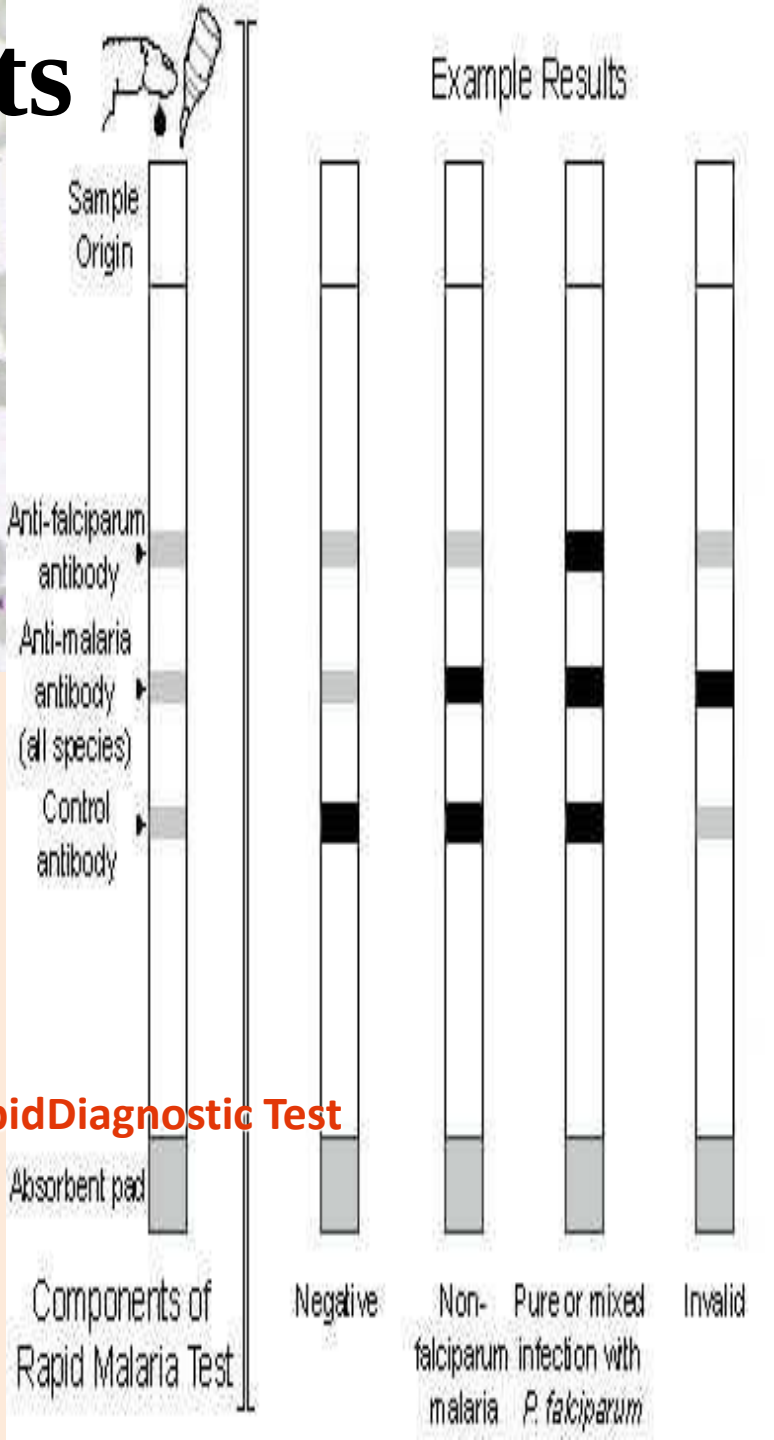
1. Peripheral smear study
2. Quantitative Buffy Coat (QBC) test
3. CBC
   - Anemia
   - Leukopenia, or leukocytosis
   - No eosinophilia
   - Rapid Diagnostic Tests (RDTs)
   - Para Sight F test
   - OptiMal Assay
   - The immuno chromatographic test (ICT Malaria P. f. test)
   - Polymerase Chain Reaction
   - Detection of antibodies by Radio immuno assay, immunofluorescence or enzyme immuno assay

Diagnostic test Results

- **Peripheral smear study Smear**







RapidDiagnostic Test

Treatment

Antimalarial Drugs:

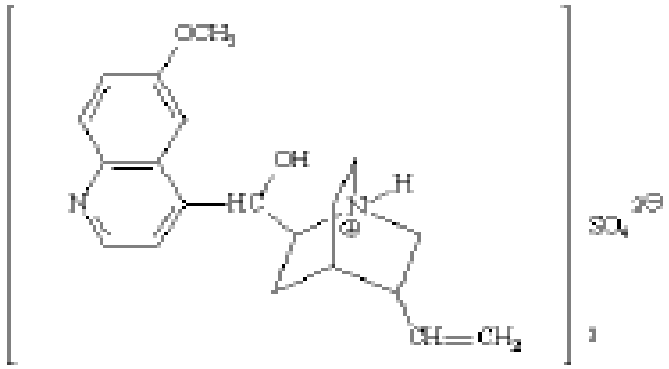
- **Chloroquine 600 mg (2 tabs) initially**
  - **300 mg (1 tab) in 6 hrs 300 mg (1 tab) QD for 2 days**
  - **COMPLICATED OR SEVERE INFECTIONS : I.V. QUINIDINE or quinine**

Sulfadoxine-pyrimethamine (Fansidar®)

- **Mefloquine (Lariam®)**
- **Atovaquone-proguanil (Malarone®)**
- **Quinine**
- **Doxycycline**
- **Artemisin derivatives (not licensed for use in the United States, but often found overseas)**

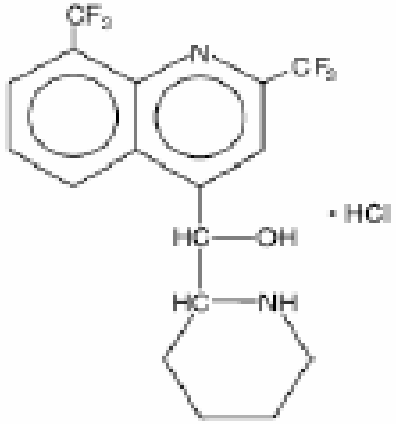
Drugs Of Choice:

A. Parent Compound



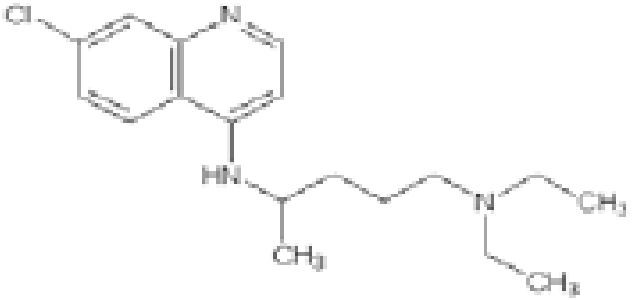
Quinine

C. Newer Derivative



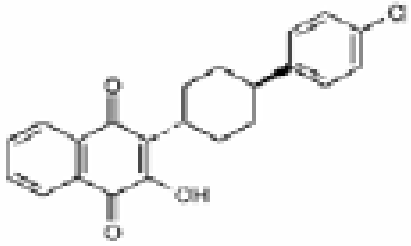
Mefloquine

B. Older Derivative: extensive resistance

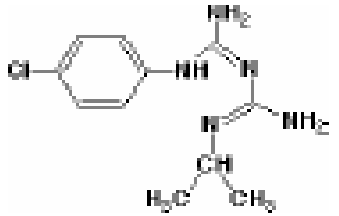


Chloroquine

D. Drugs of choice



Atovaquon



Proguanil

Prevention and Control

- **Elimination of mosquitoes**
- **Drainage of standing water (but agricultural irrigation is becoming more common)**
- **Widespread use of pesticides (DDT was the most effective)**
- **Local use of insecticides in the homePrevention of bites**
- **Appropriate clothing**
- **Insect repelants**
- **Bed nets**
- **most bites occur at dusk and through the night**
- **nest**
- **more effective if treated with insecticide**

Vaccine

- **NYVAC - Pf. 7: This vaccine blocks transmission of the parasite from vertebrate host to mosquitoes**
- **Gamete Vaccine: When the antibodies are taken up by the mosquitoes, gametes escaping the RBCs will be neutralized, thus preventing fertilization and reducing transmission.**
- **Sporozoite vaccines containing CSP, generated by recombinant DNA technology, combined with potent T-cell epitopes for higher immunogenicity seem to inhibit early liver-stages of the parasite**

References

- **Text Book OF Medical Parasitology**
- **www.wikipedia.com**
- **www.malaria.com**
- **www.malariasite.com**
- **www.parasitology.com**