

The Malarias:

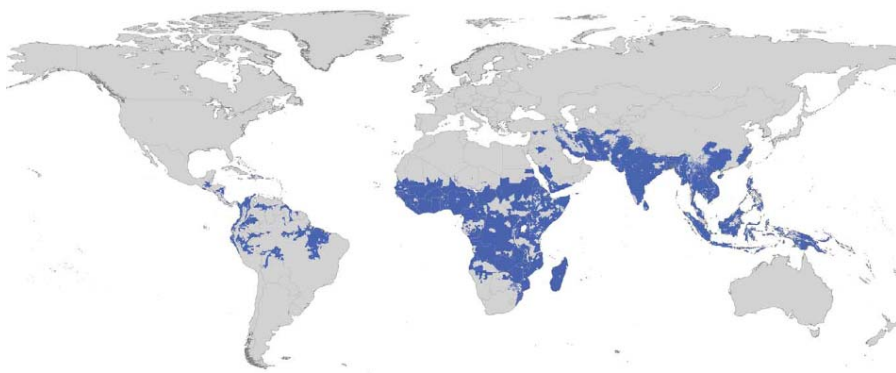
Plasmodium falciparum

Plasmodium vivax

Plasmodium malariae

Plasmodium ovale

Distribution of Plasmodium falciparum



Distribution Of Plasmodium vivax

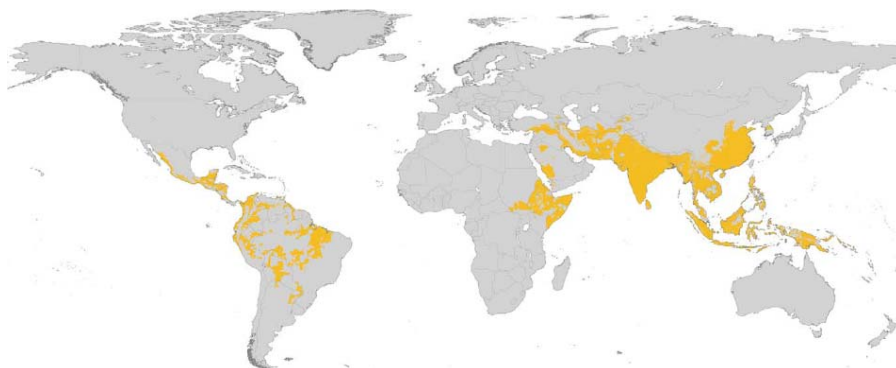
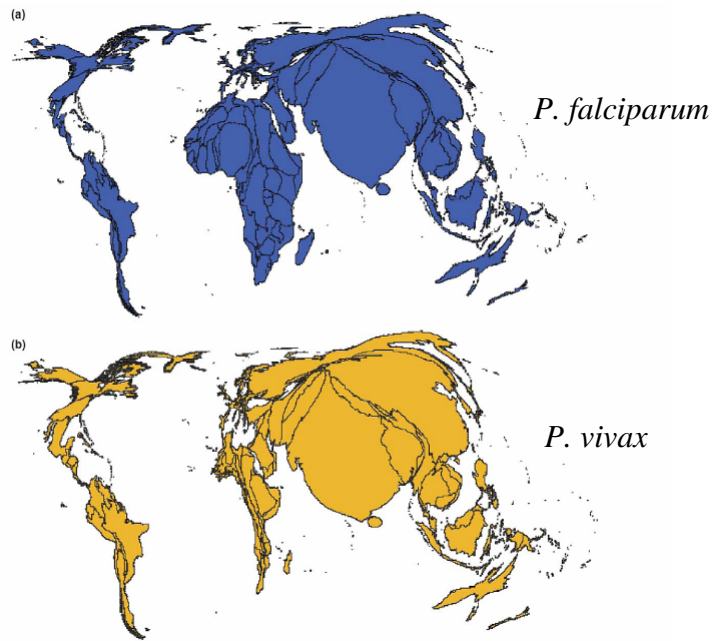


Table 2. PAR of malaria derived from extractions using the global spatial limits for *P. falciparum* and *P. vivax* in 2005

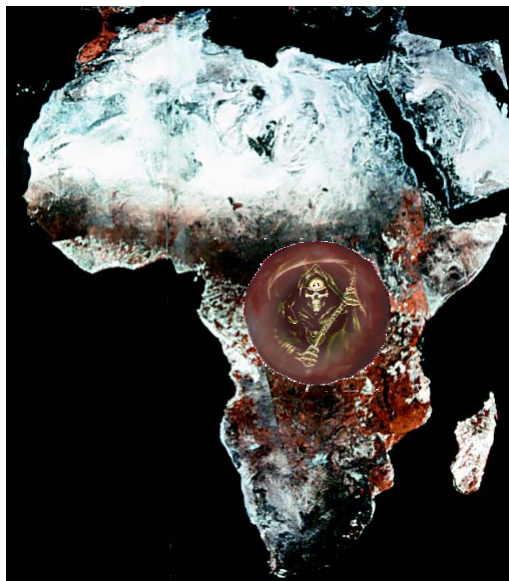
WHO region	<i>P. falciparum</i> risk ^a	<i>P. vivax</i> risk ^a
SEARO	1.252	1.347
AFRO	0.525	0.050
WPRO	0.438	0.890
EMRO	0.245	0.211
AMRO	0.050	0.078
EURO	0.000	0.020
Total	2.510	2.596

^aThe risk is given in billion (1,000,000,000) persons. Abbreviations: WHO, World Health Organization; SEARO, South East Asian Regional Office; AFRO, African Regional Office; WPRO, Western Pacific Regional Office; EMRO, Eastern Mediterranean Regional Office; AMRO, American Regional Office; EURO, European Regional Office.

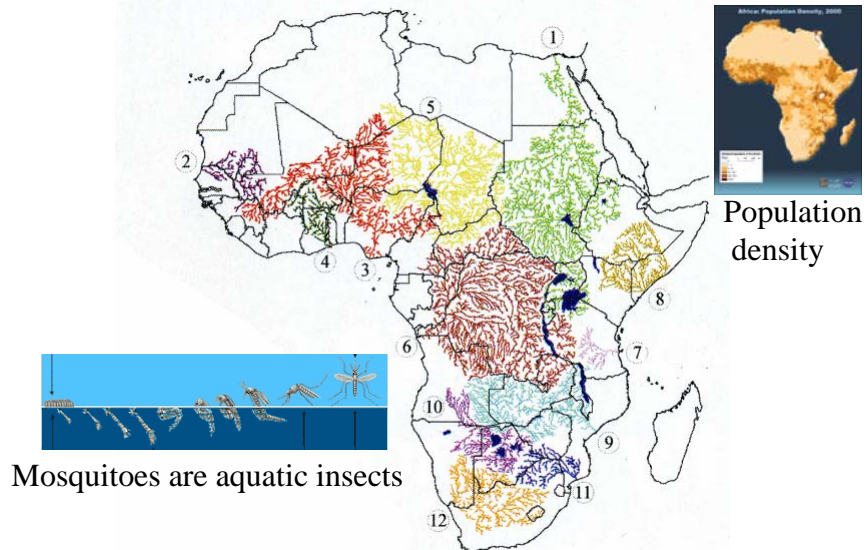
Global Risk By Country-Proportionality Plot



3 million deaths/yr. 1 million in Africa,
mostly children below the age of 5



Watersheds of the African Continent



World Situation

- Approx. 2 billion infections/yr
- Economic and social development reduced
- 27% of the world lies within the malaria transmission zone
- New unstable transmission area: Bangladesh
- Impact of malaria on population change ?



Malarious Area of the United States

1934-5



Malaria put bite on Jersey man

By JANET A. HINES
Staff Writer



A mosquito bite put 19-year-old college student Vincent Battista in the hospital, where doctors diagnosed him with an illness that hasn't been contracted in New Jersey since 1991.

Battista had malaria. "He had a better chance of winning the lottery than contracting malaria," said infectious disease specialist Dr. Patricia Ruggeri-Weigle of Westfield. "There's a one-in-8-million chance of someone in this state contracting malaria without leaving the country."

Centers for Disease Control and Prevention experts said they are aware of Battista's case but are not worried about a widespread outbreak as the mosquito population diminishes at the onset of cooler weather.

"The cold climate is not conducive to ongoing transmission — mosquitoes can't thrive in it," said Dr. Lawrence Baratz of the centers. "By the time health departments identify these cases, transmission has stopped."

The state Department of Health and Senior Services is in the process of confirming the doctors' diagnosis, spokesman Dennis McGowan said.

"Once we confirm that it is malaria, we will try to identify where the mosquito contracted the parasite," McGowan said. "Malaria is not common in New Jersey. The mosquito would have had to pick it up from someone who is infected and doesn't realize it."

The disease attacks red blood cells and is more common in tropical climates. The source is a specific breed of mosquito, called *Anopheles quadrimaculatus*, which is prevalent in New Jersey, McGowan said.

However, cases of the mosquito transmitting the disease are extremely rare in this country, he said.

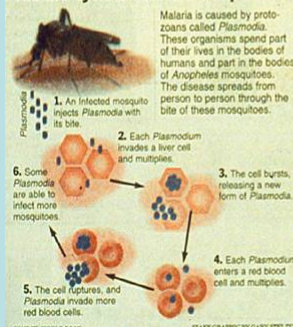
The disease is usually contracted when people travel to countries where there are malaria epidemics and return home with the illness, Baratz said. Most people receive inoculations before they visit those countries.

Each year, the centers receive about 1,200 malaria reports. Ten or fewer are transmitted to people who receive the disease while living in the United States. The last reported cases in New Jersey occurred in Monmouth and Camden counties in 1991, Baratz said.

There are four types of malaria, and some forms are deadly, Ruggeri-Weigle said. In Battista's case, doctors are treating him with a two-week program of drugs to stave off future recurrences. But there is a chance that the malaria will reappear years from now.

Battista of North Plainfield, who was afflicted with malaria, is fully recovered. Left, a graphic describes the life cycle of the malaria parasite.

The life cycle of the malaria parasite



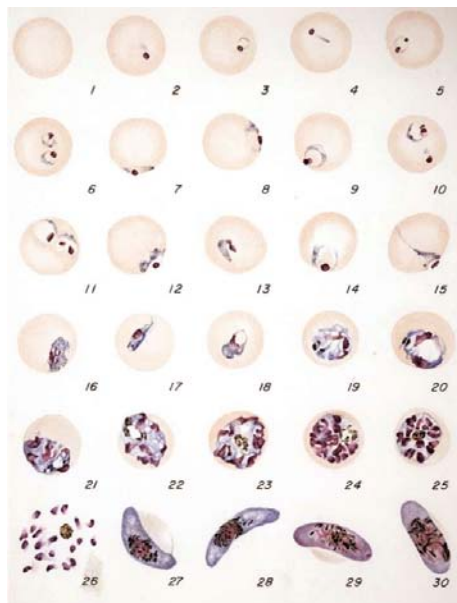
STAFF PHOTO BY MARY SCORSE
Top, Vincent Battista of North Plainfield, who was afflicted with malaria, is fully recovered. Left, a graphic describes the life cycle of the malaria parasite.

See MALARIA, A-4

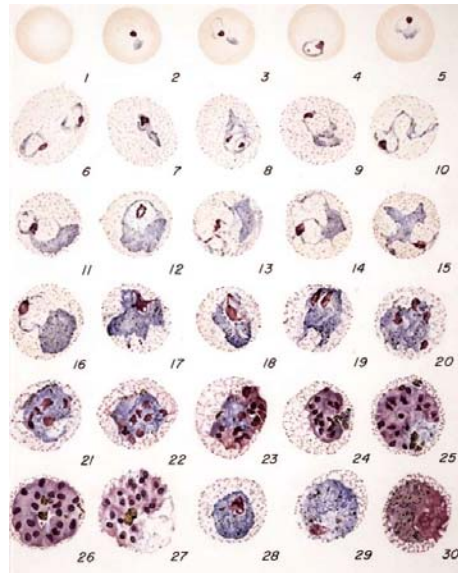
Adult *Anopheles dirus* taking a blood meal from one of the authors (RWG)



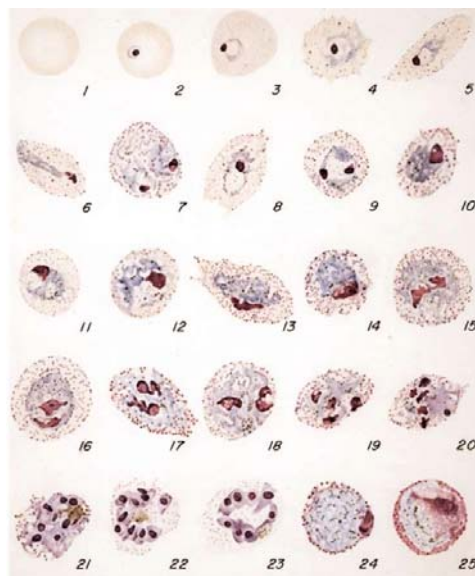
Plasmodium falciparum



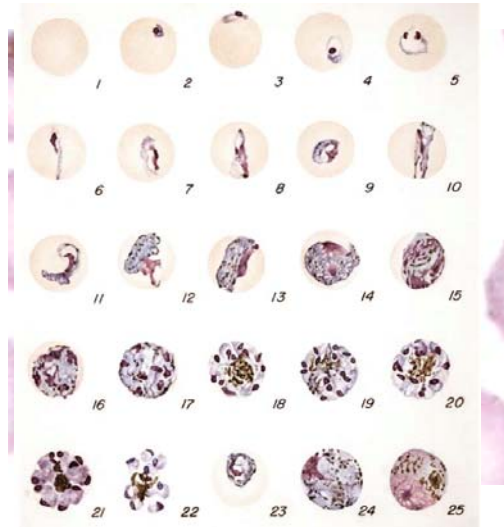
Plasmodium vivax



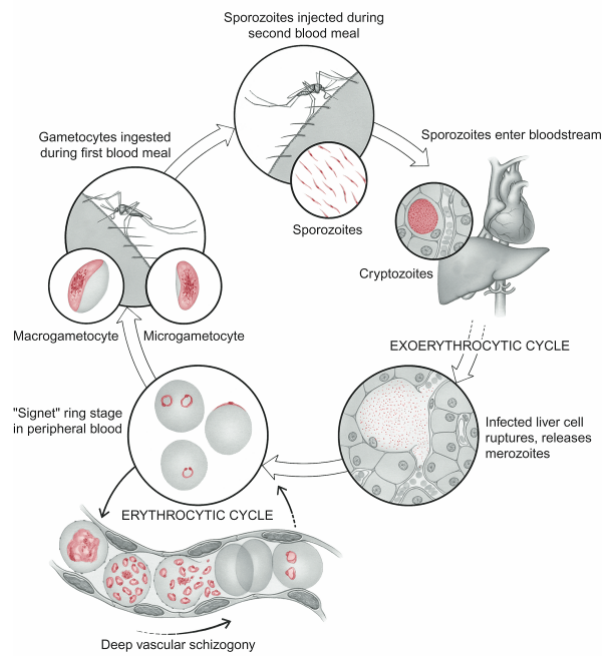
Plasmodium ovale



Plasmodium malariae



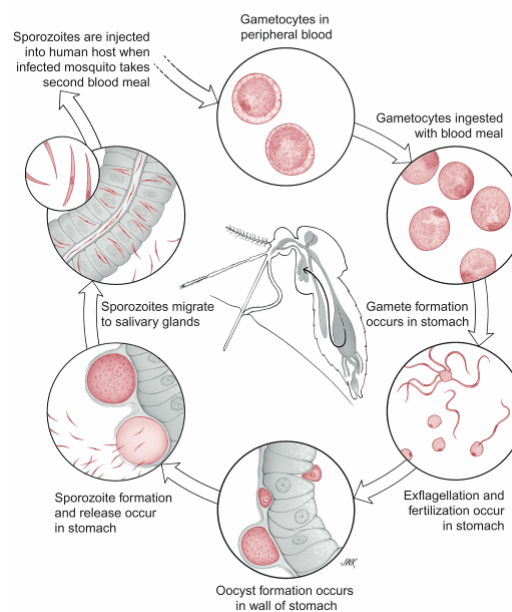
Plasmodium falciparum



Adult *Anopheles dirus* taking a blood meal from one of the authors (RWG)



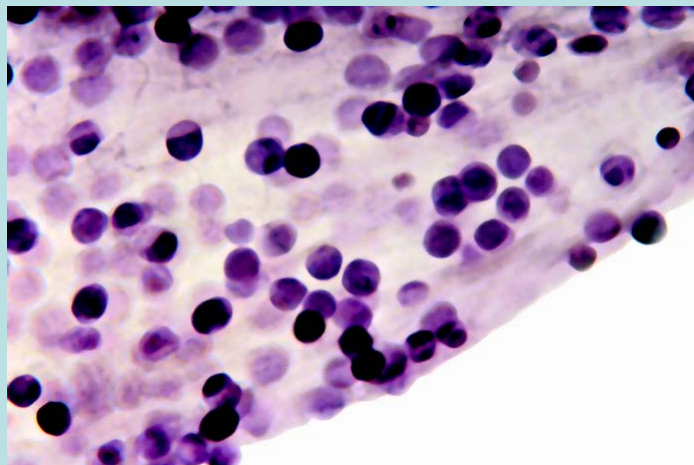
Mosquito Cycle (Sporogony)



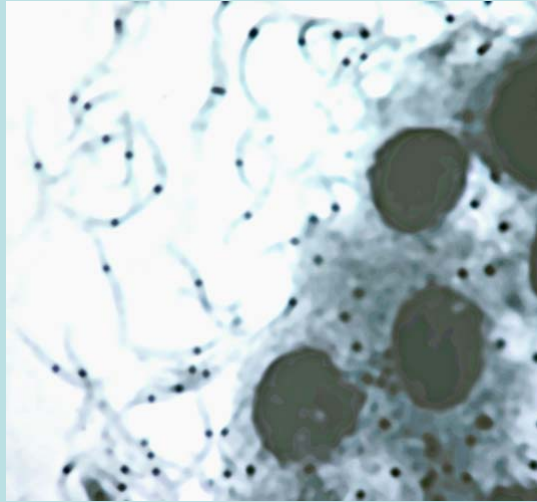
Ex-flagellation of the microgametocyte
of a malaria parasite in mosquito stomach



Portion of an infected mosquito stomach.
Note numerous oocysts on outer wall.



Sporozoites of malaria in infected mosquito stomach preparation

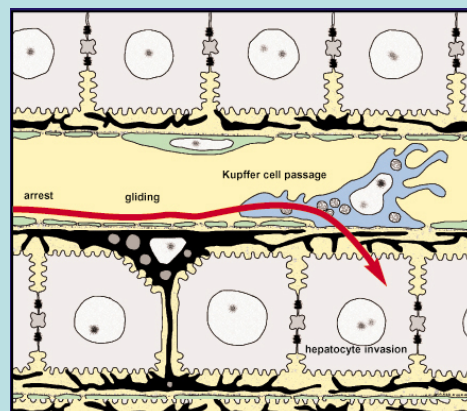


Light micrograph



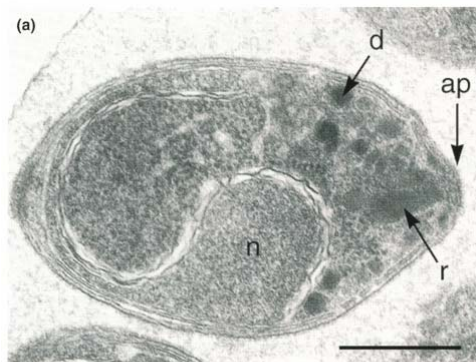
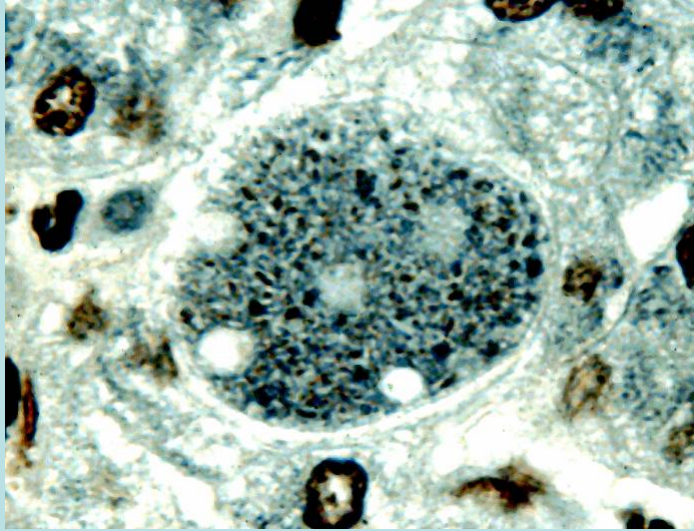
SEM Photo: Photini Simis

Entry Of Sporozoites Into Parenchymal Cells Of The Liver

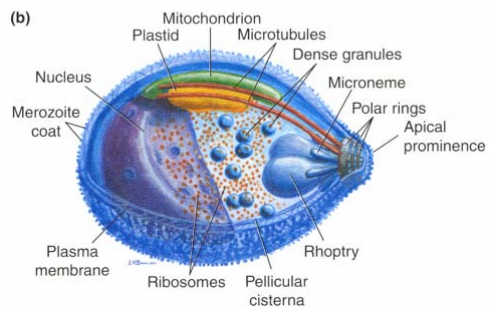


From: Ute Frevert
NYU School of Medicine

Exo-erythrocytic stages of malaria in liver parenchymal cell



Plasmodium Anatomy

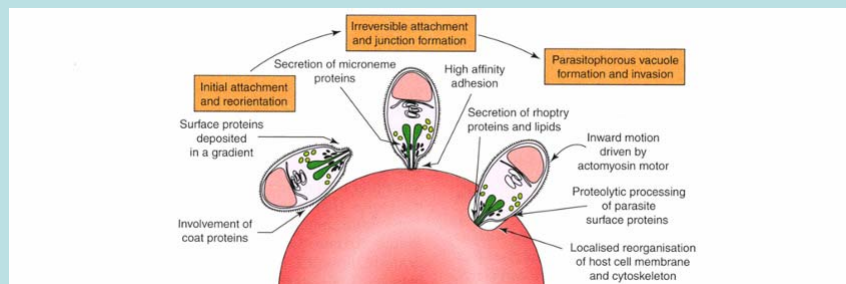


Transmission EM of merozoite entering a red cell.

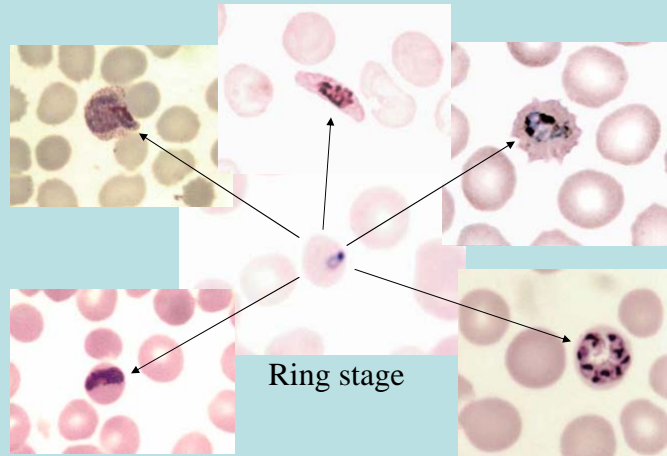
Note points of attachment



Mechanisms of Red Cell Invasion By Plasmodium



Erythrocytic stages of malaria:
All infections begin with the ring stage
regardless of the species

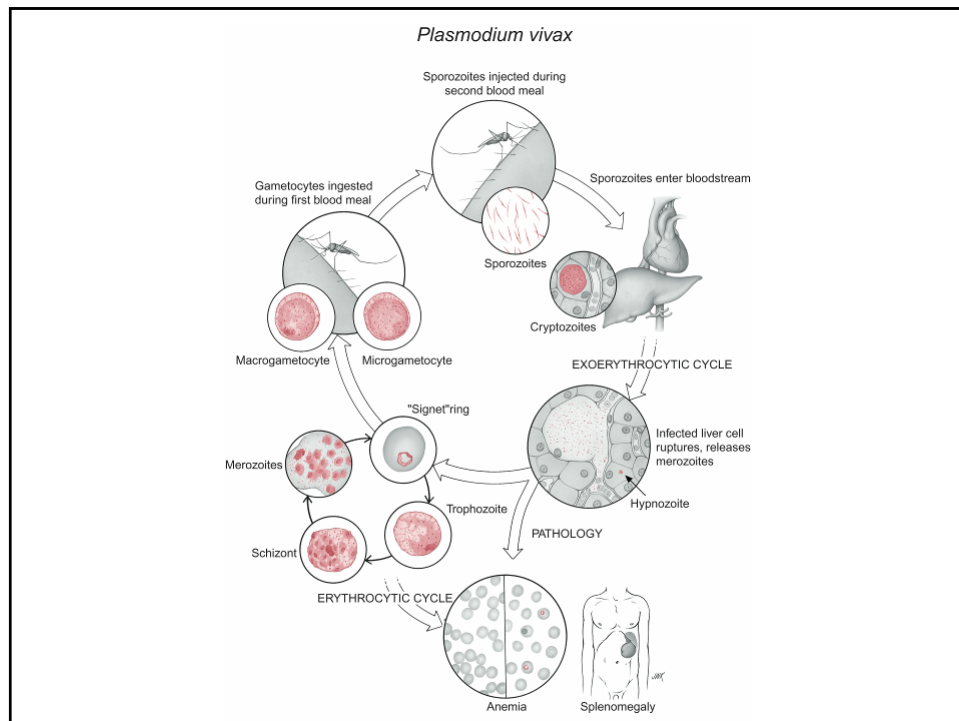


Pathogenesis

- 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 micro-circulation 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**

Clinical Signs & Symptoms

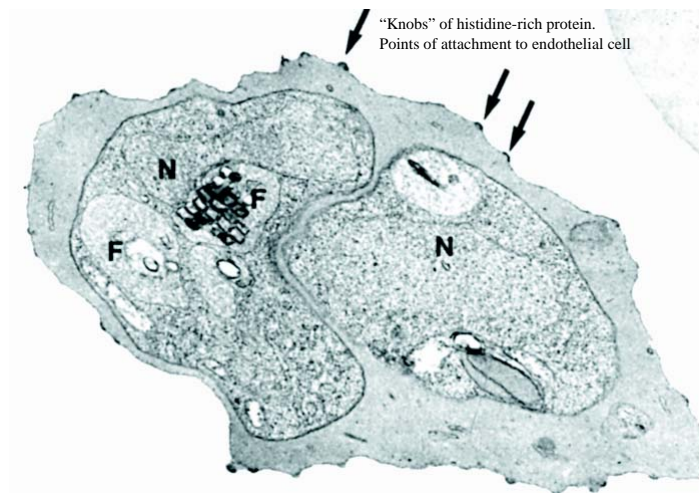
- Fever, paroxysms of shaking chills
- Tertian vs quartan fever pattern
- Symptoms when other organs involved
- Hemolysis: icterus, jaundice, enlarged spleen



Susceptibility to malaria, antibody production, and lethality.

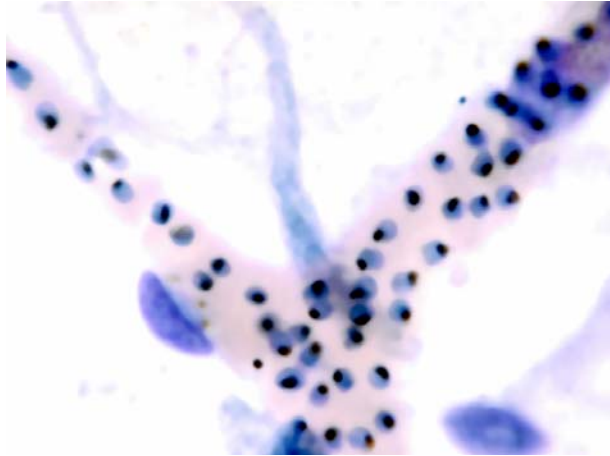


Transmission EM: RBC infected with *P. falciparum*



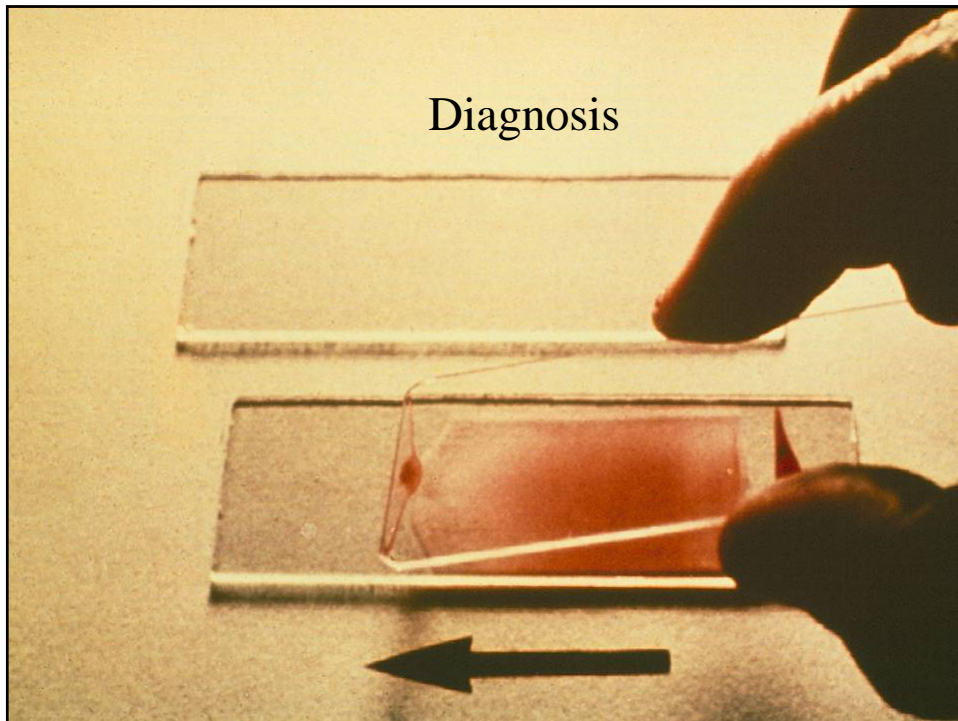
N = Nucleus; F = food vacuole

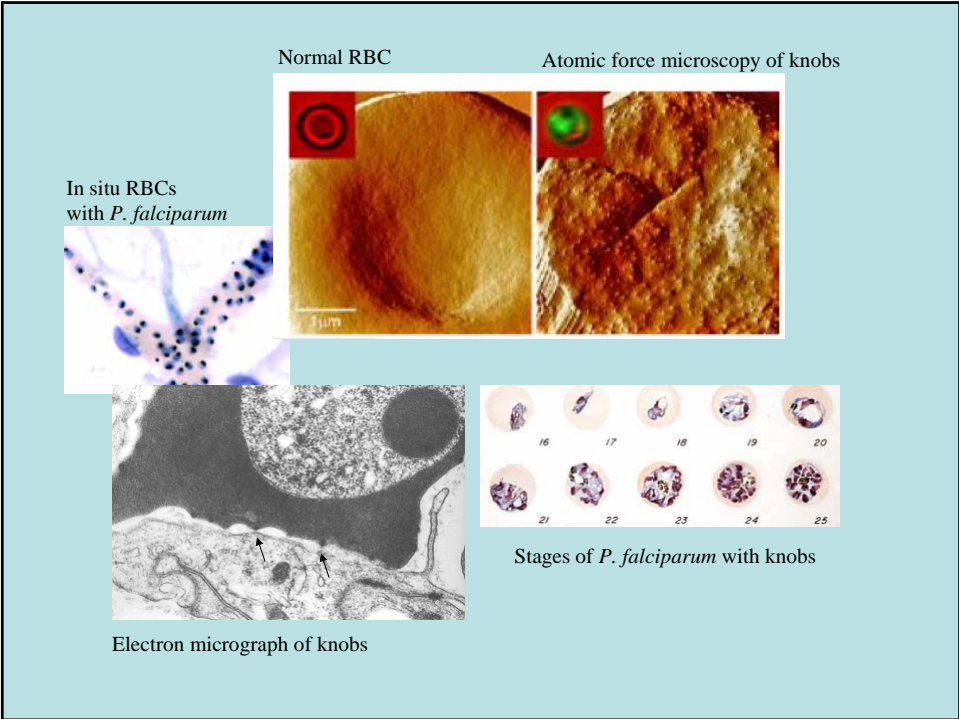
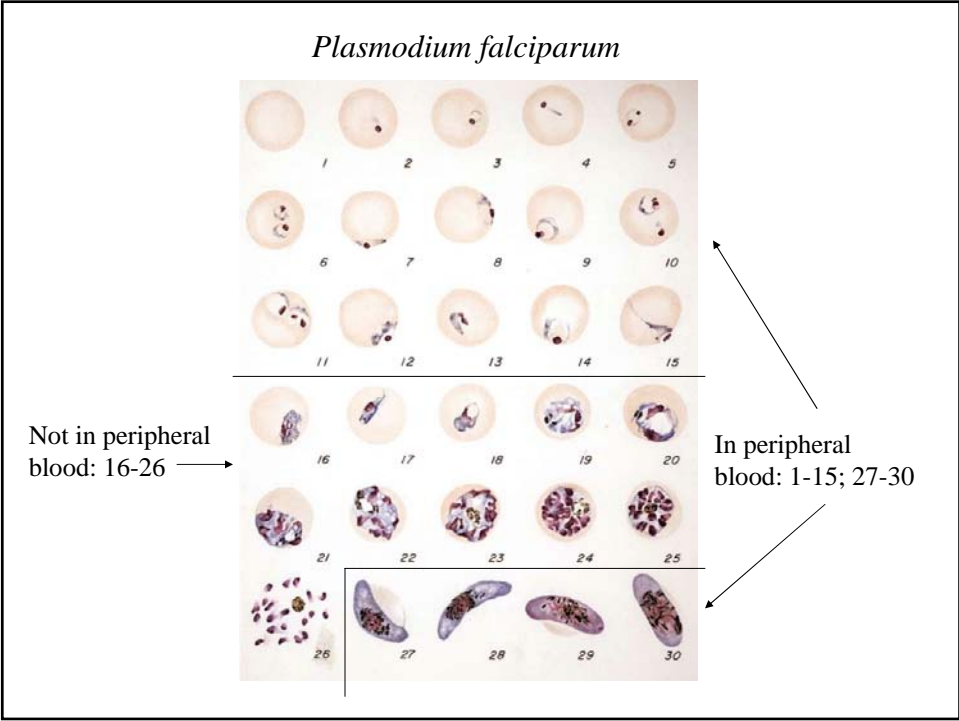
Cerebral malaria: experimental infection in monkey



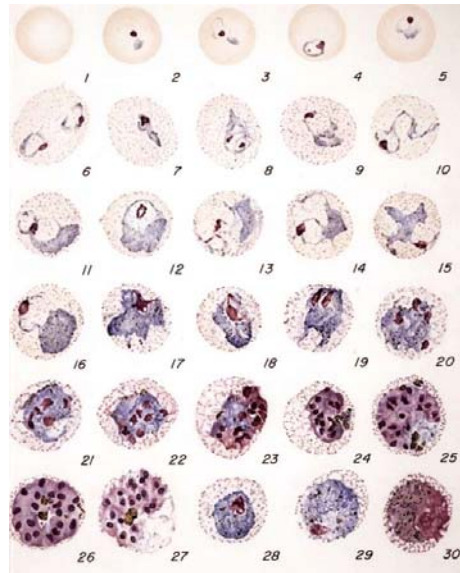
stain: tissue Giemsa

Diagnosis



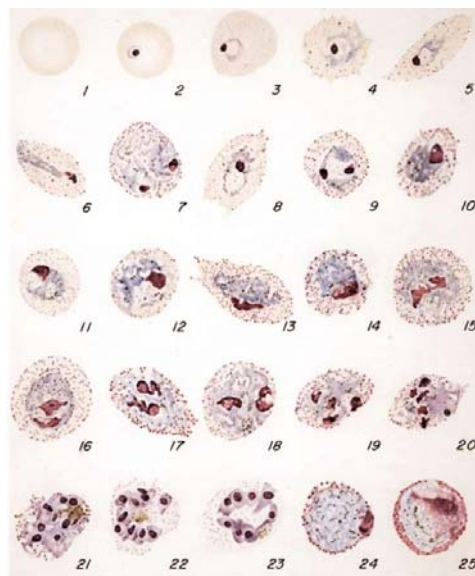


Plasmodium vivax



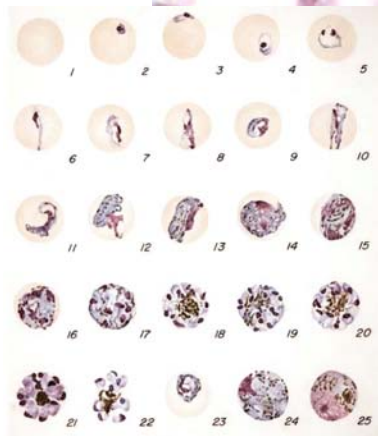
Infected RBCs larger
than non-infected RBCs,
Schüffner's dots

Plasmodium ovale



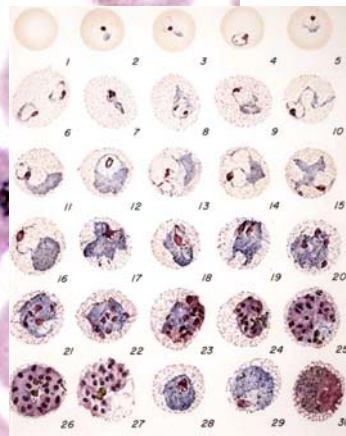
Same as *P. vivax*

Plasmodium malariae



Infected RBCs same size as non-infected RBCs,
No Schüffner's dots

Plasmodium vivax

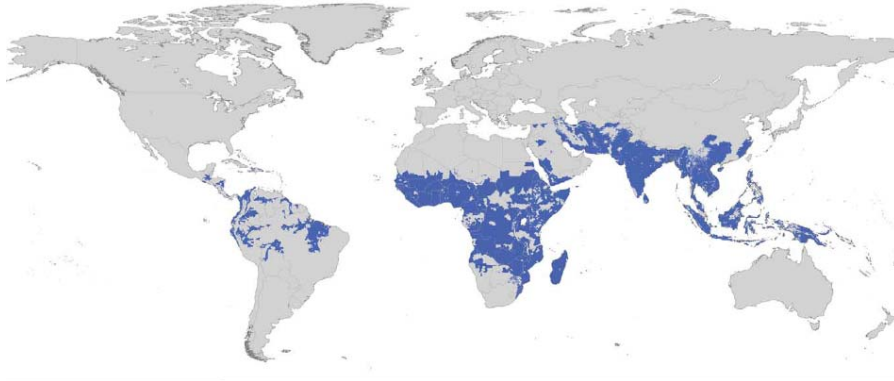


Infected RBCs enlarged

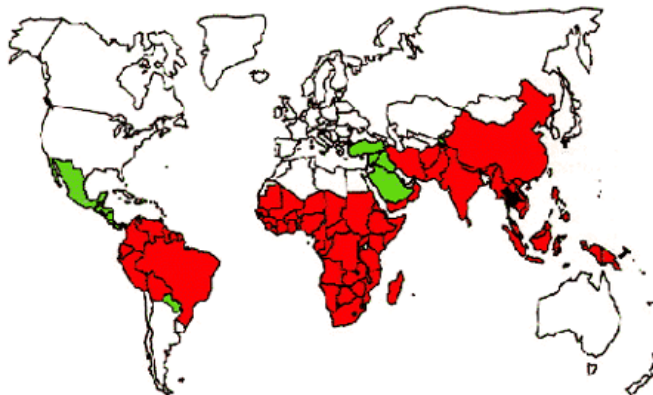
Treatment

- Type of malaria
- Knowledge of regional resistance
- Severity of illness (oral vs intravenous)
- Age of patient

Distribution of Plasmodium falciparum



Drug-resistant Malaria



Red - chloroquine resistant

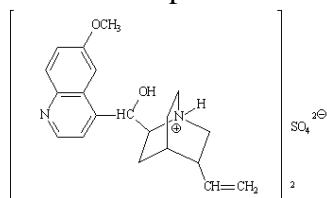
Green - chloroquine sensitive

Black - chloroquine and mefloquine resistant

The diagram illustrates the parasite's hemozoin (HZ) detoxification pathway and the effect of Chloroquine (CQ). The parasite is shown within a red blood cell (RBC). The parasite's cytosol contains various components: Parasite, Cytosol, and PV (parasitophorous vacuole). The pathway involves the conversion of heme (h) to hemozoin (Hz) by the enzyme Stacking enzyme. This process is coupled with the conversion of CO₂ to CO₂ (likely a typo for CO₂ to CO₂ or CO₂ to CO₂). The resulting HZ is then excreted from the parasite as a waste product. The diagram also shows the effect of Chloroquine (CQ) on the parasite's detoxification pathway. CQ is shown as a red dot that binds to the Stacking enzyme, inhibiting its activity. This leads to the accumulation of HZ within the parasite, which is labeled as a 'Parasite toxic waste dump: hemozoin (HZ)'. The diagram also shows the effect of CQ on the parasite's cytosol, where it is shown as a red dot that binds to the parasite's cytosol, inhibiting its activity. The diagram also shows the effect of CQ on the parasite's PV, where it is shown as a red dot that binds to the PV, inhibiting its activity. The diagram also shows the effect of CQ on the parasite's RBC, where it is shown as a red dot that binds to the RBC, inhibiting its activity.

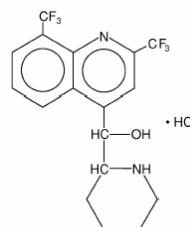
The parasite uses the protein portion of hemoglobin and discards the heme moiety as hemozoin.

A. Parent Compound



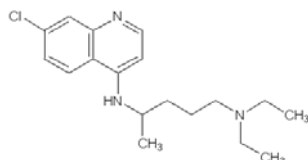
Quinine

C. Newer Derivative



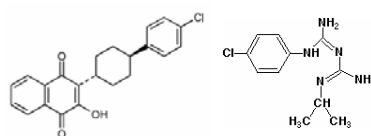
Mefloquine

B. Older Derivative: extensive resistance



Chloroquine

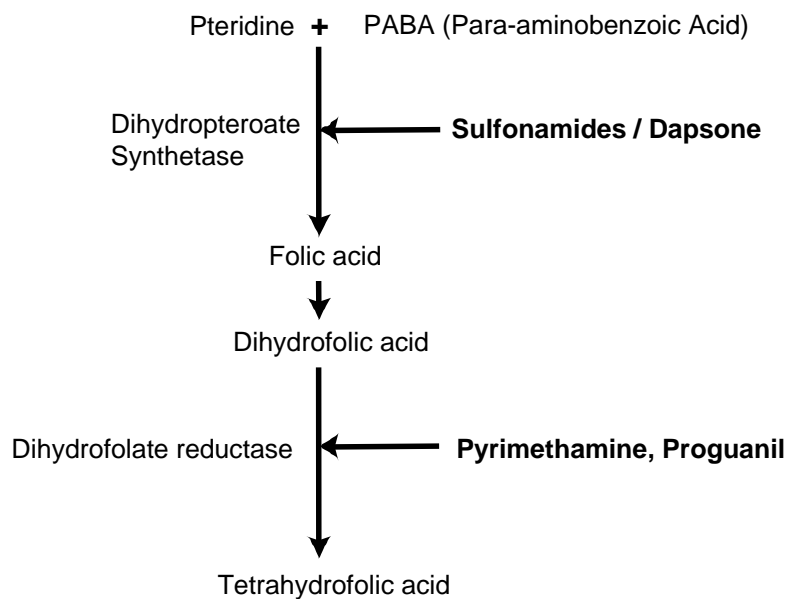
D. Drugs of choice



Atovaquon

Proguanil

Treatment: Anti-Folates



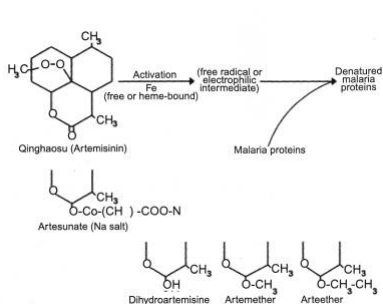
Artemisinin

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, May 2002, p. 1510-1515
0096-4804/02/0000-0 DOI: 10.1128/AAC.46.5.1510-1515.2002
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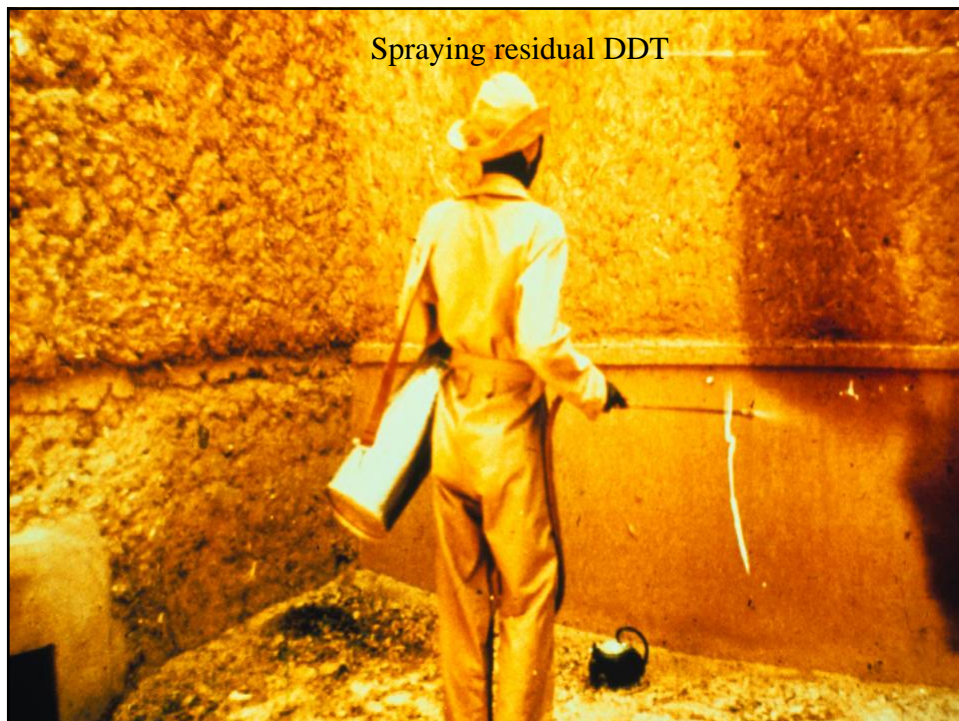
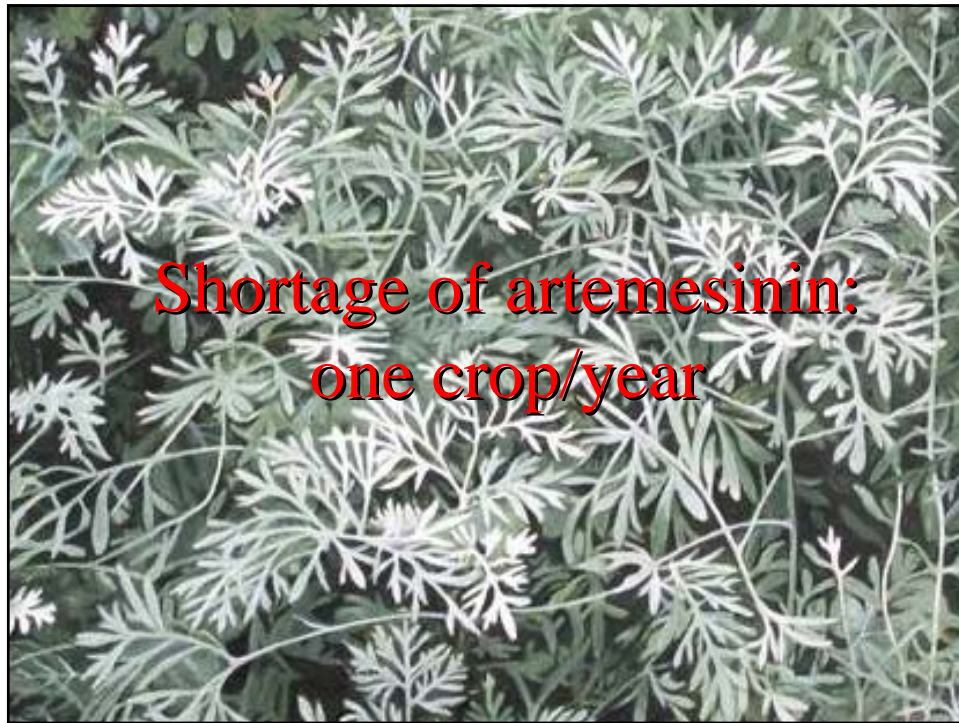
Vol. 46, No. 5

In Vitro Interactions of Artemisinin with Atovaquone, Quinine, and Mefloquine against *Plasmodium falciparum*

S. Gupta,¹ M. M. Thapar,¹ W. H. Wernsdorfer,² and A. Björkman^{1*}



Artemisia sp.



Antimalarial Prophylaxis

- North American travelers lack immunity to malaria
- Risk of acquiring malaria depends on rural travel, altitude, season of travel.
- Highest risk in low lying areas during rainy season
- Personal protection measures against mosquitoes as important as drugs.
- Insect repellants, mosquito nets, clothing covering body
- Antimalarial drugs do not prevent infection and initial liver stage

nature

Vol 438|24 November 2005|doi:10.1038/nature04024

LETTERS

The entomological inoculation rate and *Plasmodium falciparum* infection in African children

D. L. Smith¹, J. Dushoff^{1,2}, R. W. Snow^{3,4} & S. I. Hay^{3,5}



Conclusion of article: 20% of the children harbor 80% of the infections because they are bitten more often.

Q: Since mosquitoes home in on us via CO₂, body temperature and perhaps other odors, is there a genetics controlling our susceptibility to being bitten?



Types of Preventive Measures: Drugs

- Prophylaxis with medications based on knowledge of geographic resistance patterns
- Mefloquine, Doxycycline, Atovaquone-Proguanil
- Self treatment: Fansidar, Quinine
- Combination of both: Chloroquine chemoprophylaxis with standby Rx (Not Recommended!)
- MDR resistance a problem in Thailand, Cambodia and Increasingly E. Africa

Future Research

- ? Vaccine; none yet but many being tested
- New and Better drugs
 - Safety in Children
 - Safety in Pregnant Women
 - ? 1 dose



Review

TRENDS in Parasitology Vol.21 No.11 November 2005

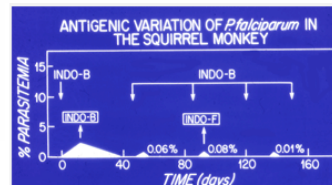
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Malaria vaccines 1985–2005: a full circle?

Geoffrey A. Targett

Gates Malaria Partnership, Department of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, 50 Bedford Square, London, UK, WC1B 3DP

Few who were actively engaged in malaria vaccine research 20 years ago (including myself) would have imagined that, in 2005, there would still be a prediction of a 10–20-year horizon before vaccines become part of malaria-control strategies. Why is it still proving so challenging to produce effective vaccines?



Variation of the Indochina strain of *P. falciparum* in the squirrel monkey: cryopreserved stabilates of Indo-B are injected at various time points, but the Indo-B phenotype (as identified using anti-Indo-B serum) is only expressed in the first peak of infection. Another variant population (Indo-F) is isolated from the third peak.
[Image: Marcel Hommel]

A major reason why there is still no vaccine

