The Malarias:

*Plasmodium falciparum*
*Plasmodium vivax*
*Plasmodium malariae*
*Plasmodium ovale*

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

<table>
<thead>
<tr>
<th>WHO region</th>
<th><em>P. falciparum</em> risk*</th>
<th><em>P. vivax</em> risk*</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEARO</td>
<td>1.252</td>
<td>1.347</td>
</tr>
<tr>
<td>AFRO</td>
<td>0.525</td>
<td>0.050</td>
</tr>
<tr>
<td>WPRO</td>
<td>0.438</td>
<td>0.890</td>
</tr>
<tr>
<td>EMRO</td>
<td>0.245</td>
<td>0.211</td>
</tr>
<tr>
<td>AMRO</td>
<td>0.050</td>
<td>0.078</td>
</tr>
<tr>
<td>EURO</td>
<td>0.000</td>
<td>0.020</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2.510</strong></td>
<td><strong>2.596</strong></td>
</tr>
</tbody>
</table>

*The 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.
3 million deaths/yr. 1 million in Africa, mostly children below the age of 5
Mosquitoes are aquatic insects.

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. HANES
Staff Writer

A mosquito bite put 18-year-old college student Mark Brown on the spot where doctors diagnosed him with a malady that hasn't been contracted in New Jersey since 1934.

"It's a better chance of winning the lottery than contracting malaria," saidd infectious disease specialist Dr. Patrick Heggie-Rogers of Eagelwood Hospital, a major malaria facility in the state.

"Mark is an exception in this area," said the doctor.

"The disease attacks red blood cells, causing the disease to be transmitted from person to person by mosquitoes. The disease is known as Plasmodium vivax, which is prevalent in New Jersey.

"Mark was treated successfully at the hospital."
Adult *Anopheles dirus* taking a blood meal from one of the authors (RWG)

*Plasmodium falciparum*
Plasmodium vivax

Plasmodium ovale
**Plasmodium malariae**

![Image of Plasmodium malariae cells](image)

**Plasmodium falciparum**

![Diagram of Plasmodium falciparum life cycle](image)
Adult *Anopheles dirus* taking a blood meal from one of the authors (RWG)

*Mosquito Cycle (Sporogony)*

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

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
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 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
Clinical Signs & Symptoms

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

![Plasmodium vivax diagram]
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 falciparum**

- Not in peripheral blood: 16-26
- In peripheral blood: 1-15; 27-30

**Normal RBC**

**Atomic force microscopy of knobs**

**In situ RBCs with *P. falciparum***

**Electron micrograph of knobs**

**Stages of *P. falciparum* with knobs**
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
Mode of Action of Chloroquine 
And Mechanisms of Drug Resistance

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

Drugs Of Choice:

A. Parent Compound

B. Older Derivative: extensive resistance

C. Newer Derivative

D. Drugs of choice
Treatment: Anti-Folates

\[ \text{Pteridine} + \text{PABA (Para-aminobenzoic Acid)} \]

\[ \text{Dihydropteroate Synthetase} \]

\[ \text{Sulfonamides / Dapsone} \]

\[ \text{Folic acid} \]

\[ \text{Dihydrofolate reductase} \]

\[ \text{Pyrimethamine, Proguanil} \]

\[ \text{Tetrahydrofolate reductase} \]

\[ \text{Dihydropteroate Synthetase} \]

\[ \text{Dihydrofolate reductase} \]

\[ \text{Tetrahydrofolate reductase} \]

**Artemesinin**

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

S. Gupta, M. M. Thapa, W. H. Werndt, and A. Bjorkman

*Artemisia sp.*
Shortage of artemisinin: one crop/year

Spraying residual DDT
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

LETTERS

The entomological inoculation rate and Plasmodium falciparum infection in African children

D. L. Smith1, J. Dushoff1,2, R. W. Snow3,4 & S. I. Hay5,6

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

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?

A major reason why there is still no vaccine
1,500 languages! 1,500 antigenic strains of *P. falciparum*!