Malaria

- Vector-borne disease
- Mosquitoes are vectors for several diseases
- Malaria exclusively vectored by Genus *Anopheles*
- *If all Anophelines could vector Malaria the disease burden would be much more than 500 million cases.* (Of 422 species worldwide, 40 are considered important vectors. *Occur almost all over the world.*)
Definitive host mosquito

Ingests 3 ul of blood with 100-300 gametes

Gametocytes
Viable for 28 days

Oocysts on gut wall

28 days
In mosquito

\[ 100's \]
Sporozoites

Within hours invades 1-2 liver cells

Plasmodium Life Cycle

Clinical signs and symptoms in erythrocytic stages of ring, trophozoite and schizont

ring

48-72 hrs

1,000's released

Merozoites in liver for seven to 10 days. P. vivax & ovale hypnozoite for Months.
*Plasmodium falciparum*: High percent rings
Source: Thomas Spahr and David Sullivan JHMRI

*Plasmodium vivax*: Enlarged erythrocytes
Source: CDC/Dr. Mae Melvin

*Plasmodium malariae*: Band forms
Source: CDC/ Steven Glenn, Lab & Consultation Division

*Plasmodium ovale*: Oval or comet shape
Source: CDC/Dr. Mae Melvin
Reading:

- Global transmission patterns
- Poverty and malaria
- Socio-economic costs of malaria
- Long-term demographic consequences
- Human and physical capital
- Effect on foreign investment, trade, movement of people
Figure 1 Global distribution of malaria. The changing global distribution of malaria risk from 1946 to 1994 shows a disease burden that is increasingly being confined to tropical regions.

High risk of malaria
- 1994
- 1966
- 1946

Figure 2 Global distribution of per capita GDP. The global pattern of income distribution is highly uneven, with average income levels significantly lower in tropical regions.

GDP per capita 1995
- US$450–1,999
- US$2,000–4,999
- US$5,000–9,999
- US$10,000–15,999
- US$15,000–31,100
- No data
Clinical Complications of Malaria

*P. falciparum*
1. Cerebral coma
2. Anemia
3. Pulmonary edema
4. Renal Failure
5. Shock
6. Lactic acidosis
7. Hypoglycemia
8. Tropical splenomegaly
9. Pregnancy
   a. Maternal death
   b. Stillbirth
   c. Low birth weight
   d. Anemia

*P. vivax (P. ovale)*
1. Splenic rupture
2. Anemia (mild)
3. Debilitating fevers
4. Higher TNF-α per parasite

*P. malariae*
1. Immune complex
2. Glomerulonephritis, leading to nephrotic syndrome
• 100 countries in malaria endemic areas.
• half in sub-Saharan Africa.
• 2.4 billion at risk.
• 300 to 500 million cases each year.
• 1.0 to 2.7 million deaths in children.
• Malaria constitutes 25% of child mortality in Africa.
• 90% of all malaria mortality is in under children under 5.
• Low birth weight, preterm delivery, cerebral malaria, and severe malarial anemia are major causes of mortality.
• Sequelae from severe clinical complications include cognitive impairment, behavioral disturbances, spasticity, and epilepsy as well as vision, hearing, and speech impairments.
**Burden of Malaria in the World**

- 300-500 million malaria cases in the world
- 1.5 to 2.7 million deaths due to malaria
- 90% disease burden in Africa, South of Sahara

**Estimated Burden of Disease in Disability Adjusted Life Years (DALYs)**

(WHO Report 2001)

<table>
<thead>
<tr>
<th>Region</th>
<th>Total DALYs</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>World</td>
<td>40,213,000</td>
<td>-</td>
</tr>
<tr>
<td>Africa</td>
<td>35,748,000</td>
<td>88.89</td>
</tr>
<tr>
<td>The Americas</td>
<td>111,000</td>
<td>2.76</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>1,945,000</td>
<td>4.83</td>
</tr>
<tr>
<td>Europe</td>
<td>21,000</td>
<td>0.052</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>5,16,000</td>
<td>1.28</td>
</tr>
<tr>
<td>South East Asia</td>
<td>1,874,000</td>
<td>4.66</td>
</tr>
<tr>
<td>India</td>
<td>1,311,800</td>
<td>(70% of SEAR DALYs)</td>
</tr>
</tbody>
</table>

**Situation Analysis of Malaria in India**

- 1 billion population at risk of malaria
- 10 million population under SP treatment
- 2 million cases reported by NAMP
- 800-1000 malaria deaths reported by NAMP
- 6 major vectors-resistant, exophilic and or endophilic behavior
- New malaria ecotypes identified
- Spraying produces transient control
- Widespread mono-drug resistance, multi-drug resistance in *P. falciparum*
- Inadequate resources
- 1 billion US dollars loss due to malaria

**Malaria Profile of India (1961-2001)**

[Graph showing malaria cases and prevalence over time]
Malaria Control History in India
1946: India started using DDT
1953: NMCP is started
1958: NMCP becomes the NMEP
1959: The first time vector resistance is first detected in India (in Gujarat)
1965: Malaria begins to re-emerge
1976: Peak of malaria cases in reemergence period
1977: India starts MPO and PfPC
1985: Only 2 million annual cases of malaria in India
1991: Peak of P. falciparum cases
1994: Large scale epidemics, primarily in eastern India and Western Rajasthan

India’s official figures show that every year, malaria infects 1.5-2 million people, killing 500 to 800 of them. But these figures are huge underestimates. The World Health Organization (WHO) says there are 100 million cases of malaria in its South-East Asia Region (which includes India), with 70 per cent contributed by India. This would imply that India has a staggering 70 million cases. –VP Sharma
Role of Vectors in Malaria Transmission in India

<table>
<thead>
<tr>
<th>Malaria Vectors</th>
<th>Disease Potential</th>
<th>Total malaria cases (%)</th>
<th>Pf cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rural &amp; Urban Vector</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>An. culicifacies</td>
<td>+</td>
<td>65</td>
<td>55</td>
</tr>
<tr>
<td>An. stephensi</td>
<td>++</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>Regional Vector</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>An. fluviatilis</td>
<td>++</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>An. minimus</td>
<td>+++</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>An. dirus</td>
<td>+++</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Coastal Vector</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>An. sundaicus</td>
<td>++</td>
<td>0.4</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Broad categorization based on 1996 NAMP data.
+ Low       ++ Medium       +++ High

Biological Variations Among members of An. culicifacies Sibling Species Complex

<table>
<thead>
<tr>
<th>Biological Behaviour</th>
<th>An. culicifacies Sibling Species</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthropophilic index (%)</td>
<td></td>
<td>0-4</td>
<td>0-1</td>
<td>0-3</td>
<td>0-1</td>
<td>80</td>
</tr>
<tr>
<td>Biting Activity</td>
<td>All night</td>
<td>All night</td>
<td>All night</td>
<td>Till midnight</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak Biting Time</td>
<td>10-11 pm</td>
<td>10-11 pm</td>
<td>6-9 pm</td>
<td>6-9 pm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vector Potential</td>
<td>Vector</td>
<td>Non-vector</td>
<td>Vector</td>
<td>Vector</td>
<td>Vector</td>
<td></td>
</tr>
<tr>
<td>Sporozoite Rate</td>
<td>0.51</td>
<td>0.04</td>
<td>0.3</td>
<td>0.4</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Resistance to DDT</td>
<td>Slow</td>
<td>Fast</td>
<td>Fast</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resistance to HCH</td>
<td>Fast</td>
<td>Fast</td>
<td>Fast</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resistance to Malathion</td>
<td>Slow (9-10 yrs.)</td>
<td>Medium (6-7 yrs.)</td>
<td>Fast (4-5 yrs.)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Malaria Treatment Cost of an Adult in India

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Cost (Rs.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroquine</td>
<td>3.50-10.00</td>
</tr>
<tr>
<td>Chloroquine injection + fluids</td>
<td>200.00</td>
</tr>
<tr>
<td>Sulfadoxine Pyrimethamine</td>
<td>7.00-30.00</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>240.00-300.00</td>
</tr>
<tr>
<td>Artemether injections</td>
<td>390.00-1600.00</td>
</tr>
<tr>
<td>Arteether injections</td>
<td>275.00</td>
</tr>
<tr>
<td>Artesunate injections</td>
<td>1120.00</td>
</tr>
<tr>
<td>Quinine tables + Tetracycline</td>
<td>270.00-210.00</td>
</tr>
<tr>
<td>Quinine injections + IV fluid + Tetracycline</td>
<td>800-910</td>
</tr>
</tbody>
</table>

*Antipyretics @ Rs. 5.00-10.00 per treatment

I/V fluid may be required during Artemisinin treatment

Chronology of drug resistance in SEA Region

- **CHLOROQUINE**
  - 1962 Thailand
  - 1969 Myanmar
  - 1970 Bangladesh
  - 1973 India
  - 1981 Indonesia
  - 1981 East Timor
  - 1984 Nepal
  - 1985 Sri Lanka
  - 1985 Bhutan

- **SULFADOXINE-PYRIMETHAMINE**
  - 1979 India
  - 1980 Indonesia
  - 1980 Myanmar
  - 1985 Thailand
  - 1997 Nepal

- **QUININE**
  - 1983 Thailand
  - 1986 India

- **MEFLOQUINE**
  - 1989 Thailand

Status of Insecticide Resistance in *A. culicifacies*

- **DDT + DL + MLN**
- **DDT + DL**
- **DDT**
- **NO DATA AVAILABLE**
Malaria in Pregnancy

- Pregnant women attract twice the number of mosquitoes than non-pregnant women
- There is a greater susceptibility to *P. falciparum* than *P. vivax* during pregnancy
- Low birth weight babies in malarious areas are 2 to 4 times more likely to experience failure in school.

Endless Vicious Cycle of Malaria

- Malaria is the leading cause of anemia
- Malaria affects cognitive development and learning abilities of children
- Malaria is a risk factor of neuro-sensory and behavioral development in children
- Malaria—one clinical febrile episode of malaria consumes 5,000 k Cal.
This view is stunningly naive. DDT residual house spraying is an inexpensive, highly effective, practice against malaria, and it has been approved by the World Health Organization. In it, trained sprayers apply a small quantity of DDT on the interior walls and eaves of homes in endemic regions. The quantities involved are minimal (2 g/m²) and, unlike agricultural uses which inject tonnes of DDT into the outdoors, indoor house spraying results in little harmful release to the environment. For the amount of DDT used on a cotton field, all the high risk residents of a small country can be protected from malaria.²
Malaria Control in Karnataka in Partnership with PHC System

- Major silk producing region. Farmers unwilling to allow the use of DDT
- High malaria incidence and deaths
- Major Breeding habitats of *An. culicifacies*
  - Wells: Species A (Vector Species)
  - Streams: Species B (Non-Vector Species)
  - All wells mapped and fishes released
  - Malaria cases declined sharply

Rise of malaria in DDT sprayed villages. In 1998 fishes were released in problem villages.

Impact of Fishes on Malaria

Malaria cases

- Population 38000 in 95 villages
- Malaria cases

Graph showing the decline in malaria cases with the release of fishes in 1998.
Interventions

• Integrated management – poverty alleviation strategies, better access to health-care
• Cost-effective case management
• Local solutions (ecotypes)
• Insecticide-treated bednets
• Indoor residual spraying
• Larviciding (predatory fishes)
• Filling breeding sites, paddy field drainage
New Tools in Malaria Control

- **MALARIA DIAGNOSIS**
  - Dipstick/pLDH tests
    - **TREATMENT**
    - Artemisinin & Drug Combination
  - **ENVIRONMENT**
    - Health Impact Assessment
  - **VECTOR CONTROL**
    - Situation specific based on stratification, An. Sibling species, Bioenvironmental Methods, Treated Bed Nets, *Bacillus thuringiensis*, Neem Based Repellents, Selective Spraying
Rapid Diagnosis
Immunochromatographic Test
That Detects Malaria Antigens

Sensitivity 90-95%
Specificity 72-92%

Inaccuracies of clinical diagnoses

• Malaria is difficult to diagnose clinically
• In studies > 70% of +ve diagnoses are non-parasitaemic.

QBC Test
Advantages of mosquito nets with insecticides

Hungry mosquitoes do not wait in the room, they are either killed or repelled after contact with the net.

Mosquitoes die or escape after landing on the net.

Mosquitoes fail to find holes or other small opening to enter.

A person sleeping in the same room without a net also receives some protection.

Neem oil treated bednets, bedsheets or pillowcovers etc.
Research

Larvicidal effects of a neem (Azadirachta indica) oil formulation on the malaria vector Anopheles gambiae
Fredros O Okumu¹,², Bart GJ Knols³ and Ulrike Fillinger*⁴

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* Corresponding author

Figure 1
Percentage larval mortality, pupation and adult emergence (as proportion of original numbers tested) of 3rd-4th instar larvae of An. gambiae following exposure to various concentrations (0.5–32 ppm) of neem oil (N) or corn oil (C). Adult emergence values are percentages of the total number of mosquitoes tested as larvae.
Images and graphs from:

- http://www.pitt.edu/~super1/lecture/lec17341/001.htm
- http://ocw.jhsph.edu/courses/malariology/lectureNotes.cfm
- http://www.sumanasinc.com/scienceinfocus/plasmodium/plasmodium.swf