Malaria: A Global Perspective and Prospects for Elimination

Rima Shretta
Background

- Spread by the female anopheles mosquito; caused by plasmodium parasite:
  - P. falciparum, P. vivax, P. ovale, P. malariae, P. knowlsei
- 3.3 billion people living in 109 countries are at risk of malaria
- 350 million–500 million new cases annually
- 1 million people die every year due to malaria
- 35% of countries suffer 98% of global death toll
- 90% of deaths caused by malaria occur in Africa
Background

- Accounts for 18% of under-five mortality in Sub-Saharan Africa (global average: 8%)
- Cause of 10% of all maternal deaths annually:
  - Repeated infections result in chronic anemia particularly dangerous to young children and pregnant women
- 30,000 cases in visitors to tropical countries
Every 30 seconds a child in Africa dies of malaria
Burden of Malaria in Sub-Saharan Africa, 1999-2004

Mathers, et al., 2006, *Global Burden of Disease and Risk Factors*
Economic Impact of Malaria

- Malaria causes and results in poverty
  - Malaria costs Africa at least US$ 12 billion in direct losses
  - Malaria costs may be 40% of total health expenditures in endemic countries
  - Impacts on work productivity, drug supply systems and school attendance and education
  - An estimated 10% of the income of an African family is consumed by malaria treatment
Distribution and Transmission of Malaria

- Where the environment provides – water, vegetation, temperature, low altitude
- Transmission differs depending on local factors:
  - Rainfall patterns
  - Proximity of mosquito breeding sites to people
  - Types of mosquito species in the area
- “Malaria endemic“ regions have a fairly constant number of cases throughout the year
- In other areas there are "malaria seasons" usually coinciding with the rainy season.
- Epidemics
  - Parasite introduced into areas where people have little or no immunity to malaria
  - People with low immunity move into areas where malaria cases are constant
Transmission of *Plasmodium* from Mosquito to Human to Mosquito

*P. falciparum*
*P. vivax*
*P. ovale*
*P. malariae*
*P. knowlesi*
Clinical Manifestations of the Malaria Burden

Infected Mosquito

Infective Human

Acute febrile illness

Chronic effects

Infected Human

Pregnancy

Fetus

Maternal

Anemia

Neurologic

Cognitive

Developmental

Severe illness

Respiratory distress

Hypoglycemia

Cerebral malaria

Impaired growth and development

Malnutrition

Long-term sequelae

Infant and fetal mortality

Low birth weight

Abortion, stillbirth

Acute illness

Long-term sequelae

High-risk or Vulnerable Populations

- Infants and children under five years
  - Infants are vulnerable to malaria from approximately 3 months of age, when immunity acquired from the mother starts to wane
- Pregnant women
  - Malaria in pregnancy increases the risk of maternal anemia, stillbirth, spontaneous abortion, low birth weight and neonatal death
- Co-infection and interaction between malaria and HIV/AIDS
  - Placental malaria increases the potential for mother-to-child transmission of HIV. Similarly HIV positive patients are more likely to get malaria and vice versa
- Migrant populations
- Non-immune travellers

Highest death rates are in children under 5 years of age
Clinical Cases of *Plasmodium falciparum* in 2005

<table>
<thead>
<tr>
<th>Region</th>
<th>Population at risk (million)</th>
<th>Cases (%) (million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>521</td>
<td>365 (215 - 374)</td>
</tr>
<tr>
<td>South East Asia</td>
<td>1,314</td>
<td>119 (66 - 224)</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>142</td>
<td>15 (9 - 26)</td>
</tr>
<tr>
<td>Eastern Med.</td>
<td>176</td>
<td>12 (5 - 25)</td>
</tr>
<tr>
<td>Americas</td>
<td>55</td>
<td>4 (2 - 8)</td>
</tr>
<tr>
<td>Europe</td>
<td>4</td>
<td>1 (0 - 1)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2,211</strong></td>
<td><strong>515 (298 – 659)</strong></td>
</tr>
</tbody>
</table>

### Clinical Cases of *Plasmodium vivax* in 2005

<table>
<thead>
<tr>
<th>Region</th>
<th>Population at risk (millions)</th>
<th>Infections/year (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>South East Asia</td>
<td>1,347</td>
<td>90-248</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>89</td>
<td>20-77</td>
</tr>
<tr>
<td>East Mediterranean</td>
<td>211</td>
<td>11-34</td>
</tr>
<tr>
<td>Americas</td>
<td>78</td>
<td>10-28</td>
</tr>
<tr>
<td>Europe</td>
<td>20</td>
<td>1-4</td>
</tr>
<tr>
<td>Africa</td>
<td>50</td>
<td>—</td>
</tr>
<tr>
<td>Central Asia</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2,596</strong></td>
<td><strong>132-391</strong></td>
</tr>
</tbody>
</table>

10 countries estimated to have 90% of cases in regions other than Africa, 2006

WHO. World Malaria report (2008)
Estimated incidence of malaria per 1000 population (2006)

WHO. World Malaria report (2008)
Malaria in the United States

- Malaria transmission in the United States was successfully interrupted in the 1950's
- CDC continues to conduct malaria surveillance to detect locally acquired cases
- *Anopheles* mosquito still exists in the United States: risk of re-introduction
- 2007: CDC received reports of 1,505 cases of malaria
  - All but one of these cases were acquired outside of the United States; one was acquired through a blood transfusion
The History of Malaria

- **400 BC:** Hippocrates attributed malaria to ingestion of stagnant water
- **1820:** Quinine isolated from cinchona bark
- **1897:** Ronald Ross and role of mosquito in malaria transmission
- **1899:** Ross attempted to eradicate malaria from England by trying to eliminate larvae from stagnant pools
- **1901:** US Army leads a successful anti-mosquito drive in Havana, Cuba; use of pyrethrum
- **1921-22:** Larvivorous fish used in control of mosquitoes in California
- **1934,1946:** Chloroquine discovered
- **1939:** Dichloro-diphenyl-trichloroethane (DDT) discovered
- **1955:** WHO Global Malaria Eradication Program launched
- **1965:** Eradication Program successful in Europe, but cases re-emerge in Asia
- **1969:** Global Malaria Eradication Program abandoned
The History of Malaria

- 1972: DDT banned
- 1998: Roll Back Malaria (RBM) Campaign launched
- 2000: African heads of state pledge to halve mortality due to malaria by 2010
- 2000: MDGs agreed by every member state
- 2005: World Bank Booster and US President’s Malaria Initiative launched
- 2005: Gates Foundation pledges US$ 258 million for R&D
- 2007: G8 pledges US$ 60 billion for health systems in Africa and advance MDGs related to HIV, TB and malaria
- 2008: UN Secretary General calls for Universal Coverage
- 2008: RBM Global Malaria Action Plan launched
Global Malaria Control Strategies

- Early diagnosis and prompt and effective treatment
- Prevention through use of personal protection (Long Lasting Insecticide Treated Nets [LLINs]) and other vector control measures (Indoor Residual Spraying [IRS], larviciding, environmental management)
- Prevention of malaria during pregnancy (LLINs, Intermittent Preventive Treatment [IPTp])
- Early detection, prevention and rapid response to epidemics
Future Technologies

- Intermittent Preventive Treatment in Infants (IPTi)
- Vaccines (pre-erythrocytic, blood stage, transmission-blocking)
- Genetic modification of vectors
Early Diagnosis

- Parasitological/biological
  - Microscopy
  - Rapid Diagnosis Tests (RDTs)
- Clinical Diagnosis
- WHO recommends parasitological diagnosis before treatment except in cases where it is not available
- 20 of 45 countries in Africa and 51 of 64 countries outside of Africa use parasitological testing
Challenges to Diagnosis

- Microscopy
  - Access
  - Training and human resource capacity

- Rapid Diagnosis Tests
  - Cost
  - Quality Assurance

- Clinical diagnosis: potential for over-treatment
Effective Treatment

Plasmodium falciparum
- Artemisinin based Combination Therapies (ACTs)
  - Artemether/lumefantrine
  - Artesunate/aminodiquin
  - Artesunate/mefloquine
  - Artesunate/sulfadoxine-pyrimethamine
  - Dihydroartemisinin/piperaquine
- 78 countries are using ACTs
  - 130 million treatments procured in 2008 compared to 5 million in 2004
  - Distribution of funding

Plasmodium vivax
- Chloroquine where sensitive; ACTs plus primaquine to prevent relapse

Severe plasmodium infections
- Quinine, artesunate, artemether plus ACT
Challenges to Effective Treatment

- Drug resistance
  - Emergence of chloroquine resistance in 1970’s; SP in 2000’s
  - Low level of artemisinin resistance in SE Asia
- Most patients access treatment in the private sector
  - Access to and cost of effective medicines in private sector
- Poor quality/counterfeit medicines
- Rational use
- Poor drug management systems: forecasting, procurement, distribution
- Use of monotherapies
- Limited WHO pre-qualified products
- In 11 of 13 countries surveyed in 2007-8, fewer than 15% of children received an ACT
Personal Protection and other Vector Control

- Long Lasting Insecticide Treated Nets [LLINs])
  - Mass campaigns
  - Routine distribution through health facilities
  - 58 countries adopted WHO recommendation of nets for all
  - Nearly 140 million LLINs distributed in 2007-8 in Africa
  - 31% of households own at least one net; 24% of children sleep under a net

- Indoor Residual Spraying
  - DDT
  - 44 countries implementing IRS
Challenges to Effective Vector Control

- Long Lasting Insecticide Treated Nets [LLINs]
  - Coverage and replacement
  - Use (cultural, heat, other uses)
  - Cost
  - Pyrethroid resistance
  - Use of WHOPES recommended nets

- Indoor Residual Spraying
  - Vertical and intrusive
  - Human resource intensive
  - Cost
  - Insecticide resistance
Prevention of Malaria in Pregnancy

- Prenatal clinic attendance high
- Free distribution of LLINs to pregnant women in prenatal clinics
- WHO recommends Intermittent Preventive Treatment (IPTp) in high transmission areas. Current treatment of choice is at least two doses of sulphadoxine-pyrimethamine (SP)
  - 37 countries adopted IPTp by 2009
  - First attendance sometimes late in pregnancy
  - Only 20% receive a second dose of SP
Financing for Malaria Control

- Total funds increased from US$ 0.3 billion in 2003 to US$ 1.7 billion in 2009
  - Global Fund for HIV/AIDS, TB and Malaria
  - United States President’s Malaria Initiative (PMI)
  - World Bank Booster Program
  - UNITAID
  - Affordable Medicines Facility for Malaria (AMFm): 216 million treatments in Phase 1: US$ 110 million for supporting interventions

- Distribution of funding

- In 2010, an estimated $ 6.2 billion will be needed to support commodity purchases as well as institutional strengthening and research
Global Commitment to Malaria

- 4 February 2008: UN Secretary-General announced the appointment of a Special Envoy to mobilize global support for action on malaria
- 25 April 2008: UN Special Envoy calls for universal access to malaria prevention and treatment
- Since 2000, global partnerships and advocacy have increased exponentially
Recent Global Advocacy on Malaria

- Youssou N’dor Foundation
- Yvonne Chaka Chaka (Roll Back Malaria Goodwill Ambassador)
- Princess Astrid
- NYC marathon: “Malaria No More” team
Can Malaria be Eradicated/Eliminated?
Bill and Melinda Gates listen to a question at the forum on malaria on Wednesday in Seattle.

**WHO chief joins Gateses' call to eradicate malaria**

Some at Seattle meeting see risk in high expectations

October 17, 2007
By TOM PAULSON
P-I REPORTER

The director-general of the World Health Organization declared Wednesday in Seattle that the Geneva-based agency, which coordinates international public health efforts, would seek to eradicate one of the planet's leading killers, malaria.
Can Malaria be Eradicated/Eliminated?

- Eradication/elimination endorsed by WHO and Roll Back Malaria Partnership.
- Eradication of malaria, theoretically possible, is not likely to be feasible within the medium term using existing control tools.
- Malaria elimination (cessation of local transmission) is a realistic short- to medium-term goal for an increasing number of countries that are already bringing malaria under control.
The Global Malaria Action Plan (GMAP) is a global framework for action around which those working against malaria can coordinate their efforts.

**GMAP Targets**

- **Achieve** universal coverage by 2010 and **sustain** universal coverage indefinitely;
- **Reduce** global malaria cases from 2000 levels by 50% in 2010 & by 75% in 2015;
- **Reduce** global malaria deaths from 2000 levels by 50% in 2010 & to near zero in 2015;
- **Eliminate** malaria in 8-10 countries by 2015 and afterwards in all countries in the pre-elimination stage today; and
- **In the long term**, **eradicate** malaria world-wide through progressive elimination in countries.

By meeting these targets, the malaria MDG will be achieved and there will be progress towards the other MDGs.
What is Meant by Universal Coverage?

- **Prevention**
  - 100% of the population at risk is provided with locally appropriate preventive interventions.
  - Coverage is defined as:
    - **LLINs**: one long lasting insecticidal net for every two people
    - **IRS**: a household is routinely sprayed with indoor residual spraying
    - **IPTp**: every pregnant woman living in a high transmission setting receives at least 2 doses of an appropriate antimalarial drug during her pregnancy

- **Case management**
  - 100% of patients receive locally appropriate case management interventions.
  - Coverage is defined as:
    - **Diagnosis**: prompt parasitological diagnosis by microscopy or RDTs
    - **Treatment**: treatment with effective drugs within 24 hours after the first symptoms appear
GMAP proposes 3-part global strategy to achieve targets

1. CONTROL
   - Scale-up for impact (SUFI)
   - Sustained Control

2. ELIMINATION

3. RESEARCH
Global Distribution of Malaria

Progress
Global Progress Towards Malaria Control

- 27 countries including 5 in Africa have reported reductions of > 50% of cases and deaths between 1990-2006
- Reductions associated with scaling up of IRS, LLINs and ACTs
- 8 countries are in the pre-elimination stage (2009), 10 implementing elimination strategies (6 entered elimination stage in 2009). Nine have interrupted transmission and in stage of prevention of re-introduction
- Examples:
  - Inpatient deaths decreased by 53% in Sao Tome and Principe and 57% in Zanzibar
  - Zambia: all-cause child mortality rate reduced by 35%
# Zanzibar Progress on Malaria

## Impact of ACT use for 24 months in 13 health facilities, North A district, Zanzibar, 2002-2005

<table>
<thead>
<tr>
<th>Measure of impact</th>
<th>Measurement method</th>
<th>Before ACT intervention, 2002</th>
<th>After ACT intervention, 2005</th>
<th>% decline</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTs only, public sector</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5y in-patient malaria cases</td>
<td>Routine</td>
<td>1261</td>
<td>296</td>
<td>77</td>
</tr>
<tr>
<td>&lt;5y in-patient malaria deaths</td>
<td>Routine</td>
<td>40</td>
<td>10</td>
<td>75</td>
</tr>
<tr>
<td>&lt;5y out-patient malaria cases</td>
<td>Routine</td>
<td>20634</td>
<td>4817</td>
<td>77</td>
</tr>
<tr>
<td>&lt;5y % asexual parasite +</td>
<td>Survey</td>
<td>9.0</td>
<td>5.3</td>
<td>41</td>
</tr>
<tr>
<td>&lt;5y all-cause mortality</td>
<td>Vital event registration</td>
<td>133</td>
<td>64</td>
<td>52</td>
</tr>
<tr>
<td>ACTs+ITNs</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;5y % asexual parasite +</td>
<td>Survey</td>
<td>9.0</td>
<td>0.3</td>
<td>97</td>
</tr>
</tbody>
</table>

Zanzibar Progress on Malaria

Outpatient Malaria Cases (confirmed and non-confirmed) per 1000 of the population

Ali, et al 2007, RBM EARN Meeting
Rwanda, 2001-2007, 19 health facilities

In-patient malaria and non-malaria cases in children <5 years

Ethiopia 2003-2007, 7 in-patient facilities

In-patient malaria and non-malaria cases in children <5 years old

Malaria In-patient Cases and Deaths (all ages) 2001-2008: Eritrea

Malaria In-patient Cases and Deaths (all ages) 2001-2008: Sao Tome and Principe
Future Actions Needed

- Halt the manufacture, marketing and use of oral artemisinin monotherapies
- Scale-up access to diagnostic testing for malaria
- Strengthen routine surveillance for malaria and regular monitoring of antimalarial drug efficacy
- Support operational research as an integral part of malaria programming to learn as we implement and continuously refine our delivery
- Capacity building on commodity management and case management and use of technologies
- Continued commitment for research for new technologies
- Continued donor commitment. US$ 5-6 billion required annually to ensure high coverage and maximal global impact. Ensure success in large countries with high burdens
Some References

www.who.int/malaria
http://rbm.who.int
http://www.cdc.gov/malaria
25 April 2011
Achieving Progress and Impact
WORLD MALARIA DAY
"If you think you're too small to be effective, you have never been in bed with a mosquito."

Bette Reese