Malaria Control in Africa - Rolling Back the Map

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Southern Health Association
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US Malaria, circa 1850

Fig. 218. Malaria distribution in the United States circa 1850.
Global Malaria Eradication Program, 1955-1969

Why Malaria Still Matters

Malaria, which had been eliminated or effectively suppressed in many parts of the world, underwent a resurgence in the last 3 decades.

Attributable to many factors -- social, political, economic, and the emergence and spread of drug-resistant parasites and insecticide-resistant mosquitoes.

The global effects of this disease threaten public health and productivity on a broad scale, and impede the progress of many countries toward democracy and prosperity.

World Malaria Situation

• 3 billion people (40% of world population) at risk of malaria
• ~300 million cases each year
• Causes 1 million deaths worldwide per year - mostly young children under 5 years in sub-Saharan Africa
• Costs > $12 billion per year in direct losses (illness, treatment, premature death) but much more in lost economic growth
World Malaria Situation

- ~10,000 travelers from Europe, Japan and North America (~2,000) contract malaria each year
- No vaccine; effective drugs expensive & counterfeited
- Resistance: parasites to drugs & vectors to insecticides

Distribution of *P. falciparum* Stratified by Endemicity Class

Malaria is a Disease of Poverty

Distribution of *P. falciparum* Stratified by Endemicity Class

Why is this map deceptive?

Geographic distribution of malaria

Where do most people live?

World map adjusted for population

How much money is spent on health care?

World map adjusted for health care spending

Malaria in the World

Maps from:

Sulfadoxine-Pyrimethamine resistance
Mefloquine resistance
Chloroquine resistance

Rapid Emergence, and Rampant Spread of Drug-resistant Malaria
Malaria Control

- Unprecedented funding and enthusiasm: Roll Back Malaria (WHO), Global Fund to Fight AIDS, Tuberculosis & Malaria, President’s Malaria Initiative, World Bank, Gates Foundation, etc.
- Gates Foundation meeting in 2007 - talk about malaria elimination / eradication
Clinical Presentation

Symptoms
• Fever, chills, sweats
• Headaches
• Nausea and vomiting
• Body aches, general malaise

Physical Exam
• Elevated temperature, perspiration
• Weakness
• Enlarged spleen and liver
• Mild jaundice
Clinical Presentation

Severe Malaria
– Coma, severe anemia, hypoglycemia, respiratory failure, renal failure
– High mortality rate

Diagnostic Testing

• Now recommended for all suspect malaria patients
  – Fever in a child under 5 years old
• Rapid diagnostic tests
• Microscope slides
• Clinical diagnosis where lab & / or staff not available
• Children < 5 years – Integrated Management of Childhood Illness (includes diagnosis)
Plasmodium falciparum
Thin blood film

Treatment

- Artemisinin containing compounds (artemether-lumefantrine = Coartem®) for uncomplicated malaria
- Intravenous then oral quinine for severe / complicated malaria
U. S. President’s Malaria Initiative (PMI)

United States Agency for International Development (USAID) / CDC Project

President’s Malaria Initiative

- 30 June 2005, President Bush announced a new 5-year, $1.2 billion initiative to rapidly scale up malaria control interventions in 15 high burden countries in Africa

- Global Health Initiative continues PMI
### Funding Levels and Coverage

<table>
<thead>
<tr>
<th>Year</th>
<th>Anticipated Funding Level</th>
<th>Coverage</th>
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<tbody>
<tr>
<td>2006</td>
<td>$30 million</td>
<td>3 countries</td>
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<tr>
<td>2007</td>
<td>$135 million</td>
<td>7 countries</td>
</tr>
<tr>
<td>2008</td>
<td>$300 million</td>
<td>15 countries</td>
</tr>
<tr>
<td>2009</td>
<td>$300 million</td>
<td>15 countries</td>
</tr>
<tr>
<td>2010</td>
<td>$500 million</td>
<td>15 countries</td>
</tr>
<tr>
<td>TOTAL</td>
<td>$1,265 million</td>
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### Countries Selected for PMI

**First Year (FY06):**
- Angola, Tanzania, Uganda

**Second Year (FY07):**
- Malawi, Mozambique, Rwanda, Senegal

**Third Year (FY08):**
- Benin, Ethiopia, Ghana, Kenya, Liberia, Madagascar, Mali, Zambia
PMI Goal and Targets

• Goal: To reduce malaria-related mortality by 50% in 15 selected countries

• Targets: To achieve 85% coverage of vulnerable groups with four key interventions

PMI Interventions

• Artemisinin-based combination therapy (ACTs) - Coartem®

• Insecticide-treated bed nets (ITNs) – “herd immunity”

• Intermittent preventive treatment in pregnancy (IPTp) - Fansidar®

• Indoor residual spraying (IRS), urban & periurban – “herd immunity”
What will PMI fund?

- Commodities
  - Antimalarial drugs for treatment of uncomplicated malaria (ACTs)
  - Rapid diagnostic tests
  - Long-lasting nets
  - Equipment and supplies for IRS (pyrethroids & DDT)

Zambia

- Population - 13 million, 45% < 15 years old, 2.5 million households
- Malaria incidence rate in 2009 - 239 / 1000 population
- Malaria is a leading cause of illness and death in Zambia
- Malaria contributes 20% to maternal deaths and 40% to under 5 year old deaths
Malaria hot spots in Zambia.

Predicted Parasitemia Risk for Children <5 years in Zambia.
Malaria presents a major burden to Zambia’s population, healthcare system and economy

- Malaria is endemic throughout Zambia with seasonal and geographic variations
- Leading cause of illness and death
  - 3 million cases of malaria and 3000 deaths per yr
- Estimated GDP loss of 1.5% per year
  - Low productivity, high expenditure on medicines, supplies & control programs

2006-2010 National Malaria Strategic Plan set a package of malaria control interventions

INDOOR RESIDUAL SPRAYING

- *Anopheles gambiae and A. funestus* main vectors; feed evenings or late at night
- Gorge themselves with blood
- Move to vertical surface and digest meal
- If insecticide on surface, they die
Indoor Residual Spraying

IRS Districts, 2009
IRS Coverage by Household & Population, Zambia, 2003-2010
Modes of ITN distribution

National Objective
- Ensure 100% of households have at least three ITNs
- Ensure at least 85% utilization rates

Strategies
- Mass distribution (door-to-door, through schools or health centers)
- Malaria in pregnancy (Mama Safenite®, antenatal clinics)
- Commercial distribution (PermaNet®)
- Last kilometer distribution (NetsforLife)

Types of ITNs
- Permanet®, Olyset®, Netprotect®

ITNs Planned for Procurement and Distribution in Zambia, 2009-2011
ITN Distribution – Issues

• Availability of vehicles for transport from district to communities
• Effort to track down to facility / distribution point level to link back with routine malaria disease reports
• Efficiency – is there a better way to get the nets out?
Zambia ITN Distribution, All Programs, 2004-2007

Numerator: all ITNs distributed to date per district
Denominator: 3*estimated household count per district

Source: NMCC, ITN distribution database

Zambia ITN Distribution – All programmes
2006-2008

Numerator: all ITNs distributed to date per district
Denominator: 3*estimated household count per district

Source: NMCC, ITN distribution database
Zambia ITN Gap Assessment
2009
Adjusting for IRS

Source: NMCC

- No Gap
- Low Gap (<25%)
- Medium Gap (≤50%)
- High Gap (>50%)
- Critical (>75%)

Source: NMCC
MALARIA IN PREGNANCY

• Pregnant women often carry the malaria parasite without symptoms
• Placenta does not have resistance to parasites and is often infected
• Complications
  – Miscarrages
  – Low birthweight
  – Maternal mortality
MALARIA IN PREGNANCY

• Intermittent Preventive Therapy in Pregnancy (IPTp)
  – 2-3 doses of sulfadoxine-pyrimethamine (SP or Fansidar®) during antenatal care visits
• Priority in bed net distribution

Malaria in Pregnancy Research
Dubowitz / Ballard: Demonstrating the Heal to Ear Maneuver

Dubowitz / Ballard Gestational Age Determination
Malaria in Pregnancy Research

• Sulfadoxine-pyrimethamine (SP) in vivo drug efficacy study
  – Does this drug still work to clear malaria parasites in pregnant women?
  – Enroll pregnant women with asymptomatic parasitemia, give SP and follow weekly to see if parasites clear

Malaria in Pregnancy Research

• SP birth outcomes effectiveness study
  – Do SP given in the 2nd and 3rd trimester of pregnancy prevent negative birth outcomes?
  – Enroll women at time of delivery and compare number of SP doses taken with birth outcome
  – Dubowitz score, placental biopsy for malaria and maternal blood smear for malaria
Placental Biopsy for Malaria – does anyone have a scalpel handle?

Tropical Disease Research Center Staff
Diagnostic Test Kits and Treatment Stock Outs

- Rapid diagnostic test kits
- Artemisinin-containing compounds for treatment
- SP for pregnant women

Pilot to Determine Best Method for Drug / Supply Delivery and Inventory in Zambia, 2009-2010
Malaria Indicator Survey 2008

Methods

• Representative probability sample
  – Rural and urban
  – First stage: 181 standard enumeration areas (SEAs) in 71 of 72 districts
  – Second stage: 25 households selected after all households mapped by PDA / GPS
  – 4405 households surveyed

• Household questionnaire
  – To identify members and demographics of household

Malaria Indicator Survey 2008

Methods

• Women’s questionnaire
  – Age 15 - 49 years

• Testing for children under 6 years of age
  – Parasitemia by both microscopy and RDT
  – Anemia

• PDA used for sampling and recording of data
# Malaria Indicator Surveys, 2006 & 2008, Zambia

<table>
<thead>
<tr>
<th>Indicator</th>
<th>MIS 2006</th>
<th>MIS 2008</th>
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<tbody>
<tr>
<td>Household Ownership of at Least One ITN</td>
<td>44.4</td>
<td>62.3</td>
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<tr>
<td>Pregnant Women Slept Under ITN Previous Night</td>
<td>23.7</td>
<td>49.8</td>
</tr>
<tr>
<td>Children &lt;5 Years Slept Under ITN Previous Night</td>
<td>22.8</td>
<td>41.1</td>
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<tr>
<td>Household Protected by at Least One ITN or IRS</td>
<td>43.2</td>
<td>65.5</td>
</tr>
<tr>
<td>Severe Anemia Rates, Children &lt;5 Years Old</td>
<td>13.3</td>
<td>4.3</td>
</tr>
<tr>
<td>Parasitemia Rates, Children &lt;5 Years Old</td>
<td>21.8</td>
<td>10.2</td>
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</table>
In-patient Malaria and Anaemia, Children <5 years Old by Year, 1\textsuperscript{st} and 2\textsuperscript{nd} quarter 2000-2008, Zambia

WHO Draft Report, HMIS Data, Zambia, 2009

THE EPIDEMIC SCORECARD

2 MILLION DEATHS A YEAR
6 MILLION NEW CASES A YEAR, AND CLIMBING

MALARIA

1 MILLION DEATHS A YEAR
300-500 MILLION NEW CASES A YEAR

TUBERCULOSIS

1 MILLION DEATHS A YEAR
10 MILLION NEW CASES A YEAR

HEPATITIS B VIRUS

1 MILLION DEATHS A YEAR
2 MILLION NEW CASES A YEAR

DIARRHEAL DISEASES

1.6 MILLION DEATHS A YEAR
2.7 BILLION NEW CASES A YEAR

AIDS

3.1 MILLION DEATHS A YEAR
3.5 MILLION NEW CASES A YEAR

42 MILLION PEOPLE ARE H.I.V. POSITIVE

MEASLES

1 MILLION DEATHS A YEAR
24 MILLION NEW CASES A YEAR

YELLOW FEVER

30 DEATHS A YEAR
2,000 NEW CASES A YEAR

DENGUE FEVER

1 MILLION DEATHS A YEAR
2 MILLION NEW CASES A YEAR

SARS

25 MILLION DEATHS A YEAR

HOWARD MARKEL & STEPHEN DOYLE
THE NEW YORK TIMES OP-ED APRIL 30, 2003
Clinical Complexities of HIV Care in Malarious Africa

• Anaemia from HIV and / or malaria
• Diagnostic challenges
  – Fever ≠ malaria – consider TB, pneumonia, sepsis
  – Parasitemia in semi-immune adults may not indicate malaria illness
• Atypical symptoms of malaria – gastrointestinal and respiratory

Impact of Malaria on HIV

• Increase in viral loads for up to 6-19 weeks
• Transient decrease in CD4 counts
• Potential for increased HIV transmission
• Unclear impact on HIV progression
Impact of HIV on Malaria

- Partial loss of malaria immunity in semi-immune patients
- Increased risk of uncomplicated malaria & increased parasite density
- Increased risk of severe malaria, correlates with CD4 counts
- Increased mortality from malaria
- Worsening of malaria-related anemia

Impact of HIV on Treatment of Malaria in Zambia

- 971 patients enrolled, 33% were HIV infected
- Treatment failure with sulfadoxine-pyrimethamine or artemether-lumefantrine not associated with HIV infection
- HIV infected patients with CD4 <300 had an increased rate of recrudescence

Malaria Research Activities – Zambia

- Sulfadoxine-pyrimethamine drug effectiveness and efficacy in pregnancy
- ITN longevity
- Community health worker compensation
- Saliva malaria diagnostics
Malaria Research Activities – Zambia

• Economics – cost effectiveness of interventions & impact of malaria on industry
• Impact of active case detection & treatment
• Vector insecticide resistance & vector mapping
• Field efficacy of larvicides

Malaria Vaccine Development

• Antigenic variation
• Pre-erythrocyte stage
  – circumsporozoite protein – RTS, S
  – leading candidate vaccine
  – 30-50% effective preventing clinical malaria in phase IIb trials
• Erythrocyte stage
  – merozoite proteins
• “We may not know enough about malaria to develop an effective vaccine”

Pierce BK and Miller LH. J Immunol 2009;5171-7
Challenges

- Net misuse / abuse
- Low net utilization (approx. 43% - 2008 MIS)
- Inadequate storage and transport at district
- Late disbursement of funds
- 2010: 1.7 M ITN gap
- IRS refusals
- Insecticide resistance

Key Lessons Learned - ITNs

- Improving utilization of existing nets will require new approaches
- PermaNet® longevity is unknown in Zambia
- Replacement and disposal strategies need to be put in place
Key Lessons Learned - IRS

- Insecticide resistance monitoring is needed
- Insecticide rotation is likely to begin in 2011 to mitigate resistance concerns

Children Saved by Vector Control Based on 2011-2015 Scale Up
New Directions

- Expansion of indoor residual spraying
- Use of electronic medical record for surveillance
- Collaboration on supply chain enhancement
- Use net longevity study data to plan future net purchases and replacement

Malaria Prevention for Expats in Africa

- Recommended by CDC for travelers to any location in Zambia
- Decisions by long-term residents based on local data about transmission
- Drugs to use
  - Larium® (mefloquine)
  - Doxycycline
  - Malarone® (atovaquone/proguanil)
- www.cdc.gov/travel