Overview

- Malaria 101: Early history, biology, and epidemiology
- The first push for malaria eradication (1950–1970)
- Worsening of malaria control (1990s)
- New focus and scale-up success (2000–2010)
  - Is eradication possible now?
History: Major Scientific Milestones

Charles Alphonse Laveran
Demonstrated parasites in patient’s blood, 1880

Ronald Ross
Discovered *Anopheles* mosquito as vector, 1897

Giovanni Batista Grassi
Demonstrated life cycle from mosquito to man, 1898–1899
Malaria Biology: The Human Malaria Parasites

- Intra-erythrocytic protozoan
- Human malaria: 4 major species
  - *Plasmodium falciparum*
  - *Plasmodium vivax*
  - *Plasmodium ovale*
  - *Plasmodium malariae*

- **P. falciparum**
  - Potentially fatal severe disease
    - Red blood cell destruction → severe anemia
    - Sequestration in cerebral vessels → coma
  - Multi-drug resistant
Malaria Biology: Vectors of Human Malaria

- >400 species of Anopheles mosquitoes found worldwide; ~50 transmit malaria
- Each species occupies distinct ecological niche
- Major African vectors tend to bite indoors and at night
- Biting and resting behavior affect transmission potential and control
Malaria Global Burden, 2008

- ~250 million clinical cases per year; 80% in Africa
  - Children aged <5 years and pregnant women most affected
- >800,000 deaths per year; >90% in Africa
- Disability from severe forms of the disease
- Annual economic burden
  - GDP → 1.3% loss

GDP, Gross domestic product
Prevalence of *P. falciparum* Malaria in Children Aged 2–10 Years

Events Leading up to the Global Malaria Eradication Program

- Early successes in mosquito control (Panama Canal)
- Effective interventions, chloroquine and DDT, became available after WWII
- Availability of good diagnosis with microscopy
- 8th World Health Assembly launches Global Eradication Campaign (1955)
Eradication Strategies 1950–1970

- “Magic bullet”: DDT indoor residual spray (IRS)

- Assumptions
  - People stay indoors at night
  - *Anopheles* mosquito bites at night, rests indoors on house walls, and receives a toxic dose of DDT

- Other major activities
  - Antimalarial drug treatment: Patients, occasionally as mass treatment
  - Surveillance to detect and eliminate any reservoirs
Eradication Successes

Malaria was eliminated in 37 countries during 1950–1978
### What Were the Problems?

<table>
<thead>
<tr>
<th>Category</th>
<th>Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical</td>
<td>Insecticide and drug resistance</td>
</tr>
<tr>
<td>Logistics</td>
<td>Supply chain failures</td>
</tr>
<tr>
<td></td>
<td>Poor delivery of IRS</td>
</tr>
<tr>
<td>Strategic</td>
<td>Rigidity</td>
</tr>
<tr>
<td></td>
<td>Lack of research</td>
</tr>
<tr>
<td></td>
<td>Africa not included</td>
</tr>
<tr>
<td>Financial</td>
<td>Funds diverted elsewhere</td>
</tr>
<tr>
<td>Sociocultural</td>
<td>Lack of community buy-in and participation</td>
</tr>
<tr>
<td></td>
<td>Decreasing acceptance of IRS</td>
</tr>
</tbody>
</table>

IRS, Indoor residual spraying
Consequent Change in Strategy (1970s)

- **22\textsuperscript{nd} World Health Assembly (1969)**
  - “Suspended” eradication campaign
  - Goal became control to “Minimize the health damage by malaria”
    - Less ambitious
    - Strategy adapted to local context

- **Shift from prevention with insecticides/DDT to antimalarial treatment**

- **Integrate activities into primary health care**
Worsening of Malaria Control (1990s)

- Decreased funding
- Intensification and spread of chloroquine resistance
Renewed Optimism in the New Millennium

- New partnerships
- New funding
- New political leadership in endemic countries
- New tools (drugs, bed nets)
A COMMITMENT TO MALARIA CONTROL AND PREVENTION: THE FIRST STEPS TOWARDS ELIMINATION

John R. MacArthur, MD, MPH
Chief, Program Implementation Unit
Division of Parasitic Diseases and Malaria
Center for Global Health
Centers for Disease Control and Prevention
Overview

- Roll Back Malaria and U.N. Millennium Development Goals
- President’s Malaria Initiative (PMI)
  - PMI under two presidents
  - Goals, targets, and funding
  - Focused interventions
  - CDC’s role in PMI: Strategic information
- Results achieved
  - Significant reductions in malaria transmission
Roll Back Malaria (RBM)

- **Global partnership**
  - Launched in 1998
  - WHO, UNICEF, UNDP, World Bank

- **Global framework**
  - Coordination of activities
  - Mobilization of resources
  - Establishment of technical working groups
  - Establishment of subregional networks

- **Global Malaria Action Plan**
  - Launched September 25, 2008, by RBM partnership
  - Scaling up for impact
  - Sustaining control over time

www.rollbackmalaria.org

UNICEF, United Nations Children’s Fund

UNDP, United Nations Development Program
Goal 4: Reduce child mortality
Goal 5: Improve maternal health
Goal 6: Combat HIV/AIDS, malaria, and other diseases
- Target 6c: Have halted by 2015 and begun to reverse the incidence of malaria and other major diseases
  - Incidence and death rates associated with malaria
  - Children under 5 sleeping under insecticide-treated bednets
  - Children under 5 with fever who are treated with appropriate anti-malarial drugs
International Financial Disbursements to Malaria Endemic

U.S. dollars (millions)


PMI, President’s Malaria Initiative
GF, Global Fund
President’s Malaria Initiative (PMI)

- On June 30, 2005, President Bush announced a new initiative to rapidly scale up malaria control interventions in high-burden countries in Africa
  - 5-year and $1.2B investment
- Challenged other donors to increase their funding
- PMI is led by USAID and co-implemented with CDC

Source: S. Craighead/White House (12/14/06)
PMI Goal and Targets

- **Goal:** Reduce malaria-related mortality by 50% in 15 selected countries
- **Targets:** Achieve 85% coverage of vulnerable groups with 4 key interventions (~270 million residents)
**PMI Interventions**

- **Artemisinin-based combination therapies (ACTs)**
- **Insecticide-treated bed nets (ITNs)**
- **Indoor residual spraying (IRS) (where appropriate)**
- **Intermittent preventive treatment in pregnancy (IPTp)**
## PMI Funding Levels and Coverage

<table>
<thead>
<tr>
<th>Year</th>
<th>Funding Level</th>
<th>No. Countries Covered</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>$30 M</td>
<td>3</td>
</tr>
<tr>
<td>2007</td>
<td>$135 M</td>
<td>7</td>
</tr>
<tr>
<td>2008</td>
<td>$300 M</td>
<td>15</td>
</tr>
<tr>
<td>2009</td>
<td>$300 M</td>
<td>15</td>
</tr>
<tr>
<td>2010</td>
<td>$500 M</td>
<td>15</td>
</tr>
<tr>
<td>TOTAL</td>
<td>$1,265 M</td>
<td></td>
</tr>
</tbody>
</table>
President Obama signals support for global health including malaria (September 2008)

The White House launches Global Health Initiative
- U.S. Government will invest $63 billion over 6 years

PMI is now a major component of GHI

"We will not be successful in our efforts to end deaths from AIDS, malaria, and tuberculosis unless we do more to improve health systems around the world, focus our efforts on child and maternal health, and ensure that best practices drive the funding for these programs."

—President Barack Obama, May 5, 2009
CDC’s Mandate in PMI: Strategic Information

- U.S. Congress (through the Lantos-Hyde Act, 2008) charged CDC to take a leading role in strategic information
  - Monitoring and evaluation
  - Surveillance
  - Operations research

- CDC is advising the U.S. Malaria Coordinator on priorities for these activities and being a key implementer

An Act
To authorize appropriations for fiscal years 2009 through 2013 to provide assistance to foreign countries to combat HIV/AIDS, tuberculosis, and malaria, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the “Tom Lantos and Henry J. Hyde United States Global Leadership Against HIV/AIDS, Tuberculosis, and Malaria Reauthorization Act of 2008”.

http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_bills&docid=f:h5501enr.pdf
PMI Focus: 15 African Countries

Angola
Benin
Ethiopia
Ghana
Kenya
Liberia
Madagascar
Malawi
Mali
Mozambique
Rwanda
Senegal
Tanzania
Uganda
Zambia
PMI Focus: Additional African Countries

Nigeria and the Democratic Republic of Congo account for the 23% of the world’s burden of the falciparum malaria.
Proportion of Households with at Least 1 Insecticide-Treated Bed Net (ITN) from 2 Survey Points

Data source: Demographic Health Survey, http://www.measuredhs.com
Proportion of Children Aged <5 Years Who Slept Under an ITN the Previous Night

Children <5 years old sleeping under an ITN


Data source: Demographic Health Survey, http://www.measuredhs.com
Zanzibar: Intervention Coverage and Malaria control

Intervention coverage percent (IRS, ITN, ACT)

Malaria positivity rate %

ITN, Insecticide-treated bed net
IRS, Indoor residual spraying
ACT, Artemisinin-based combination therapy
Declines in All-Cause Mortality in Children Aged <5 Years, 7 PMI Countries, 2003–2010

Data source: Demographic Health Survey, http://www.measuredhs.com
Resistance – A Lurking Threat

- Emergence of insecticide resistance in Africa
  - DDT, pyrethroids
- Emergence of artemisinin resistance in Southeast Asia
  - Thai-Cambodia border
Significant reductions in all-cause mortality

- Tanzania 19%
- Madagascar 22%
- Ghana 28%
- Zambia 29%
- Senegal 30%
- Rwanda 32%
- Kenya 36%

Massive scale-up of control interventions has been followed by substantial decreases in all-cause mortality in children aged <5 years

Initiative-wide impact assessment is under way
CDC’s SCIENTIFIC EVIDENCE BASE FOR SCALE-UP AND POSITIONING FOR MALARIA ELIMINATION

S. Patrick Kachur, MD, MPH
Chief, Strategic and Applied Sciences Unit
Division of Parasitic Diseases and Malaria
Center for Global Health
Centers for Disease Control and Prevention
Overview

1. Scientific evidence: Basis for current interventions
2. Global Malaria Eradication Research Agenda
3. CDC operational research priorities, 2010
1. Scientific Evidence: Basis for Current Malaria Interventions

- Artemisinin-based combination therapies (ACTs)
- Insecticide-treated bed nets (ITNs)
- Indoor residual spraying (IRS) (where appropriate)
- Intermittent preventive treatment in pregnancy (IPTp)
### Efficacy of ITNs on All-Cause Child Mortality from 4 Randomized Controlled Trials in Africa

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treated nets</th>
<th>Control</th>
<th>log [Relative rate] (SE)</th>
<th>Relative rate</th>
<th>Relative rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td></td>
<td>IV,Fixed,95% CI</td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Controls with no nets</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kenya (Nevill)</td>
<td>11596</td>
<td>11439</td>
<td>-0.3425 (0.157)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ghana (Binka)</td>
<td>18457</td>
<td>18054</td>
<td>-0.1985 (0.093)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burkina Faso (Habluetzel)</td>
<td>14773</td>
<td>14118</td>
<td>-0.1508 (0.1139)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kenya (Phillips-Howard)</td>
<td>17833</td>
<td>18099</td>
<td>-0.1744 (0.058)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.83 [ 0.76, 0.90 ]</td>
<td></td>
</tr>
</tbody>
</table>

**17% protective efficacy against child mortality before age of 5 years**

**Could save 5.5 lives for every 1,000 children protected**
People without nets experienced the same benefit if they lived within 300 meters of net users – reduction in:

- Parasite infection (odds ratio=0.59)
- Malaria illness (odds ratio=0.52)
- Anemia (odds ratio=0.53)
- Child mortality (hazard ratio=0.72)
Survival benefit lasted beyond 6 years

Mortality rates
- Infants: 113/1,000
- Children 1–5 years old: 28/1,000

Survival benefit lasted beyond 6 years

Mortality rates
- Infants: 113/1,000
- Children 1–5 years old: 28/1,000
Additional Lessons from the KEMRI/ CDC ITN Trial and Follow-up Studies

- Providing nets to 65% of older children and adults would protect even children without nets.

Preventing Childhood Malaria in Africa by Protecting Adults from Mosquitoes with Insecticide-Treated Nets

Gerry F. Killeen¹ ², Tom A. Smith³, Heather M. Ferguson¹ ⁴ ⁵, Hassan Mshinda¹, Salim Abdulla¹, Christian Lengeler³, Steven P. Kachur¹ ⁶

1 Ifakara Health Research and Development Centre, Ifakara, Morogoro, United Republic of Tanzania. 2 Department of Biological and Biomedical Sciences, University of Durham, Durham, United Kingdom. 3 Department of Public Health and Epidemiology, Swiss Tropical Institute, Basel, Switzerland. 4 Division of Infection and Immunity, Glasgow University, Glasgow, United Kingdom. 5 Division of Environmental and Evolutionary Biology, Glasgow University, Glasgow, United Kingdom. 6 United States Public Health Service Commissioned Corps and Malaria Branch, Division of Parasitic Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America.

Adam Nadel, Freelance

KEMRI, Kenya Medical Research Institute
ITN, Insecticide-treated mosquito net
Policy Impact of the KEMRI/ CDC ITN Trial and Follow-up Studies

Established the evidence-base for widespread scale-up and universal coverage

FROM EVIDENCE TO POLICY
Continued progress in scale-up and elimination will require improved tools for malaria control and surveillance

- **Scale-up**: Aims to reduce morbidity and mortality
- **Elimination**: Aims to reduce transmission
  - Basic reproduction number <1.0

2. Global Malaria Eradication Research Agenda

- New tools and systems to accommodate:
  - Drugs
  - Vaccines
  - Diagnostics
  - Insecticides

- Strategies to manage resistance to antimalarial drugs and insecticides for public health:
  - Combination treatments
  - Combined delivery systems
  - Rotational or mosaic deployment

http://malera.tropika.net
Global Malaria Eradication Research Agenda

- **Alternative vector interventions**
  - ITNs and spraying work against mosquitoes indoors
  - Some mosquitoes feed and rest outdoors
    - Larviciding
    - Spatial repellants, baited traps

- **Drug interventions for reducing transmission**
  - Mass screen and treatment
  - Transmission-blocking agents

- **Surveillance: Detecting and responding to local transmission**

ITN, Insecticide-treated bed net
3. CDC Operational Research Priorities in 2010

- Optimize current malaria control interventions
- Establish role for new and revisited interventions
  - Research and development
  - Clinical and field trials of new interventions
- Integration with other initiatives
Research and Development: Field-Ready, High-Sensitivity Test for Malaria

- WHO now calls for universal access to malaria diagnosis and treatment for every case of suspected malaria

- Diagnostic confirmation
  - Minimize the overuse of treatments
  - Improves detection and treatment of other causes of illness
  - Forms the basis of a reliable system for monitoring malaria and malaria control

Light microscopy

Rapid antigen detection
- As endemic countries approach elimination, highly sensitive tests become more critical
- Current diagnostic formats will improve management of malaria illness
- Elimination may rest on molecular assays
  - Available only in reference laboratories far from remote areas
Research and Development: Field-Ready, High-Sensitivity Test for Malaria

- CDC and University of Georgia
- Novel system for molecular diagnosis
- Real-time fluorescence loop-mediated amplification: Real LAMP
  - Detection of malaria parasites at very low numbers
  - Without access to reference laboratory staffing and equipment
  - Validation of the first generation prototype on specimens from Tanzania completed

Phase III malaria vaccine trial in Kenya

- First candidate vaccine to reach this stage of development
- One of 11 sites in 9 countries
- Could reduce clinical malaria by up to 35%, severe malaria by 49%

Clinical and Field Trials of New Interventions

When will we have a vaccine that can eliminate malaria?
- Current vaccine within 18–24 months
- Will reduce illness burden, not transmission
- Hundreds of other candidates in development
- Millennia of co-evolution confound development
Clinical and Field Trials of New Interventions

- **Combined impact of ITNs with indoor residual spraying**
  - Northern Ghana (starting 2011)

- **Combined impact of ITNs with insecticide-treated durable wall liners**
  - Lakeside Malawi (starting 2011)

ITN, Insecticide-treated bed net
Integration Opportunities

- Community-based control/elimination
- Integrated case management interventions
- Integrated vector control
- Integrated surveillance, monitoring and evaluation
From Scale-Up to Elimination: the Role of Partnership

- Creative partnerships within the U.S. government
  - Within Department of Health and Human Services
  - With U.S. government partners
- Partnerships beyond our system
Malaria Elimination: A Global Partnership Perspective

Richard W. Steketee MD, MPH

Director of Science
Malaria Control and Evaluation Partnership in Africa (MACEPA), PATH

Centers for Disease Control and Prevention
Public Health Grand Rounds, November 2010
“Now is the time to act. We should not ignore the shrinking of the malaria map, which has been successfully unfolding over the past century.”
Malaria Elimination

- Today’s opportunity for elimination success – why today?
- African country example of a move toward elimination
- A partnership perspective in transitioning from scale-up to elimination
- Opportunities for CDC to make a difference:
  - A perspective from outside
Malaria Landscape

• From Scale Up for Impact (SUFI) to Elimination
From Scale Up for Impact (SUFI) to Elimination
Malaria Elimination: Why Today?

- Between the Global Malaria Eradication Program and the start of Roll Back Malaria (1975 – 2000) was a time of science

- The scientists identified:
  - Prevention directed to the biology of the vector and able to be delivered proactively and to the most vulnerable
Malaria Elimination: Why Today?

- The scientists identified:
  - Treatment with combined drugs to optimize efficacy and delay resistance
  - Diagnostics that can be deployed close to home and in facilities and can clarify where malaria transmission, illness, and death is occurring
Malaria Elimination: Why Today?

- The scientists are seeking:
  - New/improved prevention, diagnostics and treatment
  - New interventions (vaccines, larval control, repellants)

- And we already have the ‘final intervention’ – surveillance for infection detection and transmission containment
Malaria Elimination: Zambia Example

Transmission intensity, 2006

Predicted parasitaemia prevalence
- < 0.1
- 0.1 - 0.3
- 0.3 - 0.5
- > 0.5

Copyright Licensed to the Malaria Atlas Project (MAP) at www.map.ac.uk, under a Creative Commons Attribution 3.0 license (http://creativecommons.org/licenses/by/3.0/). Note: The accuracy is approximate at the equator. Projection: Peters conical.
Zambia: Malaria Intervention Scale-Up 2001–2010

Percent Coverage of Interventions

- % households with at least one ITN
- % children slept under ITN last night
- % pregnant women slept under ITN last night
- % pregnant women received 2+ doses IPTp
- %HH with an ITN or IRS

ITN, Insecticide-treated bed net
IRS, Indoor residual spraying
IPTp, Intermittent preventive treatment in pregnancy
Reported Malaria Cases per 1,000 and Numbers of RDTs Delivered in Kazungula, Zambia

ITNs and IRS introduced

ITNs, Insecticide-treated bed net
IRS, Indoor residual spraying
RDTs, Rapid diagnostic tests
ITNs and IRS introduced

- **2005**: 981 cases per 1,000 population
- **2006**: 887 cases per 1,000 population
- **2007**: 346 cases per 1,000 population
- **2008**: 21 cases per 1,000 population
- **2009**: 18 cases per 1,000 population

**ITN**, Insecticide-treated bed net
**IRS**, Indoor residual spraying
**RDTs**, Rapid diagnostic tests
Reported Malaria Cases per 1,000 and Numbers of RDTs Delivered in Kazungula, Zambia

- **ITNs and IRS introduced**
- **RDTs introduced**

Malaria cases per 1,000 population

- 2005: 981
- 2006: 887
- 2007: 346

Number of RDTs Used

- 2005: 275
- 2006: 1625
- 2007: 346
- 2008: 21
- 2009: 18

**Legend**
- ITN, Insecticide-treated bed net
- IRS, Indoor residual spraying
- RDTs, Rapid diagnostic tests
Incidence Rates for All Districts in Southern Province, Zambia

Malaria cases per 1,000 population

- Provincial
- Choma
- Gwembe
- Itezhi-tezhi
- Kalomo
- Kazungula
- Livingstone
- Mazabuka
- Monze
- Namwala
- Siavonga
- Sinazongwe

68
Partners: Elimination is on some but not all of their agendas

- WHO, UNICEF, World Bank, UNDP
- US-PMI
- Bill and Melinda Gates Foundation
- Roll Back Malaria
- CDC?

*Consider embracing Elimination!*
A Partnership Perspective on CDC Engagement

- Focus on Africa, but work elsewhere (you do this)
- Work with many partners (you do this)
  - US-President’s Malaria Initiative (PMI), WHO and others
- What will CDC do with its own resources and focus
  - Do “Control” via US-PMI (you do this)
  - Do “Science of Elimination” on CDC’s dime (do this more explicitly and bring CDC’s strengths)
  - Do “Capacity Building” from CDC’s strengths
Surveillance as an intervention to reduce transmission

"Surveillance indicates epidemiological and remedial action.
…to detect cases...these are registered, treated and followed up with an investigation of the source and other possible cases;
…to discover transmission, establish its causes, eliminate residual foci, and to end transmission and avoid its resumption; and
…to substantiate that elimination has been achieved."

CDC – Doing “Science of Elimination”

- Surveillance as an intervention to reduce transmission
  - Diagnostics
  - Use of antimalarial drugs
  - Investigation procedures
- Test this “intervention” and its ability to contain transmission
CDC – Doing “Capacity Building”

- Capacity development for information management (building on surveillance for transmission reduction)
  - A “Stop Malaria” model (take a lesson from “Stop Polio”)
  - FELTP/FETP model in malaria-endemic countries
- Partner for this work

FELTP, Field Epidemiology Laboratory Training Program
FETP, Field Epidemiology Training Program
A Partnership Perspective on CDC Engagement

- Elimination and eradication require a long view…
  - and CDC should exercise its strength in “sustained public health focus” amidst competing priorities
Global Partnership Role for Elimination

- Bring a durable commitment

- Provide leadership in the “science of elimination”
  - Development of new tools and testing new strategies
  - Train the next generation

- Actively seek strategic partnerships en route to malaria elimination

- Elimination/Eradication is not for the faint of heart!