Conquering Malaria

DCP2, Juba, Southern Sudan, June 9-11, 2008

Dr. Dismas Ongore

Introduction

- 107 countries and territories at risk
- 50 percent of the world's population
- > 3 billion people at risk
- 1 - 3 million deaths each year
- 515 million cases annually
  - Majority Africa
- 5 billion clinical episodes resembling malaria

Introduction contd…

- In Southern Sudan the leading cause of morbidity
  - 27% in 2002
  - 28% in 2003
  - 29% in 2004
  - 27% in 2005
  - 22% in 2006
- In terms of mortality (health facilities)
  - 24% of the deaths in 2003
  - 21% in 2004

Etiology/Causes

- Four species of the genus *Plasmodium*
  - *P. falciparum*
  - *P. vivax*
  - *P. ovale*
  - *P. malariae*.
- Human infection
  - Sporozoites
  - Mature in the liver
  - Merozoites
  - Gametocytes

Distribution

- *P. falciparum*
  - Haiti, Papua New Guinea, and Sub-Saharan Africa
    - Causes most deaths
- *P. vivax*
  - Central America and the Indian subcontinent
- *P. malariae*
  - Throughout Sub-SaharanAfrica,
- *P. ovale*
  - Unusual outside Africa,
  - Less than 1 percent of isolates

Distribution S. Sudan

- *Plasmodium falciparum* dominant parasite
  - *M*ore than 90% of all morbidity
- *Plasmodium vivax* important
  - Border regions with Ethiopia
- Limited data on parasite prevalence
  - Malariometric survey Malakal and Wau
  - Prevalence rate 30-40% < 5 years

Transmission

- Female Anopheles mosquitoes
  - In Africa
    - Principally *Anopheles gambiae*, *Anopheles funestus*
- In Southern Sudan
  - The major vectors are
    - *Anopheles gambiae s.s*.
    - *A. Arabiensis*
    - *A. Funestus*
  - Little known about their relative distribution

Epidemiology

- *Stable malaria*
- > 1 infected human bite per person per day
- morbidity and mortality early childhood
- Some immunity develops against disease
- Most infections asymptomatic by adulthood
- Frequent, intense, year round transmission

Unstable malaria

- Transmission
  - Low
  - Erratic
  - Focal
- Full protective immunity
  - Not acquired
- Symptomatic disease
  - At all ages

An epidemic or complex emergency?

- Changes in
  - Environmental
  - Economic
  - Social conditions
  - Due to
    - Heavy rains
    - Migrations of refugees or workers
    - Breakdown in malaria control and prevention services
  - In areas with unstable malaria

Epidemiology South Sudan

- Suitable for malaria transmission
  - Transmission perennial
    - Seasonal variations
  - Peak malaria incidence
    - Towards the end of the rainy season
  - Malaria transmission
    - Southern parts (7-8 months)
    - Northern parts (5-6 months)

Epidemiology S. Sudan contd...

- More localized outbreaks do occur
- Caused by
  - Environmental and climatic factors
  - Movement of (Internally Displaced Persons) IDPs
    - Little immunity
    - Into areas of high transmission
  - Lack of access to treatment in some areas

Manifestations

- Uncomplicated falciparum malaria
  - Mortality rate of approximately 0.1 percent
- Anemia
  - Quite common
    - Among young children
    - In areas of stable transmission
    - In presence of resistance to drug
- Coma
  - Ominous feature of falciparum malaria,
  - Associated with death rates
    - 20 percent among adults
    - 15 percent among children.

Manifestations contd…

- Convulsions
  - Usually generalized and often repeated
  - In up to 50 percent of children with cerebral malaria
- Neurological sequalae
  - In < 3 percent of adults
  - 10 to 15 percent of children surviving CM
  - Repeated seizures, and deep coma

Diagnosis

- Confirmatory diagnosis
  - Microscopy
- Newer diagnostic tests using
  - Antigen detection methods (RDTs)
    - Being evaluated
    - Promising
    - Limitations in relation
      - Species, sensitivity
      - Parasite quantitation,
      - Field feasibility
      - Costs

Diagnosis S. Sudan

- Introduction of the ACT
  - Need exists to increase the capacity for diagnosis
  - In order to avoid unnecessary treatment.
- For peripheral health facilities
  - Rapid Diagnostic Tests (RDTs) recommended
  - Children under 5 treated on clinical diagnosis
  - Older patients tested wherever RDTs are available

Interventions and their effectiveness

- Malaria can be conquered by
  - Use of priority antimalarial services
    - Full coverage
    - Access
  - Diagnosis
    - Clinical, microscopy, RDTs
  - Patient management
    - Diagnosis, treatment, counseling, education and referral
  - Judicious use of insecticides
    - To kill and repel the mosquito vector
- Control of epidemics.

Interventions and their effectiveness contd…

- Eliminating malaria
  - Distant goal
  - Huge challenge because of
    - Widespread *Anopheles* breeding sites
    - Large number of infected people
    - Use of ineffective antimalarial drugs
    - Inadequacies of
      - Resources
      - Infrastructure
      - Control programs

Interventions and their effectiveness contd…

- The Roll Back Malaria Partnership
  - Began in 1998
  - Aims to halve the burden of malaria by 2010
  - Has developed strategies and targets
  - Making substantial progress
    - Success in
      - Brazil
      - Eritrea
      - India
      - Vietnam

Interventions and their effectiveness contd…

- Early diagnosis and effective treatment
  - Lends credibility to the malaria program
  - Strengthens confidence in the health care system
  - Raises the esprit of clinicians and public health workers.
  - Can cure infection
  - Prevent further morbidity
  - Prevent progression to severe disease and death
  - Arrest transmission

Interventions and their effectiveness contd…

- Requires
  - Timely and accurate diagnosis
  - Use of efficacious drugs
  - Education of patients and their families
    - About the disease
    - Home management, and prevention
    - Referral to higher levels of the health system

Interventions and their effectiveness

- Critical issues
  - *Timelines*
    - Untreated 1 in 250 will progress to severe disease
    - Provided within 24 hours of the onset of symptoms and signs
  - *Diagnosis and effective drug treatment*
    - Based on detection of the parasite
    - Based on clinical grounds
  - Monitoring the therapeutic efficacy of drugs
  - *Location of clinical management*
    - Through health facilities
    - Near the home when access is limited

IPT in Pregnancy

- Recommended in pregnancy
  - Two curative doses
  - SP given during the second and third trimesters
- IPTi in infancy involves
  - Giving infants treatment doses during
    - Vaccination
    - Well-baby visits to health clinics
    - Not practiced in S. Sudan

IPT in Pregnancy contd…

- Southern Sudan
- IPT adopted
  - Follow WHO guidelines
    - At least 2 doses of SP are recommended
  - NGOs and health workers sensitized
  - Exact data on the coverage level for IPT2
    - Not yet available

Insecticide-Treated Nets

- ITNs (bednets, curtains, and other materials)
  - Major strategies of malaria control
  - Kill or repel mosquitoes
  - Provide personal protection
  - Effectiveness depends on
    - Acceptability
    - Affordability
    - Accesibility

Insecticide-Treated Nets contd…

- It is contingent on
  - The habits, biology, and susceptibility of the vector
  - Compliance of the human population
  - Concentration of insecticide on or in the fiber
  - Re-treating ITNs
    - Semi-annually
    - Just before the annual peak in transmission
    - Major logistical and financial challenge

Insecticide-Treated Nets contd…

- Efficacy
  - More than 50 percent protective efficacy
  - 29 percent protection against severe malarial disease
  - Substantial protection against anemia
  - Reduced child mortality by 18 percent
  - Demonstrated in many trials

Indoor Residual Spraying

- The application of long-lasting insecticides
- Effective for upto six months on the walls of dwellings
- Repel mosquitoes from entering houses
- Impart a lethal dose of the insecticide on the mosquito
- Most effective against indoor-biting (endophilic) mosquito vectors

Indoor Residual Spraying contd…

- Main criterion for choosing an insecticide
  - Vector susceptibility
  - Post feeding behavior
- Compounds used
  - Organophosphates
  - Carbamates
  - Pyrethroids
  - Organochlorines (DDT)

Indoor Residual Spraying contd…

- The effectiveness depends on
  - Cost
  - Toxicity
  - Acceptability of the insecticide
  - Residual effects
  - Local political and international partnership commitment.
  - Evidence from many large scale trials

Vector Control S. Sudan

- In the late 70's and early 80's
  - Indoor residual spraying and larviciding was implemented
    - By the local vector control units
    - Around the major towns and municipalities
    - Interventions stopped in 1983 due to the collapse of infrastructure and public services

Vector Control S. Sudan contd…

- Long-lasting insecticidal nets (LLINs) are the main strategy at present, particularly for the rural and remote areas
- The major targets for LLINs are pregnant women andChildren under 5 years of age
- Nets are procured through GFATM, UNICEF, and Sudan Health Transformation Project funded by USAID

Vector Control S. Sudan contd…

- Long-lasting insecticidal nets (LLINs)
  - Distributed by NGOs for free through health facilities and Communities
  - Sold at highly subsidized prices, US$ 1.00 for a mash net, through social marketing funded by DFID and implemented by PSI.
- Use of locally made “damuria” net
- Use of LLIN version of the “damuria”

Vector Control S. Sudan contd…

- Limited data on coverage of households
- A UNICEF multi-cluster (2000) indicated
  - Maximum coverage of 36% of children under the five
  - Less than 5% under an ITN
- Accuracy of estimates questionable
  - More detailed information needed
- Estimates on the number of nets distributed
  - Total net output (mash and damuria): 45,000 in 2003 and 2004, 253,000 in 2005, 700,000 expected in 2006
- Commercial sector still quite weak

Health Education and Counseling

- The provision of information via newspapers, radio, or television
- Health counseling interactive
- The provision of information to households
  - Needed in all endemic communities
  - Should cove the importance of early treatment and where to access it, the use of referral services, and the significance of full compliance with treatment
- The necessary information can be provided by communities and voluntary health workers

Economics of malaria control interventions

- Cost-effectiveness
  - Wide range of malaria control interventions
- Very low-income country range per DALY averted
  - ITNs (US$19 to US$85)
  - Residual spraying (US$32 to US$58)
  - Chemoprophylaxis for children (US$3 to US$12)
  - IPT for pregnant women (US$4 to US$29)
  - Case-management improvements (US$1 to US$8)

Insecticide-Treated Nets.

- Analysis based on WHO TDR delivery mechanism
- Treatment of nets done by
  - Householders
  - Community health workers
  - Program staff
- Insecticide with
  - Permethrin (Lasts for six months)
  - Deltamethrin (Effective for a year)
- Activities undertaken:
  - Training of staff and community health workers
  - Campaign to inform the community about the intervention
  - Procurement and transport of the insecticide and nets
  - Initial treatment
  - Re-treatment of the nets

Insecticide-Treated Nets contd...

- Calculated for each intervention for two scenarios
  - Nets distributed to households
  - Treatment arranged for existing nets
- With one treatment per year using deltamethrin
  - Mean cost per DALY averted: US$11 (90 percent range of US$5 to US$21)
- 2 treatments of permethrin per year mean CER
  - US$17 (90 percent range of US$9 to US$31)

Insecticide Residual Spraying.

- Four insecticides considered for analysis
  - DDT
  - Malathion
  - Two pyrethroids, deltamethrin and lambdacyhalothrin.
- When one round of spraying was done per year
  - CERs for the four insecticides (Range from US$5 - $18)
- With two rounds per year;
  - Costs increased
  - Effectiveness remained the same
  - All the CERs approx. doubled from US$11 - $34

IPT during Pregnancy

- Cost-effectiveness analyzed assuming
  - Primigravid women are given 2-3 doses of SP at a prenatal clinic
- Benefit to the mother and child analyzed by
  - Decreased childhood mortality
  - Changes in the incidence of severe anemia
- Effect of IPT estimated on neonatal mortality rate
- The CER for IPT using SP had a
  - 90 percent range from US$9 to US$21 with a mean of US$13
  - Average total cost-effectiveness had a mean of (US$24, 90 percent range of US$16 to US$35)

Change in First-Line Drug

- Cost-effectiveness analyzed of changing first-line therapies to SP and to ACT
- Patient-management model used
  - Patient presents with uncomplicated malaria and progresses
    - To full recovery
    - Recovery with neurological sequelae
    - Death
- Changes in three potential drug policies considering the use of either chloroquine or SP
    - SP or amodiaquine as a second-line drug
    - Quinine as the third-line drug
    - Cost-effectiveness of policy switches to either SP or ACT examined

Change in First-Line Drug contd...

- Switch from chloroquine to SP is cost-effective when chloroquine resistance is above 35 percent and it is less than $150 per DALY averted
- Switching from chloroquine to ACT is cost-effective when Chloroquine resistance is around 37 percent
- Switching from SP to ACT is cost-effective when SP resistance reaches 12 percent
- High resistance to SP arises when it is used as a first-line therapy

Results and Interpretation

- All interventions can be considered attractive when a cutoff of US$150 per DALY averted
- ITNs are cost-effective if the coverage is already high
- IPT is economical if prenatal care coverage is sufficient
- Comparison between ITNs and IRS globally
  - Both are equally effective
  - Choice should be based on operational feasibility

Results and Interpretation contd...

- Widespread approaches toward drug use may result in increased drug resistance and cost
- First line treatment:
  - Switch from chloroquine to SP is unlikely to be costly
  - Switch from chloroquine to ACT is likely to be costly
- Resistance to ACT is essentially nonexistent

Results and Interpretation contd...

- Switching to ACT becomes cost-effective especially when SP resistance surpasses 12 percent
- Switch from chloroquine to ACT is highly cost-effective at resistance above 37 percent
- Studies indicate remarkable effectiveness of the ACT artemether-lumefantrine
- Accessibility to ACTs will increase as its cost decreases

Affordability and Scaling Up

- CE analyses can identify the most efficient interventions to implement
- Some interventions are affordable
  - Prevention of the childhood malaria with ITNs has high total cost thus requires external financial assistance
- More information on affordability is needed

Affordability and Scaling Up contd…

- Full coverage of children under 5 years with ITNs cost US$2.81 million per 1 million persons, assuming the provision of nets combined with two rounds of permethrin treatment
- Full coverage of children under 5 years with IRS cost US$4.01 million per 1 million persons with using deltamethrin two rounds
- Strategic approaches for national ITN upscaling
  - Social marketing (e.g. Malawi and Kenya)
  - Assisted commercial sector development (e.g. Senegal, Mali, and Tanzania)
  - Total free distribution to children at the time of measles vaccination (e.g. Togo)

Affordability and Scaling Up contd…

- Important feature of all of the approaches:
  - Cost per distributed net decreases significantly, as the acceccability increases
- Additional actions targeted at the main high-risk groups
  - e.g. Voucher scheme in Tanzania (Free ITN for every pregnant woman)
- Re-treatment of ITNs on a large-scale
  - Formidable operational issue
    - Free distribution of insecticide **(**e.g. Vietnam and China)
    - Long-lasting insecticidal nets
    - Substantial commitment by donors and governments **(**Per capita expenditure around US$4)

Research priorities

- Four major areas identified by WHO Scientific Working Group on Malaria

1. Patient management for uncomplicated malaria in children and in pregnancy

- Evaluation of treatment effectiveness
- Evaluation of access to treatment
- Home management
- Evaluation of alternative delivery systems
- Evaluation of ACT
- Delivery approaches via the public and private sectors

2. Prevention research to focus on

- New approaches to drug-based malaria prevention, including IPT in children and during pregnancy
- Strategies for scaling up the use of ITNs.

Research priorities contd…

3. **Innovative approaches**
   - Sequencing the DNA of *P. falciparum* and *A. gambiae*
     - Discover and develop drugs
     - Diagnostics
     - Vaccines
     - Insecticides
4. **Social, economic, and policy research to focus on**
   - Methodology for measuring socioeconomic status
   - Balance of public private partnerships
   - Ethical, legal, and social issues pertaining to new malaria-related tools

Affordability and Scaling Up

ACT and long-term affordability

- Additional annual costs of ACT
  - US$300 million to US$500 million globally
- Other costs
  - Drugs for non malarial fevers
  - Health system strengthening required
    - Improved drug regulation
    - Pharmacovigilance
    - Diagnostics
    - Implementation of drug policies
- Changed the economic landscape of malaria control
  - Innovative approaches at the global level
    - GFTAM
    - Other agencies and organizations