DEVOTED TO REDUCING MALARIA DEATHS & SUFFERING IN HUMANITARIAN CRISIS
Malaria Prophylaxis in Pregnant Women

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GOALS FOR UNDERSTANDING

• Global Scope of malaria and maternal malaria
• Importance of pregnant women in context of malaria
• Malaria in humanitarian crisis
• Intermittent Preventative Treatments
• Means for measuring coverage and impact
GLOBAL SCOPE OF MALARIA

- 3.3 billion people at risk worldwide
- 98% of Malarial deaths in Africa
- Second leading cause of death from infectious diseases after HIV/AIDS in Africa
MALARIA FAST FACTS

• WHO estimates a child dies every 45 seconds from Malaria
  – Makes up 20% all childhood deaths

• 50 million women become pregnant in Malaria endemic areas yearly
  – Half in areas where *P. falciparum* endemic
• Red: Malaria Everywhere

• Yellow: Malaria in Provence

• Green: No Known Malaria

http://cdc-malaria.ncsa.uiuc.edu/
MALARIA DURING PREGNANCY

• Leads to 5-12% of all low birth weights in children worldwide
• Contributes to 35% of all preventable low birth weights in children worldwide
  • Low birth weights can lead to premature births and intrauterine growth retardation
• 75,000-200,000 infant deaths worldwide each year attributed to malarial infection during pregnancy
PREGNANT WOMEN AT HIGH RISK

- Pregnant women have an increased susceptibility to contracting malarial infection because of changes in their immune system related to the pregnancy.

- Pregnant women more susceptible to *P. falciparum* specifically because of placenta provides a novel intervillous space for cytoadherence.
MATERNAL IMMUNE RESPONSE

- Typically, immunity built up after several years as the human’s cytoadherence molecules are depleted.

- When women become pregnant, placenta develops a new space for cytoadherence.

- Even if the woman had built up previous immunity in her endothelial cells, the placental lumen provides a new location for parasite development.
EFFECTS OF MULTIPLE PREGNANCIES

- Acquired immune effects seen in the differences of severity of malarial infection depending if the woman is primigravida, or multigravida, because of the idea of “pregnancy immunity.”
- Mother loses previously acquired immunity once pregnant, during pregnancy able to regain some of that immunity
  - Will counteract infection in subsequent pregnancies
EFFECTS OF MULTIPLE PREGNANCIES

- Primigravidae women less likely to have immunity from infection
- Multigravidae women, more likely because of “Pregnancy Immunity”
  - Mother loses previously acquired immunity once pregnant, during pregnancy able to regain some of that immunity
  - Will counteract infection in subsequent pregnancies
DIAGNOSIS

• Pregnant women difficult to diagnose because of differences in placental and peripheral blood parasitaemia
  • Placenta could have many infected red blood cells while none detected from peripheral blood
  • Placental malaria often not diagnosed
CLINICAL MANIFESTATIONS

- Depends on level of acquired immunity pre-pregnancy

- High/stable transmission: mothers generally asymptomatic even though immunity wanes during pregnancy
  - Maternal anemia, low birth weight

- Low/unstable transmission areas: mother and fetus at risk for most severe consequences
  - Maternal anemia, severe malarial disease, low birth weight, premature birth, fetal loss
CONTEXT HUMANITARIAN CRISIS: TSUNAMI

- Population migration
  - Women with low immunity moving into areas of high transmission or vice versa

- New pools of standing water
  - Perfect breeding grounds for mosquitoes

- Close proximity of people with active infections and non-infected persons
HISTORY MALARIA PREVENTION

• 1950s first preventative malaria strategies with chemoprophylaxis with chloroquine
• 1980s became a public health issue
• Chloroquine resistance and poor adherence (weekly/bi-monthly administration required) led to poor effectiveness
• 2004 Intermittent preventative treatment (IPT) replaced chemoprophylaxis
INTERMITTENT PREVENTATIVE TREATMENT

• Administration of a single, curative dose of an effective anti-malarial drug
  • Current recommended drug is sulfadoxine-pyrimethamine
  • Administered at least two times during pregnancy
    • After first trimester and first sign of quickening
    • Doses must be at least one month apart
Some instances of resistance
2005 WHO convened to review the efficacy of IPT-SP
- Used children <5 as a measure
- Found that at its lowest, efficacy dropped to 61% but still deemed effective
- Data is hard to extrapolate to pregnant women, and randomized controlled trials must deal with ethical issues because mortality outcomes are used as measures
TREATMENT RESTRICTIONS

- Pregnant women shouldn’t take Primaquine (typically used to prevent relapse of *P. vivax* and *P. ovale*)
  - associated risk of intravascular haemolysis in the mother and fetus

- Tetracyclines and doxycycline excluded for adverse effects on bone growth with fetus
LOOKING FORWARD

• Further research needed surrounding sulfadoxine-pyrimethamine
  • Optimal timing and dosage
  • Resistance/efficacy
• Mefloquine: Newest alternative
  • Long half life like sulfadoxine-pyrimethamine, but more research needed to deem safety
  • Still expensive
ANTENATAL CARE RECOMMENDATIONS

• 4 visits recommended, with 3 after first quickening
  • IPT should be administered at all 3 visits past first trimester to increase chance of receiving at least 2 doses IPT
  • HIV+ mothers have recommended dosage of at least 3 because of higher likelihood of infection and parasite densities
• Combination with other interventions important
ANTENATAL CARE RECOMMENDATIONS

http://www.cdc.gov/malaria/malaria_worldwide/reduction/iptp.html

DEVOTED TO REDUCING MALARIA DEATHS & SUFFERING IN HUMANITARIAN CRINES
INSECTICIDE TREATED NETS

• Should be given to all pregnant women in areas of malaria transmission

• Only safe method of prevention for pregnant women during first trimester

http://www.cdc.gov/malaria/malaria_worldwide/reduction/itn.html
CASE STUDY COTE D’IVOIRE

- Conducted between March and September 2008
- 6 antenatal facilities selected, with requirement of also providing HIV prevention of mother to child transmission
- Estimated placental malaria rate from neighboring, Ghanaian data, at 15%
- Goal: Evaluate coverage and effectiveness of IPT-SP since 2004 Implementation based on WHO guidelines
CASE STUDY COTE D’IVOIRE

- 2,044 women
- All gave birth at one of six selected clinics
- Blood samples taken from umbilical cord and placenta right after birth
  - Blood sample taken from neonate 2 hours after birth
CASE STUDY COTE D’IVOIRE: RESULTS

- 83.7% of women had received at least one dose of IPT-SP
- 49.8% had received at least two doses
  - no significant differences found for age, gravidity, or HIV status of the mother
CASE STUDY COTE D’IVOIRE: RESULTS

- Clear dose-effect relationship with IPT-SP and placental malaria
  - 82% reduction in placental malaria for the women who had taken at least two doses of IPT-SP
  - 68% reduction in placental malaria for those women who had taken one dose of IPT-SP
CASE STUDY COTE D’IVOIRE: RESULTS

- Overall, there was a decrease of placental malaria prevalence, to 4.8%
  - compared to 2004 African studies recorded prevalence rates of 10.6-20.5%
  - Data sets hard to compare because of location of data collection and population characteristics, such as the proportion of primigravidae women.
CASE STUDY COTE D’IVOIRE: TAKEAWAYS

• Only 53% of women visited the antenatal clinic at least three times.
• Challenges to coverage:
  • staff shortages to deliver the dosage
  • limited drug supplies
  • difficulty to access of antenatal care
PROGRESS INDICATORS

• 2007, WHO outlined several important indicators that should be routinely measured both in clinics and through household surveys

• Evaluate progress/effectiveness of intervention delivery, and outcomes and impact.

BOX 2. Recommended indicators for monitoring and evaluation of programmes to control malaria during pregnancy

Output indicators
• percentage of antenatal clinic staff trained: pre-service, in-service or during supervisory visits in the control of malaria during pregnancy during the past 12 months (including intermittent preventive treatment, counseling on use of insecticide-treated nets and case management for pregnant women);
• percentage of health facilities reporting stock-out of the recommended drug for intermittent preventive treatment (currently sulfadoxine-pyrimethamine) in the past month or in the determined period (according to national guidelines).

Outcome indicators
• percentage of pregnant women receiving intermittent preventive treatment under direct observation (first dose, second dose, third dose, according to national guidelines);
• percentage of pregnant women who report having slept under an insecticide-treated net the previous night.

Impact indicators*
• percentage of low-birth-weight singleton live births (< 2500 g), by parity;
• percentage of screened pregnant women with severe anaemia (haemoglobin < 7 g/dl) in third trimester, by gravidity.

* Influenced by other factors, such as nutrition, hookworm infection and pre-term birth

### SAMPLE SURVEY

#### Section: VI. PREGNANCY AND INTERMITTENT PREVENTIVE TREATMENT

<table>
<thead>
<tr>
<th>Question</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>301</td>
<td>ENTER IN 3/2 THE NAME AND SURVIVAL STATUS OF THE MOST RECENT BIRTH. Now I would like to ask you some questions about your last pregnancy that ended in a live birth, in the last 6 years.</td>
</tr>
<tr>
<td>302</td>
<td>FROM QUESTIONS 212 AND 216 (LINE 01)</td>
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<tr>
<td>303</td>
<td>HEALTH PROFESSIONAL</td>
</tr>
<tr>
<td></td>
<td>DOCTOR _____________ A</td>
</tr>
<tr>
<td></td>
<td>NURSE/MIDWIFE ____________ B</td>
</tr>
<tr>
<td></td>
<td>AUXILIARY MIDWIFE _____________ C</td>
</tr>
<tr>
<td></td>
<td>OTHER PERSON __________ D</td>
</tr>
<tr>
<td></td>
<td>TRADITIONAL BIRTH ATTENDANT ___________ E</td>
</tr>
<tr>
<td></td>
<td>OTHER (SPECIFY) ___________ X</td>
</tr>
<tr>
<td></td>
<td>NO ONE ________________ Y</td>
</tr>
<tr>
<td>304</td>
<td>DURING THIS PREGNANCY, DID YOU TAKE ANY DRUGS IN ORDER TO PREVENT YOU FROM GETTING MALARIA?</td>
</tr>
<tr>
<td></td>
<td>YES ___________________ 1</td>
</tr>
<tr>
<td></td>
<td>NO ___________________ 2</td>
</tr>
<tr>
<td></td>
<td>DON'T KNOW _______________ 3</td>
</tr>
<tr>
<td>305</td>
<td>WHICH DRUGS DID YOU TAKE TO PREVENT MALARIA?</td>
</tr>
<tr>
<td></td>
<td>RECORD ALL MENTIONED.</td>
</tr>
<tr>
<td></td>
<td>IF TYPE OF DRUG IS NOT DETERMINED, SHOW TYPICAL ANTIMALARIAL DRUGS TO RESPONDENT.</td>
</tr>
<tr>
<td></td>
<td>SPFsansidar __________ A</td>
</tr>
<tr>
<td></td>
<td>Chloroquine ___________ B</td>
</tr>
<tr>
<td></td>
<td>OTHER (SPECIFY) ___________ X</td>
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<tr>
<td></td>
<td>DON'T KNOW _______________ 4</td>
</tr>
<tr>
<td>306</td>
<td>CHECK 305.</td>
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<td></td>
<td>DRUGS TAKEN FOR MALARIA PREVENTION</td>
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<td></td>
<td>CODE A CIRCLED</td>
</tr>
<tr>
<td></td>
<td>CODE A NOT CIRCLED</td>
</tr>
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</table>

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