Malaria during pregnancy

- Approximately 45 million pregnancies occur annually in malarious areas
  - ~25 million of those in sub-Saharan Africa
- Perinatal effects depend on intensity of transmission
  - Low and High malaria transmission area
Malaria during pregnancy in high/moderate transmission area

Impact of disease

- In sub-Saharan Africa MIP is estimated to account for:
  - 8 – 14% of low birth weight
  - 8 – 36% of preterm delivery
  - 3 – 8% of all infant deaths
  - 2 – 15% of maternal anemia
Malaria during pregnancy high/moderate transmission area

*P. falciparum* malaria

- Asymptomatic Infection
  - Placental Sequestration
    - Nutrient Transport
      - Low Birth Weight
        - Risk of Infant Mortality

- Maternal Anemia
WHO recommendation for control of MIP in high/moderate malaria transmission area

- Insecticide-Treated Nets
- Effective Case Management
- Intermittent Preventive Treatment (IPT)
- Anemia prevention
## Intermittent preventive treatment (IPTp) with SP: program effectiveness evaluations

<table>
<thead>
<tr>
<th>Site</th>
<th>Study design</th>
<th>Anemia</th>
<th>Placental parasitemia</th>
<th>Birth weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malawi, Verhoeff 1998</td>
<td>Observational: Delivering women; comparing 2 or 3 doses of SP vs. 1 dose</td>
<td>Mean Hb increased (multigrav. only)</td>
<td>NS</td>
<td>LBW decreased, Mean BW increased</td>
</tr>
<tr>
<td>Malawi, Rogerson, 2000</td>
<td>Observational: Delivering women; number of doses of IPTp/SP vs. outcome measures</td>
<td>Mean Hb increased, anemia decreased (2-dose only)</td>
<td>Reduced (1 and 2 doses)</td>
<td>LBW decreased, Mean BW increased</td>
</tr>
<tr>
<td>Kenya, Van Eijk, 2004</td>
<td>Observational: Delivering women; number of doses of IPTp/SP vs. outcome measures</td>
<td>NA</td>
<td>Reduced</td>
<td>LBW decreased, Mean BW increased</td>
</tr>
<tr>
<td>Burkina Faso, Sirima 2006</td>
<td>Program evaluation: ANC/DU; number of doses of IPTp/SP vs. outcome measures</td>
<td>NS</td>
<td>Reduced (2 and 3 doses)</td>
<td>LBW decreased (3 doses)</td>
</tr>
</tbody>
</table>

SP = sulfadoxine-pyrimethamine; Hb Hemoglobin; LBW Low birth weight
NS = not statistically significant (p > 0.05)
Program collaboration with ANC

• Schedule of 4 ANC visits for normal pregnancy
• First visit before quickening where LLIN is given
• Three visits after quickening and IPTp given at each scheduled ANC (but not more frequently than monthly interval)
Intermittent preventive treatment

Fetal growth velocity

1 2 3 4

Conception Quickening Pregnancy Birth
Status of IPTp policy and implementation in Africa

2001

2008

IPTp policy
Very little or no malaria (7)
No IPT policy
Increasing SP resistance

- Meta analysis (ter Kuile JAMA 2007)
  - Shows IPTp-SP remains efficacious even with in-vivo SP resistance in <5yo of up to 50%
  - So WHO expert technical committee recommends that in countries that are already implementing IPTp-SP, continue to do so and evaluate its effectiveness (generic protocol for measuring IPTp-effectiveness currently being finalized)

- Monitoring of SP resistance in pregnant women:
  - Therapeutic efficacy
  - Preventive efficacy

- Alternate antimalarial drug (even ACTs) as option for IPT
  - Good safety profile
  - Efficacy
  - Program feasibility

ISTp???
IPTp with SP: summary of evidence and benefits

- 2 doses of IPT with SP is associated with:
  - Reduction in 3\textsuperscript{rd} trimester maternal anemia
  - Reduction in placental malaria parasitemia
  - Reduction in low birth weight
- At least 2 doses required for optimal benefit
- Regimen is safe and well tolerated
- Not recommended in HIV\textsuperscript{+} women receiving daily CTX
HIV Among Pregnant Women in sub-Saharan Africa

- Estimated 27 million people in Africa living with HIV/AIDS
- 55% of sub-Saharan Africa adult HIV infection in reproductive-age women
- Estimated increase in MIP attributable to HIV is 5.5% and 18.8% for populations with HIV prevalence of 10% and 40%
# Effect of HIV on Malaria

Kisumu, Kenya, 1996-1999

<table>
<thead>
<tr>
<th>N=2539</th>
<th>Prevalence</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV (24.9%)</td>
<td>HIV+ 29.1</td>
<td>HIV- 17.1</td>
</tr>
<tr>
<td>Peripheral malaria</td>
<td>30.7</td>
<td>18.1</td>
</tr>
<tr>
<td>Placental malaria</td>
<td>9.4</td>
<td>3.1</td>
</tr>
<tr>
<td>Hospitalization (all causes)</td>
<td>4.3</td>
<td>2.7</td>
</tr>
</tbody>
</table>

van Ejik et al. AIDS, 2003
## Effect of HIV on Malaria

<table>
<thead>
<tr>
<th>Characteristics of HIV+ and HIV- pregnant women in Malawi</th>
<th>HIV+ (n=152)</th>
<th>HIV- (n=2,601)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral parasitemia at enrollment</td>
<td>54.4%</td>
<td>41.7%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Peripheral parasitemia at delivery</td>
<td>34.7%</td>
<td>18.2%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Placental malaria infection</td>
<td>38.2%</td>
<td>22.5%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Reported fever at enrollment</td>
<td>36.8%</td>
<td>21.0%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Geometric mean parasite density/µl (primigravida)</td>
<td>4,390</td>
<td>1,375</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Steketee R.W et al. 1996, HIV and Malaria in Pregnancy, AJTMH 55 suppl 55
Effect of IPT on placental parasitemia, by HIV status

- Case Management
- 2 doses
- monthly

HIV+ vs HIV-

* p<0.01
HIV infection, Pregnancy and Malaria - program overlap -

• Intervention overlaps
  – Diagnosis
  – Treatments: complexity and costs of Tx, resistance; potential for drug interactions; systems of pharmacovigilance
  – OI prophylaxis with CTX (an antimalarial)
  – HIV-infected persons need malaria prevention
HIV infection, Pregnancy and Malaria -conclusion-

• Coordinated action by Malaria, HIV and Reproductive Health programs
  – To strengthen antenatal and delivery care services:
    • ITNs & IPT for malaria: VCT & PMTCT
    • Laboratory support
    • Prompt treatment with highly effective antimalarial drugs to HIV-infected persons with malaria
• Questions