P. vivax malaria: the neglected malaria and why it matters

MMV Stakeholders’ Meeting
6-8 November 2012, Delhi, India

Kamini Mendis
Global spatial limits of *P. vivax* transmission

RBC Duffy negativity >95%
*Plasmodium vivax* “0%” in endemics
~ 1% in travellers

Guerra, CA et al. PLoS Negl Trop Dis 2010 4 (8), 774
Proportion of P.vivax infections increase as malaria is controlled
(annual data from Sri Lanka 1980 – 2012)
The proportion of P. vivax higher in countries where transmission intensity is low – SEARO countries, 2009

Annual Parasite Incidence of Malaria (per 1000)

Proportion of P. vivax infections

R² = 0.444
(blue) Asia: Bangladesh, Bhutan, Cambodia, China, India, Indonesia, Lao PDR, Malaysia, Myanmar, Nepal, Papua New Guinea, Philippines, Solomon Islands, Sri Lanka, Thailand, Vanuatu and Vietnam,

(green) Eastern Mediterranean: Afganistan, Iran, Iraq, Oman, Pakistan, Saudi Arabia, Syria and Yemen.

(pink) Latin America: Argentina, Belize, Bolivia, Brasil, Colombia, Costa Rica, Dominican Republic, Ecuador, El Salvador, Guatemala, French Guyana, Guyana, Haiti, Honduras, Mexico, Nicaragua, Panama, Peru, Suriname and Venezuela.

(orange) Central Asia & the Caucasus: Armenia, Azerbaijan, Tajikistan and Turkey.
Persistent liver forms cause relapses – GENERATION OF CASES WITHOUT INOCULATION

Preferentially invades reticulocytes – LOWER PARASITE DENSITIES

Continuous IN VITRO CULTURE STILL NOT POSSIBLE

Mature gametocytes appear in peripheral blood simultaneously with asexual stages – PARASITE HAS ESCAPED EVEN BEFORE PATIENT PRESENTS FOR TREATMENT

Shorter development in mosquito – LESS SUSCEPTIBLE TO VECTOR CONTROL MEASURES WHICH REDUCE THE MOSQUITO LIFE SPAN.

Distinctive biological features of P. vivax
<table>
<thead>
<tr>
<th>P. falciparum</th>
<th>P. vivax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrives in highly favourable transmission conditions to outcompete <em>P. vivax</em></td>
<td>Can persist under a variety of less favourable conditions</td>
</tr>
<tr>
<td>Also more vulnerable to any form of malaria control</td>
<td>Less amenable to current control methods sp., early treatment than to transmission control</td>
</tr>
<tr>
<td>Does poorly in well managed human environments</td>
<td></td>
</tr>
</tbody>
</table>

As more powerful antimalaria campaigns are put into effect, primarily against *P. falciparum*, the residual burden of malaria will become increasingly that of *P. vivax*.
**P. vivax** malaria: 75 - 90 million cases annually

Other estimates: 132 - 391 million (Hay et al., 2004, Price et al., 2007)

Mendis K et al., 1998
Global distribution of *Plasmodium vivax* cases (1993 – 1997)

- **C.America & Caribbean (4%) [84%]**
- **Travellers (0.02%) [10-30%]**
- **C.Asia & Caucasus (<1%) [99%]**
- **Eastern Mediterranean 15% [80%]**
- **Korea (<1%) [100%]**
- **S.America (11%) [70%]**
- **Africa 13% [4%]**
- **Asia 56% [48%]**
Clinical burden of *P. vivax* malaria

- **Acute infection**
  - extremely debilitating febrile illness

- **Reputation of being a benign, non-life threatening**
  - but severe and fatal infections have and are being reported
  - high TNF-alfa levels, transiently even higher than those in severe and complicated *P. falciparum* infections

- **Anaemia** – main pathological consequence, both acute and chronic

- **Effects on pregnancy**
Vivax malaria occurs characteristically in low endemic situations.

Both adults and children suffer from vivax malaria.

Where vivax prevails, males (15-50 yrs) are at high risk.

School children suffer high absenteeism and impaired learning.

Massive economic and social costs, and cost to human and nation development.
Current, key antimalarial interventions

**Prevention**
- Insecticide-treated bednets/
  - Long-lasting ITNs
- Indoor Residual Spraying
- Selective methods of VC

**Diagnosis & Treatment**
- Microscopy •
- Rapid Diagnostic Tests •
- Chloroquine/Artemisinin-based combination therapies (ACTs) + primaquine

**Effective surveillance and response system**

IEC/BCC

Advocacy
Prophylactic and treatment failure and confirmed resistance of *P. vivax* to chloroquine 2010

Source:

- Red: *P. vivax* prophylactic or treatment failure, resistance confirmed
- Orange: *P. vivax* prophylactic or treatment failure
Currently effective medicines against *P. vivax*

**Against asexual blood stages**
- Chloroquine
- Mefloquine
- All current ACTs (except AS-SP)

**Against dormant liver stages**
- Primaquine
  - Risk of AHA in G6PDd patients
  - Long course of therapy
- Tafenoquine – phase II b trials

**MEDICINES NEEDED**
- a medicine directed against pre-erythrocytic stages which is
  - short-course therapy,
  - safe
  - long half-life or as implants?
- medicines against the blood stages of *P. vivax* – which synergise with anti-relapse medicines
Global distribution of *Plasmodium vivax*

maximum distribution 19th century (pink)
late 20th century (purple)
“the ghost of a man, a sufferer from his cradle to his grave; aged even in childhood and laying down in misery that life which was but one disease.”

John Macculloch, 1827

- and he or she laid down that life, on average, by around 20 to 25 years of age.

An allegory of malaria

The ghost of the swamp (Maurice Sand, 1823-1889). An allegory of malaria.