This chapter reviews (i) the adoption of policies and implementation of programmes to expand access to and utilization of intermittent preventive treatment of malaria in pregnancy and in infants and (ii) progress in the development of two new therapeutic tools for malaria prevention: seasonal malaria chemoprevention and malaria vaccine.

5.1 Intermittent preventive treatment

5.1.1 Intermittent preventive treatment of pregnant women

The countries which had adopted intermittent preventive treatment for pregnant women (IPTp) with sulfadoxine-pyramethamine (SP) as national policy by the end of 2010 include 35 high-burden countries in sub-Saharan Africa spanning two WHO Regions, and also Papua New Guinea (Table 5.1).

For 21 of the 36 high-burden countries which have adopted IPTp as national policy, consistent data for 2010 were available from NMCPs on both the second dose of IPTp (numerator) and the number of women who had attended antenatal care at least once (denominator). Approximately half of women attending antenatal clinics (52%, inter-quartile range 47%–61%) received a second dose of IPTp in countries which responded (Figure 5.1).

Information on the proportion of all pregnant women receiving the second dose of IPTp can be derived from household surveys. Data on IPTp for pregnant women from surveys in 2009–2011 were available for 12 countries in Africa, representing a combined population of 409 million. Although some low IPTp coverage rates for two doses may be attributable to the fact that some pregnant women do not attend ANC or only make a single ANC visit, a substantial proportion of all pregnant women nonetheless did not receive a second dose of IPTp. In 2009–2011, the percentage of women who received two doses of IPTp during pregnancy ranged from 5% in Namibia to 69% in Zambia (Figure 5.2); the weighted average remained low, at 23%, primarily due to low coverage rates in Nigeria and the Democratic Republic of the Congo.

Table 5.1
Adoption of Policies for Intermittent Preventive Treatment for Pregnant Women (IPTp)

<table>
<thead>
<tr>
<th>Policy</th>
<th>Africa</th>
<th>Americas</th>
<th>Eastern Mediterranean</th>
<th>Europe</th>
<th>South-East Asia</th>
<th>Western Pacific</th>
<th>Grand Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPTp used to prevent malaria during pregnancy</td>
<td>33</td>
<td>N/A</td>
<td>2</td>
<td>N/A</td>
<td>N/A</td>
<td>1</td>
<td>36</td>
</tr>
<tr>
<td>Number of endemic countries/areas</td>
<td>43</td>
<td>23</td>
<td>12</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>106</td>
</tr>
<tr>
<td>Number of P. falciparum endemic countries/areas</td>
<td>43</td>
<td>18</td>
<td>8</td>
<td>0</td>
<td>9</td>
<td>9</td>
<td>87</td>
</tr>
</tbody>
</table>

Source: NMCP reports

Source: Household survey data
5.1.2 Intermittent preventive treatment of infants

Intermittent preventive treatment in infancy (IPTi) with SP is the administration of a full therapeutic course of SP delivered through immunization services at defined intervals corresponding to routine vaccination schedules – usually at 10 weeks, 14 weeks, and approximately 9 months of age – to infants at risk of malaria. WHO recommends IPTi in countries with moderate to high malaria transmission, where levels of parasite resistance to SP are low. So far no country has adopted IPTi as national policy since its recommendation in 2009; however, the IPTi implementation guidelines were released only in September 2011, and eight countries recently met to discuss possible implementation.

5.2 New therapeutic tools for malaria prevention

The scale-up of currently available tools for malaria prevention and treatment has resulted in substantial progress in malaria control in many countries. However, new tools are needed, especially in countries where there is high malaria transmission potential. Two new therapeutic tools currently in development for malaria prevention are seasonal malaria chemoprevention and malaria vaccines.

5.2.1 Seasonal malaria chemoprevention

Seasonal malaria chemoprevention (SMC), previously termed intermittent preventive treatment in children, is defined as the intermittent administration of full treatment courses of an effective antimalarial medicine during the malaria season to prevent malarial illness. The objective of SMC is to maintain therapeutic antimalarial drug concentrations in the blood throughout the period of greatest malarial risk.

SMC has been studied most frequently in areas with seasonal malaria transmission where the main burden of malaria is in older children, rather than in infants, and the main risk of clinical malaria is restricted to a few months each year. WHO is presently assessing the potential role of SMC for use as an additional malaria measure strategy in different malaria epidemiological settings.

As a first step in the policy development process, the Technical Expert Group (TEG) on Preventive Chemotherapy was convened in May 2011 to review the current evidence on the efficacy, safety and feasibility of large-scale implementation of SMC, and to assess the risks and potential benefits. The report of this consultation will be presented to the newly established Malaria Policy Advisory Committee (MPAC) in early 2012. The MPAC will review the recommendations of the TEG together with additional analysis carried out since the consultation, and advise WHO on the potential role of SMC in the control of malaria. In accordance with this advice, a WHO policy recommendation will be formulated in the first quarter of 2012.

5.2.2 Malaria vaccine development

An effective vaccine against malaria has long been envisaged as a valuable addition to the available tools for malaria control. There are as yet no licensed malaria vaccines. A single candidate vaccine is currently being assessed in phase 3 clinical trials, and approximately 20 other projects are in phase 1 or phase 2 clinical trials.

Vaccine candidate RTS,S/AS01: The RTS,S/AS01 vaccine targets P. falciparum. It comprises a fusion protein of a malaria antigen with hepatitis B surface antigen, and includes a new potent adjuvant. Now in phase 3 clinical trials, the vaccine is being developed in a partnership between GlaxoSmithKline and PATH Malaria Vaccine Initiative (MVI), with funds provided by the Bill & Melinda Gates Foundation to MVI. The vaccine manufacturer's target group for this vaccine is African infants resident in malaria-endemic countries, with vaccination administered at 6–14 weeks of age, together with other vaccines administered routinely to infants.

The first of three sets of results from the phase 3 trial were published in October 2011 and were consistent with results from the phase 2 trials (1). Conducted at 11 trial sites in seven countries across sub-Saharan Africa, the preliminary results from the phase 3 trial showed that the vaccine reduced the incidence of clinical malaria by 55% when evaluated over 12 months following the third dose; this conclusion was based on data from the first 6000 children, aged 5–17 months.

A preliminary analysis for efficacy against severe malaria was made when 250 cases accrued in both the 5–17 month and 6–14 week age groups in the trial. This analysis found an efficacy of 35% with variable follow-up from zero to 22 months after the third dose. The full trial results will become available to WHO in late 2014 and will include 30 months' safety and efficacy data from the target group aged 6–14 weeks, together with data on an 18-month booster dose and site-specific efficacy data.

The Joint Technical Expert Group on Malaria Vaccines, set up by the WHO Global Malaria Programme and Department of Immunization, Vaccines & Biologics in April 2009, has advised that, in the light of the published results to date, a policy recommendation could be made once the full trial results become available. The timelines of the phase 3 trial may allow a policy recommendation in 2015, subject to vaccine performance. This vaccine will then be considered for potential addition to the current WHO recommended malaria preventive measures.

Other malaria vaccine candidates in development: Several other scientifically promising vaccine candidates are currently being explored, but their development is at least 5–10 years behind that of RTS,S/AS01. Details are provided in the rainbow tables1, WHO’s comprehensive annually updated spreadsheets of global malaria vaccine project activity.

In the longer term WHO is committed to working with malaria vaccine stakeholders towards the 2025 goal set out in the malaria vaccine technology roadmap – a vaccine with at least 80% efficacy against clinical malaria. WHO also participated in the

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1 Malaria Vaccine Project Spreadsheets (known as ‘the rainbow tables’): www.who.int/vaccine_research/links/Rainbow/en/index.html
malaria eradication R&D agenda (malERA)\(^1\) consultative process which supported the concept of a vaccine that can interrupt malaria transmission. The long-term goals for malaria vaccines will therefore include not only protection against clinical malaria, but also impact against malaria transmission as a core feature of vaccine performance (2).

5.3 Conclusions

Scale-up of intermittent preventive treatment of pregnant women: There has been substantial progress in scaling up IPTp in several countries, but implementation has been slow in many others. Overall progress in achieving coverage targets across high burden malaria-endemic countries has lagged behind the scale-up of other malaria control measures. This limited progress is unlikely to be related solely to low ANC attendance, as ANC attendance is fairly high in Africa, and even among women attending the clinics, IPTp coverage is only moderate. Simplified IPTp messages and health worker training have been shown to improve IPTp coverage (3). To facilitate scale-up, malaria control programmes should encourage ANC attendance and identify barriers to implementation. Some countries (Benin, Senegal, Ghana and Mali) have already decided to document the barriers to the implementation of IPTp as well as to the attendance of ANC. As the effectiveness of IPTp with SP is sensitive to changes in malaria burden and the level of resistance to SP, a decreasing malaria burden or increasing resistance to SP may render IPTp with SP a less attractive intervention in some areas. In such situations, programmes may need to reorient their malaria prevention efforts in pregnancy towards other approaches.

Implementation of intermittent preventive treatment of infants: The recent WHO policy recommendation for IPTi is based on results from seven studies on IPTi with SP in areas of moderate to high transmission of malaria, with varied levels of other malaria control measures in place. These studies showed that IPTi delivered through EPI services provides protection in the first year of life against clinical malaria and anaemia, as well as reductions in hospital admissions for patients with malaria parasitaemia and admissions for all causes. Introduction of this new intervention builds on established collaboration between malaria and other maternal and child health programmes in the distribution of ITNs through EPI services and delivery of IPTp in antenatal clinics. These established relationships should facilitate implementation in countries wishing to add IPTi to their malaria control efforts. The efficacy of IPTi is dependent upon resistance levels to SP, and, as for IPTp, new regimens are under investigation. These new regimens may prove useful where SP resistance prohibits IPTi implementation.

Development of policy on new tools for malaria control: An assessment of seasonal malaria chemoprevention will be one of the first tasks taken up by WHO’s newly established Malaria Policy Advisory Committee. While much progress has been made in scaling up existing interventions, further efforts will be required to introduce and widen the application of new tools. The MPAC will have an important role in policy development on new tools for malaria control, an essential step towards making the tools available in the communities that will benefit from them.

\(^1\) The Malaria Eradication Research Agenda (malERA) initiative was a consultative initiative aimed at identifying current knowledge gaps and new tools needed for malaria eradication; it concluded its activities in 2011.

References
