EDITORIAL

Malaria Prevention in Pregnancy: When Will the Prevention Programme Respond to the Science

The article by Okoko and colleagues (1) in this issue of the Journal presents an interesting scenario. By its title, the article draws attention to the comparison with seminal work done between 1966 and 1972 when Sir Ian McGregor and colleagues monitored malaria infection at delivery and birth outcomes in more than 6,000 women in urban and rural parts of western Gambia (2). In a much smaller sample of women delivering during the rainy season in eastern Gambia in 1997, Okoko and colleagues observed very similar findings. In essence, nothing has changed in the 30 intervening years.

The article by McGregor and colleagues, in combination with similar reports by others (3), led to discussions of the importance and appropriate approaches to the prevention of malaria in pregnancy. The World Health Organization (WHO) published recommendations for antimalarial chemoprophylaxis in pregnancy in 1986 (4) and noted the importance of an initial treatment dose, because many asymptomatic women were infected at the time of their first antenatal clinic visit. Studies elsewhere in Africa in the 1980s and 1990s showed the benefit of various treatment and or chemoprophylaxis regimens on the reduction of malaria, maternal anaemia, low birth-weight, and premature delivery (5,6). Work by others in the Gambia contributed to the growing recognition that effective interventions, including the use of antimalarial drugs (7,8) and insecticide-treated bednets (9), could be applied and could markedly reduce the adverse effects from malaria. Yet, good scientific inquiry and published articles have not led directly to changes in national policy and implementation of these policies at the local level. Okoko and colleagues note in their introduction that “the use of antimalarial chemoprophylaxis is still not uniformly practised in the Gambia,” and they conclude that “a workable policy needs to be put in place.”

Recent studies in African settings have addressed the issue of a ‘workable policy.’ With the recognition that health systems have difficulty in delivering regular chemoprophylaxis to pregnant women (10), investigators in several settings demonstrated that intermittent preventive treatment (IPT) with effective and safe antimalarial drugs can achieve important reductions in frequency of malaria and its consequences (11,12). These interventions can be particularly cost-effective (13) and reduce the intolerable burden of malaria in pregnancy. The 20th WHO Expert Committee Report recommends, “intermittent treatment with an effective, preferably one-dose antimalarial drug delivered in the context of antenatal care should be made available to primi- and secundigravidae as an appropriate and effective method for reducing the consequences of malaria in pregnancy in highly-endemic areas.” In follow-up of this guidance, dialogue between the malaria community and the reproductive health community is underway with the intent to incorporate the malaria-prevention strategy into antenatal care programmes widely in malarious areas of sub-Saharan Africa and to assure necessary supplies of drugs. Like all proven and important public-health prevention strategies, this will need continued attention and much advocacy from the malaria and reproductive-health community, and advocacy and demand from the mothers (and their babies) who will benefit.

This approach using IPT has been facilitated by having sulphadoxine-pyrimethamine (SP)*, an antimalarial therapy that still has good efficacy in these semi-immune women, is a single-dose treatment, is not bitter, and is relatively well-tolerated. Importantly, studies of IPT with SP in pregnancy in numerous settings have clearly demonstrated its efficacy and effectiveness in programmes (6). Because of the single-dose treatment, the effectiveness of the programme essentially matches the efficacy of the drug as long as health workers can give it under observation in the clinic. If and when we

* Editor’s note: According to the package insert, contraindications include infants aged less than two months, and pregnancy at term and during the nursing period because sulfonamides pass the placenta and are excreted in the milk and may cause kernicterus.
have to move from SP to alternative drugs or drug combinations that require multi-day dosing, this will be more challenging (i.e. the effectiveness of the programme may decrease because of incomplete adherence to the full regimen) but still important.

Most of the world’s malaria is prevalent in Africa, and the efforts noted above will offer important benefit for this most-affected population. However, in the non-African settings where overall intensity of transmission is lower and where Plasmodium vivax and multidrug-resistant P. falciparum (MDRPf) coexist, the issues are more challenging. First, there are limited data showing that P. vivax does what P. falciparum does in the placenta (14); thus, the consequences of P. vivax on pregnancy are unclear and may differ from the consequences of P. falciparum. Since this impact is not well-characterized, health officials have less reason to try to preemptively address P. vivax in pregnancy. So, at the moment, there are no recommendations for chemoprophylaxis or IPT that are meant to cover P. vivax. As for MDRPf, it too is not exactly the same as the situation is or will become in Africa. In general, the frequency of transmission and, thus, the likelihood of repeated exposure every year so that an adult has substantial ‘semi-immunity’ to malaria is much lower in Asia, South East Asia, and the Americas—the places where MDRPf is common. Thus, pregnant women in these settings tend to have lower immunity, are more likely to develop clinical illness with their infection, and the situation may lend itself to a case-management approach instead of a presumptive treatment or prophylaxis. As for drugs to use, most data on treating MDRPf in pregnancy come from Thailand where they have used mefloquine, and now mefloquine + artesunate with success (15). The WHO is currently evaluating the safety data on artemisinin compounds in pregnancy, and this evaluation will be important in determining recommendations on the combination drug approach for MDRPf in pregnancy.

For areas with both P. vivax and MDRPf, important questions remain. Is P. vivax a significant public-health problem in pregnancy, and is that problem amenable to antimalarial drugs for treatment, preemptive treatment or prophylaxis? For P. falciparum and MDRPf, the frequency and intensity of transmission and the prevailing human immunity need to be understood. For example, how prevalent is P. falciparum in pregnant women, are women infected with P. falciparum typically symptomatic or asymptomatic, and will a case-management strategy (i.e. prompt recognition of illness and prompt treatment) be sufficient; or will healthcare providers need a preemptive approach? What drugs will be effective in this MDRPf environment; and will these be appropriate for pregnant women? Even after these questions can be answered, the challenges currently seen in the African setting—whether we can establish a workable programme—will remain.

The prevention of malaria during pregnancy is a key element of the global Roll Back Malaria Partnership strategy, especially in sub-Saharan Africa. To date in Africa, Malawi, Kenya, Uganda, Tanzania, and Zambia have adopted the use of IPT in pregnancy as part of their national strategy, and many other countries in Africa are considering such changes. Recent data from a national survey in Malawi showed that two-thirds of pregnant women received at least one antimalarial treatment dose; however, less than one-third received the recommended 2-dose treatment regimen (16). Thus, policy change alone is not sufficient to establish full implementation of this strategy. Having said that, the widespread adoption and application of this malaria-prevention strategy could mean that the Gambia and many other countries will be able to experience and report on reductions in malaria in pregnant women and the commensurate improvements in maternal and newborn health and survival. One would hope that we will not need to wait another 20 years for this action and that the scientific community will not be faced with replicating past studies to demonstrate the consequences of inaction.

REFERENCES

5. Garner P, Brabin BJ. A review of randomized controlled trials of routine antimalarial drug prophylaxis during pregnancy in endemic malarious
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