A rational approach to malaria control in pregnancy in sub-Saharan Africa: the need for a link between scientific research and public-health interventions

Since 1964, about 300 articles reporting, directly or indirectly, on malaria-control measures during pregnancy have been published. A recent Cochrane review on malaria prevention in pregnant women (Gulmezoglu and Garner, 1998) identified only 14 trials meeting the authors' strict inclusion criteria. Different antimalarial drugs (chloroquine, pyrimethamine, mefloquine or dapsone–pyrimethamine) and different chemoprophylaxis regimens (daily, weekly, fortnightly and monthly) were used in these trials. The results indicate that chemoprophylaxis has a consistent beneficial effect on the clinical episodes of malaria and on anaemia (in terms of mean haemoglobin concentrations or packed-cell volumes), particularly in primigravidae, and appears to improve birthweights. However, there is little direct evidence that routine antimalarial chemoprophylaxis results in lower mortality in the mother or infant. In The Gambia, reduction of low birthweight by chemoprophylaxis was estimated to reduce neonatal and infant mortalities by 42% and 18%, respectively, among the children of primigravidae, and by 6% and 4%, respectively, among the children of multigravidae (Greenwood *et al.*, 1992). In Malawi, low birthweight from all causes contributed to 80% of all neonatal deaths, 45.7% of perinatal deaths and 37.8% of infant mortality (Slutsker *et al.*, 1996). Reduction in the incidence of low birthweight could therefore lead to substantial reductions in childhood mortality, although further, direct evidence of this outcome is required. While it is generally accepted that effective measures to prevent malaria in pregnancy can have a significant benefit on the health of mothers and neonates, several critical issues remain to be explored.

The emergence and spread of parasites resistant to commonly used drugs, such as chloroquine, can only complicate the choices which face the health managers who are responsible for malaria prevention during pregnancy. The results of studies in Thailand, on the use of quinine, mefloquine, artemisinin and combination therapy against multidrug-resistant *Plasmodium falciparum*, have demonstrated that new regimens can be effective in areas where no chemoprophylaxis is available (McGready *et al.*, 1998). Drug resistance will be a major obstacle in any future control strategy. The experience gained in Thailand is highly relevant to the emerging problem of drug resistance in Africa. The use of artemisinin compounds has been shown to reduce gametocyte carriage, and this may be an additional reason to explore the use of these drugs in pregnancy.

Whether insecticide-treated bednets could be of some benefit to pregnant women living in malaria-endemic areas remains an open question, as initial studies have shown only moderate if any effect on the reduction of anaemia in primigravidae (D'Alessandro *et al.*, 1996; Shulman *et al.*, 1998). The usefulness of several, intermittent and presumptive treatments with sulfadoxine–pyrimethamine (SP) has been recently explored. Reductions in the prevalences of peripheral parasitaemia and placental malaria at delivery and in maternal anaemia, and increases in mean birthweight, have been reported (Verhoeff *et al.*, 1998; Gulmezoglu and Garner, 1998; Shulman *et al.*, 1998). However, these benefits may be reduced by HIV infection, which appears to have a detrimental effect on the efficacy of SP (Verhoeff *et al.*, 1999; Parise *et al.*, 1999). It is possible that placental malaria increases the risk of the perinatal transmission of HIV, although, as yet, there are no published data to indicate this. There is also little information from urban areas, which generally experience relatively low transmission intensities, and there has yet to be a comparison of the effectiveness of SP treatment between areas with seasonal and continuous transmission. Malaria

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in epidemic-prone countries has been little studied. There is also a scarcity of information on the effects of vivax malaria in pregnancy, although the results of recent studies, in Thailand and India, show that it has important effects on birthweight and anaemia (Nosten *et al.*, 1999; Singh *et al.*, 1999).

One of the major problems for programme managers and implementers remains how to translate the information produced by scientific research into feasible and sustainable programmes. Should selected groups, such as primigravidae (who are the most susceptible) or adolescent girls (who, in general, are difficult to reach and often illiterate, and have low social status) be targeted?

There is a need to review all the existing data critically (not only those from the randomized, controlled trials that are included in the Cochrane reviews). The total of our current knowledge needs to be assembled and regularly reviewed, as a basis for promoting the best strategies available and for identifying important gaps in our knowledge. The choice of 'best strategies' will only be rational if the scientists collaborate more closely with the policy-makers and health managers. This collaboration involves the evaluation of current practices as well as the promotion of new ones. It is hoped that the promotion of the necessary dialogue will be fostered by a number of groups and international agencies. As a contribution to this process, a new network has been established with the title of PREMA (the PREgnancy, Malaria and Anaemia network). A key aim of PREMA is to decrease the burden of malarial disease among pregnant women and babies living in endemic areas, by promoting effective control strategies.

The specific objectives of the new group were considered at the 'Multilateral Initiative on Malaria' meeting in Durban in March 1999, whose participants included representatives of the World Health Organization. These objectives are outlined below.

(1) To review and inform on the 'state of the art' concerning malaria and anaemia in pregnancy, including burden of disease, programme strategies and research priorities, by:
   (a) compiling and reviewing the available data on the burden of disease caused by malaria and anaemia in pregnancy;
   (b) creating an inventory of current, national, malaria-control policies aimed at pregnant women, and their implementation status;
   (c) compiling and reviewing the data available on efficacy, effectiveness, safety, acceptability and operational feasibility of the different strategies for malaria and anaemia control during pregnancy, under different epidemiological settings; and
   (d) informing policy-makers and national governments on the 'state of the art' concerning malaria and anaemia in pregnancy, and on research findings and their implications for malaria control and maternal-health programmes in endemic countries.

(2) To identify gaps in our knowledge and develop and promote appropriate research protocols when needed.

(3) To address specific technical issues that are critical for the control of malaria and anaemia in pregnancy, through partnerships, between the scientific and control communities, in malaria control and maternal health.

(4) To provide technical support for the design and implementation of effective programmes for control of malaria and anaemia in pregnancy, through antenatal-care services.

(5) To develop and foster national expertise on malaria and anaemia in pregnancy and facilitate inter-country collaboration.

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