Few Options for Treating Malaria in Pregnancy

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LISBON — Malaria in pregnancy is the greatest challenge the disease poses, said Dr. Theonest K. Mutabingwa at the 12th International Congress on Infectious Diseases.

Each year, 50 million women become pregnant in malaria-endemic areas worldwide, including 30 million in sub-Saharan Africa. Those who are infected often develop placental parasitemia, a leading cause of low birth weight, infant mortality, and severe maternal anemia in tropical regions.

This is true even when the mother's infection is asymptomatic, as is typical in regions where malaria transmission is intense and many adults have developed immunity to the disease, explained Dr. Mutabingwa of the Seattle Biomedical Research Institute and the National Institute for Medical Research in Muheza, Tanzania.

WHO guidelines say quinine, a drug with an inconveniently lengthy treatment course, is the most effective antimalarial that's safe for use during pregnancy.

For this reason, it is recommended that malaria in pregnancy be diagnosed and treated. And that's where matters become so difficult. Microscopy, the standard diagnostic method in the developing world, isn't sufficiently sensitive to reliably detect asymptomatic infection in pregnant women who may have placental parasitemia despite having a negative peripheral blood smear. A rapid diagnostic test using a malaria-specific antigen that is suitable for rugged field use would be a major advance, he said.

Moreover, the resistance of malaria parasites to chloroquine and sulfadoxine-pyrimethamine has become so pervasive that the latest World Health Organization malaria guidelines, issued earlier this year, have demoted these agents from their longtime status as first-line therapy in favor of artemisinin-based combination therapies, except in pregnancy, where the older drugs' well-established safety record earned them a reprieve. The WHO guidelines call quinine—a drug with an inconveniently lengthy treatment course—the most effective antimalarial that's safe for use throughout pregnancy.

The big emerging problem as older antimalarials give way to artemisinin combination therapies and other drugs in the developmental pipeline is that pregnant women have been systematically excluded from participation in clinical trials of all newer agents. There is an urgent need to rectify this situation and begin evaluating the safety of antimalarial agents in pregnancy, Dr. Mutabingwa said at the congress sponsored by the International Society for Infectious Diseases.

Women in their first and second pregnancies are known to be particularly vulnerable to the deleterious effects of malaria. But in a recent study involving 453 infants, 69 of them born to mothers with placental malaria, Dr. Mutabingwa and colleagues discovered a surprising effect of gravidity on infant malaria. Babies born to mothers with placental malaria at delivery were 41% more likely to have parasitemia during infancy. No surprise there. But although parasitemia was more common in primigravid than multigravid women, the opposite was true in their infants. First-born infants of mothers with placental parasitemia were less likely to develop malaria in infancy than were babies born to multigravid women with placental malaria (PLos Med. 2005 December 2(12): e407; doi: 10.1371/journal.pmed.0020407).

Unfortunately, targeting malaria control measures specifically at women in their first two pregnancies as a means of improving mother-child health is rendered impractical in many areas because of the complicating factor of the HIV epidemic. HIV-infected women in malarial regions have a high prevalence and density of peripheral and placental parasitemia in all pregnancies, not just their first two.

For this reason, the most practical antimalarial strategy today in a region such as sub-Saharan Africa is to use intermittent preventive therapy and presumptively treat anemic pregnant women as having malaria. Historically, two or more antenatal doses of intermittent preventive therapy with sulfadoxine-pyrimethamine were known to be effective in reducing infection and parasite load, but drug resistance has greatly reduced the usefulness of this regimen. ■