**New Options for HIV in Pregnancy Worldwide**

**BY DIANA MAHONEY**

**New England Bureau**

**BOSTON —** Short-term treatment with one or more antiretroviral drugs starting in late pregnancy may significantly reduce the likelihood that HIV-infected women will transmit the virus to their newborns and that the women will develop nevirapine resistance, research has shown.

The practice of giving pregnant women with HIV a single dose of nevirapine (Viramune) during labor has significantly reduced maternal-child transmission rates in the developing world. It also has been heralded as an optimal approach for lowering the mother-to-child transmission rate in the United States, where women in developing countries should not be subjected, said Dr. McIntyre of the perinatal HIV research unit at the University of Witwatersand, Johannesburg, South Africa. In this country, this has been seen as a U.S. and pharmaceutical company conspiracy.

The value of nevirapine monotherapy should be reassessed, Dr. McIntyre stressed, in light of new evidence suggesting that possible alternatives to the single-dose, single-drug regimen may be as effective at preventing vertical HIV transmission minus the potential for drug resistance.

In one of the studies presented at the conference, which was sponsored by the Foundation for Retrovirology and Human Health, 349 HIV-infected pregnant women in the West African nation of Cote d'Ivoire began therapy with a combination of zidovudine (AZT) and lamivudine (3TC) [Epivir in the U.S.] in their 32nd week of pregnancy through 3 days post partum, in addition to single-dose nevirapine during labor, reported lead investigator Francois Dabis, M.D., of Victor Segalen University Hospital, reported lead investigator Francois Dabis, M.D., of Victor Segalen University Hospital.

**BY ERIK GOLDMAN**

**Contributing Writer**

**NEW YORK —** Macrophage migration inhibition factor, a newly characterized cytokine that inhibits cortisol and increases production of inflammatory cytokines, may be the key to understanding depression during pregnancy, Brad D. Pearce, Ph.D., said at a symposium sponsored by the National Alliance for Research on Schizophrenia and Depression.

Pregnant women seeking treatment for major depression have markedly higher levels of macrophage migration inhibition factor (MIF) than do nondepressed pregnant women of similar age.

In general, MIF levels are slightly elevated in pregnant vs. nonpregnant women, but the difference is insignificant compared with the difference between depressed and nondepressed pregnant women, said Dr. Pearce of the department of psychology at Emory University, Atlanta.

"We all hear that pregnancy is a time of joy, a natural high, and that pregnancy-related hormones are protective. The data, however, collide with these truisms," said Dr. Pearce, noting that roughly 7% of all American women experience episodes of major depression during their first pregnancies. The proportion increases to 12%-14% for second and third pregnancies.

The prevalence of major depression among nonpregnant women is roughly 8%. So, on a statistical basis, pregnancy is hardly protective and may actually increase the incidence of depression, particularly in multiparous women, he said.

"There are some very big changes in body chemistry during pregnancy. The shift in the balance of hormones, cytokines, cortisol, and many other things can be huge and very complex. Some women feel bliss; many others become depressed," he noted.

Depression during pregnancy can have significant complications. It is predictive of preterm labor and delivery, as well as other obstetrical complications, and is linked to an increased risk of behavioral and social problems in the children. "The physiological changes caused by depression during pregnancy result in changes in maternal-fetal interaction, which can have adverse effects on the fetal brain," Dr. Pearce said.

Antidepressant drug therapy, however, is not a neutral, risk-free proposition during pregnancy. Although none of the major antidepressant drug classes is considered strongly teratogenic, many commonly used medications have been linked to adverse obstetrical outcomes, including preterm delivery.

Dr. Pearce and his colleagues at Emory have been looking at potential biologic mediators involved in depression during pregnancy with the hope of eventually identifying targets for novel treatment strategies.

They've focused largely on inflammatory cytokines, many of which are consistently elevated among individuals with major depression. Patients with chronic inflammatory disorders, characterized by elevated cytokine levels, often have comorbid depression. Some cytokines used as drugs in the treatment of serious illnesses like cancer can actually induce symptoms of depression if given intravenously.

MIF is a fairly recent discovery, and it has attracted considerable attention among immunologists and infectious disease researchers. "It is a very unique protein. It is not like any of the other cytokines. It is really in its own family," Dr. Pearce said.

MIF is produced endogenously by a number of different immune cells and appears to block the action of cortisol. This results in an overall up-regulation of inflammation because cortisol normally inhibits inflammatory signaling molecules. MIF is also a modulator of catecholamine metabolism. Interestingly, MIF is also produced in large quantities by the hippocampus. "Nobody knows yet what it is doing there in the brain," he said.

If the connection between elevated MIF levels and depression is born out in future studies, Dr. Pearce believes that MIF may be useful as a prognostic marker for both depression and pregnancy complications like preterm labor. Prepregnancy depression predicts depression during and after pregnancy, he said.

"It seems that MIF levels predict postpartum outcomes," Dr. Pearce commented.

"Continuing to debate these early papers is like doing a thesis on the Wright brothers' first flight when you already have a 747 that flies."

Peter Levine, CEO of Correligic Systems Inc.

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"...and pregnancy complications like preterm delivery. We therefore must continue to aggressively expand access to services and improve our ability to offer the most effective drug regimens in all instances."