Antiretrovirals During Pregnancy: A Note of Caution

To The Editor—In their editorial about antiretrovirals in pregnancy, Watts and Mofenson note that as antiretroviral treatment (ART) is rolled out more widely for pregnant women in resource-limited settings, it will be critical to carefully monitor pregnancy outcomes, including congenital anomalies, preterm birth, stillbirth, and infant mortality, to assess risks and benefits of the different regimens [1].

We want to caution against another potential adverse effect of the maternal triple-drug ART regimen during pregnancy and breast-feeding (the World Health Organization's option B strategy [2]): pregnancy-related neuropsychiatric disorders including postpartum depression (PPD). Specifically, in the option B strategy, all human immunodeficiency virus (HIV)–positive pregnant women, regardless their $CD4^+$ T-cell count, will be treated with a regimen that includes the nonnucleoside reverse-transcriptase inhibitor efavirenz. Efavirenz, however, is known to cause neuropsychiatric side effects, including anxiety and depressive symptoms [3]. In a pharmacokinetic study in Uganda, up to 69% of participants experienced adverse central nervous system symptoms attributable to efavirenz in the first 2 weeks after initiating an efavirenz-based regimen [4]. The incidence of neuropsychiatric side effects during efavirenz therapy is correlated with plasma concentrations, and African

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populations exhibit greater variability in efavirenz concentrations than other ethnic groups [4]. Elevated concentrations are in turn correlated with, among other factors, the cytochrome P450 isoenzyme 2B6 G>T polymorphism [5]. A high proportion of the HIV-positive population in southern Africa have this polymorphism [6] and therefore are at increased risk of neuropsychiatric side effects of efavirenz.

PPD is the most common neuropsychiatric disorder in pregnancy and affects approximately 13% of women [7, 8]. Because use of efavirenz during pregnancy has been limited in the past towing to concerns about teratogenicity, it is unknown whether pregnancy-related neuropsychiatric disorders, including PPD, may be exacerbated by efavirenz use. However, there is evidence suggesting that patients with a history of depression have a greater risk of developing depression during efavirenz therapy [9]. Therefore, HIV-seropositive African pregnant women with perinatal depression may be at increased risk for developing a very serious form of PPD when they initiate an efavirenz-containing regimen.

Healthcare workers and pregnant women need to be aware of this potential adverse effect. Women who initiate an efavirenz-based regimen should be screened for perinatal depression [10], and, within the surveillance system for adverse events proposed by Watts and Mofenson [1], data about maternal mental health should be collected.

Note

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Robert L. Colebunders[1] and Landon Myer[2]

[1]Institute of Tropical Medicine and University of Antwerp, Belgium; and [2]School of Public Health & Family Medicine, University of Cape Town, South Africa

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Correspondence: Robert Colebunders, Institute of Tropical Medicine, Nationalestraat 155, 200 Antwerp, Belgium (bcoleb@itg.be).

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