STUDY POPULATION. A total of 39 antiretroviral therapy–exposed and 24 control children were assessed.

METHODS. This was a prospective, controlled, cross-sectional study. The Bailey Scales of Infant Development and Vineland Adaptive Behavior scales were performed at 18 to 36 months of age. Control children were born to HIV-uninfected women with similar anticipated social and economic backgrounds. Results were compared by using analysis of covariance and χ² analysis.

RESULTS. All scores were lower for children who were exposed prenatally to antiretroviral therapy. However, when maternal substance use during pregnancy was controlled for, there were no significant differences between the groups in any of the domains assessed. Children in both groups who were exposed to maternal substance use scored significantly lower in most domains than children who were not exposed.

CONCLUSIONS. HIV and antiretroviral therapy–exposed HIV-uninfected children had lower development and adaptive behavior scores compared with children who were not exposed to HIV or anti-HIV drugs. It is important to note that these differences were not significant when maternal substance use was considered. In this prospective study, exposure to perinatal anti-HIV therapy was not associated with neurodevelopmental abnormalities.

REVIEWER COMMENTS. This small study demonstrated that maternal substance use impacted the neurodevelopment of children to a far greater extent than exposure to anti-HIV drugs. In this study, at least, any negative impact of antiretroviral drugs on infant neurodevelopment was masked by the maternal substance use. This is not to say that exposure to combination anti-HIV medications may not have an impact on childhood development. Studies with similar designs to this one, in larger numbers of children for whom maternal substance use is not a confounding factor, will be required to address this issue fully.

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CCR5 Deficiency Increases Risk of Symptomatic West Nile Virus Infection

PURPOSE OF THE STUDY. Chemokine receptor 5 (CCR5) is critical for survival of mice infected with West Nile virus (WNV). CCR5Δ32 is a defective CCR5 found predominately in white individuals. Approximately 1% of the white population in the United States have homozygous CCR5Δ32 and completely lack CCR5 function. Individuals with CCR5Δ32 have an innate resistance to infection with HIV, because most HIV that is transmitted sexually or perinatally uses the CCR5 as a coreceptor with CD4 for HIV attachment to target cells. CCR5 inhibitors are in development, because most individuals with homozygous CCR5Δ32 seem to be immunologically normal. The purpose of this study was to determine if the presence of CCR5Δ32 homozygosity increases the risk for symptomatic WNV infection.

STUDY POPULATION AND METHODS. Three cohorts of patients were studied: 2 WNV-positive and 1 WNV-negative but with symptomatic illness in which WNV was considered. Genotypes of CCR5 were defined for each subject in the 3 cohorts.

RESULTS. In the group of healthy white random blood donors, CCR5Δ32 homozygotes represented 1% of the total. In contrast, CCR5Δ32 homozygotes represented over 4% of white subjects in the one WNV cohort and 8% in the second cohort. CCR5Δ32 homozygosity was significantly associated with fatal outcome in one of the cohorts.

CONCLUSIONS. The authors concluded that CCR5 mediates resistance to symptomatic West Nile infection.

REVIEWER COMMENTS. The immune system has evolved over the millennia to provide generally protective functions for the human host. That a particular chemokine receptor was maintained throughout this evolutionary process suggests a survival advantage. One percent of the white population in the United States have a genotype that eliminates functional CCR5. This mutation emerged in northern Europe and probably had no significant negative impact on that population. However, it seems that host defense against WNV depends on sufficient CCR5 engagement. CCR5 blockade is an emerging strategy in the treatment of HIV infection. It is possible that blockade of CCR5 will subsequently result in an increase risk for invasive WNV infection. If the CCR5 inhibitors continue through development, this potential complication must be anticipated.

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