infection increases an estimated 46%, from 1.4 infections/100,000 persons during 1997 to 2.0 infections/100,000 persons during 2001 [8].

Readers interested in the legal context of this discussion, including the administrative law judge’s initial decision to uphold the FDA’s proposed prohibition of the use of fluoroquinolones in poultry, are referred to FDA docket number 00N-1571 [9].

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10. The Journal of Infectious Diseases 2005; 191:1566–7. This article is in the public domain, and no copyright is claimed. 0022-1899/2005/19109-0026

Safety of Stavudine during Pregnancy
To the Editor—In the 15 December 2004 issue of the Journal of Infectious Diseases, Wade et al. present a study that is inappropriately entitled “Pharmacokinetics and Safety of Stavudine in HIV-Infected Pregnant Women and Their Infants: Pediatric AIDS Clinical Trials Group Protocol 332” [1]. The pharmacokinetic work is necessary and commendable, but it is impossible to assess, even grossly, the tolerance to this molecule after perinatal exposure with such a small number of study participants (n = 10). It is not reasonable to include the notion of safety in the title and to conclude in the Abstract and Discussion that this molecule is safe to use during pregnancy.

In addition, Wade et al. raised no questions concerning the potential interference of nucleoside analogues with mitochondrial [2–7] or nuclear [8] DNA in the fetus. Regardless of how we choose to interpret the increasing quantity of data from studies in animals and humans on this type of toxicity, these data cannot be ignored. I understand that it was not the aim of Wade et al.’s study to identify specific biological markers, but it is interesting to note that hypoglycemia (n = 1) and hyperkalemia (n = 3) may be such indicators.

Furthermore, the limited hematologic data presented by Wade et al. should not be underemphasized: 5 of the 10 infants in their study developed grade 3 neutropenia, which does not correspond with what has been observed after exposure to zidovudine [9], or the combination of zidovudine and lamivudine [10].

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References

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Reply to Blanche

To the Editor—On behalf of all of the authors of “Pharmacokinetics and Safety of Stavudine in HIV-Infected Pregnant Women and Their Infants: Pediatric AIDS Clinical Trials Group Protocol 332” [1], I would like to respond to Blanche’s correspondence [2] by pointing out that our study was a phase 1 study and, as such, was designed to preliminarily address the pharmacokinetics and safety of stavudine (d4T) during pregnancy. Thus, we agree that, as a phase 1 study, it did not address the issue of safety in large numbers of women and infants, and we did not imply that it did. Also, we did not conclude that d4T is safe but rather that it was well tolerated by all of the pregnant women in our study who received it. The laboratory toxicities seen in the infants were fully described, and the roles played by in utero exposure to d4T and/or lamivudine or by neonatal exposure to zidovudine were discussed as probable causes of the toxicities; in these infants, the toxicities resolved without requiring treatment. The infants received only single doses of d4T at weeks 1 and 6. We did not describe d4T as being well tolerated by the infants; rather, we pointed out the observed toxicities and noted that they may have been secondary to in utero drug exposure. The study was not designed to assess mitochondrial toxicity in this small number of infants; however, the issue of the potential mitochondrial toxicity of d4T was included in the Discussion, and we concluded that d4T should be used with caution during pregnancy, especially if combined with didanosine. It is clear that additional studies with larger numbers of pregnant women are necessary to fully understand the safety profile of d4T in pregnant women and their infants and that long-term follow-up of infants exposed in utero to antiretroviral drugs is required to assess any late adverse outcomes of such exposure.

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Hepatitis C Virus Genotype and the Natural History of HIV-1 Disease: Potential Role of GB Virus C in the Hemophiliac Population

To the Editor—Yoo et al. [1] recently reported that, in individuals coinfected with HIV-1 and hepatitis C virus (HCV), infection with HCV genotype 1 was associated with an increased risk for progression to AIDS-related mortality. Their study suggested that HIV-1-infected individuals with HCV genotype 1 infection had higher HCV RNA levels and lower absolute CD4+ T cell counts than did those without HCV genotype 1 infection. Whether this observation is a direct effect of HCV genotype 1 infection or the result of a confounding factor is a question that needs to be further explored. A possible confounding factor may be the status of GB virus C (GBV) infection in these individuals. This RNA virus has been found in hemophiliacs [2], and the common routes of exposure to both HIV-1 and GBV suggest that coinfection with the 2 viruses may be common; such coinfection has been noted especially frequently in hemophiliacs with HIV-1 infection [3], but it has also been noted in patients with other modes of acquisition of HIV-1 [4].

There have been multiple recent reports suggesting that, in patients coinfected with HIV-1 and hepatitis G, progression of HIV-1 infection may be delayed [3–7]. Differences in GBV infection status among the subjects in the Yoo et al. study might partly explain the differential CD4+ T cell counts noted in individuals with HCV genotype 1. It would be of interest to know whether the authors explored this possibility.

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