Maternal-Fetal Transmission of HIV

A number of recent studies on mechanisms and prevention of in utero and intrapartum transmission of HIV infection were reviewed at the Los Angeles meeting by Yvonne Bryson, MD, from the Los Angeles Pediatric AIDS Consortium and the University of California at Los Angeles.

The rate of transmission of HIV from infected mothers to infants is estimated at 13% to 40%. Prospective study data suggest that 30% to 50% of infected infants acquire infection in utero, with there being evidence suggesting that most acquire it late in gestation; most of the remainder acquire infection intrapartum, with an added risk of transmission of 14% having been attributed to breastfeeding. A definition of in utero infection proposed by Dr Bryson and colleagues consists of positive viral quantitative co-culture within 48 hours of birth followed by subsequent positive co-cultures, with intrapartum infection being defined as negative co-culture within 48 hours of birth followed by positive co-cultures within 90 days. A study by Dr Bryson's group has shown that infants acquiring infection in utero have more rapid progression of disease, regardless of SI vs NSI HIV phenotypes, indicating that those with positive quantitative PCR or co-culture findings at birth should be targeted for early antiretroviral treatment and *Pneumocystis carinii* pneumonia (PCP) prophylaxis.

Transmitters vs nontransmitters in prospective study group

Dr Bryson and colleagues analyzed immunologic and virologic factors in a subgroup of infected mothers who were enrolled in a prospective study of vertical transmission of HIV; in the prospective study, transmission had occurred in 25 of 82 infants with known infection status (30.5%) and of 111 with any follow-up (22.5%). The subgroup in which risk factor analysis was performed consisted of 61 women, 58 of whom were asymptomatic, 19 of whom had received zidovudine during pregnancy and/or during labor and delivery, and six of whom were entered in the blinded ACTG protocol 076 (discussed below). The analysis showed significant differences between nontransmitters and transmitters with regard to measures of cell-associated HIV (ie, quantitative DNA PCR and quantitative co-culture), measures of cell-free HIV (ie, ICD p24 antigen and quantitative plasma culture), and CD4+ cell count. Further, it was found that the presence of autologous neutralizing antibody in the mother was associated with decreased risk of transmission. This finding was particularly significant among women transmitting infection in utero, only 11% who had measurable antibody titer (>10).

Citing studies by other groups, Dr Bryson related that the finding that a relatively homogenous viral population appears to be transmitted in maternal-fetal cases, as well as adult cases, may be due to the escape of the transmitted strain from neutralizing antibody. In one study indicating a correlation between autologous neutralizing antibody and reduced transmission, it was found that nontransmitters also had broader range of antibody against heterologous viral isolates; in Dr Bryson's analysis, sera from nearly all of the transmitting mothers assessed failed to neutralize the first isolate from the infected infant. Additional analysis showed that neutralizing antibody titers correlated significantly with maternal CD4+ cell counts and quantitative DNA PCR and co-culture findings. As related by Dr Bryson, the overall findings support the attempt at therapeutic intervention aimed at reducing maternal viral load or enhancing maternal autologous neutralizing antibody levels.

Absence of transmission by zidovudine recipients

A striking finding of the analysis was that no transmission of HIV occurred in the 19 infants of women receiving zidovudine, compared with 11 (32%) of 35 infants of women not receiving the drug. Zidovudine recipients had received dosages of 500 to 1000 mg/d during pregnancy and/or during labor and delivery on the basis of having CD4+ cell counts <500/μL or inclusion in a phase I study (ACTG 082; n = 6): 12 received oral zidovudine antepartum for a mean of 16.5 weeks and an intrapartum infusion; four received oral drug antepartum only for a mean of 17.8 weeks; three received only an intrapartum infusion. Three were enrolled in ACTG 076 and were not included in this analysis. As noted by Dr Bryson, the women receiving zidovudine had lower CD4+ cell counts than did the remainder of the patients, with the mean count being equivalent to that in the group of transmitters (402 vs 420/μL) and markedly lower than that in the other nontransmitters (803/μL).

Significant preventive effect of zidovudine in ACTG 076

As related by Dr Bryson, these findings have been followed by reporting of an interim efficacy analysis of the double-blind, placebo-controlled ACTG 076. In this multicenter trial, HIV-infected women at 14 to 34 weeks of gestation with no prior zidovudine treatment and CD4+ cell counts >200/μL were randomized to receive oral zidovudine 500 mg/d and a zidovudine infusion during labor and delivery or placebo, with their newborns receiving oral zidovudine for 6 weeks or placebo. At the time of interim analysis, with data current as of late December 1993, 477 of an anticipated approximately 800 women had been enrolled, with the group having a median age of 25 years, median CD4+ cell count of 550/μL and treatment having begun at a median gestational age of 26 weeks. A total of 364 infants had known infection status at the time of analysis; infection was observed in 13 (8.3%) of 180 in the zidovudine group and in 40 (25.5%) of 184 in the placebo group, a highly significant difference ($P = 0.00006$). No significant toxicity was observed in mothers or infants, with the zidovudine infants having a slight decrease in hemoglobin count that corrected spontaneously. As related by Dr Bryson, further evaluation of the data will include analysis of the characteristics of the zidovudine mother-infant pairs for whom transmission occurred, including viral load and viral phenotype, compliance with and duration of treatment, mode of delivery, and presence or absence of drug resistance, as well as examination of such issues as the contribution of postnatal zidovudine treatment to the findings. ■