ADDITIONAL DISCUSSION OF THE EFFECT OF PRENATAL TREATMENT ON SYMPTOMATIC CT

Drugs such as spiramycin are likely to prevent MTCT in some cases or only decrease parasitic burden in others. Some of the cases in which the parasitic burden was decreased were likely to be shifted from the severe disease or demise group to the mild disease group. The net benefit of a drug that decreases MTCT rates in some cases while only decreasing parasitic burden in others is a significant reduction in severe disease and death but only a “weak” benefit in MTCT transmission.

Cortina-Borja et al,6 in a recent analysis of data from 293 infants with CT from 14 European centers in 6 countries, showed that antepartum treatment was associated with a 76% lower odds of severe neurologic sequelae (at a median 4-year follow-up) or death (by 2 years of age; OR: 0.24; 95% CI: 0.07–0.71). In this composite outcome of severe neurologic sequelae, severe bilateral visual impairment was included (Fig 4). The effect of the antepartum treatment was large and, for women who knew that their fetus was infected (on the basis of AF PCR assay results), the number of infected fetuses who needed to be treated (NNT) to prevent 1 case of CT with severe neurologic sequelae was 3 (95% CI: 2–15), after maternal acute infections at 10 weeks of gestation. The respective NNT for maternal acute infections at 20 weeks of gestation was 6 (95% CI: 3–28) and for maternal infections at 30 weeks of gestation was 18 (95% CI: 9–75). Without knowing the infection status of the fetus, the respective NNTs at 10 weeks, 20 weeks, and 30 weeks of gestation were 28, 20, and 32, respectively. These NNT estimates apply to women with documented seroconversion during pregnancy. The authors had calculated the number of women needed to be treated to prevent 1 case of SNSD as a clinically meaningful measure for counseling women about the absolute difference in the probability of their child developing SNSD with and without treatment. They used the posterior probability distributions and 95% credible interval calculated from the regression model to estimate the NNT for women after a positive prenatal diagnosis (positive AF PCR result; i.e., the number of women with an infected fetus who need to be treated). With maternal seroconversion at 10 weeks, the risk of SNSD in treated infants was 25.7% and in untreated infants was 60%, with an absolute risk difference of 33.3% and an NNT of 3. Respectively, the NNT was 6 for maternal seroconversion at 20 weeks and the NNT was 18 for maternal seroconversion at 30 weeks. To estimate the NNT for women without prenatal diagnosis (without AF PCR results), they multiplied the difference in probability with the estimated risk of MTCT of toxoplasmosis derived from a meta-analysis of all available cohort studies.1

Published data from the Danish neonatal screening experience113 also revealed relatively low rates of symptomatic CT in Denmark, despite using only neonatal screening for CT and not routine antepartum screening/treatment.113 The prevalence of CT in Denmark113 during the screening period 1999–2007 was 1.6 CT cases per 10 000 live births. An earlier study in Denmark by Schmidt et al194 showed that among the 55 confirmed CT cases identified through neonatal screening (1999–2002), 27% (15 of 55) had clinical manifestations (4% [2 of 47] had chorioretinitis...
only, 11% [5 of 47] had intracranial calcifications only, 9% [4 of 47] had intracranial calcification and chorioretinitis, and 2% [1 of 47] had intracranial calcification, chorioretinitis, and hydrocephalus when evaluated at birth, but at the 3-year follow-up, 41% (7 of 17) had clinical manifestations.

Some additional factors that also might contribute to the observed low rates of severe CT in countries with routine antepartum screening and treatment programs are decreases in the *T. gondii* burden over time, reduction in the dose or types of *T. gondii* in undercooked meat or from soil, copathogens, or other secular changes in clinical care and public health surveillance over time. However, the incremental effect of these factors, beyond the effect of antepartum screening/treatment programs, has not been studied.

When differences over time are evaluated by using data from observational studies, one should consider that unmeasured confounders also could contribute to observed differences. However, in the field of CT, the recently accumulated evidence from several large-scale observational studies provided consistently supportive evidence for a large treatment effect from antepartum screening and treatment programs in reducing the MTCT risk and the risk of severe CT.