Future Research

We suggest that the effect of prenatal treatment should be tested out using an ordinary double-blind placebo-controlled clinical trial with randomization on an individual basis.

Additionally, better estimates of the burden of disease should be made, including population statistics. How many children in a certain population will suffer from the consequences of congenital toxoplasmosis? The observational studies give little detail as to the degree of disability and illness experienced by these children. Such data are also needed for evaluation of public health actions.

We also suggest that controlled community trials could be performed to estimate the effect of primary prevention directed against established risk factors. Thus, one could randomize health care districts to have intervention or no intervention, where the intervention might consist of detailed advice to women in early pregnancy to modify behaviour with respect to consumption of raw or undercooked meat and unwashed vegetables, and behaviour with respect to contact with cat faeces.

References


Commentary: Efficacy of prenatal treatment for toxoplasmosis: a possibility that cannot be ruled out

P Thulliez

In their retrospective cohort study of 554 mother-child pairs, Gilbert et al. did not detect a significant effect of prenatal treatment on the risk of vertical transmission of toxoplasmosis. This result is not surprising as there were very few untreated women and the analysis of no treatment versus pyrimethamine-sulphadiazine was restricted to half of the cohort who did not undergo amniocentesis. The confidence interval (0.57–3.03) for the odds ratio (1.06) for no treatment compared with pyrimethamine-sulphadiazine was therefore very wide and could include a doubling in the risk of transmission in untreated women. Thus an absence of evidence of prenatal treatment effect does not exclude a clinically important beneficial effect.

A further problem is that most of the untreated women were infected during the third trimester of pregnancy. Figure 4 shows that only three women infected before 28 weeks of gestation were not treated. The remaining 28 untreated women were infected after 28 weeks. The effect of treatment in the third trimester cannot be generalized to the whole of pregnancy. Finally, the authors explain their findings by suggesting that vertical transmission occurs soon after infection, during parasitaemia. This hypothesis is not supported by any scientific studies in humans. On the contrary, one study found that the sensitivity of prenatal diagnosis was lower in early than mid pregnancy, suggesting that vertical transmission may be delayed for some women infected in early pregnancy.

In the second report by Gras et al., the authors unexpectedly found no evidence that prenatal treatment with pyrimethamine-sulphadiazine was more effective than spiramycin in reducing...
the risks of intracranial or ocular lesions in congenitally infected infants by 3 years of age. A potential explanation for this result is that mothers who transmitted the infection to their fetus soon after infection were more likely to be treated with pyrimethamine-sulphadiazine than mothers infected at the same gestation but in whom transmission was delayed until later in pregnancy. These two groups may not be comparable as fetuses infected earlier in pregnancy have a higher risk of clinical signs. This explanation is suggested by the fact that mothers infected before 32 weeks were only given pyrimethamine-sulphadiazine if the diagnosis of fetal infection was positive (i.e. vertical transmission occurred between maternal infection and the date of fetal sampling). Other mothers infected before 32 weeks were treated with spiramycin until delivery, either because the prenatal diagnosis was negative or not attempted. In this latter group, transmission occurred either after amniocentesis or at some unknown time between the date of maternal infection and delivery, that is later during gestation than in the group receiving pyrimethamine-sulphadiazine.

There are two further explanations for the lack of effect of pyrimethamine-sulphadiazine. Firstly, there was a long delay before pyrimethamine-sulphadiazine was started. This was because the study was carried out more than 6 years ago, when mouse inoculation was the standard fetal diagnostic test and pyrimethamine-sulphadiazine treatment would have been delayed for 3–6 weeks until results were known. Today, PCR analysis of amniotic fluid is widespread. Results are available in one day and women with infected fetuses are treated much earlier. Secondly, women in the study given pyrimethamine-sulphadiazine actually received an alternating regimen with spiramycin. The periods of spiramycin treatment may have led to parasitic relapses in fetal tissues, as shown in experimental models. The current treatment policy for women with a positive prenatal diagnosis is to prescribe continuous treatment with pyrimethamine-sulphadiazine until delivery. The data reported by Gilbert et al. and Gras et al. provide no convincing evidence that this policy should change.

References