Reviewer's report

Title: Assessment of laboratory methods used in the diagnosis of congenital toxoplasmosis during maternal treatment with spiramycin in pregnancy

Version: 6 Date: 8 August 2013

Reviewer: Florence Robert-Gangneux

Reviewer's report:

The study is now well defined and analyzed and deserves publication. However, the authors should add in the Discussion a sentence to temper their conclusions, since the weakness of the study resides in that data were collected on a limited series (68 cases), and there are many children lost to follow-up (more than two third), which can bias the analysis. In addition, it should be stated in the flowchart how many infected children were diagnosed using other techniques such as mouse inoculation, and what was the outcome in these cases (clinical signs, maternal treatment).

Specific points remain to be edited:

Table 1: the title should be: « Positivity of biological markers of congenital toxoplasmosis in infected newborns from mothers treated with spiramycin (Group 1) and from untreated mothers (Group 2) ».

The first head column should read: “biological test”, since PCR is not a serologic test. The lines “negatives” must be deleted (redundant, since they can be easily calculated from the number of positive tests and the total number). Translate the foot note in English.

Table 2: the title should be: “Frequency of clinical manifestations of congenital toxoplasmosis in newborns from mothers treated with spiramycin (Group 1) and from untreated mothers (Group 2) ”. Instead of “Presence” in the first column, it could be: “any of the following clinical signs”. Translate the foot note in English. What do the authors mean by “systemic toxoplasmosis”? Define the clinical signs associated.

Methods. §2.1. Population. « 44 mothers were treated with 3g of spiramycin per day, administered 3 times a day ». Do the authors mean 3g x3 (=9g) per day or 3x1g per day (which is below the regimen classically recommended).

§2.2. It is strange that congenital toxoplasmosis could be diagnosed solely on « clinical alteration compatible to the congenital infection in the absence of other diagnosis (Chagas disease, syphilis, rubella, cytomegalovirus, HIV, HTLV, hepatitis B and C) ». This is not a criteria of congenital toxoplasmosis ! but can help consider the patient « as suspect of ».

Results. A statistical test comparing the frequency of congenital toxoplasmosis in both groups (61.4% vs 79.2%) is still lacking. I understand that 17/19 women of group 2 underwent a serologic testing during the first trimester and were negative, thus they seroconverted later on. As the transmission rate increases
with the term of pregnancy, this could explain the higher rate of infected neonates observed in group 2 and could bias the interpretation about the effect of maternal treatment. How many women from group 1 seroconverted after the first trimester? Is the proportion similar? This must be verified.

The authors probably mean «The laboratory markers of congenital infection (T. gondii DNA detection through PCR, specific IgM and IgA antibodies) were more frequently positive in the infected NBs of group 2, although not statistically significant», as stated in the next sentence («treatment with spiramycin did not interfere significantly with the laboratory markers of congenital T. gondii infection»). Delete «The sensitivity of markers was higher for infants in group 2», since it is not proven by statistics. The impact of treatment on clinical signs is now well documented despite the probably low impact on vertical transmission.

«The presence of serological markers for toxoplasmosis was not associated with greater severity of congenital infection»: even a positive PCR?

Discussion: the % of symptomatic neonates in groups 1 & 2 cited in the text (70.3 and 31.5%) differ from Table 2.

Beware: «Cortina-Borja et al [46] found no reduction of severe neurological sequelae in children»: of course they did! they found an effect whatever the treatment (spiramycin or pyrimethamine-sulfadiazine).

«This latter study resulted in 31%...» should be replaced by «in our study» to avoid confusion.

End of Discussion: «treatment based on sulfadiazine, pyrimethamine and folic acid instead of spiramycin»: in case of proven fetal infection.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.