Serological and molecular screening of umbilical cord blood for Toxoplasma gondii infection; a reply to Botein et al

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Serological and molecular screening of umbilical cord blood for *Toxoplasma gondii* infection;

A reply to Botein et al.

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To the Editor,

We have read the paper by Botein et al. [1] (https://doi.org/10.1111/tid.13117) on the screening of umbilical cord blood for *Toxoplasma gondii* to prevent transplantation-transmitted infections. Indeed, as explained by the authors, there could be a risk of disseminated infection in the recipient if the cord blood (CB) contains circulating *Toxoplasma* parasites, an occurrence which is possible only if the fetus has been congenitally infected. Congenital infection occurs when the mother acquires primary infection during pregnancy. Considering a 30% seroprevalence of *Toxoplasma gondii* infection in Egypt, [2] and a risk for acquiring toxoplasmosis during pregnancy previously estimated to be about 1% in a population of roughly similar prevalence, [3] along with an overall transmission rate to the fetus of 30%, one would expect to observe 0.21 seroconversions in the 100 women included in this study. Of note, the sensitivity of PCR on cord blood is not 100%, even in the absence of specific treatment of the mother, [4] thus the number of cases detected by PCR would be even lower. In contrast to this estimation drawn from well-established data, Botein et al. found a positive PCR in 11 CB samples suggesting a seroconversion rate of about 52% among women who were seronegative at the beginning of pregnancy. Although it can be argued that Egyptian women may have a greater risk of infection due to poorer knowledge regarding hygienic measures to prevent toxoplasmosis, this seroconversion rate is simply unrealistic. Overall, these findings raise suspicion of possible contamination, as frequently observed with nested PCR methods, which are therefore in no way a reference molecular diagnostic method.

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Another point is the interpretation of the CB serological results. The detection of anti-*Toxoplasma* IgG in CB reflects the presence of specific IgG in maternal serum, meaning that the mother is either immunized (chronically infected) or has seroconverted during pregnancy, so it is poorly informative regarding the risk of fetal infection. By contrast, the detection of specific IgM, which are not transferred through the placental barrier, indicates fetal production of specific IgM, and therefore fetal infection. The presence of anti-*Toxoplasma* IgM alone in CB is rare, as it would imply that the fetus has been infected simultaneously with the mother shortly before birth (no passive transfer of maternal IgG, as they would not yet be synthesized by the mother), and unrealistic to occur in 6%.

Specific IgM detection is in fact one of the biological tools to diagnose congenital toxoplasmosis at birth. However, the sensitivity of IgM detection ranges from 45% to 85%.[5] Consequently, the absence of IgM in CB cannot exclude newborn infection, thus there is indeed a risk of having circulating parasites in IgM-negative CB from infected neonates. In this setting, maternal serological screening at delivery would be more appropriate to exclude CB potentially risky for recipients, i.e. CB from mothers who acquired toxoplasmosis during pregnancy and of whom 30% may have transmitted *Toxoplasma* parasites to their fetus. As mentioned by the authors, specific anti-*Toxoplasma* IgM can be detected months after infection. In our experience, more than 95% of women who seroconverted in early pregnancy still present with IgM at delivery (unpublished data). Provided that the sensitivity of ELISA is high, and the test is designed for diagnostic purposes, the approach to screen mothers, and to exclude those with *Toxoplasma*-specific IgM antibodies from CB donation, would be simple and more appropriate than a nested PCR.

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Authors Contribution statement

FRG and ODjDj both conceived the letter. FRG drafted the letter and ODjDj revised it, and they both approved the final version.

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