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Title: Congenital cytomegalovirus infection: disease burden and screening tools: towards newborn screening
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Screening newborns for congenital cytomegalovirus infection

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To the Editor:

Dr Boppana and colleagues' concluded that dried blood spot (DBS) real-time PCR assays are not suitable for screening newborns for congenital CMV infection due to their insufficient sensitivity.

[Boppana et al. published in JAMA (2010) results of a multicenter study in which 20 448 newborns were screened for congenital CMV infection by means of rapid culture of saliva specimens and 2 different in-house DBS real-time PCR assays. Congenital infection was confirmed by means of rapid culture of saliva or urine in 92 infants. Sensitivity and specificity of these PCR assays were at most 34.4% and 99.9%, respectively. Negative and positive predictive values were 99.8% and 91.7%, respectively. The authors stated that, DBS real-time PCR assays have limited value for screening newborns for congenital CMV infection because of insufficient sensitivity.]

We believe that this is a premature conclusion, based on a number of considerations that were not sufficiently discussed in this article.

First, the sensitivity of DBS testing is highly variable, largely depending on the nucleic acid extraction methodology used, so conclusions cannot be generalized. It appears that this problem can be reduced by using optimized techniques that differ from those applied in the study by Boppana et al [Qiagen M48 robot (MagAtract) extraction using two 3-mm disks of dried blood]. In addition, performing independent triplicate testing to increase sensitivity has been advocated, an approach not used in this study.

Second, it should be clear what the clinical relevance is of the cases that were missed. These cases will likely involve the samples with the lowest or even absent viral loads, and there is evidence that such cases are associated with lower risks of late-onset sequelae, including hearing loss. Sensitivity should be judged by patients in whom hearing loss is eventually caused by CMV. The intended follow-up of the infants with congenital CMV infection in this study will reveal the clinical outcome, and these data should be awaited before discarding the screening test that was used.

Third, we are concerned about the possible inclusion of very common but generally harmless postnatal CMV infections. Oropharyngeal contamination during vaginal delivery might cause positive saliva samples soon after birth, as has been shown for herpes simplex virus. Sampling in this study was mainly performed on the day of birth. Confirmation of the presumed congenital infections was carried out at a mean age of more than 6 weeks, although it is commonly accepted that only CMV infections diagnosed within the first 2 or 3 weeks can be considered proof of congenital CMV infection. If postnatally infected neonates were indeed included, this would falsely suggest a lower sensitivity of DBS testing.
References


