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Dried Blood Spot Polymerase Chain Reaction Screening for Congenital Cytomegalovirus Infection

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To the Editor

We applaud Kharrazi et al for their population-based study of the prevalence of congenital cytomegalovirus (CMV) infection in a large cohort of California newborns in *The Journal* (1). The study retrospectively performed polymerase chain reaction (PCR) testing for CMV on archived dried blood spots (DBS) collected for routine newborn screening. The authors point out, and the accompanying editorial (2) re-emphasizes, that universal screening of newborns for congenital CMV infection is a worthy goal. Kharrazi et al also correctly observe that PCR technology is amenable to high throughput screening of large numbers of specimens, as would be required of a newborn CMV screening program. They propose, on the basis of their study, that PCR performed on DBS could become a useful screening method.

Kharrazi et al (1) and Pass (2) both note that the sensitivity and specificity of DBS PCR for detecting CMV DNA remain unknown, in the absence of a large, population-based, prospective comparison of this methodology to a culture-based assay. Ironically, the study they call for was published (3) while their manuscripts were under review. A comparison of DBS CMV PCR to saliva rapid culture prospectively demonstrated that 92 of 20,448 (0.45%) newborns screened at seven medical centers in the United States as part of the NIDCD CHIMES study were infected with CMV. Using a single-primer PCR assay, the sensitivity of the DBS PCR was only 28.3% (95% confidence intervals 17.4-41.4%). Although a two-primer assay was slightly (but not significantly) more sensitive [34.4% (95% confidence intervals 18.6-53.2%)], neither was deemed adequately sensitive to be appropriate for universal screening (3,4), as 64 of 92 (70%) of the infected babies were missed by DBS PCR (3).

It might be argued that the most important goal of a universal screening program for congenital CMV is to identify infants at risk for subsequent adverse outcomes, such as developmental delay or sensorineural hearing loss, rather than those infected with CMV [most of whom will not suffer sequelae (5)]. If DBS PCR positivity correlates with eventual hearing and

developmental outcome, the sensitivity of the assay for all infection may become less important. Clinical outcomes data from the ongoing CHIMES study may provide answers to these questions.

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