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Performance of virological testing for early infant diagnosis: a systematic review

The World Health Organization recommends that HIV-exposed infants receive virological testing for HIV infection between four and six weeks of age and treatment with antiretroviral (ARV) therapy as soon as the diagnosis is made. Despite efforts to expand mother-to-child transmission prevention programs, only an estimated 50 percent of HIV-exposed infants are tested within the first two months of life. Understanding testing performance characteristics and determining the diagnostic accuracy of virological testing at birth as well as at six weeks using dried blood spots among HIV- and ARV-exposed infants may help guide testing and HIV treatment regimens. The authors conducted a systematic review to assess the diagnostic accuracy of virological testing at birth, as well as the performance of dried blood spot testing for at-risk infants at six weeks. A systematic literature review by two independent reviewers was performed on studies published between Jan. 1, 2009 and Jan. 30, 2015. The final analysis included estimates of the sensitivities and specificities of the virological testing performed. From 2,243 publications screened, five manuscripts were selected for review. The authors concluded that the performance of polymerase chain reaction (PCR) at birth demonstrated low sensitivity and high specificity, which was consistent with the difficulty of detecting intrapartum infections at birth. The review also found high sensitivity and specificity with the use of dried blood spots collected at four to six weeks of life in HIV- and ARV-exposed infants. The evidence to support the accuracy of PCR virological testing was, overall, limited and of low quality. The authors concluded that the timing of early infant diagnosis of HIV using PCR needs to be assessed further, particularly with regard to preventing mother-to-child transmission. While there are benefits to PCR testing at birth, the low sensitivity of the test may result in false-negative results and undiagnosed HIV infections in infants. These infants would need repeat testing several weeks later to confirm the diagnosis.

Mallampati D, Ford N, Hanaford A, et el. Performance of virological testing for early infant diagnosis: a systematic review. *J Acquir Immune Defic Syndr.* 2017;75(3):309–314.

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Evaluation of a rapid molecular drug-susceptibility test for tuberculosis

Multidrug-resistant tuberculosis is defined by resistance to isoniazid and rifampin. It results when treatment is ineffective due to improper antibiotic selection or administration, among other factors. Incorrect diagnosis and treatment of drug-resistant tuberculosis may be associated with morbidity, mortality, and ongoing infection. For uncomplicated multidrug-resistant tuberculosis, the World Health Organization recently endorsed a new shortened treatment plan of nine to 12 months that uses fluoroquinolones and the second-line injectable drugs aminoglycosides and capreomycin. The authors conducted a clinical study in which they assessed the diagnostic accuracy of a new investigational assay for the rapid detection of *Mycobacterium tuberculosis* and mutations associated with fluoroquinolones, aminoglycosides, and isoniazid resistance. They conducted a blinded, multicenter, prospective diagnostic study to compare the investigational assay against phenotypic culture-based drug-susceptibility testing and DNA sequencing. The assay involves a new cartridge, for use with the GeneXpert platform, for the rapid detection of 25 mutations that are associated with resistance to fluoroquinolones,

aminoglycosides, and isoniazid. Adults in Seoul, South Korea, and Zhengzhou, China, who had symptoms of pulmonary tuberculosis were enrolled in the study. The results showed that the assay detected *M. tuberculosis* mutations associated with resistance to the investigated drugs. The assay holds promise as a rapid point-of-care test to guide therapeutic decisions for patients with tuberculosis. The results could be available in two hours, which would help, on a global scale, with same-day therapeutic decision-making. Existing GeneXpert instruments have the potential to be upgraded to include this newer testing platform.

Xie YL, Chakravorty S, Armstrong DT, et al. Evaluation of a rapid molecular drug-susceptibility test for tuberculosis. *N Engl J Med.* 2017;377(11):1043–1054.

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