Congenital Cytomegalovirus Infection
The Elephant in Our Living Room

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Congenital cytomegalovirus (cCMV) can be considered an elephant in our living room. Since Weller published his landmark article in 1971 reporting the ubiquity of the problem of cCMV infection in the United States and stressing its major public health importance, cCMV has been recognized as a common congenital infection that can cause liver disease, thrombocytopenia, hearing and vision loss, microcephaly, and neurodevelopmental disorders. Despite how long we have known how common and destructive CMV can be, little has been done to stop this virus from affecting our newborns.

A logical next step toward getting our sights on the elephant in our living room is to screen newborns for cCMV infection at birth. Two approaches have been proposed: targeted CMV testing (or targeted CMV screening) of newborns with failed hearing screens and universal CMV screening of all newborns. Both approaches are evaluated by Gantt and colleagues in this issue of JAMA Pediatrics. Because cCMV infection is a common cause of congenital hearing loss, many hospitals and 2 states (Utah and Connecticut) have already adopted targeted CMV testing (or targeted CMV screening) for newborns who fail their newborn hearing screens. Universal newborn CMV screening, however, remains elusive. If adopted, universal newborn CMV screening will appropriately rob CMV of its invisible elephant in the living room status and force us to see the pachyderm on our couch. The newborns identified through screening will benefit from sensory and neurodevelopmental follow-up, speech and language programs, and educational accommodations to optimize their potential. Severely affected infants may require antiviral treatment, surgical procedures, and hearing devices to help them successfully navigate their childhood and adolescence.

Through the programs that identify these newborns, clinicians, audiologists, laboratories, policy makers, and public health officials also will be forced to face the tens of thousands of newborns born each year with cCMV infection and to develop practical and effective management and prevention strategies.

Does cCMV hit the mark? Does it satisfy accepted criteria for newborn screening? Is it worthy of universal screening and for acceptance to the Recommended Uniform Screening Panel? For a newborn condition to be considered a worthy candidate for universal newborn screening, the condition should represent a significant public health problem. Congenital CMV hits the bull’s eye here! It is a common congenital infection present in 0.4% to 1% of newborns that for decades has been underappreciated. It is a common cause of progressive sensorineural hearing loss as well as ocular and visual disorders, microcephaly, developmental and motor disabilities, liver disease, and growth failure.

An accurate, reliable, validated, and low-cost method of detection should also be available and preferably tested in prospective population-based studies. Another near-the-center target hit! Detection of cCMV can be easily performed using a variety of tests, including viral culture and shell vial culture assay on urine or saliva samples and CMV DNA polymerase chain reaction or other nucleic acid test detection methods on urine, saliva, or dried blood spot (Guthrie cards) samples already obtained for newborn screening of genetic and metabolic disorders. These detection methods have been validated in large-scale population studies. Congenital CMV infection has a diagnostic window of opportunity in the first 21 days of life, however, after which the diagnosis is confounded by perinatal transmission from maternal sources, such as cervical vaginal secretions during delivery and breast milk feedings, and from postnatal sources from blood product transfusions and person-to-person transmission. Therefore, CMV testing in the newborn period is key. Furthermore, screening programs for all newborns would eliminate “the diagnostic odyssey” experienced by many children with cCMV who present after the newborn period.

A condition under consideration for universal newborn screening also should have treatments or interventions with proven efficacy. Another clean shot! Randomized clinical trials have shown early neonatal treatment, initiated within the first month of life, with intravenous ganciclovir or oral valganciclovir provides benefit for newborns diagnosed with cCMV disease by improving head size growth and developmental milestones and reducing the risk for hearing loss and its progression into childhood. In addition, early identification and treatment of hearing loss, whether congenital or later onset, results in improved speech and language outcomes as well as improved behavior and school performance during childhood. For these interventions to provide the most benefit, health care systems and public health and education programs should be capable not only of conducting the screening programs, but also be braced and adequately prepared to provide the needed follow-up and indicated interventions for the tens of thousands of newborns who will be identified each year as having cCMV infection.

If cCMV hits the mark and satisfies the criteria for a condition worthy of universal newborn screening, what are the...
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for comprehensive, directed care.3 In this issue of JAMA Pediatrics, Gantt and colleagues3 have further addressed this issue and put it to rest through a comprehensive analysis for all identifiable contemporary costs related to targeted and universal screening of newborns for congenital CMV. Through their models they show targeted and universal screening of newborns for CMV are both cost-effective, with universal screening offering the larger net savings and the better opportunity for comprehensive, directed care.3

Another important consideration is will newborn screening for CMV cause harm? Because most newborns with cCMV will be asymptomatic at birth, pass their newborn hearing screen, and have no immediate or long-term consequences, a unique consideration is the psychosocial implications that most newborns with cCMV will not develop CMV-related disabilities and therefore would not directly benefit from screening and identification. Instead, screening might burden the parents and child with unnecessary testing, and even psychological suffering and anxiety. Newborns who fail their newborn hearing screen and are identified through targeted CMV screening will have a diagnosis established or refuted in the newborn period, and all of these newborns and their families will benefit. However, approximately 80% of the newborns who will be identified as having CMV infection through a universal newborn screening program will never develop disease or sequelae. For the families of these children, and for the children themselves, this may pose a psychosocial burden. Studies have addressed the issue of potential psychosocial harm and have shown parents favor universal newborn CMV screening, whether or not their children ever develop problems.12 The initial anxiety of a positive newborn CMV screening result can be ameliorated by expert advice, evidenced-based management algorithms to guide clinicians, educational materials for families, and access to hearing, vision, and developmental screening and early interventions when indicated.

Newborn screening for congenital CMV hits the mark. Whether we begin with targeted newborn testing or jump right into universal newborn screening, it is time for newborn screening for CMV. It is time to say goodbye to the elephant in our living room.

ARTICLE INFORMATION

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