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Advancing Clinical Practice through Integration of Congenital Cytomegalovirus (cCMV) Testing with Newborn Hearing Screening at Mayo Clinic

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Abstract

Although congenital cytomegalovirus (cCMV) is the leading non-genetic cause of childhood hearing loss in the United States, neither targeted nor universal screening protocols have been well established to identify cCMV in newborns. Moreover, until cCMV testing is universal, clinical protocols need to account for the complexities of individualized care in partnership with interprofessional care teams. This work addressed an immediate clinical practice need to identify cCMV with subsequent hearing monitoring of babies who test positive for cCMV. This effort focused on three primary objectives to: (a) define interprofessional, team-based approach to facilitate care pathways; (b) develop a clinical workflow for all babies who refer on inpatient hearing screening to be tested for cCMV by 21 days of age; and (c) develop a hearing monitoring plan for all babies who test positive for cCMV. The article describes the development and integration of our interprofessional, team-based approach to institute cCMV testing by 21 days of age on all babies who refer. Description of the inpatient newborn hearing screening and subsequent monitoring is also included. Our observed referral rate was lower than predicted (2.7%) from existing literature with only one positive cCMV outcome noted in the two-year span. This study demonstrates the feasibility of a hearing-targeted cCMV testing paradigm in our clinic practice.

Key Words: newborn hearing screening, CMV, cCMV, targeted screening, interprofessional collaborative care

Acronyms: AABR = automated auditory brainstem response; ABR = auditory brainstem response; ASSR = auditory steady state response; AUD = audiology; CBC = complete blood count; cCMV = congenital cytomegalovirus; CMV = cytomegalovirus; DPOAEs = distortion product otoacoustic emissions; EHDI = Early Hearing Detection and Intervention; GCE = genetics, IFD = infectious disease; JCIH = Joint Committee on Infant Hearing; LFT = liver function test; MDH = Minnesota Department of Health; MRI = magnetic resonance imaging; OAE = otoacoustic emissions; ORL = Otolaryngology; PCR = Polymerase Chain Reaction; TEOAEs = transient otoacoustic emissions

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Babies born with congenital cytomegalovirus (cCMV) infection may present with immediate and long-term health problems, one of which is hearing loss detectable at birth or developing later in childhood (reviewed by Goderis et al., 2014 and WHO, 2021). cCMV is common in the United States presenting in 1 out of 200 babies (~0.6%; Centers for Disease Control and Prevention [CDC], 2020; Fowler et al., 2018). Of babies infected with cCMV, about 10% are symptomatic at birth, 10 to 15% are asymptomatic at birth yet develop hearing loss or other neurological impairments at a later onset, and the remaining majority (75–80%) are asymptomatic (Boppana et al., 2013; CDC, 2020; Goderis et al., 2014; Kenneson & Cannon, 2007). Symptomatic babies may exhibit multiple system conditions because

of cCMV which may include thrombocytopenia, hyperbilirubinemia, or central nervous system involvement such as microcephaly with significant neonatal morbidity and mortality (e.g., Rawlinson et al., 2017).

Sensorineural hearing loss is the most common diagnosis for a baby infected with cCMV, whether symptomatic or asymptomatic for other systems' involvement (Naing et al., 2016). Estimates suggest that cCMV accounts for 25 to 40% of total hearing loss in children (Goderis et al., 2014). Sensorineural hearing loss occurs in approximately 20 to 40% of babies with multisystem involvement and is a single system finding in 5 to 10% of cCMV cases (Dollard et al., 2007; Fowler & Boppana, 2006, 2018; Goderis et al., 2014; Rawlinson et al., 2017). Although this is counter-intuitive, hearing loss has not been included in the definition of symptomatic cCMV; asymptomatic cCMV is a distinct category and can include hearing loss (Petersen et al., 2020; Rawlinson et al., 2017). Therefore, asymptomatic cCMV cases may present with hearing loss as the only clinical finding (Fowler & Boppana, 2006, 2018; Goderis et al., 2014).

Universal newborn hearing screening successfully detects congenital hearing impairment at birth; however, concerns for delayed onset or progressive hearing loss require longer term monitoring (Joint Committee on Infant Hearing [JCIH], 2019; World Health Organization [WHO], 2021). At this time, screening for cCMV is not performed for all newborns. The debate over universal newborn cCMV screening versus targeted screening is ongoing. However, growing evidence and clinical practice goals of universal or extended neonatal cCMV screening aimed at detection of cCMV at the earliest are progressing (e.g., Krishna et al., 2020). Hearing-targeted screening for cCMV can be one step in advancing toward the goal of universal cCMV testing for all newborns and for promoting earlier detection of delayed onset or progressive hearing loss (e.g., JCIH, 2019). That said, such targeted approaches are imperfect as they are biased toward missing cCMV positive cases with passed newborn hearing screening results (see review of considerations by Haller et al., 2020 and Krishna et al., 2020). Evidence in the realm of early detection has resulted in recommendations for inclusion of cCMV testing if sensorineural hearing loss is detected as a result of newborn hearing screening (Choi et al., 2009; Haller et al., 2020; Korver et al., 2017; Park & Shoup, 2018). Hearing-targeted cCMV screening and outcomes data (Diener et al., 2017; Fowler et al., 2017) support legislative efforts to mandate cCMV testing based on newborn hearing screening outcomes and potentially beyond (National CMV Foundation, 2021). Moreover, accounting for delayed-onset or progressive hearing loss over the first years of life is of growing importance (e.g., Cannon et al., 2014; WHO, 2021).

Early cCMV testing is critical as this is the only means to differentiate between congenital and postnatally acquired infection. Detection of cCMV can be made within the first weeks of life by detecting the virus from a culture or polymerase chain reaction (PCR) of body fluids such as urine or saliva (Boppanna et al., 2011; CDC, 2020). This is most helpful for timely detection of asymptomatic cCMV cases as positive cCMV tests within the first 14 to 21 days of life help distinguish congenital from acquired CMV (Revello & Gerna, 2002). Testing of the newborn screening card dried blood spots may permit later diagnosis of cCMV as such samples are collected in the desired timeframe and may retrospectively help to distinguish between congenital and acquired CMV (e.g., Choi et al., 2009). Only congenital CMV causes hearing loss or symptomatic disease; whereas, postnatally acquired infections are not associated with disease (e.g., Boppana et al., 2010; Choi et al., 2009; Meyer et al., 2017). In the case of cCMV, newborns who are symptomatic or asymptomatic will continue to shed and transmit the virus through bodily fluids for 18 to 30 months (Pati et al., 2016). This knowledge is critical for treatment planning and consideration for antiviral therapy (Rawlinson et al., 2017). Timely diagnosis leads to timely intervention; specifically, all treatments began before 30 days of life in initial trials validated antiviral medications (Kimberlin et al., 2003, 2015; Rawlinson et al., 2017). Similarly, continued monitoring for later onset of hearing loss in children who were positive for cCMV can help with earlier diagnosis of hearing loss, facilitate fitting of assistive hearing devices, and support earlier access to speech and language interventions (Boppana & Fowler, 2017; JCIH, 2019; Kennedy et al., 2006).

The work presented here developed from the immediate clinical practice need for Mayo Clinic Rochester and Mayo Clinic Health System (outreach clinical sites throughout Minnesota and Wisconsin) to converge on clinical practice approaches to identify cCMV and subsequently monitor babies who tested positive for cCMV in the newborn population. This effort focused on three primary study objectives that we developed (based on baseline program review from 2015–2017), deployed (January 2018), and reviewed over a two-year span (2018–2019). This article describes the development and integration of our interprofessional, team-based approach to quality improvement efforts to conduct cCMV testing by 21 days of age on all babies who refer (in at least one ear) on inpatient newborn hearing screening. It also describes the follow up process developed for ongoing hearing monitoring of this population. Specific project objectives include: (a) define interprofessional, team-based approach to facilitate care pathways; (b) develop a quality improvement strategy where all babies who refer on inpatient hearing screening get cCMV testing by 21 days of age; and (c) develop a hearing monitoring plan for all babies who test positive for cCMV, keeping in mind that some may be found to have normal hearing.

Method

Participants

All newborns at Mayo Clinic undergo newborn hearing screening according to Minnesota state guidelines (Minnesota Department of Health [MDH], 2021). The population at Mayo Clinic includes newborns who stay on a postpartum/newborn nursery unit (well child) with their

mothers and patients who stay on a Level III neonatal intensive care unit (NICU) and a Level IV NICU. Mayo Clinic Rochester has been conducting inpatient hearing screening on all newborns since 1999. The practice screens approximately 2335 newborns per year (5-year average) on the newborn nursery unit and two NICUs. Overview of the birth cohort focus for this evaluation pre- and post-screening for cCMV is detailed in Table 1.

Table 1

Overview of Birth Cohort from the Newborn Nursery Population Defined as Number of Patients Screened

		Mayo Clinic Rochester, MN Newborn Nursery Population				
Year		2015	2016	2017	2018	2019
Birth Cohort		1899	1839	1903	1882	1921
Hearing Screenings	Pass	1850	1774	1800	1747	1803
	Refer/ Fail	49	65	103	135	118

Note. Screening results of pass in both ears and the target for this investigation of referred in one or both ears also depicted for 2015 to 2019. The thick vertical line delineates baseline (2015–2017) prior to implementation of the congenital cytomegalovirus (cCMV) screening triggered by refer/fail on newborn hearing screening (active since 2018).

Newborn Hearing Screening Protocol

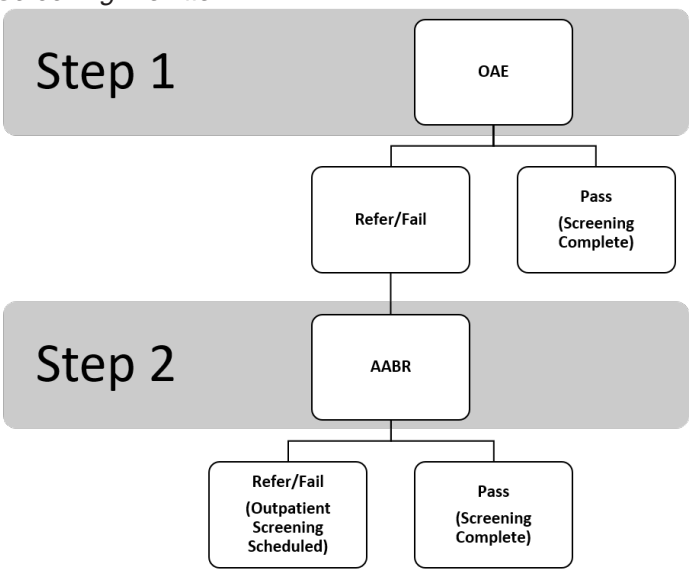
Audiology staff, including audiology assistants and audiologists, conduct the newborn hearing screenings at Mayo Clinic Rochester. On the newborn nursery unit, screening is conducted using a two-step method (See Figure 1). Otoacoustic emissions (OAE) are used as a first level screening. Screening is considered complete if there is a passing result for both ears using OAE. Automated auditory brainstem response (AABR) is conducted if there is a refer result on the first OAE screening. Screening is considered complete if there is a passing result for both ears using the AABR technology. In the NICU settings, screening is conducted using only the AABR technology. Screening is considered complete if there is a passing result for both ears. A maximum of two screening attempts are conducted during the inpatient stay. For patients on all units, risk factors for early childhood hearing loss (JCIH, 2007; 2019) are reviewed and documented.

Location

The focus of this evaluation is on the newborn nursery unit, where screening is conducted by one audiologist coordinator, seven audiology assistants, and two audiology doctoral student externs. The location of screening varies and is prioritized for family-centered care. Screening is initially offered to be conducted at the mother's bedside and with parent(s) present whenever possible. This aspect of the program lends a family-centered care emphasis and is the most common location for screening in our practice.

Figure 1

Overview of Two Step Protocol in the Newborn Hearing Screening Workflow



Note. The first level of screening (Step 1) uses otoacoustic emission (OAE) technology and the second step uses automated auditory brainstem response (AABR) technology. Refer/Fail outcomes prompt next level of screening.

Timing

Newborns on the nursery unit are typically seen for hearing screening on the first full day of life. Screening is typically completed late morning or early afternoon on the first day, so the patients may be in the range of 12 to 36 hours old when screening is completed. In either of the NICU settings, screening is conducted as the patient is getting closer to dismissal (typically within 1–2 weeks of dismissal).

Equipment

Screening is conducted using the Otodynamics Otoport TE+DP OAE+AABR equipment in all units. This is a handheld piece of equipment that plugs in to a computer kept on a cart and is transported to the newborn's location for screening. This allows the screener to be mobile and permits timely access to the electronic health record and reporting applications for maximum efficiency in the clinical practice. The handheld equipment can be transported into the mother's room without the full cart for a less obtrusive experience for the family and to maximize bedside screening opportunities.

AABR and OAE screening equipment settings are consistent across all units. Of note, the equipment that was in use from 2015 to 2018 included the ALGO 5 Newborn Hearing Screener for AABR and Otodynamics Echoport 292 for transient otoacoustic emissions (TEOAE). The Otodynamics Otoport TE+DP OAE+AABR was in use from 2018 to 2019.

Data Management

Results and risk factors are entered into an internally created database called the Early Hearing Detection and Intervention (EHDI) application (developed at Mayo Clinic Rochester, 2009). This application was designed to track

inpatient and outpatient screening as well as follow up results for newborn hearing screening. The audiologist or audiology assistant creates a note in the electronic health record as well. Results are also sent electronically to the MDH. Data is exported from the handheld units to minimize errors due to manual entry. A program coordinator maintains the internal EHDI database, oversees review of risk factors for early childhood hearing loss, monitors follow up, and directs the ongoing quality improvement initiatives.

Patient Education

Newborn hearing screening results are delivered by the examining audiologist or audiology assistant to the parent(s) at the time of the screening. Results are delivered verbally and in writing as standard practice. In person, tablet, or telephone language interpreters are used when appropriate. Two patient education brochures are offered to families. The first brochure describes the screening process and explains why hearing screening is being done for a newborn. This brochure also has a checkbox for a pass or refer result so that the family has a record of the results before hospital dismissal. The family also has access to the screening results in the electronic health record patient portal. The second brochure has a list of typical developmental milestones for speech and language abilities up to age 5 years and is intended as a reference for parents to use while monitoring their child's speech and language development.

When a baby is leaving the hospital with a refer result, the person who conducts the hearing screening documents this in the internally created EHDI database and in the note in the electronic health record and sends a message (also through the electronic health record) to the audiology scheduling team. The scheduling team contacts the family directly to schedule an outpatient rescreen appointment in 1 to 2 weeks.

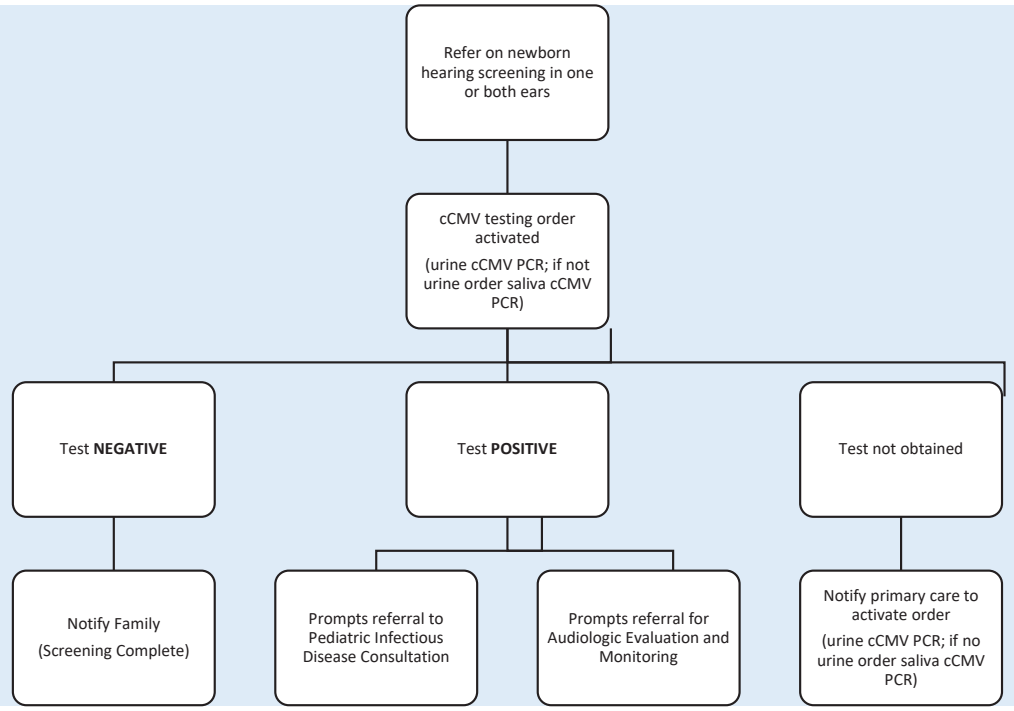
Congenital Cytomegalovirus (cCMV) Testing Protocol

For this evaluation, patients leaving the hospital with a refer result on newborn hearing screening in one or both ears were offered cCMV testing. This included patients with a refer after one attempt if a second attempt is not possible before discharge. cCMV testing was performed as urine PCR (polymerase chain reaction) or saliva swab depending on what was feasible at the time of collection prior to hospital dismissal (e.g., Rawlinson et al., 2017; JCIH, 2019). Refer to Figure 2 for workflow of cCMV testing prompted by hearing screening outcome. This was implemented in January 2018 and this article reviews the outcomes over a two-year period (2018 to the end of 2019).

In addition to the previously described process for newborn hearing screening above, the person who conducts the hearing screening also notifies the nurse caring for the patient that the patient will be leaving with a refer result (one ear or two) for hearing screening. This prompts the nurse to activate the cCMV collection order set in the electronic health record (and workflow in Figure 2). The nurse informs the family that cCMV testing is completed whenever a patient is leaving the hospital with a refer result on newborn hearing screening. The nurse collects a sample for this test (as appropriate). Urine is the preferred specimen, but saliva (buccal swab) is considered appropriate if urine cannot be collected in a timely manner.

Figure 2

Overview of cCMV Testing Workflow for Newborns Triggered by Refer/Fail On Newborn Hearing Screening by 21 Days of Life



Note. Congenital cytomegalovirus(cCMV) testing ordered and sample collected prior to hospital dismissal. PCR = polymerase chain reaction.

PCR testing is completed at the Mayo Clinic Laboratories with results reported in the electronic health record in 1 to 2 days. A PCR positive result triggers an immediate referral to the Pediatric Infectious Diseases Outpatient Clinic or a Pediatric Infectious Diseases inpatient consultation if the patient remains in the hospital. The Pediatric Infectious Disease provider then initiates an evaluation for other evidence of all organ involvement while awaiting final audiology results. If the evaluation indicates the infant has symptomatic cCMV, treatment is discussed with the parents or guardian.

Patient Education Development

cCMV testing results are delivered to the parent(s) by the managing primary care team. In a coordinated effort by the interprofessional care team, a patient education piece was created to assist the primary care providers in educating their patients and their families about cCMV and its connection to hearing loss. The piece, entitled "*Congenital Cytomegalovirus (cCMV),*" is a 12-page brochure created by Mayo Clinic Health Education and Content Services led by Audiology in collaboration with colleagues in Pediatric Infectious Disease, Genetics, Pediatric Otolaryngology, and Primary Care. Topics include a description of cCMV and causes, the relationship between cCMV and hearing loss, an overview of testing for cCMV, as well as treatment and prevention of cCMV.

Results

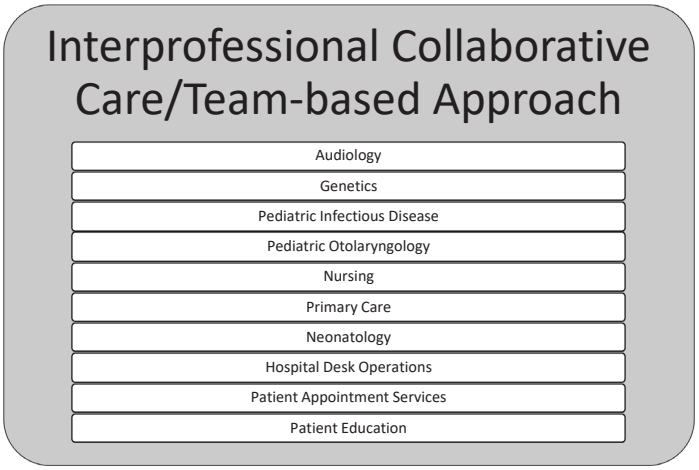
Interprofessional Collaborative Care Team Approach

An interprofessional collaborative care team was established to address this clinical practice need with the goal of initiating cCMV testing prior to dismissal from the hospital on all babies in the newborn nursery with a refer result on their newborn hearing screening. Interprofessional collaborative practice occurs when multiple health workers from different professions provide comprehensive services by working with patients, caregivers, and communities to deliver the highest quality of care across settings (WHO, 2010). The Interprofessional Education Collaborative (IPEC, 2016) further defined several competencies for teams of professionals working toward this type of practice. These include a climate of mutual respect and shared values, clearly defined roles and responsibilities, responsive and responsible communications with patients and their families as well as other professionals, and application of the principles of effective team dynamics.

For the purposes of this project, the interprofessional collaborative care team (See Figure 3) included representatives from the following specialty areas: Audiology, Genetics, Pediatric Infectious Disease, Pediatric Otolaryngology, Nursing, Primary Care (Family Medicine; Community Pediatrics), Neonatology, Hospital Desk Operations, Patient Appointment Services, and Patient Education. Representatives from the various groups worked together in smaller groups to accomplish portions of the project. For instance, pediatric expert representatives from audiology, infectious disease, genetics, pediatrics, and otolaryngology collaborated to create a patient education piece (described in Patient Education Development) designed to support primary care providers when discussing the concept of cCMV testing with parents.

Figure 3

Overview of Interprofessional Collaborative Care Team Approach



Note. There are many other collaborating providers; however, this reflects the initial launch team described in this study.

Defined Care Team Pathway for Audiology (Outpatient)

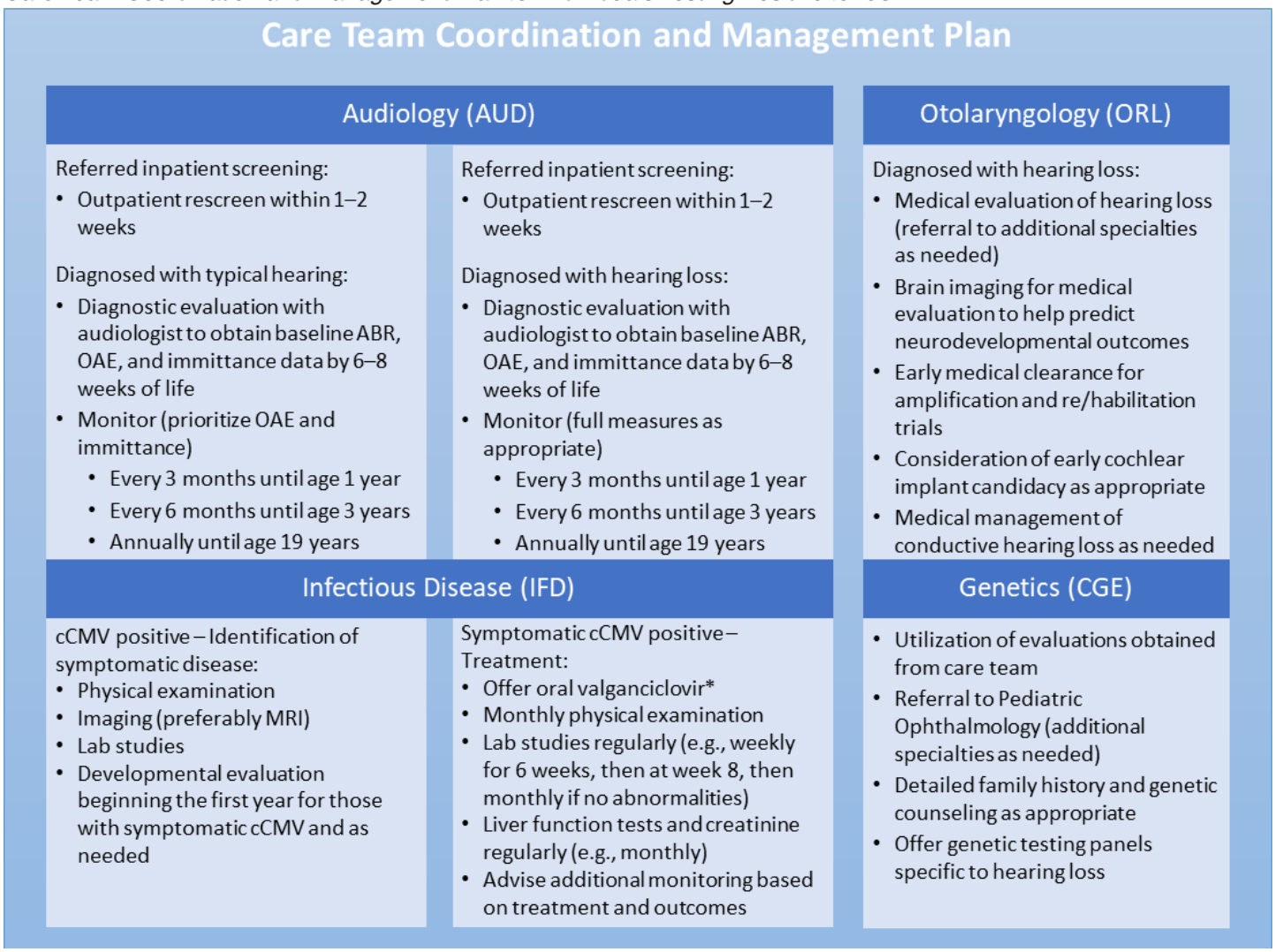
To facilitate the goal that all babies who do not pass hearing screening will undergo cCMV testing by 21 days of age, care pathways within the inpatient setting (see Figure 2 above) as well as in the outpatient setting (Figure 4) were defined as part of this project. Our objective was to develop a follow up plan for all babies who test positive for cCMV, keeping in mind that some may be found to have normal hearing. Figure 4 provides an overview of the care team coordination and plan for additional monitoring and management.

With implementation of a cCMV testing program into the clinical practice, an audiological monitoring pathway and protocol needed to be defined to account for individuals testing positive for cCMV and based on hearing status. The testing within this protocol will vary slightly depending on the patient population and individualized patient needs. Primary populations following this protocol will be patients who test positive for cCMV and who (a) Refer, miss, or refuse on newborn hearing screening and subsequently have confirmed sensorineural hearing loss, conductive hearing loss, or mixed hearing loss; and (b) Refer, miss, or refuse on newborn hearing screening and subsequently have confirmed hearing sensitivity within normal limits.

An interprofessional collaborative care team-based approach is critical when serving patients with cCMV with or without hearing loss. Clearly defined clinical pathways for the identification and management of cCMV can facilitate early intervention options. The care team needed for an effective monitoring program is one in which team

Figure 4

Care Team Coordination and Management Plan for Individuals Testing Positive for cCMV



Note. Care team coordination and management plan defined prospectively to define care pathway for individuals testing positive for congenital cytomegalovirus (cCMV) with specific focus on differences between care plan for individuals with hearing loss versus those with typical hearing. Please note this is an overview rather than exhaustive care plan in which individualized patient needs are also addressed. ABR = auditory brainstem response; OAE = otoacoustic emissions. *If initiated, valganciclovir treatment is for 6 months unless adverse effects prevent the full course of treatment.

members from different professions work in collaboration for timely identification, monitoring, and intervention as appropriate. Four of the professions (see Figure 3) are described in detail below for an overview of this approach.

Audiology

For Audiology, when babies refer on inpatient newborn hearing screening (refer to Figure 1), patients are immediately scheduled for outpatient rescreen within 1 to 2 weeks. If there is a refer result on the outpatient rescreen of hearing, then patients proceed with a scheduled diagnostic audiologic evaluation with an audiologist as soon as possible (typically, within 1–2 weeks). Audiologic evaluation may include frequency-specific threshold auditory brainstem response (ABR), auditory steady state response (ASSR), otoacoustic emissions (may include TEOAEs and distortion product otoacoustic emissions [DPOAEs]), and immittance measurements (including tympanometry and acoustic reflex testing). Evaluation and confirmation of hearing status may occur over multiple visits.

When audiologic evaluation leads to diagnosis of hearing loss, the next steps (refer to Figure 4; AUD section) are to monitor every 3 months until age 1, every 6 months until age 3, and annually until age 19. When audiologic evaluation leads to diagnosis of hearing sensitivity within normal limits, the next steps are to monitor every 3 months until age 1, every 6 months until age 3, and annually until age 19. Although the timing of the monitoring visits is the same for the two populations, the specific monitoring tools are different. The testing for the population with a diagnosis of hearing sensitivity within normal limits will focus on and prioritize objective screenings, such as OAE and tympanometry unless change in hearing is more highly suspect (modified from Figure 2 in Foulon et al., 2015).

Pediatric Otolaryngology

For Pediatric Otolaryngology, there is a close partnership with Audiology when audiologic evaluation leads to diagnosis of hearing loss (refer to Figure 4; ORL section). Additional medical evaluation of hearing loss may include detailed review of medical history, brain imaging for medical evaluation to help predict neurodevelopmental outcomes, referrals for speech and language development evaluation, et cetera. Efforts are led by otolaryngology for medical management of conductive hearing loss, which may include partnership with primary care teams. Pediatric Otolaryngology will often serve as the lead for early medical clearance for amplification or rehabilitation trials as well as the entry point for referrals for consideration of early cochlear implantation as appropriate. Specific to cCMV positive cases, additional management may include brain imaging for medical evaluation to help predict neurodevelopmental outcomes, early medical clearance for amplification and (re)habilitation trials, and consideration of early cochlear implantation as appropriate.

Genetics

For genetics, the identification of cCMV positive individuals in combination with hearing status helps guide next steps for the care plan (refer to Figure 4; CGE section). Additional work-up may include: utilization of evaluations obtained from care team, referral to pediatric ophthalmology (and other specialties as needed), and detailed family history and genetic counseling as appropriate. Targeted genetic testing is warranted, particularly, if there is a family history of hearing loss suggesting that there may be coincident cCMV as well as a genetic condition. Negative targeted genetic testing in the face of positive cCMV testing provides supporting evidence that cCMV alone would be the underlying cause of hearing loss.

Pediatric Infectious Disease

For Pediatric Infectious Disease, evaluation for evidence of symptomatic cCMV disease and treatment for symptomatic infants are the key considerations and components to manage (refer to Figure 4; IFD section). Next steps following a cCMV positive test result include physical examination; lab studies such as Complete Blood Count (CBC) with differential, liver function tests (LFT), creatinine; and brain imaging (preferably MRI). Developmental evaluation should begin at the first year for children with symptomatic cCMV on a case by case basis. Practitioners will also want to review audiology in at least 6 month intervals through age 3 years and align them with the prospective monitoring (defined in Figure 4; AUD section).

Treatment of symptomatic cCMV disease is led by Pediatric Infectious Disease in partnership with the broader care team. Specific to cCMV treatment, infants are examined at least monthly with dose adjustments of valganciclovir based on weight gain and monitoring for adverse effects of oral valganciclovir treatment including CBC with differential, liver function tests, and creatinine. Monitoring of hearing helps support the treatment which may be conducted through age 19 years based on need (as described above).

Hearing-Targeted cCMV Testing

Table 2 provides an overview of the numbers of newborns who did not pass hearing screening in both ears and cCMV testing. cCMV testing was implemented in January 2018 and here we review outcomes over a two-year period (2018 to the end of 2019) with baseline data reviewed from January 2015 to December 2017. During this time, 1882 newborns were screened in 2018 and 1920 screened in 2019 (refer to Table 1). The referral rate from newborn hearing screening is displayed by year in Table 2 with the 5-year average of 5% of newborns screened referred for hearing. Of those

Table 2

Overview of cCMV Testing Results from the Newborn Nursery Population

		Mayo Clinic Rochester, MN Newborn Nursery Population				
Year		**2015**	**2016**	**2017**	**2018**	**2019**
Hearing Screenings	Refer Rate (refer total/ birth cohort in %)	2.58%	3.53%	5.41%	7.17%	6.14%
	Refer/Fail	49	65	103	135	118
cCMV Testing	***Hypothesized***					
	Test Positive	1	2	3	4	3
	Actual					
	Test Complete				112	115
	Test Positive				0	1
	Test Negative				112	114

Note. Screening results of pass in both ears and the target for this investigation of referred in one or both ears also depicted for 2015 to 2019. The thick vertical line delineates baseline (2015–2017) prior to implementation of the congenital cytomegalovirus (cCMV) testing triggered by refer/fail on newborn hearing screening (active since 2018). The gray shading denotes hypothesized values or intentionally blank cells prior to the initiation of cCMV testing.

that refer on hearing screening, we anticipated to find about 2 to 3 babies per year from our birth cohort that would refer for our monitoring protocol based on our program data from 2015 to 2017 (see Table 2). This referral rate for cCMV was predicted based on prior evaluations at similar institutions (2.7% refer rate; Choi et al., 2009). Based on these predictions, we planned a monitoring protocol that we expected would be manageable within the framework of our existing clinical practice (see Figure 2).

Most of those individuals that referred on newborn hearing screening were tested for cCMV (83.0% in 2018 and 97.5% in 2019). No newborns were identified via targeted testing for cCMV in 2018 and only one patient was identified in 2019. This is less than our hypothesized cCMV refer rate of 4 in 2018 and 3 in 2019 (Table 2).

Discussion

Congenital cytomegalovirus (cCMV) is a cause of neurodevelopmental delay in children and a common cause of nonhereditary sensorineural hearing loss (CDC, 2020; Goderis et al., 2014; Kenneson & Cannon, 2007; Kimberlin et al., 2015). Although prevalent, cCMV has gone largely undetected because most babies that are cCMV positive are asymptomatic. The early detection of hearing loss may help identify cCMV as well as promote early intervention for hearing loss. In our practice, exploration of hearing-targeted screening for cCMV was an initial step in advancing toward the goal of universal cCMV testing for all newborns and for promoting earlier detection of delayed onset or progressive hearing loss. In this article, we described our efforts focused on defining the care pathway for the identification and audiologic monitoring of individuals who refer on newborn hearing screening and subsequently test positive for cCMV by 21 days of age in the newborn nursery population. Three primary study objectives were to (a) define the interprofessional, team-based approach to facilitate care pathways; (b) develop the clinical workflow for all babies who refer on inpatient hearing screening to get cCMV testing by 21 days of age; and (c) develop a hearing monitoring plan for all babies who test positive for cCMV.

Family-Centered Interprofessional Collaborative Care

The first objective was to establish an interprofessional collaborative care team (Figure 3) to address the immediate clinical practice need with the goal of initiating cCMV testing prior to dismissal from the hospital on all babies with a refer (in one or both ears) on their newborn hearing screening. As described above, many considerations and care team components were explored. Future considerations around defining pathways for inpatient versus outpatient screening and monitoring, internal versus external patient entry options, as well as hearing loss risk (based on degree and progression concern) will be explored. Moreover, longer term monitoring aspects warrant continued exploration given the small population and need for longer-term data (beyond the age of 19 years as described above).

Throughout the work on this project, the interprofessional care team also recognized that the child and their family are arguably the most important members of the overall team caring for the child. Family-centered care has always been a focus of the Mayo Clinic newborn hearing screening program. From the decision to offer to screen in the mother's room as well as with parent(s) present to the scheduling of outpatient appointments before dismissal whenever possible, every decision is made with the experience of each family in mind. Family-centered care means working toward a respectful partnership between the family and the professionals. It also focuses on the principles of honoring and respecting the strengths, cultures, and expertise that families and professionals each bring to the health care interaction (Family Voices, 2021; Kuo et al., 2012; American Academy of Pediatrics, 2012). The principles of family-centered care were considered during all of the work on this project. It is well documented in the literature that parent and medical professional knowledge about cCMV is quite limited. Others are working on increasing awareness of cCMV among pregnant women, those who may become pregnant, and medical professionals (see resources in the National CMV Foundation, 2021; Park et al., 2020). During our project, the creation of the patient education brochure was part of our team's efforts to increase awareness among providers and parents. One way the team could enhance these efforts in the future is to incorporate patient experience feedback and refinement of the materials.

Linking Newborn Hearing Screening and cCMV Testing

Development of a care pathway for a targeted approach to cCMV screening was the primary focus and one of the key objectives of this collaboration. Based on review of available literature, we anticipated that the newborn hearing screening program would identify more individuals with cCMV using this targeted approach to testing based on hearing screening outcomes. Specifically, we predicted a referral rate by year based on prior evaluation at a similar institution (e.g., Choi et al., 2009) which estimated about 2.7%. Our predicted estimates for the newborn nursery population is displayed by year in Table 2. As can be seen from two years of this targeted approach, we anticipated identification of approximately seven patients with cCMV. Instead, we identified only one newborn during the two years with the targeted screening (equating to a referral rate of 0.85% in 2019 and 0% in 2018). Outcomes from this study demonstrate the feasibility of a hearing-targeted cCMV testing paradigm in our clinic and establishes the framework for expanded neonatal cCMV screening or universal screening for cCMV in the future. This aligns with prior published efforts (Diener et al., 2017; Fowler et al., 2017; Haller et al., 2020; Krishna et al., 2020).

It is expected that more cCMV positive cases would be identified if a universal approach to cCMV testing were implemented. Because hearing loss that is secondary to cCMV is often progressive or later-onset in nature, a universal approach to cCMV testing and monitoring would help to identify those patients who receive a pass result on their newborn hearing screening and should be monitored for hearing changes (e.g., Haller et al., 2020). A universal cCMV testing approach would further the critical goals

of timely detection and hearing loss prevention, while promoting accessibility and affordability of care (e.g., Choi et al., 2009).

Audiologic Monitoring of Patients with cCMV Positive Outcomes

Before cCMV testing was implemented (see Figure 2), the audiologists worked to define a protocol for monitoring the newborns who test positive for cCMV. The defined protocol (see Figure 4), described earlier is similar in approach for those who have a higher degree of suspicion for or are known to have hearing loss as it is for those who continue to have results suggesting hearing that is within normal limits. The main difference is a focus on streamlined screening using more objective measures for those who continue to exhibit typical hearing in the context of a larger diagnostic assessment and monitoring plan as appropriate (e.g., Foulon et al., 2015; Park et al., 2014). There are ongoing multi-site studies from leading research centers in this realm (e.g., Choi et al., 2009; 2013; Haller et al., 2020; Park et al., 2014) validating various types of testing for cCMV and looking at the efficacy of treatment on hearing loss prevention. Findings from these continued efforts will be key for informing future changes in clinical practices and prioritizing global efforts for early detection and monitoring of hearing loss across the life span (e.g., JCIH, 2019; WHO, 2021).

Lessons Learned and Future Considerations

There are several aspects to consider when testing for cCMV, from the perspectives of the patient and their family as well as the interprofessional care teams in relation to hearing monitoring. Several of these considerations were gathered as part of the development of this clinical practice initiative and represent several areas needing further and larger scale exploration. Here we highlight considerations for social, clinical practice, and longer-term/life-span care approach.

Social considerations may include such items as the patient's birth hospital may not be their managing hospital, requiring internal and external care pathways to be clearly defined. Patient and family ability to return for frequent monitoring (e.g., travel/financial burden) may also be a factor to address for the clinical program. Patient education materials may be overwhelming or not specific to the needs of the individual. Moreover, variability may exist in expected outcomes based on elected treatment and management options. Affordability and accessibility of care also warrants future consideration.

Clinical practice considerations may include the fact that infectious disease treatment options for symptomatic cCMV symptoms require close monitoring and may have varied outcomes. The individualized treatment approach supported through the interprofessional collaborative care team is deemed to be important for this and warrants future investigation. The complexity of audiologic evaluation in young children as well as in those who are neurologically complex is also a consideration given screening tool limitations and balancing affordability of preventative monitoring. There may be limitations to appointment availability and coordinating between audiology and associated sub-specialties (e.g., Pediatric Infectious Disease, Genetics, Pediatric Otolaryngology, etc.). The timeline for cCMV testing and confirming hearing status is short to maximize treatment and management options. Until cCMV testing is universal, allowing early intervention for sensorineural hearing loss and developmental delay where appropriate (Rawlinson et al., 2017), current workflows require ordering of the test and this can increase the risk of missed tests.

Considerations across the lifespan and long-term for meeting the needs of the patient are worth immediate consideration as well as continued refinement as evidence emerges. Long term audiologic monitoring is recommended for those identified with cCMV regardless of newborn hearing screening outcome given potential risk for later onset hearing loss. The details of how often and what tools are rapidly emerging with increasing exploration as balancing accessibility, affordability, and quality of care continues to be weighed. It is our recommendation that clinical care pathways should be tailored to the individual needs of the patient and based on treatment options elected.

Conclusion

Although cCMV is the leading non-genetic cause of childhood hearing loss in the United States, there are not widespread established practices for cCMV testing universally at birth or on babies who refer on newborn hearing screening. Development of this interprofessional quality improvement project has greatly enhanced Mayo Clinic protocols and care plans for working with patients with cCMV and their families. It has also enhanced our ability to make recommendations for patients later identified with CMV. It has strengthened the interprofessional collaborative care relationships that audiology has with primary care and various specialties. Although this targeted screening project has identified fewer patients testing positive for cCMV than anticipated, it could be expected that the implementation of a program such as this could have positive implications for practices that have the resources to manage necessary referrals and follow up. Moreover, until cCMV testing is universal, clinical protocols need to account for the complexities of individualized care in partnership with interprofessional care team coordination.

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