Vestibular, Gaze, and Balance Disorders in Asymptomatic Congenital Cytomegalovirus Infection

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abstract

BACKGROUND AND OBJECTIVES: Congenital cytomegalovirus (cCMV) is the leading nongenetic cause of sensorineural hearing loss and developmental disabilities. Because there are limited data from studies of vestibular involvement in select groups of children with cCMV, the true frequency of vestibular disorders in cCMV is likely underestimated. Our objective for this study is to determine the prevalence of vestibular, gaze, and balance disorders in a cohort of children with asymptomatic cCMV.

METHODS: Comprehensive vestibular, gaze, and balance assessments were performed in 40 children with asymptomatic cCMV. The function of semicircular canals of the inner ear and vestibulo-visual tract were assessed by measuring vestibulo-ocular reflex in a computer-driven motorized rotary chair; inner ear saccular function was assessed by using cervical vestibular evoked myogenic potential; gaze stability during head movement was assessed by using clinical dynamic visual acuity, and balance was assessed by using the sensory organization test and the Bruininks-Oseretsky Test of Motor Proficiency, Second Edition. Test results for each variable were compared with those of a control group without cCMV and/or compared to age-matched normative published data.

RESULTS: Vestibular disorders were evident in 45% of the cohort on the basis of rotary chair and cervical vestibular evoked myogenic potential testing, suggesting abnormalities in semicircular canals, the utricle and saccule of the inner ear, and vestibulo-visual tracts. Additionally, 46% of the cohort had difficulties maintaining gaze during head movement, and one-third to one-half of the cohort had difficulties maintaining balance.

CONCLUSIONS: Vestibular, gaze, and balance disorders are highly prevalent in children with asymptomatic cCMV. Systematic screening for vestibular disorders will be used to determine the full clinical impact for the development of effective interventions.

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WHAT'S KNOWN ON THIS SUBJECT: Hearing loss is the most common sequela in children with congenital cytomegalovirus (cCMV), including those with asymptomatic infection. However, the prevalence and extent of vestibular, gaze, and balance disorders in cCMV, particularly in children with asymptomatic infection, is not well defined.

WHAT THIS STUDY ADDS: We document a high prevalence of vestibular, gaze, and balance disorders in children with asymptomatic cCMV, highlighting the need for routine vestibular testing in all children with cCMV, the need for future studies to determine the clinical impact, and the need for developing clinical interventions.

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The prevalence of congenital cytomegalovirus (cCMV) infection in the United States is estimated to be 4.5 per 1000 live births.[1] Sensorineural hearing loss (SNHL) is the most common and well-characterized sequela in children with cCMV, responsible for 8% to 40% of all childhood hearing loss.[2–6] Most infants with cCMV do not have clinical abnormalities at birth (asymptomatic), and ~10% to 15% of these children develop SNHL.[7–12] The natural history of cytomegalovirus (CMV)–associated SNHL is well defined, and audiological monitoring of children with cCMV[13] is recommended because SNHL is of varying severity and could be late onset, fluctuate, or progress over time.[14–16]

Although SNHL is recognized as the most common sequela of cCMV,[2,7] despite histopathologic evidence of the presence of CMV in the vestibular organ from studies of fetuses with CMV infection,[17,18] limited data exist regarding vestibular disorders[19–23] in children with cCMV. In children with SNHL[24–27] or vestibular hypofunction from birth[28–30] due to other etiologies, there is abundant evidence for progressive developmental delays, aberrant postural control, and poor gaze stability, leading to difficulties participating in sports, performing high-level gross motor functions, and reading.[31] Additionally, vestibular and balance physical therapy in these children has been shown to improve gross motor, balance, and gaze outcomes.[32,33] Our objective for this study is to determine the prevalence of vestibular, gaze, and balance disorders in children with asymptomatic cCMV identified by newborn screening.

METHODS

Study Participants

Between March 2007 and March 2012, newborns at 7 US medical centers were enrolled in the Cytomegalovirus & Hearing Multicenter Screening (CHIMES) Study within the first 3 weeks of life and tested for CMV by using rapid culture or polymerase chain reaction of saliva and/or urine. Of the 100 332 newborns screened, 449 (0.45%) were confirmed to have cCMV and were managed long-term for hearing loss outcomes for 5 years.[1,34,35] Initial newborn screening methodologies have been described previously.[34,35] Newborns who tested positive for CMV with normal physical examination findings at birth were considered to have asymptomatic cCMV and were managed long-term for hearing loss outcomes. Forty of these children enrolled at The University of Alabama at Birmingham (UAB) site of the CHIMES Study consented to participate in the current study for vestibular, gaze, and balance testing.

The control group constituted 33 healthy children without hearing loss who participated in other research protocols at UAB from whom the normative data for vestibular and balance testing were derived,[36] as detailed in the Methods section. The results of gaze and additional balance testing were compared to age-matched normative published data.[29,30,37] Institutional review board approval was obtained for this study.

Audiological Assessments

Children with cCMV underwent audiological assessments per CHIMES protocols[38] and had at least one follow-up hearing assessment in the year before performance of vestibular assessments.

Tests of Vestibular Function, Gaze, and Balance

The vestibular system is a complex network and includes (1) the semicircular canals (SCCs); (2) the otolith organ (utricle and saccule); (3) visual, somatosensory, and vestibular pathways to the brain; and (4) the vestibulospinal tracts and is primarily responsible for spatial awareness, stability of the eyes during head movement (gaze stability), and maintenance of balance. The tests used to assess the different components of the vestibular system are briefly described here and summarized in Fig 1.

SCCs and Vestibulo-Visual Tract

The integrity of the horizontal SCC and associated brainstem level reflexes is assessed by measuring the vestibulo-ocular reflex (VOR) by using videonystagmography and a computer-driven rotary chair (RC). A precise description of the RC testing protocol is described elsewhere.[36,39] An overall VOR score was calculated and considered abnormal if sinusoidal harmonic acceleration testing performed at 1.28 Hz was <1 SD of the data derived from the control group.

The function of the vestibulo-visual tract, mediated by the utricle and the central utricular pathways, is assessed by subjective visual vertical variance (SVV), which measures the participant's perception of the vertical and horizontal, and also by measuring VOR cancellation.

Saccule

Saccular function is measured by cervical vestibular evoked myogenic potential (cVEMP), per published methods.[36,39] Tympanometry preceded all protocols to ensure integrity of the middle ear. Test results <1 SD of the normative data derived from the control group were considered as low amplitude or abnormal results. The response result was coded as normal (normal response in both ears), partial and asymmetric (diminished unilaterally), partial and symmetric (diminished in both ears), weak bilaterally, or absent bilaterally.

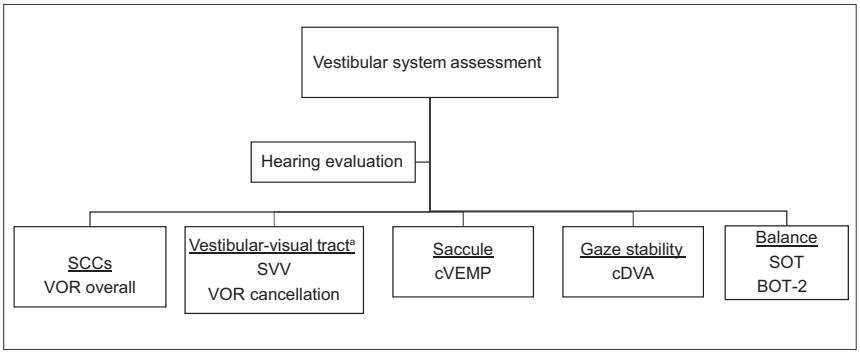

FIGURE 1
Vestibular system assessment. [a] Testing performed in an RC.

Gaze Stability

Clinical dynamic visual acuity (cDVA) is used to test the integrity of gaze stability and assess the functional use of VOR. Visual acuity completed with the head static and then as the head was passively moved at 2 Hz was measured. The difference between static and dynamic visual acuity of >2 lines was coded as abnormal, suggestive of inability to use the VOR to see clearly during head movement.[29,30]

Balance

Sensory Organization Test

The sensory organization test (SOT) is a test of static balance and postural control and was conducted with the EquiTest (Natus Medical Incorporated, San Carlos, CA) platform per published protocols. For each study participant, somatosensory, vestibular, and visual scores were calculated to determine the participant's ability to use these inputs to maintain balance.[30] Individual ratios <1 SD of the scores for the control group were considered abnormal.

Bruininks-Oseretsky Test of Motor Proficiency, Second Edition

The Bruininks-Oseretsky Test of Motor Proficiency, Second Edition (BOT-2) is a standardized gross and fine motor test for individuals aged 4 to 21 years. The balance subscale of BOT-2 includes 9 subtests and was used to assess balance in this study to yield a standard score, which was compared to age-appropriate published data.[37]

Statistical Analysis

The prevalence of vestibular, gaze, and balance abnormalities was determined for the entire group. Medians with ranges were calculated for nonnormal data, and *P* values were calculated by using Student's *t* test. The Mann–Whitney *U* test was used to calculate the differences in scores for each assessment between the two groups. *P* values <.05 were considered statistically significant. As outlined in the Methods section, for VOR, SVV, VOR cancellation, cVEMP, and SOT assessments, results <1 SD of the scores for the control group were coded as abnormal for the cCMV group. For cDVA and BOT-2, the data from the cCMV group were compared to age-appropriate published data.[29,30,37]

RESULTS

Demographic information for the entire cohort is summarized in Table 1. Of note, a majority of children from the cCMV group were Black compared with the controls (68% vs 6%; $P < .001$), consistent with demographics from the UAB site of the CHIMES Study and with higher prevalence of cCMV among Black infants.[1] There were no significant differences between maternal sociodemographic factors between children with cCMV in this study and the rest of the CHIMES cohort. Of the 40 children with cCMV, 17.5% (7 of 40) had SNHL; 6 of 7 (2 children each with mild, moderate-severe, and profound-degree SNHL and one with late-onset SNHL) with unilateral hearing loss and one child with bilateral SNHL. Results of vestibular, gaze, and balance tests for the entire group are summarized in Table 2, and a summary of test results in children with cCMV with SNHL is presented in Table 3.

RC Testing

Of the 37 children who underwent RC testing, 29 completed SCC function testing, of whom, 44.8% (13 of 29) were noted to have low VOR overall. None of the children tested had a complete absence of VOR. The median VOR gain for the cCMV group was lower compared with the control group (0.81 [range: 0.40–1.20] vs 1.01 [range 0.70–1.30], respectively; $P = .002$), as shown in Table 4.

Of the children who completed SVV testing and VOR cancellation, 20% (7 of 35) and 40.5% (15 of 37), respectively, scored outside the normal range. There was no significant difference between median scores for both the groups for these tests (Table 4). Nine of 13 children with an abnormal VOR overall, 6 of 7 with an abnormal SVV, and all the 15 children with an abnormal VOR cancellation result had normal hearing.

cVEMP

Of the 38 children who completed cVEMP testing, 44.7%(17 of 38) had a diminished or absent cVEMP response in at least 1 ear (5 with partial asymmetric response, 5 with unilateral absent response, 5 with weak bilateral responses, and 2 with a partial symmetric response). Among children with cCMV with an abnormal cVEMP, 14 of 17 had normal hearing, whereas 3 with SNHL had an

TABLE 1 Demographic Data

	cCMV Group (n = 40)	Control (n = 33)	P
Sex, n (%)			.37
Female	20 (50)	13 (39)	
Male	20 (50)	20 (60.3)	
Race and/or ethnicity, n (%)			<.001
Black	25 (67.5)	2 (6)	
White non-Hispanic	12 (25)	20 (60.6)	
White Hispanic	3 (7.5)	0	
Asian	0	8 (24)	
Multiracial	0	2 (6)	
SNHL, n (%)	7 (17.5)	0	.01
Unilateral	6[a]	—	
Bilateral	1	—	
Mean age, y, ± SD	7.52 ± 1.2	9.7 ± 1.6	<.001

—, not applicable.

[a] Two each with mild, moderate-severe, and profound unilateral SNHL.

abnormal cVEMP ipsilateral to the side of hearing loss.

cDVA

Of the 39 children with cCMV who completed cDVA testing, 48.7% (19 of 39) scored abnormal, including 15 of 19 with normal hearing, suggesting that these children have difficulty maintaining stable vision during head movement.

SOT

Thirty-nine children with cCMV completed SOT testing. The somatosensory, vestibular, and visual ratios were found to be abnormal in 23%, 53.8%, and 30.8%, respectively, suggesting difficulties integrating these inputs to maintain balance. The median SOT composite score was significantly lower in the cCMV group compared with the control group (Table 4). Interestingly, 6 of 7 children with SNHL had an abnormal SOT composite score.

BOT-2

Sixteen of the 38 (42%) children who completed BOT-2 testing scored below average compared to age-matched published data. Of those tested with an abnormal result, 13 of 16 children had normal hearing.

DISCUSSION

The current study highlights the frequent occurrence of vestibular disorders in children with asymptomatic cCMV on the basis of comprehensive vestibular, gaze, and balance testing. Given the anatomic and phylogenetic proximity of cochlear and vestibular organs in the inner ear and recognizing that SNHL is the most common sequela in children with cCMV, we anticipated vestibular disorders would be more prevalent in children with cCMV-associated SNHL. However, the findings of this study document vestibular disorders not only in children with cCMV-associated SNHL but also in children with normal hearing, suggesting vestibular involvement might be independent of hearing status.

In one of the earliest studies of vestibular system assessments in cCMV, Pappas[19] performed vestibular testing using hot and cold caloric tests in 11 children with asymptomatic cCMV. Six (54%) children were noted to have a complete lack of, or hypoactive, vestibular response with delayed gross motor skills. For the current study, we opted out of caloric test because it invokes vertigo and discomfort and only provides

TABLE 2 Summary of Vestibular Assessment Tests

	Test	Testing Completed, n	Abnormal Test Result		
			Total, n (%)	Normal Hearing, n	SNHL, n
SCC function	VOR (1.28 Hz)	29	13 (44.8)	9	4
Vestibulo-visual tract	SVV	35	7 (20)	6	1
	VOR cancellation	37	15 (40.5)	15	0
Saccular function	cVEMP	38	17 (44.7)	14	3
Dynamic visual acuity	cDVA	39	19 (48.7)	15	4
Tests of balance	Somatosensory (SOT)	39	9 (23)	5	4
	Vestibular (SOT)	39	21 (53.8)	16	5
	Visual (SOT)	39	12 (30.8)	10	2
	BOT-2	38	16 (42.1)	13	3

TABLE 3 Summary of Results for Children With cCMV and SNHL

Subject	Laterality and Severity of SNHL	1.28-Hz VOR	SVV	VOR Cancellation	cVEMP	cDVA	SOT Overall	BOT-2
1	Unilateral; L: mild	X	√	√	√	X	√	√
2	Unilateral; R: fluctuating mild	X	NC	√	√	√	X	√
3	L: moderate to severe; R: moderate to severe	X	X	√	NA	√	X	X
4	Unilateral; L: profound	NC	NC	NC	Partial and asymmetric; L: diminished	X	X	√
5	Unilateral; R: profound	NC	NC	NC	Bilateral weak	√	X	X
6	Unilateral; R: moderate to severe	X	√	√	Absent unilateral; R: absent	X	X	X
7	Unilateral R: moderate to severe	√	√	√	√	X	X	√

L, left ear; NA, not administered; NC, not completed; R, right ear; X, abnormal test result; √, normal test result.

information regarding horizontal SCC function at low frequencies. Instead, we performed comprehensive vestibular assessments using the RC to test horizontal SCC and utricular functions and cVEMP to test saccular function of the inner ear.

This study is one of the few in which comprehensive vestibular testing is performed by using an RC. Bernard et al[22] documented vestibular disorders and hearing loss in 92.3% of a cohort of children with cCMV in whom RC testing was performed. The lower prevalence of vestibular disorders in our study (44.8% with abnormal VOR overall and 20% with abnormal SVV on RC testing) is likely due to inclusion of children with only asymptomatic cCMV and fewer children with SNHL. Moreover, gaze and balance assessments were not performed in the study by Bernard et al,[22] and because their cohort predominantly included children with severe SNHL, the study findings are difficult to generalize. Vestibular disorders in children with and without hearing loss are documented in both studies, highlighting the need for vestibular screening in all children with cCMV.

Notably, 44.7% of children in our cohort who underwent cVEMP testing, including 14 children with normal hearing, had an abnormal response. In 2 previous studies, researchers performed cVEMP testing in asymptomatic infants with cCMV and documented normal cVEMP results (compared to 44.7% of children with abnormal cVEMP results in the current study) likely because of technical difficulties of sustaining the sternocleidomastoid muscle contraction needed for cVEMP testing when performed in younger age groups (testing performed at median ages of 3 and 6 months, respectively, in the previous studies versus 7 years in the current study).[20,23]

With our study, we are the first to evaluate and report gaze stability and balance disorders in children with asymptomatic cCMV on the basis of definitive testing (cDVA, SOT, and BOT-2), suggesting abnormal integration of sensory input. Previously, Karltorp et al[21] documented balance disturbances and motor delay in 88% of children in a cohort of children with symptomatic cCMV who underwent cochlear implantation, whereas Maes et al[23] documented no evidence of motor delays among children with asymptomatic cCMV. The variability in observed results for vestibular and balance testing across studies is likely due to differences in patient populations, severity of cCMV, severity of SNHL, and differences in methodologies used because of lack of evidence-based guidelines, as exist for hearing loss in cCMV.[13]

A major strength of this study is the inclusion of children with asymptomatic cCMV, identified prospectively by newborn screening, highlighting vestibular, gaze, and balance disorders in cCMV irrespective of severity of infection or hearing status. This is, so far, the largest cohort of children with asymptomatic cCMV assessed for vestibular, gaze, and balance disorders.

the few limitations of this study include the small sample size, the inclusion of a small number of children with SNHL in the cCMV

TABLE 4 Comparison of Vestibular and Balance Assessment Scores

	Vestibular Tests, Median (Range)				Balance, SOT Composite Score, Mean ± SD
	1.28-Hz VOR	SVV	VOR Cancellation	cVEMP	
cCMV cohort	0.81 (0.40–1.20)	5.28 (0.14–120.96)	0.25(0.06–0.73)	16.90 (0.60–78.66)	47.46 ± 9.85
cCMV without SNHL	0.89(0.58–1.18)	4.65(0.14–120.96)	0.27(0.11–0.73)	19.30(3.39–40.91)	48.33 ± 10.18
cCMV and SNHL	0.64(0.40–1.20)	8.10 (3.84–37.16)	0.22(0.06–0.34)	22.67(3.17–34.94)	42.67 ± 6.41
Control group	1.01 (0.70–1.30)	3.45(0.14–28.95)	0.25(0.13–0.53)	17.94 (1.33–72.83)	64.30 ± 11.85
P[a]	.002	.07	.79	.75	<.001

Parameters presented in this table are assessments that were compared between test and control subjects.

[a] Represents comparison between cCMV cohort and control group.

group, and the lack of children with SNHL in the control group. Despite the small sample size, however, we document high prevalence rates of vestibular, gaze, and balance disorders in this cohort, irrespective of hearing status, and highlight the need for universal vestibular, gaze, and balance assessments in children with cCMV. Another major limitation is that the full clinical impact of these findings on sports participation, school performance, and daily activities was not assessed through parent interviews and review of school records. Therefore, the findings of this study need to be validated in a larger cohort with clear definition of the clinical impact of these disorders to assess the need for development of interventions. It should also be noted that because the RC only measures VOR in response to medium-frequency head movements and thus only assesses the function of horizontal SCCs, future studies should include testing with the video head impulse test, which measures VOR in all canals in response to high-velocity head movements.[40]

CONCLUSIONS

In a cohort of children with asymptomatic cCMV identified by newborn screening, we document the frequent occurrence of vestibular, gaze, and balance disorders. Development of standardized vestibular, gaze, and balance testing protocols is necessary to enable identification of all affected children to determine the clinical impact and develop effective clinical interventions.

ABBREVIATIONS

BOT-2: Bruininks-Oseretsky Test of Motor Proficiency, Second Edition
cCMV: congenital cytomegalovirus
cDVA: clinical dynamic visual acuity
CHIMES: Cytomegalovirus & Hearing Multicenter Screening
CMV: cytomegalovirus
cVEMP: cervical vestibular evoked myogenic potential
RC: rotary chair
SCC: semicircular canal
SNHL: sensorineural hearing loss
SOT: sensory organization test
SVV: subjective visual vertical variance
UAB: The University of Alabama at Birmingham
VOR: vestibulo-ocular reflex

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REFERENCES

1. Fowler KB, Ross SA, Shimamura M, et al. Racial and ethnic differences in the prevalence of congenital cytomegalovirus infection. *J Pediatr*. 2018;200:196–201.e1
2. Morton CC, Nance WE. Newborn hearing screening–a silent revolution. *N Engl J Med*. 2006;354(20):2151–2164
3. Fowler KB, Boppana SB. Congenital cytomegalovirus (CMV) infection and hearing deficit. *J Clin Virol*. 2006;35(2):226–231
4. Townsend CL, Forsgren M, Ahlfors K, Ivarsson SA, Tookey PA, Peckham CS. Long-term outcomes of congenital cytomegalovirus infection in Sweden and the United Kingdom. *Clin Infect Dis*. 2013;56(9):1232–1239
5. Grosse SD, Ross DS, Dollard SC. Congenital cytomegalovirus (CMV) infection as a cause of permanent bilateral hearing loss: a quantitative assessment. *J Clin Virol*. 2008;41(2):57–62
6. Avettand-Fenoël V, Marlin S, Vauloup-Fellous C, et al. Congenital cytomegalovirus is the second most frequent cause of bilateral hearing loss in young French children. *J Pediatr*. 2013;162(3):593–599
7. Britt W. Cytomegalovirus. In: Remington JS, Klein JO, Wilson CB, Nizet V, Maldonaldo Y, eds. *Infectious Diseases of the Fetus and Newborn Infant*, 7th ed. Philadelphia, PA: Elsevier Saunders; 2011:706–755
8. Dollard SC, Grosse SD, Ross DS. New estimates of the prevalence of neurological and sensory sequelae and mortality associated with congenital cytomegalovirus infection. *Rev Med Virol*. 2007;17(5):355–363
9. Temple RO, Pass RF, Boll TJ. Neuropsychological functioning in patients with asymptomatic congenital cytomegalovirus infection. *J Dev Behav Pediatr*. 2000;21(6):417–422

10. Conboy TJ, Pass RF, Stagno S, et al. Intellectual development in school-aged children with asymptomatic congenital cytomegalovirus infection. *Pediatrics*. 1986;77(6):801–806

11. Capretti MG, Marsico C, Guidelli Guidi S, et al. Neonatal and long-term ophthalmological findings in infants with symptomatic and asymptomatic congenital cytomegalovirus infection. *J Clin Virol*. 2017;97:59–63

12. Lanzieri TM, Chung W, Flores M, et al.; Congenital Cytomegalovirus Longitudinal Study Group. Hearing loss in children with asymptomatic congenital cytomegalovirus infection. *Pediatrics*. 2017;139(3):e20162610

13. Rawlinson WD, Boppana SB, Fowler KB, et al. Congenital cytomegalovirus infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy. *Lancet Infect Dis*. 2017;17(6): e177–e188

14. Dahle AJ, Fowler KB, Wright JD, Boppana SB, Britt WJ, Pass RF. Longitudinal investigation of hearing disorders in children with congenital cytomegalovirus. *J Am Acad Audiol*. 2000;11(5):283–290

15. Fowler KB, McCollister FP, Dahle AJ, Boppana S, Britt WJ, Pass RF. Progressive and fluctuating sensorineural hearing loss in children with asymptomatic congenital cytomegalovirus infection. *J Pediatr*. 1997;130(4):624–630

16. Foulon I, Naessens A, Foulon W, Casteels A, Gordts F. A 10-year prospective study of sensorineural hearing loss in children with congenital cytomegalovirus infection. *J Pediatr*. 2008;153(1):84–88

17. Teissier N, Delezoide AL, Mas AE, et al. Inner ear lesions in congenital cytomegalovirus infection of human fetuses. *Acta Neuropathol*. 2011;122(6): 763–774

18. Gabrielli L, Bonasoni MP, Santini D, et al. Human fetal inner ear involvement in congenital cytomegalovirus infection. *Acta Neuropathol Commun*. 2013;1:63

19. Pappas DG. Hearing impairments and vestibular abnormalities among children with subclinical cytomegalovirus. *Ann Otol Rhinol Laryngol*. 1983;92(6, pt 1):552–557

20. Zagólski O. Vestibular-evoked myogenic potentials and caloric stimulation in infants with congenital cytomegalovirus infection. *J Laryngol Otol*. 2008;122(6): 574–579

21. Karltorp E, Löfkvist U, Lewensohn-Fuchs I, et al. Impaired balance and neurodevelopmental disabilities among children with congenital cytomegalovirus infection. *Acta Paediatr*. 2014;103(11):1165–1173

22. Bernard S, Wiener-Vacher S, Van Den Abbeele T, Teissier N. Vestibular disorders in children with congenital cytomegalovirus infection. *Pediatrics*. 2015;136(4). Available at: https://pediatrics.aappublications.org/content/136/4/e887

23. Maes L, De Kegel A, Van Waelvelde H, et al. Comparison of the motor performance and vestibular function in infants with a congenital cytomegalovirus infection or a connexin 26 mutation: a preliminary study. *Ear Hear*. 2017;38(1):e49–e56

24. Suarez H, Angeli S, Suarez A, Rosales B, Carrera X, Alonso R. Balance sensory organization in children with profound hearing loss and cochlear implants. *Int J Pediatr Otorhinolaryngol*. 2007;71(4): 629–637

25. Buchman CA, Joy J, Hodges A, Telischi FF, Balkany TJ. Vestibular effects of cochlear implantation. *Laryngoscope*. 2004;114(suppl 103):1–22

26. Cushing SL, Gordon KA, Rutka JA, James AL, Papsin BC. Vestibular end-organ dysfunction in children with sensorineural hearing loss and cochlear implants: an expanded cohort and etiologic assessment. *Otol Neurotol*. 2013;34(3):422–428

27. Tribukait A, Brantberg K, Bergenius J. Function of semicircular canals, utricles and saccules in deaf children. *Acta Otolaryngol*. 2004;124(1): 41–48

28. Inoue A, Iwasaki S, Ushio M, et al. Effect of vestibular dysfunction on the development of gross motor function in children with profound hearing loss. *Audiol Neurotol*. 2013;18(3):143–151

29. Rine RM, Braswell J. A clinical test of dynamic visual acuity for children. *Int J Pediatr Otorhinolaryngol*. 2003;67(11): 1195–1201

30. Christy JB, Payne J, Azuero A, Formby C. Reliability and diagnostic accuracy of clinical tests of vestibular function for children. *Pediatr Phys Ther*. 2014;26(2): 180–189

31. Braswell J, Rine RM. Evidence that vestibular hypofunction affects reading acuity in children. *Int J Pediatr Otorhinolaryngol*. 2006;70(11): 1957–1965

32. Rine RM, Braswell J, Fisher D, Joyce K, Kalar K, Shaffer M. Improvement of motor development and postural control following intervention in children with sensorineural hearing loss and vestibular impairment. *Int J Pediatr Otorhinolaryngol*. 2004;68(9): 1141–1148

33. Braswell J, Rine RM. Preliminary evidence of improved gaze stability following exercise in two children with vestibular hypofunction. *Int J Pediatr Otorhinolaryngol*. 2006;70(11): 1967–1973

34. Boppana SB, Ross SA, Novak Z, et al.; National Institute on Deafness and Other Communication Disorders CMV and Hearing Multicenter Screening (CHIMES) Study. Dried blood spot real-time polymerase chain reaction assays to screen newborns for congenital cytomegalovirus infection. *JAMA*. 2010; 303(14):1375–1382

35. Boppana SB, Ross SA, Shimamura M, et al.; National Institute on Deafness and Other Communication Disorders CHIMES Study. Saliva polymerase-chain-reaction assay for cytomegalovirus screening in newborns. *N Engl J Med*. 2011;364(22): 2111–2118

36. Almutairi A, Cochrane GD, Christy JB. Vestibular and oculomotor function in children with CP: descriptive study. *Int J Pediatr Otorhinolaryngol*. 2019;119: 15–21

37. Deitz JC, Kartin D, Kopp K. Review of the Bruininks-Oseretsky Test of Motor Proficiency, Second Edition (BOT-2). In: *Phys Occup Ther Pediatr*, vol. 27. 2007: 87–102

38. Fowler KB, McCollister FP, Sabo DL, et al.; CHIMES Study. A targeted approach for congenital cytomegalovirus screening within newborn hearing screening. *Pediatrics*. 2017;139(2):e20162128

39. Christy JB, Cochrane GD, Almutairi A, Busettini C, Swanson MW, Weise KK. Peripheral vestibular and balance function in athletes with and without concussion. *J Neurol Phys Ther*. 2019;43(3):153–159

40. Janky KL, Rodriguez AI. Quantitative vestibular function testing in the pediatric population. *Semin Hear*. 2018;39(3): 257–274

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