Congenital Cytomegalovirus and Hearing Loss: How Much Do Otologists and Pediatric Otolaryngologists Know?

Kavita Dedhia, MD
Jennifer Tomlinson, MS
Nancy Murry, MS
Albert Park, MD

Financial Disclosures

- No financial disclosures that played any role in obtaining, analyzing or presenting the data for this study

Introduction

- Most frequent congenital viral infection in developed countries
- Prevalence of congenital CMV(cCMV): 0.3-1.2%
  - Approximately 1 in 150 newborns
- Major public health implications
  - Most common viral cause of intellectual disability
  - Most common environmental cause of hearing loss
    - 21% at birth
    - 25% by 4 years of age

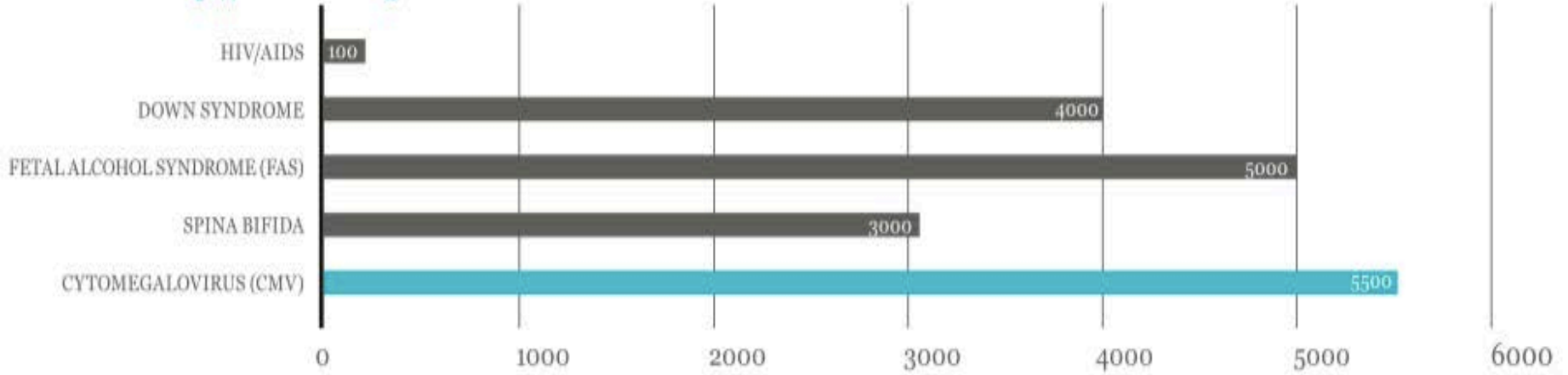
Hearing Loss Severity

- 2% of children with asymptomatic cCMV will go on to have severe-profound SNHL
- 15-35% of patients with bilateral moderate to profound SNHL due to cCMV

Awareness

US CHILDREN BORN WITH OR DEVELOPING LONG-TERM MEDICAL CONDITIONS EACH YEAR

Source: http://www.cdc.gov



WOMEN'S AWARENESS OF CONDITIONS AFFECTING CHILDREN

Source: http://www.cdc.gov

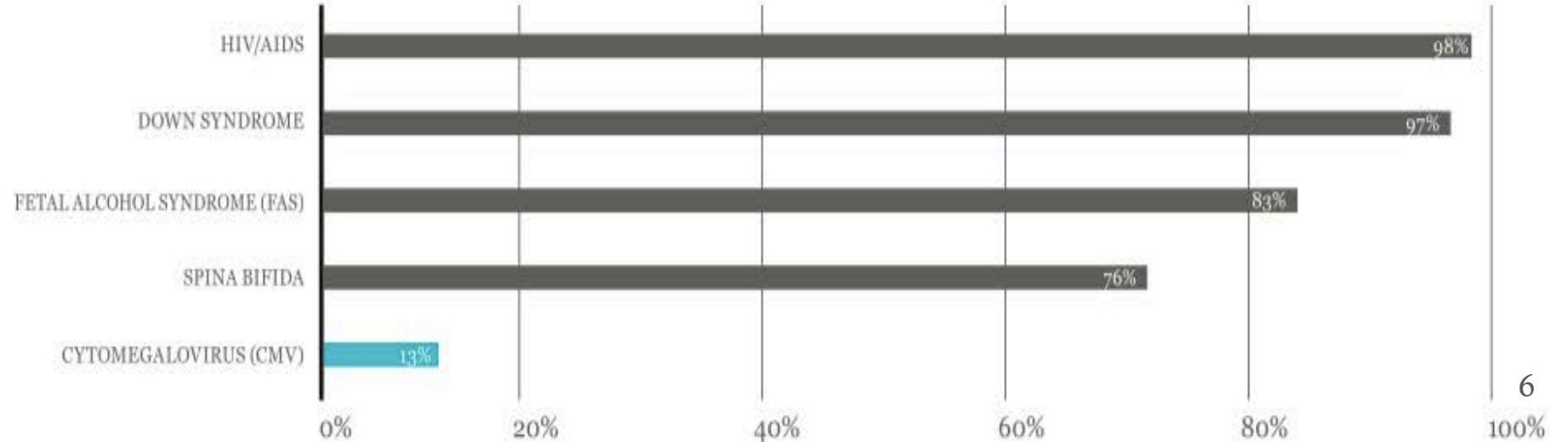


Table 1. Respondent familiarity with health conditions and illnesses (N = 207). Proportion of respondents given in parentheses. * indicates most common response.

HEALTH CONDITION	VERY FAMILIAR	SOMEWHAT FAMILIAR	NOT VERY FAMILIAR	NEVER HEARD OF THIS
Syphillis	10 (4.8)	93 (44.9)	104 (50.2)*	0
Stroke	177 (85.5)*	27 (13.0)	3 (1.4)	0
Pertussis (Whooping Cough)	36 (17.4)	109 (52.6)*	62 (30.0)	0
Cytomegalovirus (CMV)	45 (21.7)	88 (42.5)*	56 (27.1)	18 (8.7)
Down's Syndrome	156 (75.4)*	45 (21.7)	6 (2.9)	0
Tuberculosis	48 (23.2)	124 (59.9)*	35 (16.9)	0
Congenital Rubella	16 (7.7)	63 (30.4)	113 (54.6)*	15 (7.2)
Sudden Infant Death Syndrome (SIDS)	90 (43.5)	92 (44.4)*	25 (12.1)	0
Conjunctivitis (Pink Eye)	116 (56.0)*	71 (34.3)	20 (9.7)	0
Parvovirus B19 (Fifth Disease)	36 (17.4)	65 (16.9)	71 (34.3)*	35 (16.9)
Breast Cancer	103 (48.8)*	85 (41.1)	19 (9.2)	0
Group B Streptococcus	46 (22.2)	92 (44.4)*	62 (30.0)	7 (3.4)
Spina bifida	138 (66.7)*	64 (30.9)	5 (2.4)	0
Congenital Cytomegalovirus (cCMV)	43 (20.8)	63 (30.4)	70 (33.8)*	31 (15.0)
Hypertension	164 (79.2)*	38 (18.4)	5 (2.4)	0
HIV/AIDS	109 (52.7)*	87 (42.0)	11 (5.3)	0
Measles (Morbilli, Rubeola)	63 (30.4)	97 (46.9)*	47 (22.7)	0
Toxoplasmosis	21 (10.1)	84 (40.6)*	81 (39.1)	21 (10.1)
Cerebral Palsy	172 (83.1)*	33 (15.9)	2 (1.0)	0
Varicella (Chicken Pox)	121 (58.5)*	69 (33.3)	16 (7.7)	1 (0.5)

Muldoon et al.

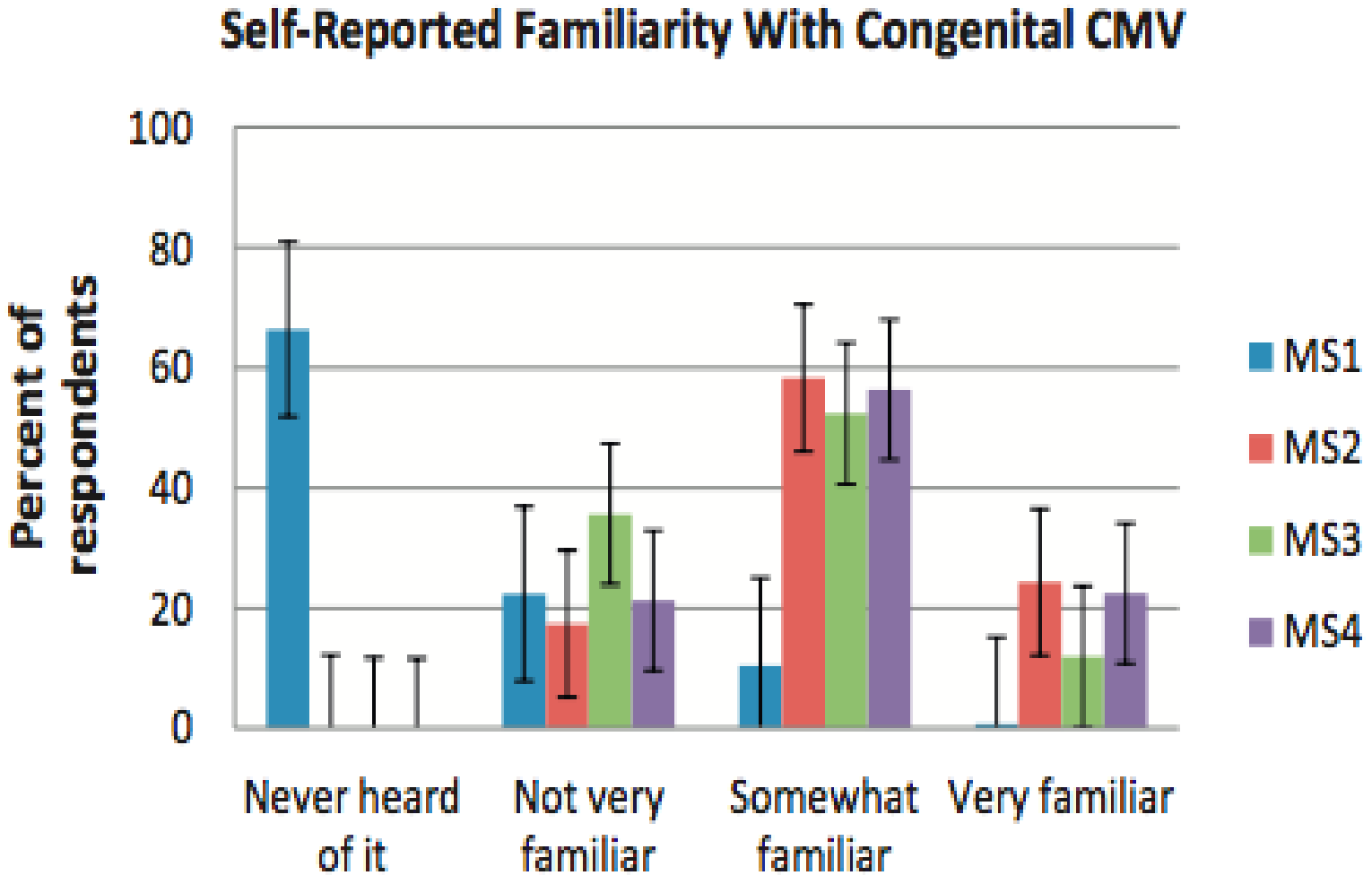


Fig. 3. Bar graph depicting self-reported knowledge and awareness of congenital CMV according to medical school year.

Table 1
Demographic variables of the respondents involved in mother and child care.

Characteristics	Number (%)	Mean transmission route score (max. possible = 7)	Mean adult symptom score (max. possible = 7)	Mean postnatal symptom score (max. possible = 12)	Mean long-term effect score (max. possible = 9)
Gender					
Male	65 (26.4)	3.2	4.9	7.4[a]	5.2
Female	181 (73.6)	3.5	4.8	7.6	5.2
Career stage					
Resident	181 (73.6)	3.3[a]	4.8	7.3[a]	5.0
Senior doctor	65 (26.4)	3.8	4.9	8.3	5.5
Parenthood					
Having children or pregnant	205 (83.3)	3.8	4.9	7.9	5.3
No plans for children	41 (16.7)	3.4	4.8	7.5	5.3
Field of expertise					
Pediatrics	85 (34.5)	4.2[a]	4.8[a]	8.9[a]	6.2[a]
Gynecology and obstetrics	18 (7.3)	3.2	4.9	8.2	5.4
Oto-rhinolaryngology	13 (5.3)	3.2	4.5	6.9	5.3
General practice	121 (49.2)	2.8	4.9	8.2	5.4
Infectious diseases (incl. medical microbiology)	9 (3.7)	5.1	5.1	8.2	5.7
Total	246	3.4	4.8	7.5	5.2

[a] $P < 0.05$.

A.M.H. Korver et al. / Journal of Clinical Virology 46S (2009) S11–S15

Awareness and Knowledge of cCMV in French Health Care Providers

Table 2
Knowledge concerning the route of transmission of CMV.

Knowledge concerning CMV transmission	Total number of respondents (n = 800) (%)	Number of medical doctors (n = 359) (%) (a)	Number of midwives (n = 409) (%) (b)	Number of laboratory physicians (n = 32) (%) (c)	p; OR (95 CI), a vs. b	p; OR (95 CI), b vs. c	p; OR (95 CI), a vs. c
Right answers							
Kissing	645 (81)	319 (89)	298 (73)	28 (88)	0,001; 2,9 (1,9–4,5)	0,06; 0,4 (0,09–1,1)	0,7; 1,1 (0,2–3,5)
Changing diapers	544 (68)	251 (70)	270 (66)	23 (72)	0,24; 1,2 (0,8–1,6)	0,49; 1,3 (0,3–2,4)	0,56; 1,3 (0,5–3,3)
Breast milk	184 (23)	93 (26)	73 (18)	18 (56)	0,006; 1,6 (1,1–2,4)	0,001; 0,1 (0,07–0,4)	0,001; 0,2 (0,1–0,6)
Blood contact	315 (39)	154 (43)	139 (34)	22 (69)	0,01; 1,4 (1–1,9)	0,001; 0,23 (0,09–0,53)	0,005; 0,3 (0,1–0,7)
Sexual intercourse	228 (28)	97 (27)	102 (25)	29 (91)	0,5; 1,1 (0,7–1,5)	0,001; 0,03 (0,006–0,1)	0,001; 0,03 (0,007–0,1)
Wrong answers							
Air	316 (39)	165 (46)	143 (35)	8 (25)	0,001; 1,5 (1,1–2,2)	0,02; 1,6 (0,6–4,2)	0,02; 2,5 (1–6,7)
Direct skin contact	125 (16)	54 (15)	69 (17)	2 (5)	0,49; 0,8 (0,5–1,3)	0,11; 3 (0,7–27)	0,2; 2,6 (0,64–23)
Combination	28 (3,5)	18 (5)	3 (0,70)	7 (22)	0,001; 7 (2–38)	0,001; 0,01 (0,003–0,09)	0,001; 0,13 (0,04–0,4)
Do not know	15 (1,9)	3 (1)	12 (3)	0 (0)	0,03; 0,3 (0,005–1)	–	–

A.G. Cordier et al. / Journal of Clinical Virology 55 (2012) 158–163

Study Objective

- Otolaryngologists commonly evaluate children with SNHL
- To evaluate the knowledge base of cCMV amongst pediatric otolaryngologists, otologists, and neurotologists

Methods

- IRB approval obtained
- Survey Contents
  - Demographics of respondents
  - Symptoms
  - Transmission
  - Prevalence and effect on hearing loss
  - Diagnosis
  - Individual practice patterns

Methods

- Survey sent through email list serve for members of the following societies
  - American Society of Pediatric Otolaryngology (ASPO)
  - American Otology Society (AOS)
  - Informed consent was signed prior to opening the survey
- Descriptive analysis was performed
- Wilcoxon rank sum test was used to compare differences between groups

Results: Demographics

- 70 total respondents, all MD
- **100% familiar with cCMV**

- **Type of specialty**
  - Pediatric 14%
  - Neurotology 17%
  - Otology 1%
  - Did not answer 69%
- **Years of practice**
  - ≤5 years 31%
  - 6-15 years: 21%
  - ≥16 years: 47%
- **Practice environment**
  - Private 17%
  - Academic 79%
  - Other 3%
- **% of Practice peds SNHL**
  - 1-25%: 83%
  - ≥ 26%: 17%

What symptoms are associated with cCMV	Number	%
Hearing loss	70	100%
Intellectual disability	65	94%
Vision loss	57	81%
Microcephaly	54	77%
Motor disabilities	52	76%
Seizures	51	73%
Death	42	61%
Hepatomegaly	46	67%
Splenomegaly	42	60%
Intrauterine growth restriction	52	79%
Petechia/Purpura	**32**	**49%**
I do not know	4	6%

- **50% knew at least 90% of symptoms**
- **74% knew at least 50% of symptoms**

Which of the following are routes of transmission for CMV? (Pick all that apply)	Number	%
Kissing	42	61%
Changing diapers	32	46%
Breast milk	37	53%
Blood transfusion	43	61%
Sexual Intercourse	36	51%
Sharing food with children	33	47%
I do not know	**20**	**29%**

- **41% more than 80% correct**
- **56% more than 50% correct**
- **20% with 0 correct**

Which of the following statement(s) regarding cCMV is/are true? (pick all that apply)	Number	%
True		
Up to 15% of children with asymptomatic cCMV can develop hearing loss	27	39%
Up to 75% children with symptomatic cCMV will develop hearing loss	21	30%
cCMV is the most common environmental cause of hearing loss	33	47%
False		
Up to 30 % of children with asymptomatic cCMV can develop hearing loss	24	34%
Up to 95% of children with symptomatic cCMV will develop hearing loss	5	7%
I do not know	14	20%

- 23% had at least 75% correct answers
- 54% at least 50% correct

What test(s) can be performed to diagnose cCMV status? (Pick all that apply)	Number	%
True		
Dried blood spot CMV PCR at any age	23	33%
Dried blood spot (DBS) prior to 3 weeks of age	28	41%
Urine PCR/culture prior to 3 weeks of age	44	63%
Saliva CMV Culture with confirmation with Urine PCR/Culture prior to 3 weeks of age	44	63%
False		
Serologic CMV IgG testing at any age	11	16%
Urine PCR/culture at any age	10	14%
Saliva CMV Culture at any age	6	9%
Serologic IgM testing at any age	7	10%
I do not know	**14**	**20%**

Which test(s) can definitively establish a diagnosis for cCMV in children >3 weeks of age?	Number	%
True		
Dried blood spot testing	25	36%
False		
Serology for IgM and IgG for CMV	27	39%
Imaging studies including CT and MRI	9	13%
Urine PCR/culture for CMV	16	23%
Saliva culture for CMV	8	11%
I do not know	20	29%

Practice Patterns	Number	%
Do you incorporate any type of cCMV testing for children with SNHL?		
Always	8	11%
Sometimes	22	31%
Rarely	20	29%
Never	20	29%
Do you offer DBS CMV PCR testing for your patients?		
Yes	16	23%
No	52	76%
Do you offer antiviral therapy or refer to infectious disease specialist for antiviral therapy for cCMV infected children?		
Yes, only if they are symptomatic	15	21%
Yes, for symptomatic children and asymptomatic children that fail the hearing screen	28	40%
No	12	17%
I don't know	15	21%

	N	Median Symptom Score (%)	Median CMV Effect on HL Score (%)	Median Diagnosis Score (%)	Median Transmission Score
% of Practice Pediatric SNHL					
1-25%	58	**73**	**25**	**50**	50
>26%	12	**100**	**75**	**67**	91.5
p-value*		**0.006**	**<0.0001**	**0.009**	0.052
Years of Experience					
0 to 15	37	91	50	67	50
>=16	33	73	50	50	50
p-value*		0.42	0.72	0.43	0.53
Type of Practice					
Private	13	55	25	50	33
Academic	55	91	50	50	50
p-value*		0.058	0.36	0.19	0.10

Limitations

- Small sample size
- Only sent to a group of otolaryngologist more familiar with pediatric hearing loss
  - Results could be inflated
- Cannot differentiate between correct response and guessing
- Did not specifically address knowledge of treatment

Discussion

- Our study highlights the significant knowledge gap amongst pediatric otolaryngologists, otologists and neurotologists regarding cCMV
- As expected, providers whose practice encompassed >25% pediatric SNHL were more knowledgeable about cCMV than their counterparts

Discussion

- Most providers do not incorporate cCMV testing into their diagnostic algorithms
- Although treatment of patients with symptomatic cCMV is standard of care, 38% either did not know or would not send them for treatment

Conclusion

- This survey suggests a meager understanding and insufficient implementation of cCMV testing by physicians who are expected to be the most competent to treat pediatric HL

Conclusions

- Due to the time sensitivity of definitive diagnosis, we feel strongly that all otolaryngologists who may encounter a child with SNHL be well-versed in diagnosis and management of cCMV
- We recommend increasing awareness on this topic through greater education/awareness in residency programs, as well as continuing medical education

Congenital Cytomegalovirus and Hearing Loss: How Much Do Otologists and Pediatric Otolaryngologists Know?

Albert Park, MD

Chief Pediatric Otolaryngology

University of Utah

ValEAR Trial
a CMV Study

HEALTH
UNIVERSITY OF UTAH

Disclosures:

- NIH U01 PI CMV multi-institutional study (Park)
- NIDCD R01 co-I Cochlear Implantation (Park)
- Valganciclovir – not FDA approved for congenital CMV

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Urine PCR/culture at any age	10	14%
Saliva CMV Culture at any age	6	9%
Serologic IgM testing at any age	7	10%
I do not know	14	20%

CMV Diagnosis:

- Best if testing when child less than 2-3 weeks of age
- Postnatal infection not associated with hearing loss
- Urine culture or PCR. Saliva- breastmilk contamination
- DBS testing offers diagnosis older child but poor sensitivity

Saliva vs Urine for CMV Screening:

- Two large studies indicate high false positive rate with saliva PCR testing
- Saliva obtained immediately after birth
- 26-41% false positive
- Associated with lower viral load BUT low viral load seen in both true positive and false positive samples
- **If you obtain a positive saliva PCR result, you should obtain a confirmatory urine PCR before the child is 3 weeks of age**
- **Consider just ordering a urine CMV PCR**

Puhakka et al. JPIDS 2018; Leruez-Ville et al. Clin Infect Dis 2017

What is the Sensitivity of DBS Testing?

- CHIMES March 2007-2008
- 7 US Medical Centers
- Compared saliva rapid culture to DBS CMV PCR (single and double primer)
- 92/20,448 infants CMV based on saliva cx
- Sensitivity DBS:
- Single primer- 28.3%
- Double primer- 34.4%
- **Should have compared to urine culture or PCR testing?**
- **Schleiss and Dollard CDC study on DBS**

Boppana S et al. JAMA 2010; 303(14): 1375-1382.

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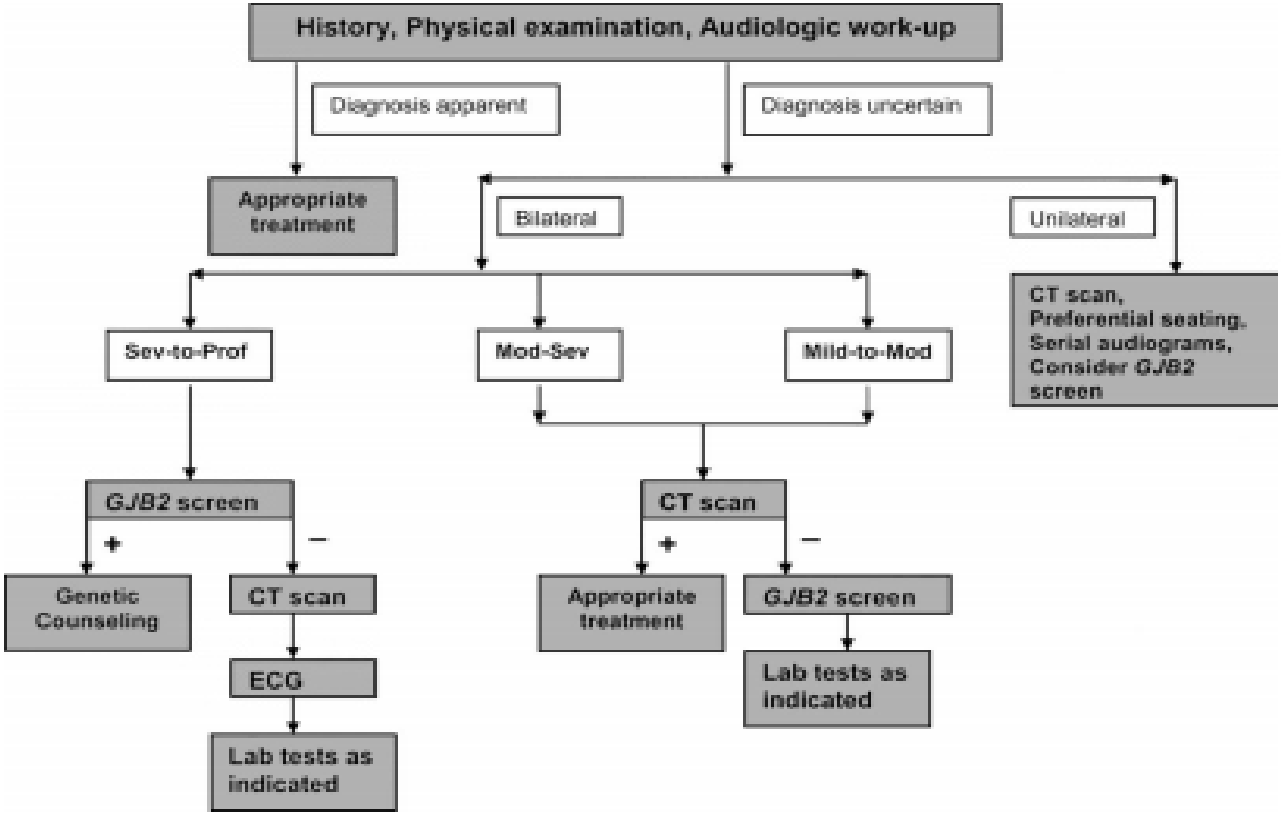
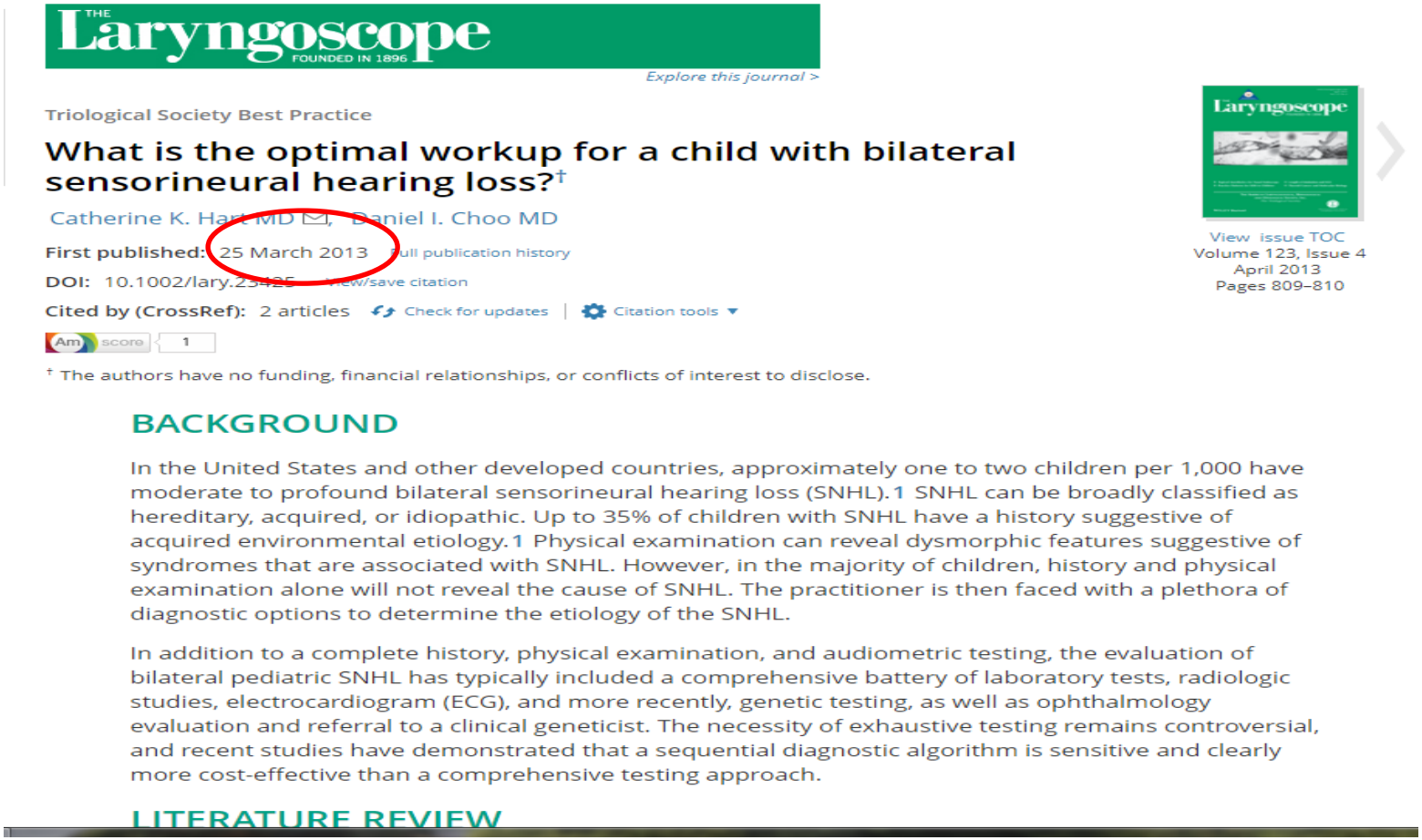
Role of CMV Testing in Pediatric Hearing Loss:



Preciado DA et al. Improved Diagnostic Effectiveness with a Sequential Diagnostic Paradigm in Idiopathic Pediatric Sensorineural Hearing Loss. Otol and Neurotology 2005

Role of CMV Testing in Pediatric Hearing Loss:



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Triological Society Best Practice

What is the optimal workup for a child with bilateral sensorineural hearing loss?†

Catherine K. Hart MD ✉, Daniel I. Choo MD

First published: 25 March 2013 Full publication history
DOI: 10.1002/lary.23425 View/save citation
Cited by (CrossRef): 2 articles Check for updates | Citation tools
Am score 1

† The authors have no funding, financial relationships, or conflicts of interest to disclose.

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BACKGROUND

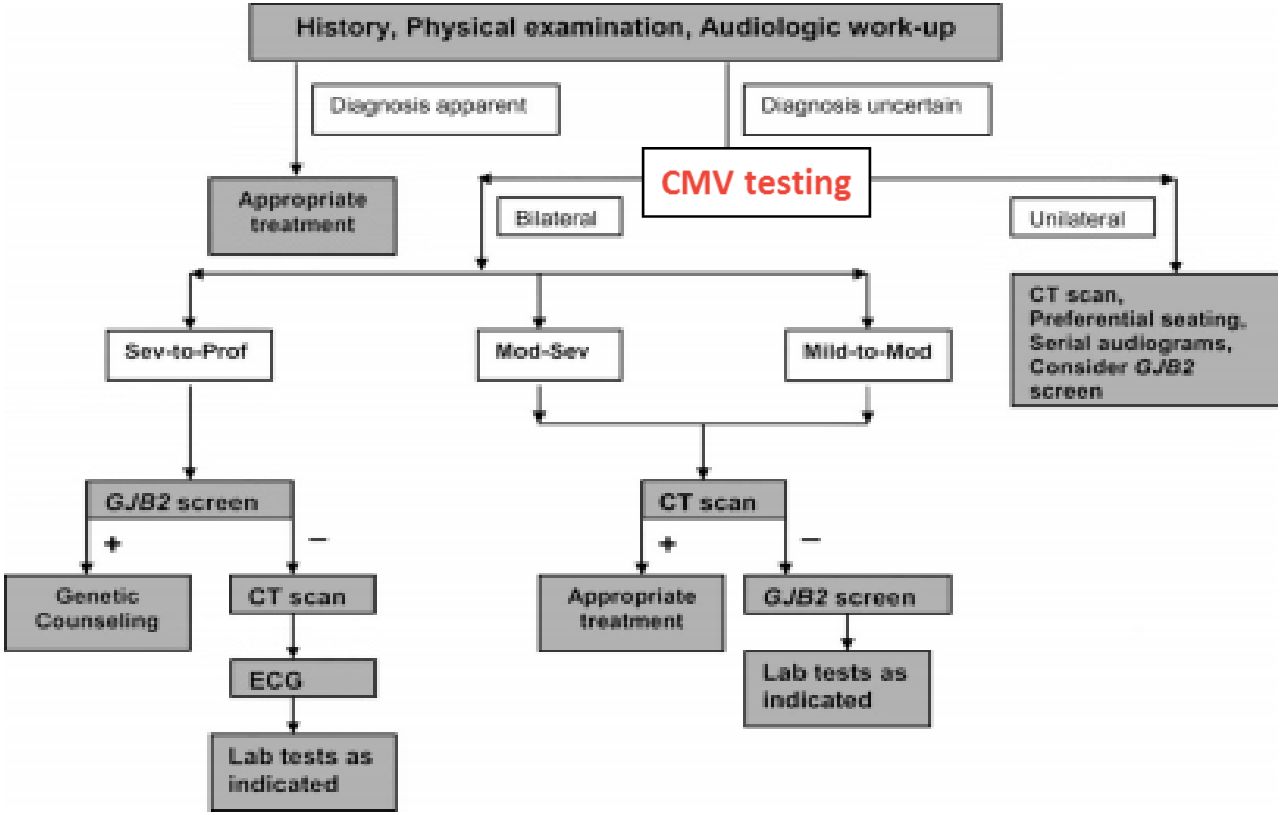
In the United States and other developed countries, approximately one to two children per 1,000 have moderate to profound bilateral sensorineural hearing loss (SNHL).1 SNHL can be broadly classified as hereditary, acquired, or idiopathic. Up to 35% of children with SNHL have a history suggestive of acquired environmental etiology.1 Physical examination can reveal dysmorphic features suggestive of syndromes that are associated with SNHL. However, in the majority of children, history and physical examination alone will not reveal the cause of SNHL. The practitioner is then faced with a plethora of diagnostic options to determine the etiology of the SNHL.

In addition to a complete history, physical examination, and audiometric testing, the evaluation of bilateral pediatric SNHL has typically included a comprehensive battery of laboratory tests, radiologic studies, electrocardiogram (ECG), and more recently, genetic testing, as well as ophthalmology evaluation and referral to a clinical geneticist. The necessity of exhaustive testing remains controversial, and recent studies have demonstrated that a sequential diagnostic algorithm is sensitive and clearly more cost-effective than a comprehensive testing approach.

LITERATURE REVIEW

Hart C and Choo D. Laryngoscope. 2013

Role of CMV Testing in Pediatric Hearing Loss:



Park et al. A Diagnostic Paradigm Including Cytomegalovirus Testing for Idiopathic Pediatric Sensorineural Hearing Loss. Laryngoscope. 2014

The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

- Chart and database review
- Children 3 yrs or younger
- May 2008-September 2013
- Sequential diagnostic paradigm

Park et al. A Diagnostic Paradigm Including Cytomegalovirus Testing for Idiopathic Pediatric Sensorineural Hearing Loss. Laryngoscope. 2014

The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

- **Confirmed Diagnosis-** positive urine or saliva CMV PCR infant < 3 weeks OR positive result infant > 3 weeks AND positive DBS

- **Probable Diagnosis-** - positive urine or saliva > 3 weeks of age AND CNS findings or progressive SNHL

Park et al. A Diagnostic Paradigm Including Cytomegalovirus Testing for Idiopathic Pediatric Sensorineural Hearing Loss. Laryngoscope. 2014

The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

- Those with negative CMV testing underwent imaging, genetics evaluation +/- EKG
- Cost analysis of the diagnostic testing (Multihospital Standardized Cost Accounting System):

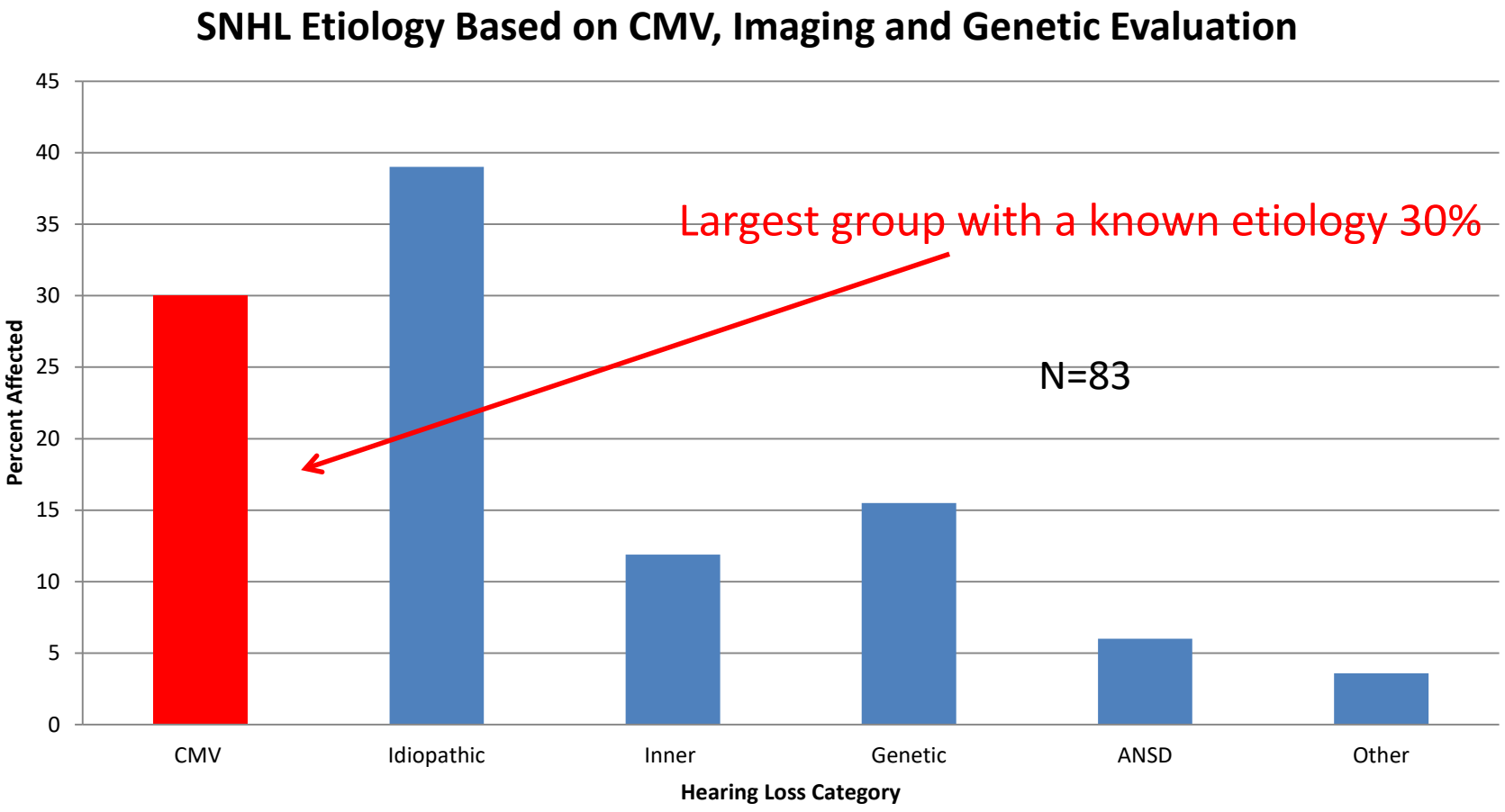
  MRI t-bone $1591

  GJB2 testing $611

  CMV PCR saliva or urine $66

Park et al. A Diagnostic Paradigm Including Cytomegalovirus Testing for Idiopathic Pediatric Sensorineural Hearing Loss. Laryngoscope. 2014

The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss



Park et al. A Diagnostic Paradigm Including Cytomegalovirus Testing for Idiopathic Pediatric Sensorineural Hearing Loss. Laryngoscope. 2014

The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

- Breakdown of CMV Patients (n=25)
- Sixteen – confirmed CMV diagnosis
- Six of sixteen diagnosed via DBS testing
- Nine- probable CMV diagnosis

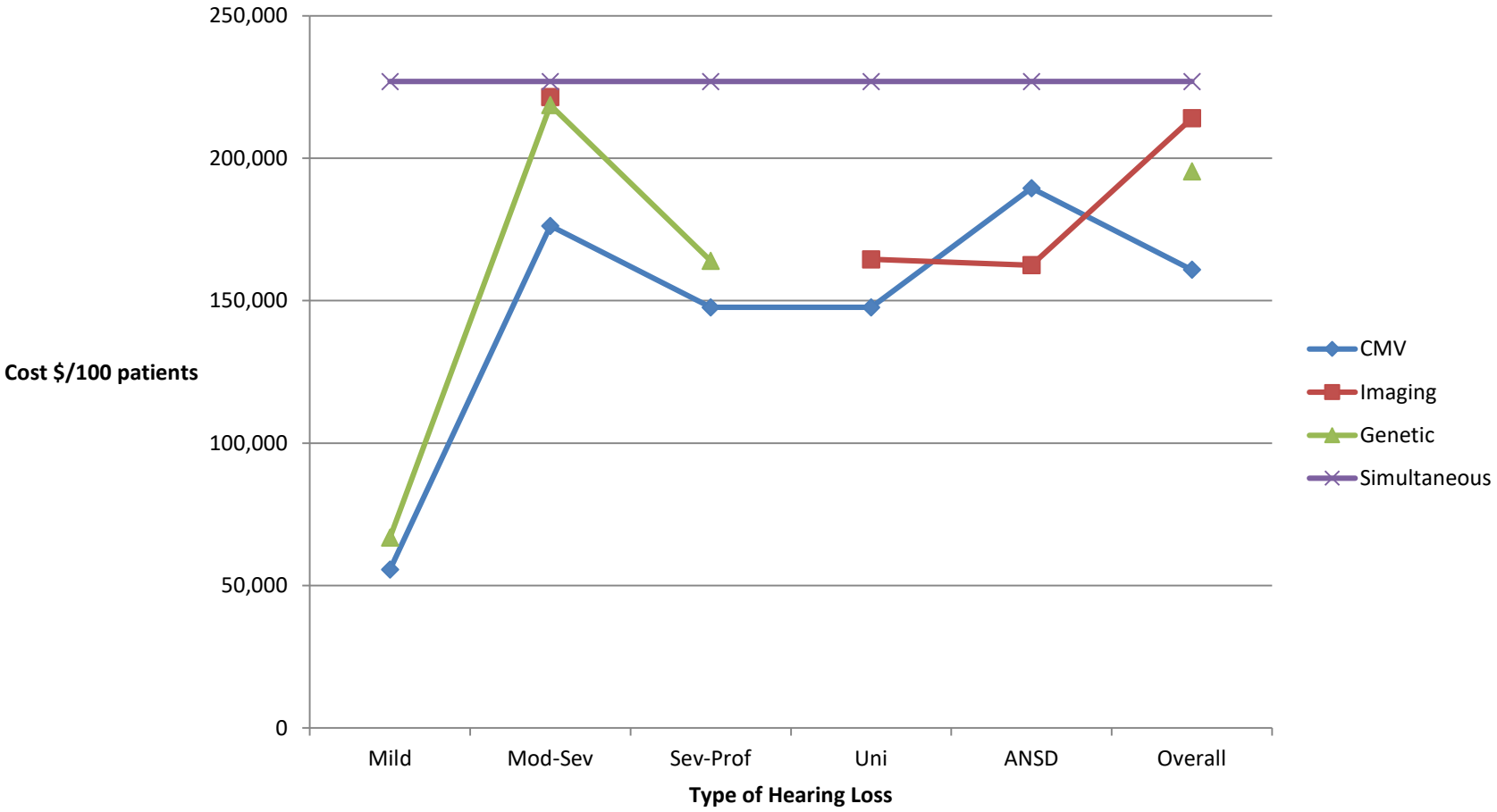
Park et al. A Diagnostic Paradigm Including Cytomegalovirus Testing for Idiopathic Pediatric Sensorineural Hearing Loss. Laryngoscope. 2014

The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

- <u>Characteristics of CMV Induced SNHL Patients:</u>
- Average age initial evaluation 352 days (range 24-1387 days)!
- Only 5 infants evaluated at one month of age or younger

Park et al. A Diagnostic Paradigm Including Cytomegalovirus Testing for Idiopathic Pediatric Sensorineural Hearing Loss. Laryngoscope. 2014

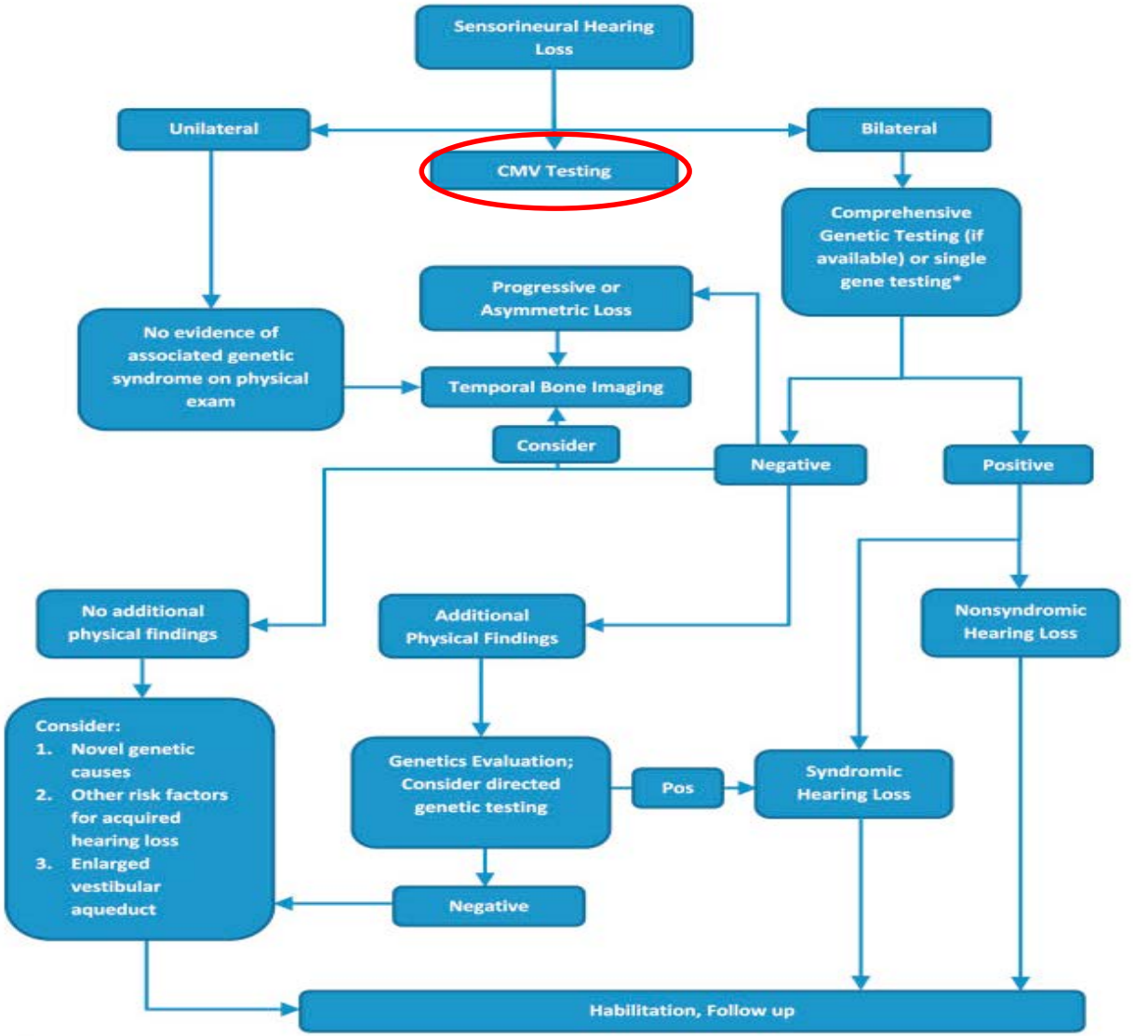
Cost Estimates Using Different Approaches for SNHL Evaluation:



Park et al. A Diagnostic Paradigm Including Cytomegalovirus Testing for Idiopathic Pediatric Sensorineural Hearing Loss. Laryngoscope. 2014

The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

- Conclusion:
- Diagnostic Paradigm incorporating early CMV testing has high yield (30%)
- DBS testing can diagnose infants > 3 weeks of age
- Average age of initial evaluation significant challenge for diagnosis
- Early CMV testing – lower cost than imaging or genetic testing



Liming BJ et al. Int. Ped. Otolaryngology Group. Int J Peds Oto 2016

Practice Patterns	Number	%
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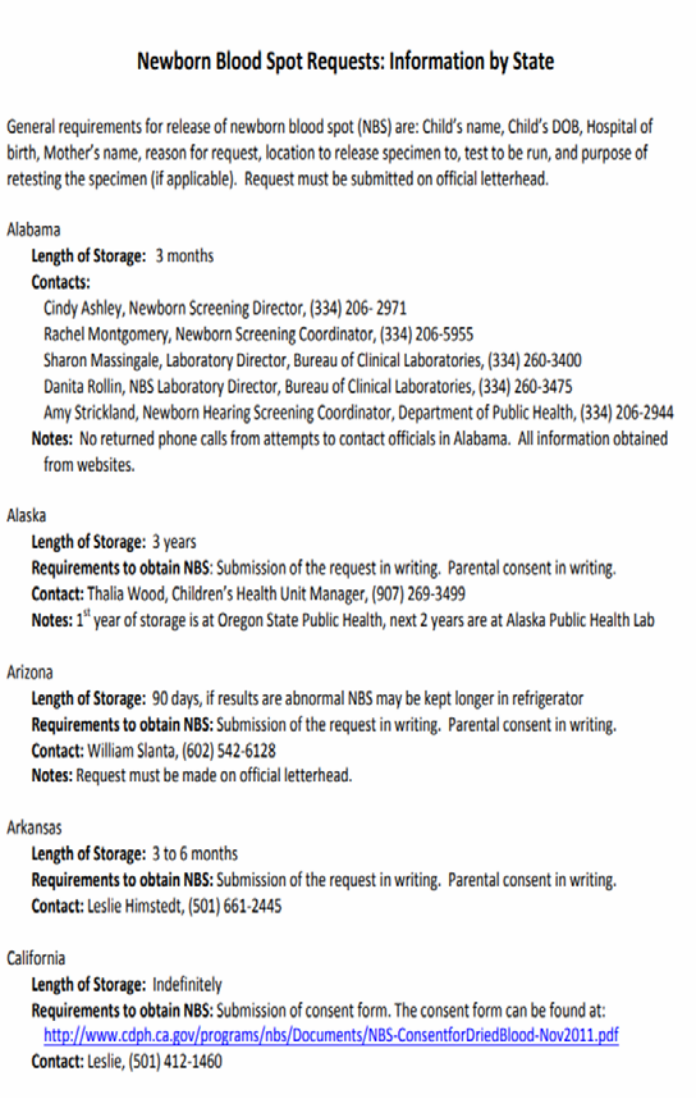
DBS Testing:

- DBS testing available every state in US
- Listing of contact
- Time sensitive
- At least 2 CLIA validated labs that can run DBS CMV PCR (Schleiss and ARUP)
- http://ltd.aruplab.com/Tests/Pub/0060040



Newborn Blood Spot Requests: Information by State

General requirements for release of newborn blood spot (NBS) are: Child's name, Child's DOB, Hospital of birth, Mother's name, reason for request, location to release specimen to, test to be run, and purpose of retesting the specimen (if applicable). Request must be submitted on official letterhead.

Alabama

Length of Storage: 3 months

Contacts:

Cindy Ashley, Newborn Screening Director, (334) 206- 2971
Rachel Montgomery, Newborn Screening Coordinator, (334) 206-5955
Sharon Massingale, Laboratory Director, Bureau of Clinical Laboratories, (334) 260-3400
Danita Rollin, NBS Laboratory Director, Bureau of Clinical Laboratories, (334) 260-3475
Amy Strickland, Newborn Hearing Screening Coordinator, Department of Public Health, (334) 206-2944

Notes: No returned phone calls from attempts to contact officials in Alabama. All information obtained from websites.

Alaska

Length of Storage: 3 years
Requirements to obtain NBS: Submission of the request in writing. Parental consent in writing.
Contact: Thalia Wood, Children's Health Unit Manager, (907) 269-3499
Notes: 1st year of storage is at Oregon State Public Health, next 2 years are at Alaska Public Health Lab

Arizona

Length of Storage: 90 days, if results are abnormal NBS may be kept longer in refrigerator
Requirements to obtain NBS: Submission of the request in writing. Parental consent in writing.
Contact: William Slanta, (602) 542-6128
Notes: Request must be made on official letterhead.

Arkansas

Length of Storage: 3 to 6 months
Requirements to obtain NBS: Submission of the request in writing. Parental consent in writing.
Contact: Leslie Himstedt, (501) 661-2445

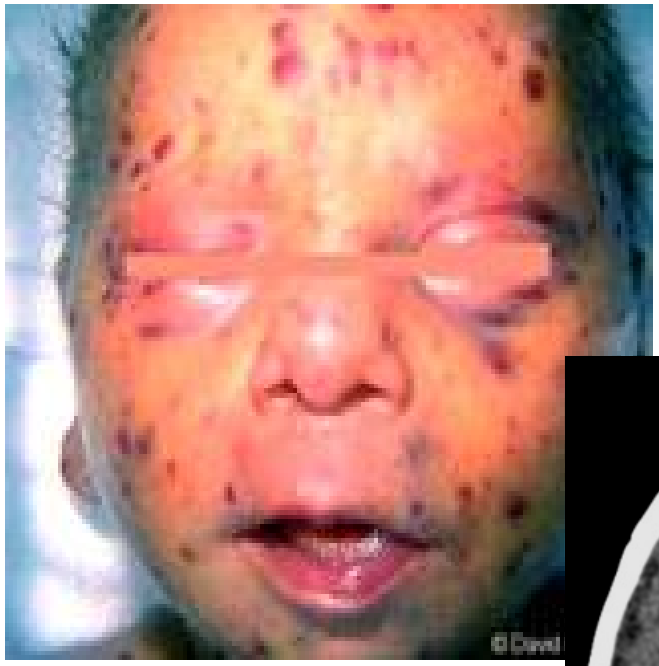
California

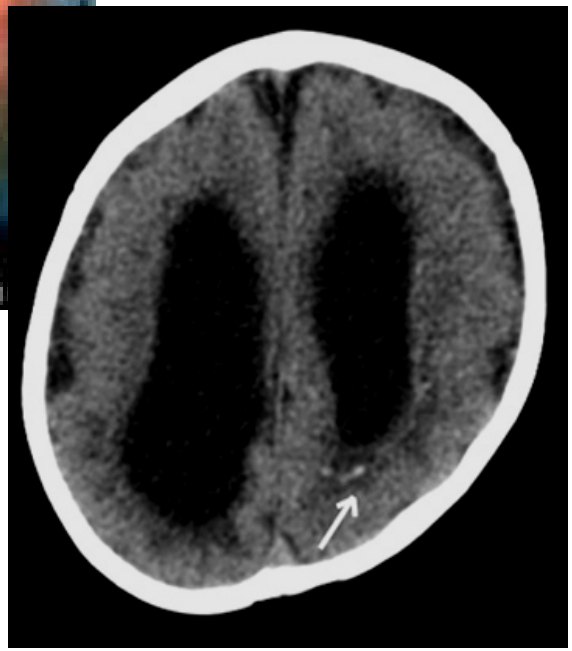
Length of Storage: Indefinitely
Requirements to obtain NBS: Submission of consent form. The consent form can be found at: http://www.cdph.ca.gov/programs/nbs/Documents/NBS-ConsentforDriedBlood-Nov2011.pdf
Contact: Leslie, (501) 412-1460

Practice Patterns	Number	%
Do you incorporate any type of cCMV testing for children with SNHL?		
Always	8	11%
Sometimes	22	31%
Rarely	20	29%
Never	20	29%
Do you offer DBS CMV PCR testing for your patients?		
Yes	16	23%
No	52	76%
Do you offer antiviral therapy or refer to infectious disease specialist for antiviral therapy for cCMV infected children?		
Yes, only if they are symptomatic	15	21%
Yes, for symptomatic children and asymptomatic children that fail the hearing screen	28	40%
No	12	17%
I don't know	15	21%

Symptomatic Congenital CMVInfection (sCMV)

- Approximately 10%
- Fetal demise
- Prematurity
- Common features:
  - Hepatomegaly
  - Splenomegaly
  - Petechiae
  - IUGR
  - Jaundice
  - Microcephaly
  - Chorioretinitis
  - Sensorineural hearing loss (50%)



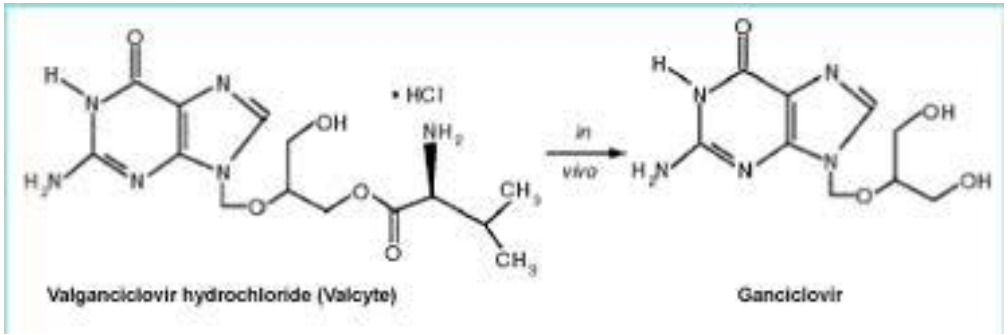


Treating the Symptomatic cCMV Infected Infant:

- Symptomatic CMV is treatable!
- General consensus that this group would benefit from antiviral therapy (valganciclovir or VGCV)

Valganciclovir (VGCV):

- L-valyl ester prodrug of ganciclovir
- Blocks viral replication
- After oral administration, it is rapidly converted to ganciclovir by intestinal and hepatic esterases
- FDA approved to prevent CMV disease for pediatric patients receiving heart or kidney transplants
- Not FDA approved for treatment of cCMV

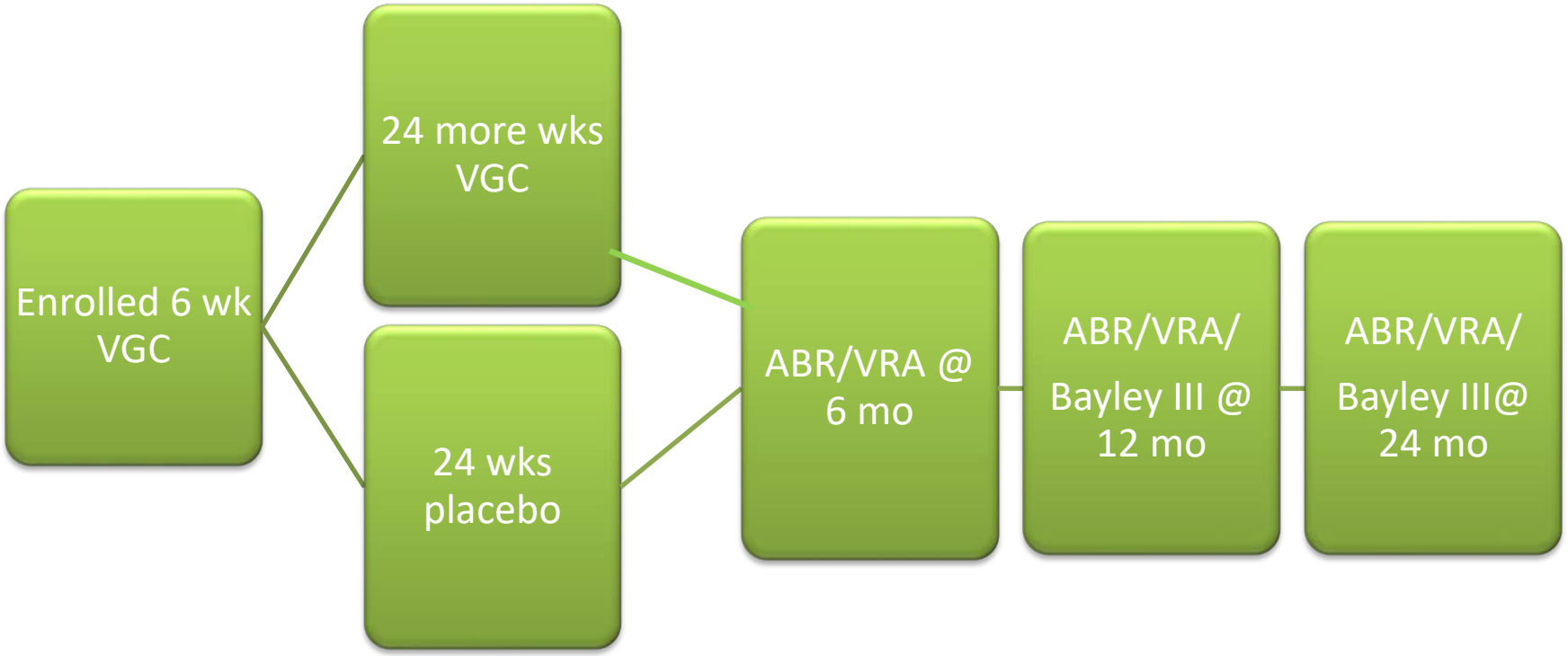


Six Months versus 6 weeks Valganciclovir (VGC) for infants with Symptomatic CMV

- Confirmation CMV from urine or throat swab-culture, shell vial or PCR
- Symptomatic CMV (1 or more): thrombocytopenia, petechiae, HSM, IUGR, hepatitis, CNS involvement (hearing loss, radiographic, CMV in CSF)
- <30 days

Kimberlin D et al. NEJM 2015

Six Months versus 6 weeks Valganciclovir (VGC) for infants with Symptomatic CMV

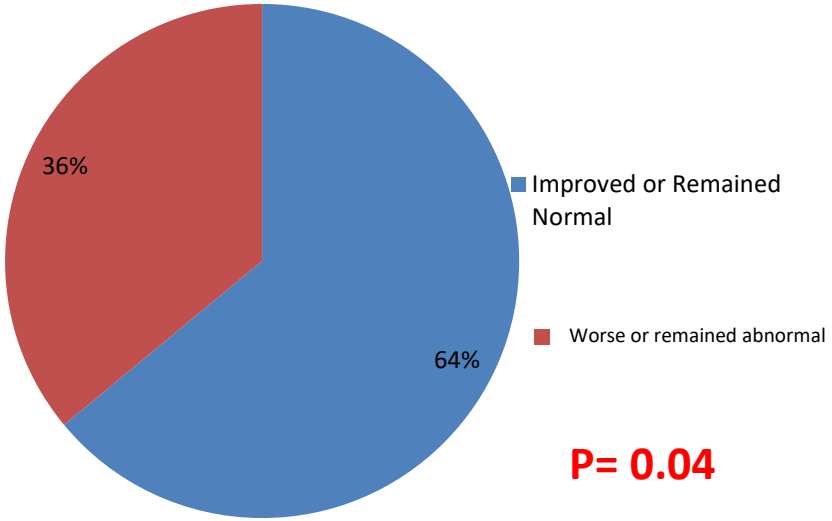


Results:

- Primary outcome- best ear hearing at 6 months – NS
- Secondary- Total ear hearing (hearing in one or both ears that could be evaluated) was more likely to be improved or to remain normal at 12 months in the 6-month group (73% vs. 57%, P = 0.01).

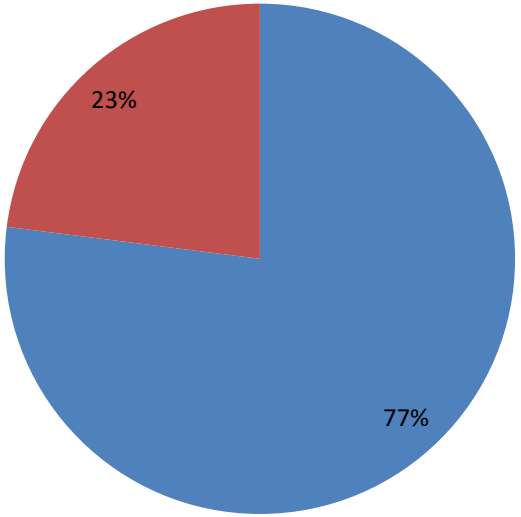
6 Weeks vs. 6 Months Valganciclovir Hearing Outcomes @ Two year Followup

6 Weeks of Treatment



P= 0.04

6 Months of Treatment



Kimberlin et al. NEJM 2015

6 Weeks vs. 6 Months Valganciclovir Bayley III Outcomes 24 mo.

	6 Week Therapy	6 Month Therapy	Adjusted P-value
Cognitive Composite	76.0±2.6	84.4±2.6	0.0236
Language Composite	72.5±2.9	84.6±2.9	**0.0037**
Receptive Communication Scale	5.2±0.5	7.3±0.5	**0.0027**
Expressive Communication Scale	5.5±0.5	7.3±0.5	0.0158
Motor Composite	74.1±3.2	85.5±3.3	0.0130
Fine Motor Scale	6.4±0.6	8.0±0.6	0.0566
Gross Motor Scale	5.3±0.5	7.0±0.5	0.0198

P-values < 0.0071 (=0.05/7) considered statistically significant using Bonferroni adjustment for multiple testing

Safety Measures:

- Grade 3 or 4 neutropenia 19% of the participants during the first 6 weeks.
- During the next 4.5 months of the study, grade 3 or 4 neutropenia -21% (6 month) vs 27% of (6-week: P = 0.64)
- 3 temporary suspension drug b/c ANC< 500
- All resumed and occurred first 6 weeks

Role of VGCV in sCMV patients:

"Based upon this study, it can be concluded that a 6-month course of oral VGCV is a well-tolerated and effective therapeutic option for infants with symptomatic congenital CMV infection."

James and Kimberlin. Curr Opinion Ped 2016

Where to go from here?

- Ongoing national survey for audiology and speech and language pathology
- ValEAR study- 30+ sites starting HT-CMV screening
- National survey of sites in ValEAR to elicit their feedback on implementing HT-CMV screening
- Certlink – General Otolaryngology segment will include CMV questions. Online alternative to the maintenance of certification for Otolaryngology
- Target national Otolaryngology and specialty meetings
- Repeat this survey in 5 years