

# Cochlear Implants in Children with Congenital CMV and/or Unilateral Hearing Loss

Stephanie Moody Antonio, MD, FACS

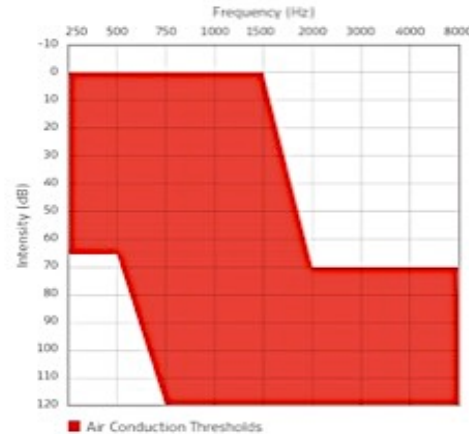
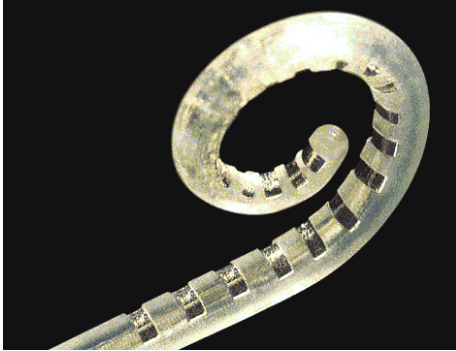
Professor

Eastern Virginia Medical School

Director, EVMS/CHKD Cochlear Implant Program

# Outline

- Introduction to CI and outcomes
- Update on CMV-related HL and treatment
- CI for single-sided deafness, a new treatment option for children
- Q&A



## Cochlear Implant

- Age 9 months and older
  - Unilateral or bilateral (sequential or simultaneous)
  - Severe to profound high frequency SNHL
  - Poor discrimination with hearing aids
  - Speech and language delay
- Stimulates the hearing nerve
- Outcomes are variable but most often shows improvement in sound awareness, speech discrimination and auditory/oral language development
- Earlier implantation provides better outcomes



## Cochlear Implant Surgery

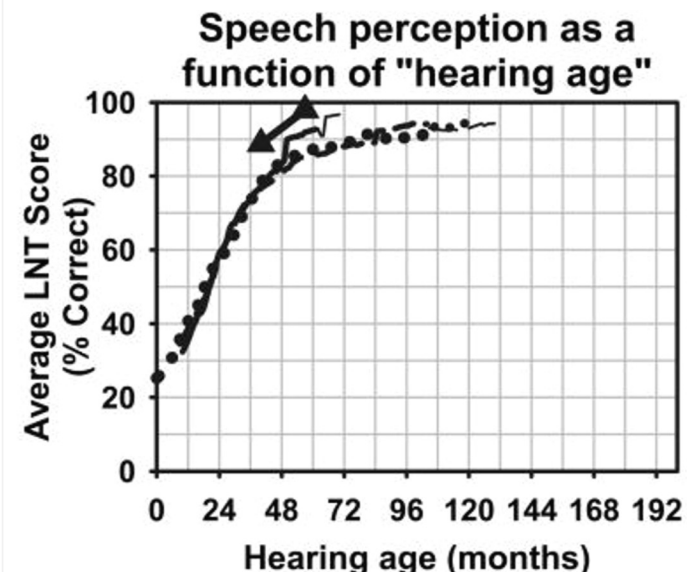
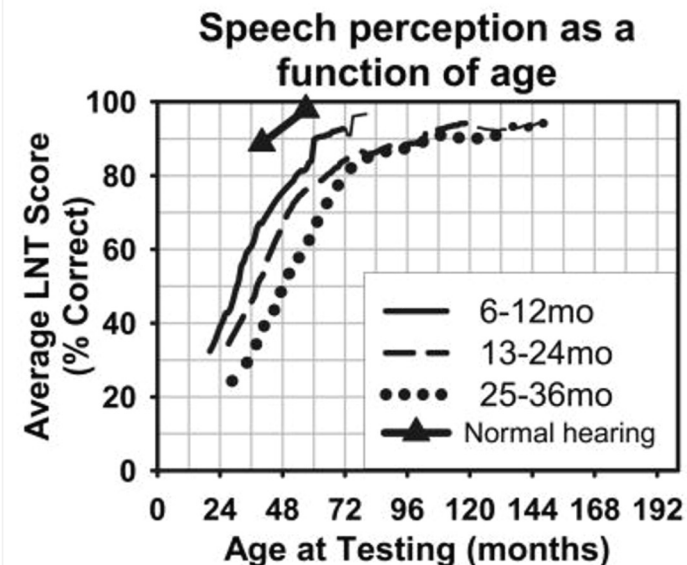
- A routine outpatient procedure
- Performed under general anesthesia
- 2-3 hours surgical time
- Requires minimal or no hair shaving
- Involves a small hidden incision
- Minimal post-operative pain
- Major complications are rare

# Advantages of early implantation

- Better auditory performance
  - Reach age appropriate norms for CAP and ITMAIS within 3 months (Colletti 2005, Holman 2013)
- Significantly better speech perception (Dunn 2014, Leigh 2013, Colletti 2009, Tajudeen 2010)
- Significantly better speech production (Leigh 2013, Schauwers 2004, Colletti 2005, Colletti 2009)
- Better vocabulary and receptive language
  - PPVT score significantly better and within the normal range for hearing peers by 3 years (Colletti 2009, Leigh 2013, Houston 2010, Miyamoto 2017)
  - Vocabulary and grammar development 10 years post-CI is closest in language age to normal hearing children (Coletti 2021)
  - 92% if implanted <12 months (Chweya 2021)

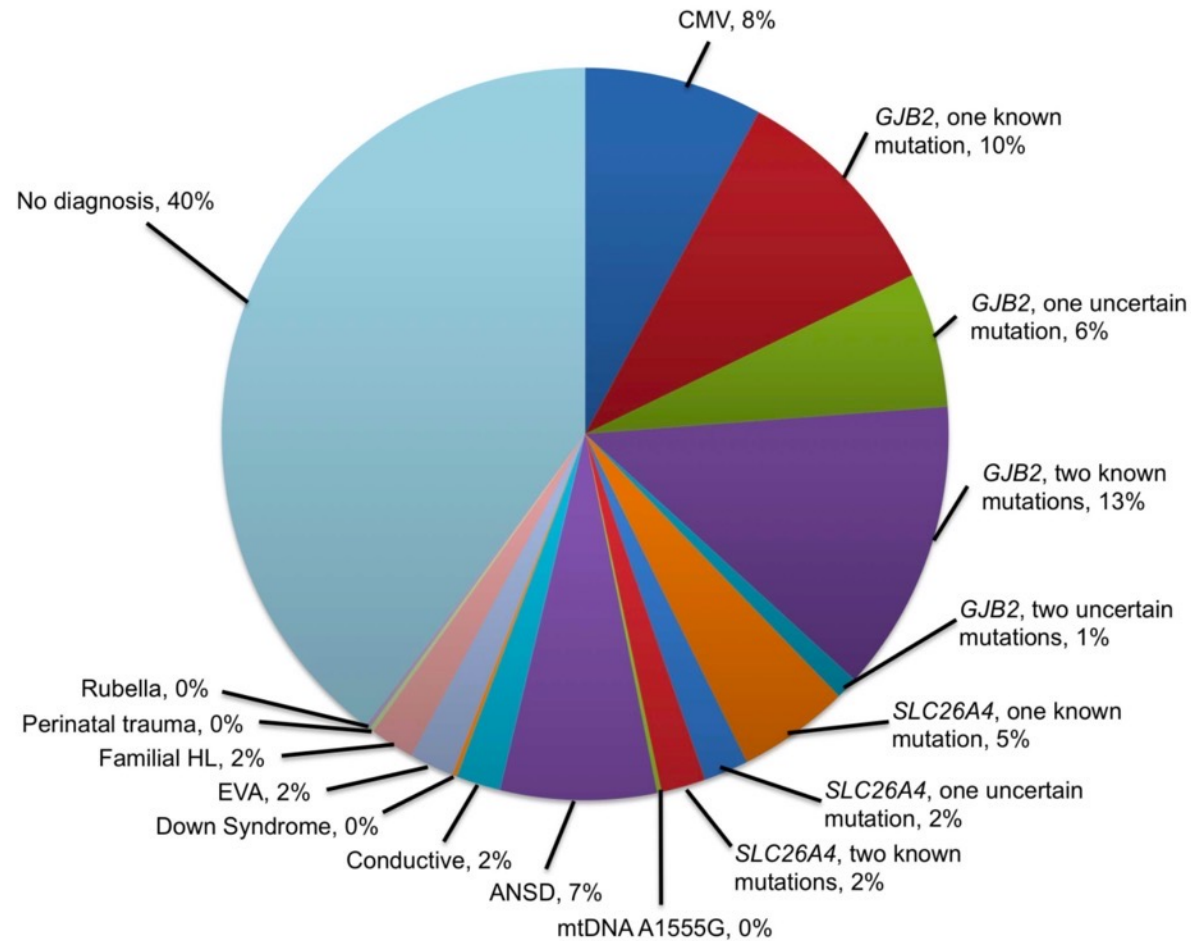
## Speech perception in congenitally deaf children receiving cochlear implants in the first year of life. BA Tajudeen, et al

- 117 subjects (35 implanted < 12 months) compared by age implanted
- Individually, most children in each group reached scores of 85% correct or higher by four years after implantation
- Children implanted earlier significantly outperformed children implanted later at ages 3, 4, 5, and 6
- Developmental Trajectory Curve: 9% advantage for those implanted in year 1 vs. year 2 (statistically significant)
- Ceiling effect by age 4-5 years



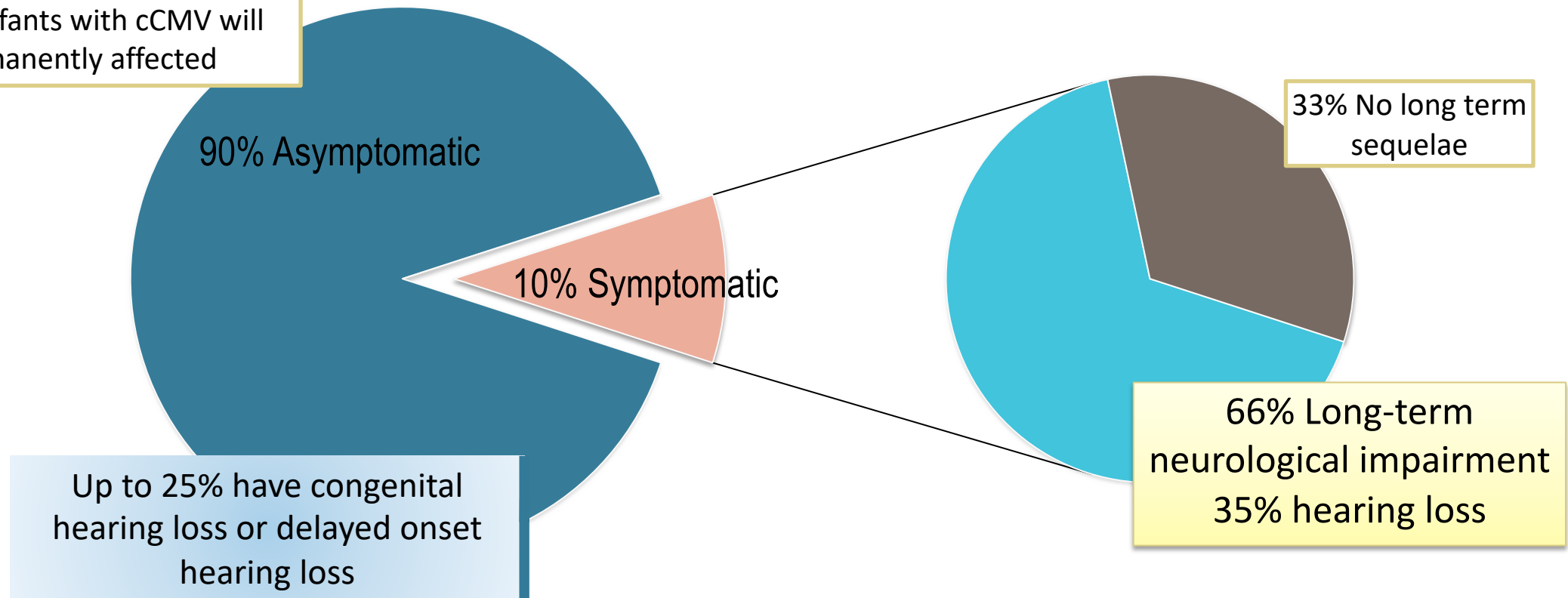
# TREATMENT OF CMV RELATED HEARING LOSS

## Etiology of childhood hearing loss



## Sequela of cCMV

1 in 5 infants with cCMV will be permanently affected



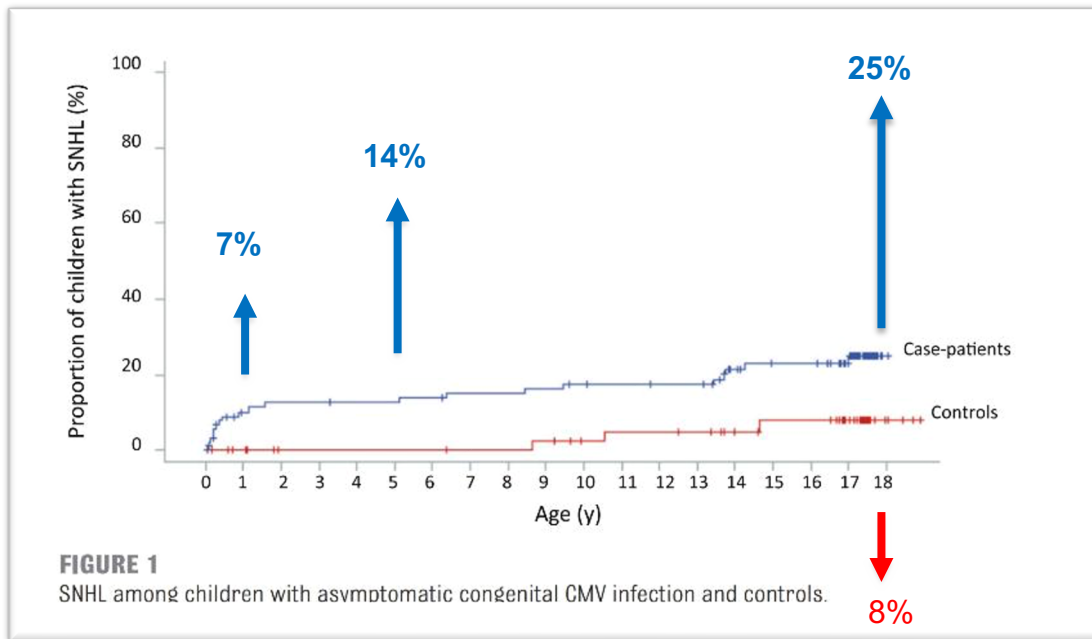
## Characteristics of cCMV-related HL

- ❑ Bilateral in >70%
- ❑ 75% is severe to profound
- ❑ Up to 30-50% is delayed onset
- ❑ Fluctuating 1 in 5
- ❑ Progressive in up to 50%
- ❑ If unilateral HL, risk of developing HL in other ear is potentially high



- Delayed HL may occur up to 18 years.
- Hearing -targeted CMV screening in newborns misses a significant number of asymptomatic cCMV cases.
- Missed cases of cCMV may present with hearing loss later.

## Natural History of “asymptomatic” cCMV-related HL



- 92 infants with **asymptomatic** cCMV compared to 51 case controls followed for 18 years
- Of all the infants with cCMV, 10% had congenital or early-onset HL
- Overall incidence of 25% in the cCMV group
- 14% of those with cCMV who had normal hearing at birth eventually developed HL
- Overall, the rate of bilateral HL in those with any HL was 50% by last assessment
- 89% had profound HL in one ear at last assessment

Lanzieri, T. “Hearing loss in children with asymptomatic congenital cytomegalovirus infection.” *Pediatrics* 2017

## Treatment of cCMV-related hearing loss

- ❑ Consider antiviral therapy
- ❑ Family Counseling and Support
- ❑ Communication options
- ❑ Hearing aids fit as young as 1 month old, before 6 months
- ❑ Early Intervention referral
- ❑ Speech and Language Therapy
- ❑ Cochlear Implantation as early as 6-9 months old



Initiated in 1<sup>st</sup> month  
Valgancyclovir  
Treated for 6 months



Audiologic monitoring  
recommended every 6  
months to 6 years and then  
annually

ORIGINAL ARTICLE

## Valganciclovir for Symptomatic Congenital Cytomegalovirus Disease

Treatment of symptomatic newborns improves developmental, language and hearing outcomes

- Prospective randomized blinded placebo controlled
- Comparing 6 weeks vs 6 months of valganciclovir (an oral medication)
- Initiated within 4 weeks of birth
- Neonates with symptomatic disease, including CNS disease and/or hearing loss

- Neurodevelopmental outcomes were significantly better in the group treated for 6 months compared to the group treated for 6 weeks, regardless of baseline neurologic status
- Hearing was more likely to be improved or remain normal at 12 months (3X odds) and at 24 months (2.6X odds) in group treated for 6 months compared to the group treated for 6 weeks



## **Valganciclovir Is Beneficial in Children with Congenital Cytomegalovirus and Isolated Hearing Loss**

Yehonatan Pasternak, MD<sup>1,2</sup>, Liron Ziv, MD<sup>1,2</sup>, Joseph Attias, MD<sup>3,4</sup>, Jacob Amir, MD<sup>2,5</sup>, and Efraim Bilavsky, MD<sup>2,6</sup>

- Retrospective review over 12 years
  - 59 infants with isolated cCMV-related HL started on antiviral therapy within 12 weeks of birth and treated for 12 months, followed 4-5 years
  - Unilateral HL in 64%
- 68.8% of ears with HL improved, most returning to normal
  - 93% of ears with mild HL improved
  - 70% with mod HL improved
  - 16% with severe HL improved
  - No deterioration in any of the uninfected ears

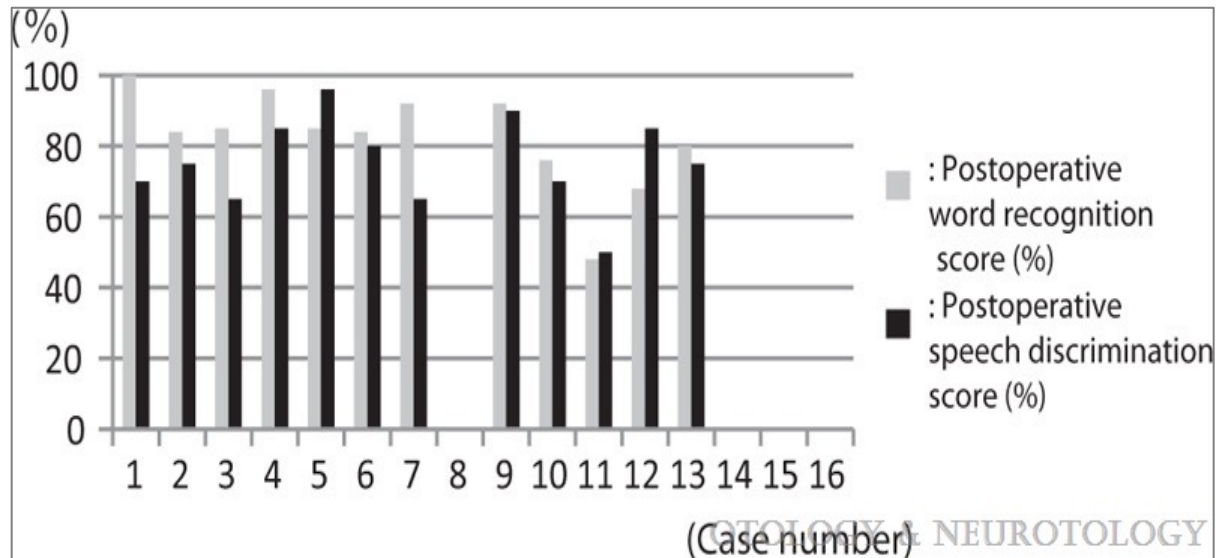
# CMV and Cochlear Implantation

- Higher risk of cognitive and neurological deficits affecting oral language outcomes
- CI improves speech comprehension vs baseline
- Language development especially speech production and intelligibility is typically slower to progress and is poorer than in other implanted children (Shin 2011, Courtois 2021)

## Long-term Outcomes of Cochlear Implantation in Children With Congenital Cytomegalovirus Infection

Yoshida, Haruo; Takahashi, Haruo; Kanda, Yukihiro; Kitaoka, Kyoko; Hara, Minoru

Otology & Neurotology 38(7):e190-e194, August 2017.

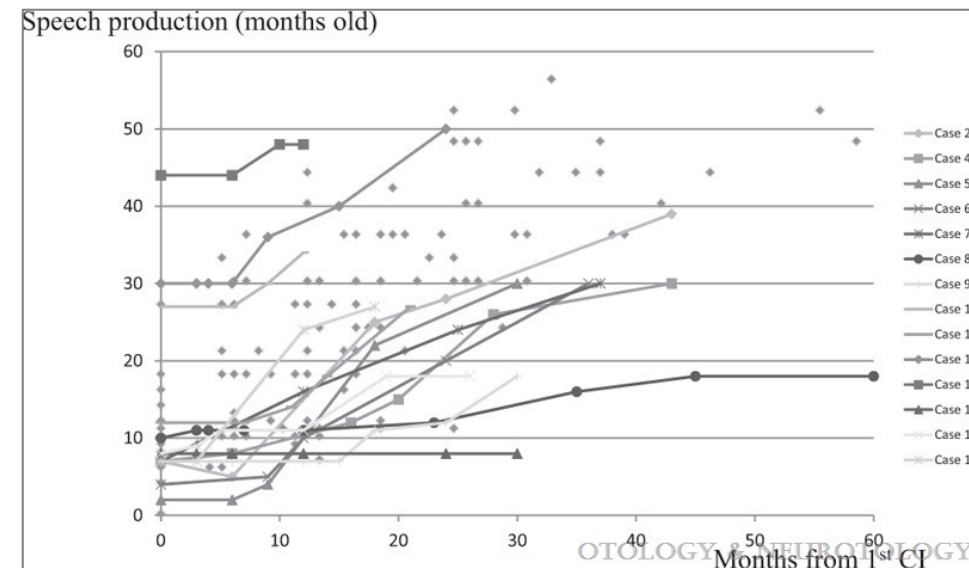
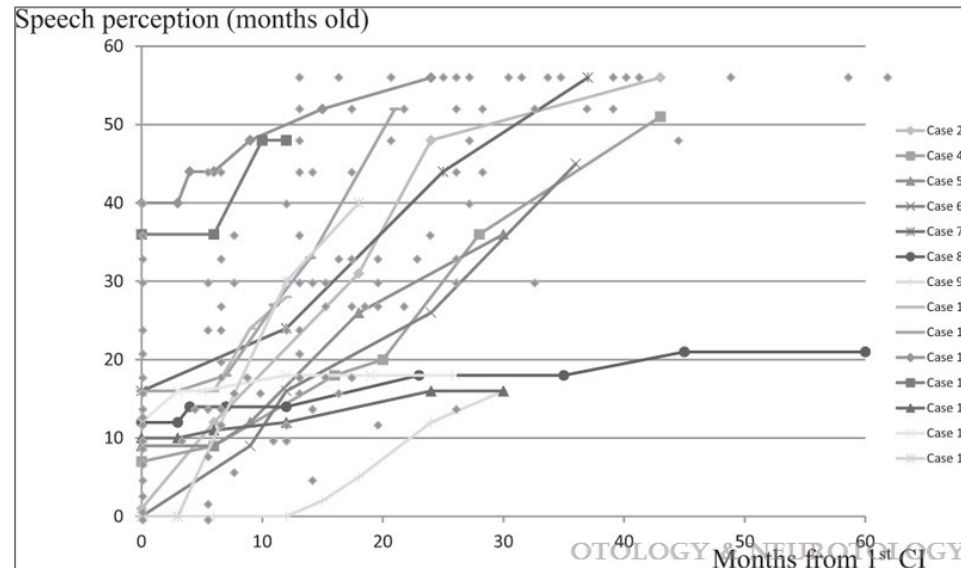


Postoperative word  
recognition score and speech  
discrimination score in 16  
cases

## Long-term Outcomes of Cochlear Implantation in Children With Congenital Cytomegalovirus Infection

Yoshida, Haruo; Takahashi, Haruo; Kanda, Yukihiro; Kitaoka, Kyoko; Hara, Minoru

Otology & Neurotology 38(7):e190-e194, August 2017.



Speech perception and speech production improved over time in CMV subjects similar to implanted subjects without cCMV. (Diamond dots show results in the non-CMV group; plots connected with lines show the results in the CMV group).

# **COCHLEAR IMPLANTATION FOR ASYMMETRIC HL AND SSD**

# Benefits of Bilateral and Binaural Hearing

- Loudness/Summation – Two ears increase the number of action potentials reaching the brainstem providing a 10dB enhancement of sound compared to unilateral stimulation
- Localization and spatial orientation– Interaural time and intensity differences enable localization of sound sources
- Spatial Hearing – The physical phenomenon of head shadow, squelch and separation of signal from noise that improve speech understanding in noise

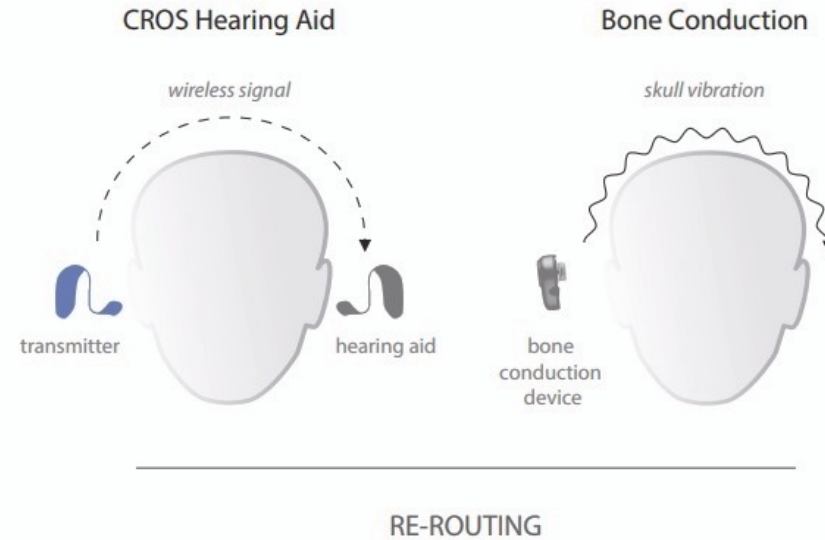
# Children suffer detrimental effects of SSD/AHL

- ❑ Developmental delays in speech and language acquisition
- ❑ Lower mean vocabulary, verbal IQ, full-scale IQ, and oral language scores
- ❑ Impaired educational progress and behavioral issues related to higher concentration needs for listening, fatigue, frustration, and easy distractibility
- ❑ Impaired visuo-spatial memory which impacts reading, math, and receptive language
- ❑ Unilateral sound deprivation leads to cortical reorganization that has negative downstream effects on attention and executive function



## Rehab options for SSD/AHL

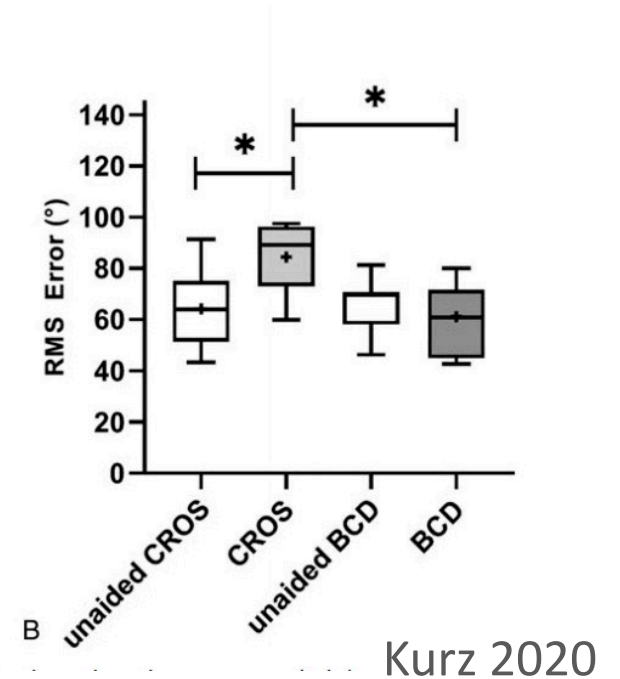
- Hearing aid
- Bone conduction devices
- CROS/BiCROS



- Route sound to better hearing ear
- Take advantage of head shadow
- Improved speech recognition in some noise conditions
- Improved QOL/patient satisfaction

## Limitations of CROS and BCD for people with SSD

- When noise is directed to the poorer ear, speech recognition deteriorates
- Do not restore spatial hearing
- Mixed outcomes for children/teens with congenital hearing loss
- No beneficial effect on the developing auditory cortex
- No benefit of sound localization
- No relief of tinnitus



Kim 2017; Kurz 2020; Peters 2015; Snapp 2020

## High rate of non-use of HAs, BCD and CROS for SSD

30-60% of patients with SSD eventually stop using their bone conduction devices

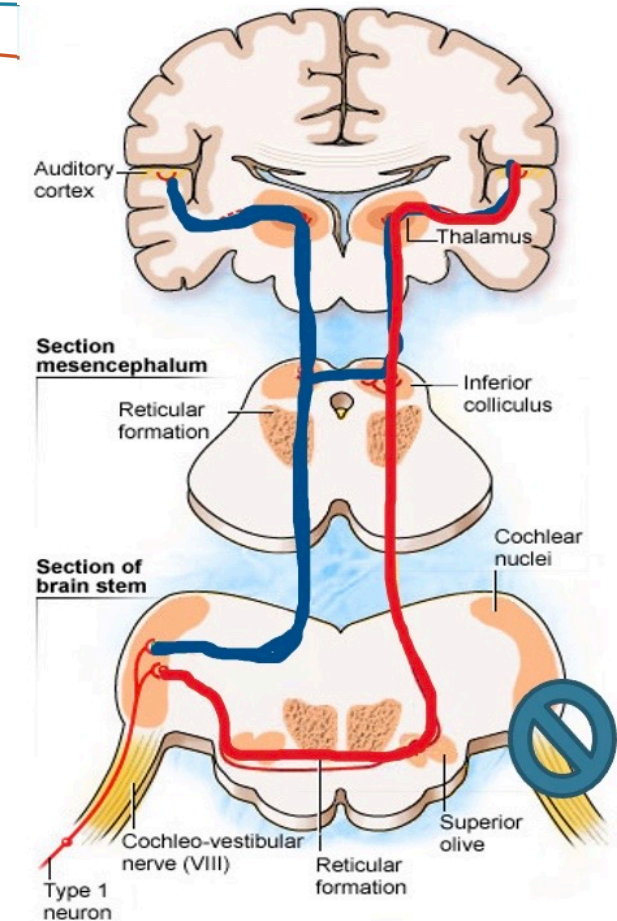
Marx 2021; Gluth 2010; Desmet 2014;  
Faber 2015

- Uncertainty of clinicians, parents and patients about clinical recommendation
- Limited benefit

Any therapeutic approach that provides suboptimal stimulation or bypasses the impaired ear is in effect non-treatment

## Aural Preference Syndrome

1. The normal balance of contralateral and ipsilateral stimulation of the central auditory system is important for spatial hearing
2. Asymmetric hearing loss during early childhood leads to a disruption of the contralateral dominance of the cortical stimulation pathways
3. Strong measurable neural pathways develop in both ipsilateral and contralateral auditory cortex, resulting in a strong neural preference for the better hearing ear

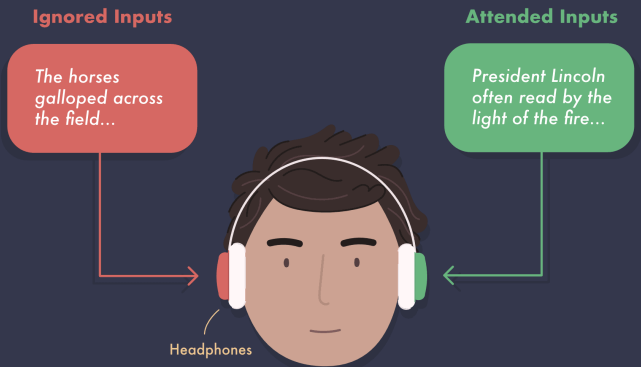


Abnormal ipsilateral neural pathways

## Aural Preference Syndrome

1. This central reorganization is difficult to overcome - resulting in persisting
  - ❑ Asymmetries in speech understanding
  - ❑ Deficits in binaural hearing, including sound localization
2. Earlier and longer hearing deprivation are associated with more significant and resistant effects
3. Limiting the long-term potential use of a congenitally impaired ear

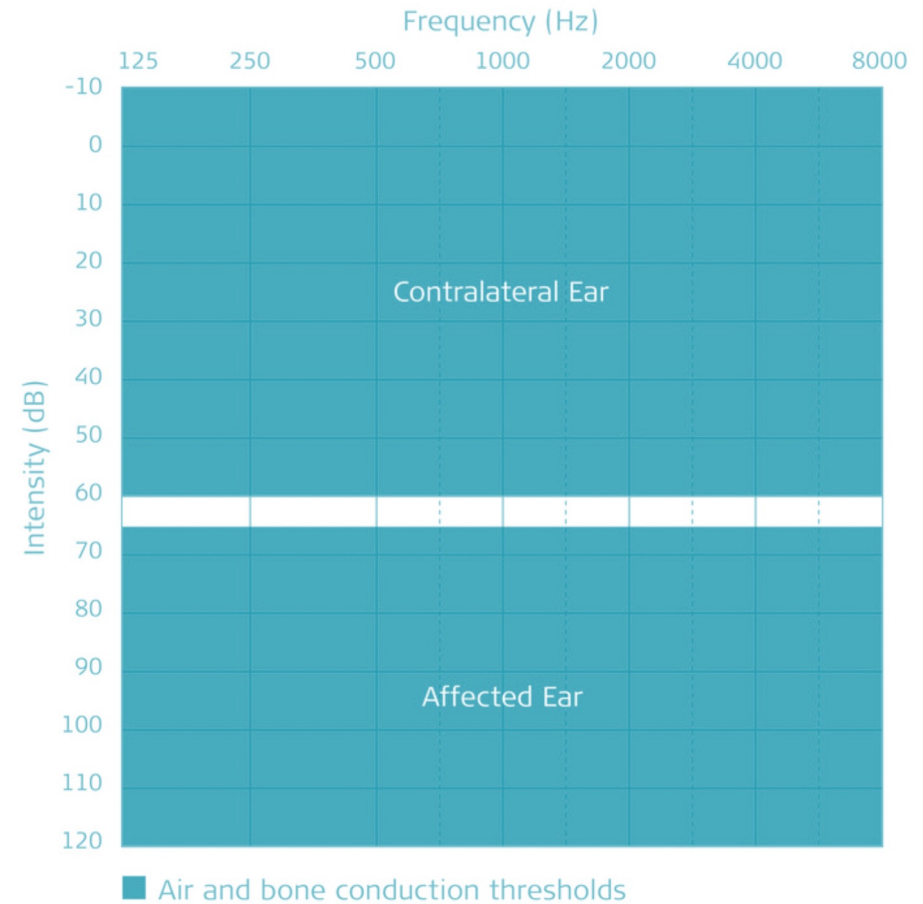
### Dichotic Listening Task



For children with unilateral atresia repaired after puberty, the atretic ear demonstrates a dichotic listening disadvantage

## Candidacy for Asymmetric SNHL and SSD

- Adults and children older than 5 years with SSD or AHL and
- Less than 10-year duration of deafness
- Individual ear analysis



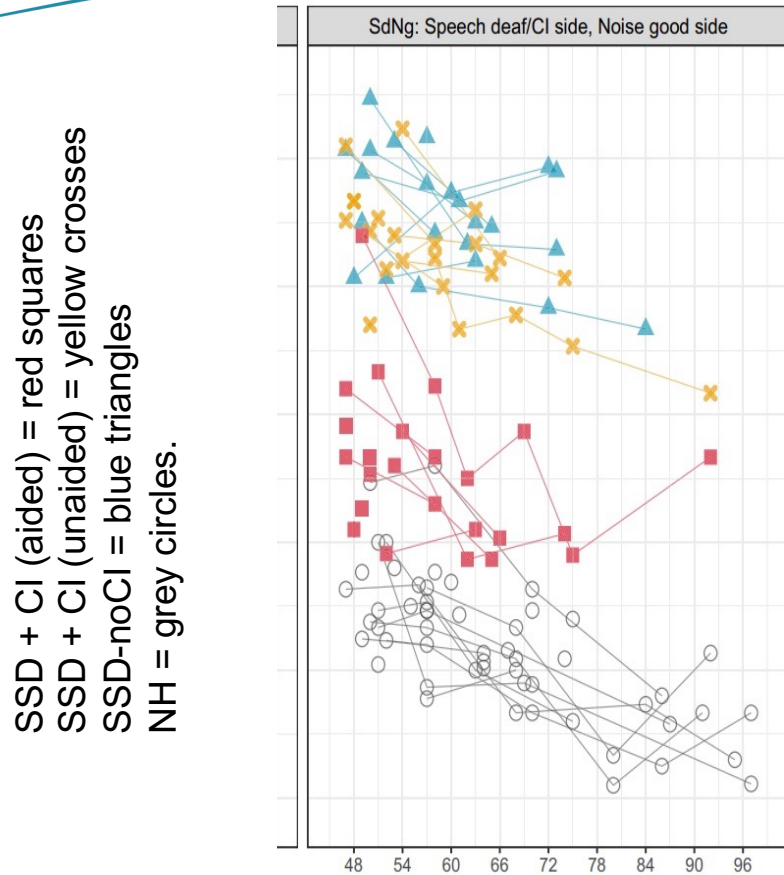


Figure 3. Individual averaged speech reception thresholds (in dB SNR) for the three spatial conditions as a function of age.

## Spatial hearing for children with prelingual SSD implanted early improves over time

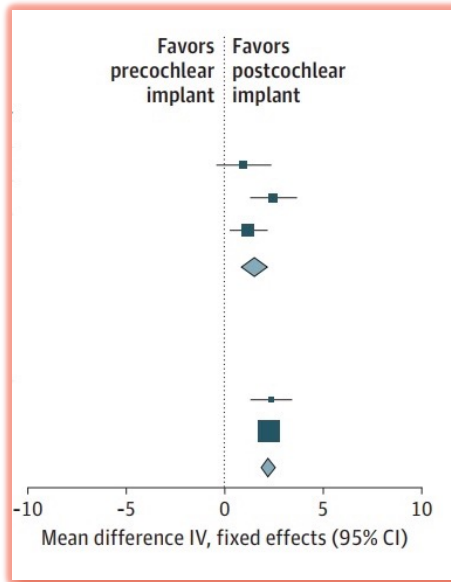
- Children with CI showed better performance compared to those without CI or with CI OFF when noise to the normal ear and speech was directed to the CI side
- Did not show worsened hearing when speech directed to the normal ear and noise to the CI side

*Arras 2022 Longitudinal auditory data of children with prelingual single-sided deafness managed with early cochlear implantation. Nature*

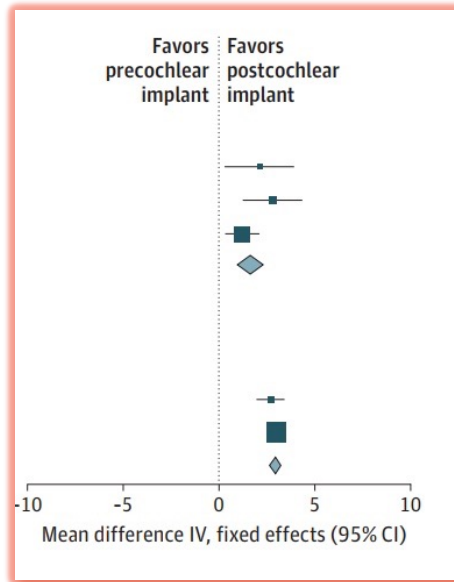
# Meta-analysis of CI for Children with SSD

12 studies, 119 children

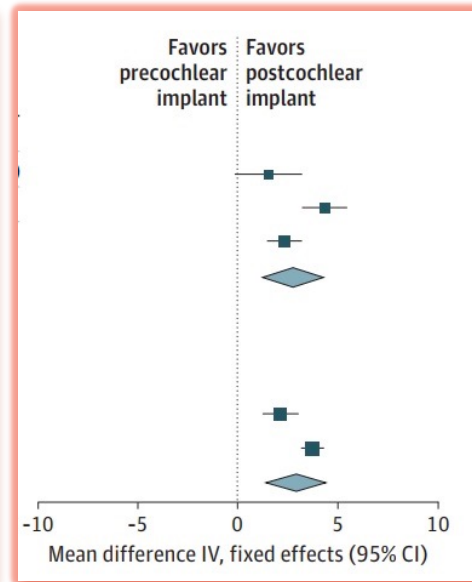
- Improvement in speech perception
  - in noise (80% of children)
  - and in quiet in (81%)
- Improved localization
- Improved subjective speech understanding, spatial hearing and sound quality



SSQ- Speech Understanding



SSQ- Spatial hearing



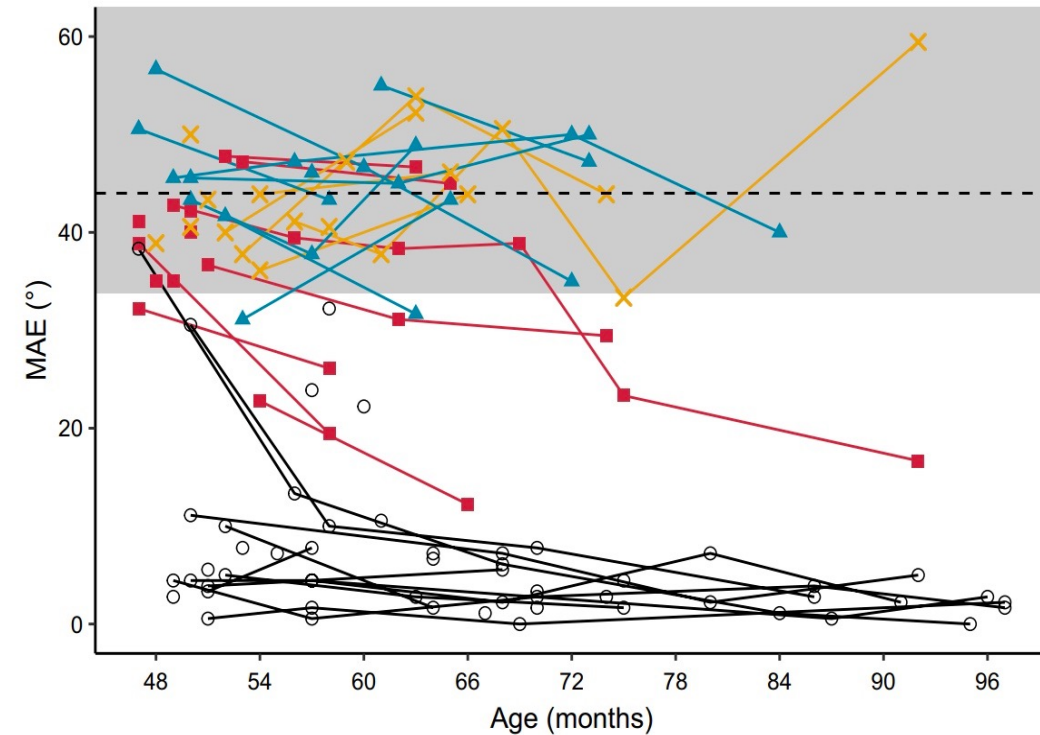
Sound Quality

Forest Plots of Mean Differences in Scores on Speech, Spatial, and Qualities (SSQ) of Hearing Stratified by Congenital vs Acquired Single-Sided Deafness

*Benchetrit Cochlear Implantation in Children With Single-Sided Deafness: A Systematic Review and Meta-analysis. JAMA Otolaryngol Head Neck Surg. 2021*

# Localization for children with prelingual SSD implanted early improves over time

- Children with congenital SSD
  - 12 with CI (avg age 13 months)
  - 12 without CI
  - Children with CI tested with CI OFF
- Control group = 26 with normal hearing



**Figure 4.** Individual mean absolute errors (in degrees) for the nine-loudspeaker condition as a function of age. SSD + CI (aided) = red squares; SSD + CI (unaided) = yellow crosses; SSD-noCI = blue triangles; NH = grey circles. The dotted line at 44° degrees corresponds to chance level performance; scores below the grey area are significantly better than chance. Red lines connect the better-than-chance scores of the SSD + CI children, to show developmental trajectories.

*Arras 2022 Longitudinal auditory data of children with prelingual single-sided deafness managed with early cochlear implantation. Nature*

# Meta-analysis of CI for Children with SSD

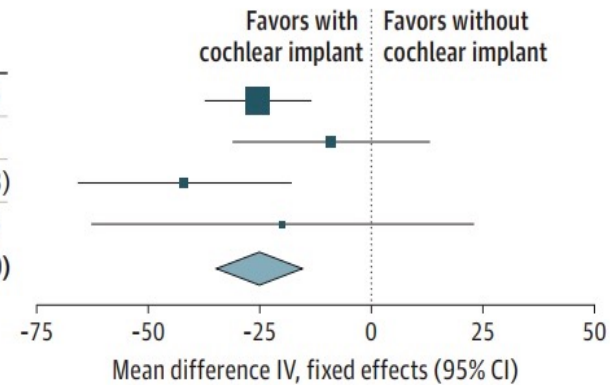
## CI improves sound localization

Figure 2. Meta-analysis Forest Plots of Mean Differences for Sound Localization

Study or subgroup	With cochlear implant			Without cochlear implant			Mean difference IV, fixed effects (95% CI)
	Mean	SD	Total	Mean	SD	Total	
Arndt et al, <sup>28</sup> 2015 (acquired)	15	5.8	9	40.5	17.3	9	-25.50 (37.42 to -13.58)
Arndt et al, <sup>28</sup> 2015 (congenital/perilingual)	32.5	19.9	4	41.5	10.5	4	-9.00 (-31.05 to 13.05)
Rahner and Plontke, <sup>34</sup> 2016	29	22	4	71	10.7	4	-42.00 (-65.97 to -18.03)
Távora-Vieira and Rajan, <sup>26</sup> 2016	43	30	2	63	8	2	-20.00 (-63.03 to 23.03)
<b>Total (95% CI)</b>			<b>19</b>			<b>19</b>	<b>-24.78 (-34.16 to -15.40)</b>

Heterogeneity:  $I^2 = 10\%$  ( $\chi^2 P = .26$ )

Effect size:  $z = 5.18$



*Benchetrit Cochlear Implantation in Children With Single-Sided Deafness: A Systematic Review and Meta-analysis. JAMA Otolaryngol Head Neck Surg. 2021*

# Outcomes

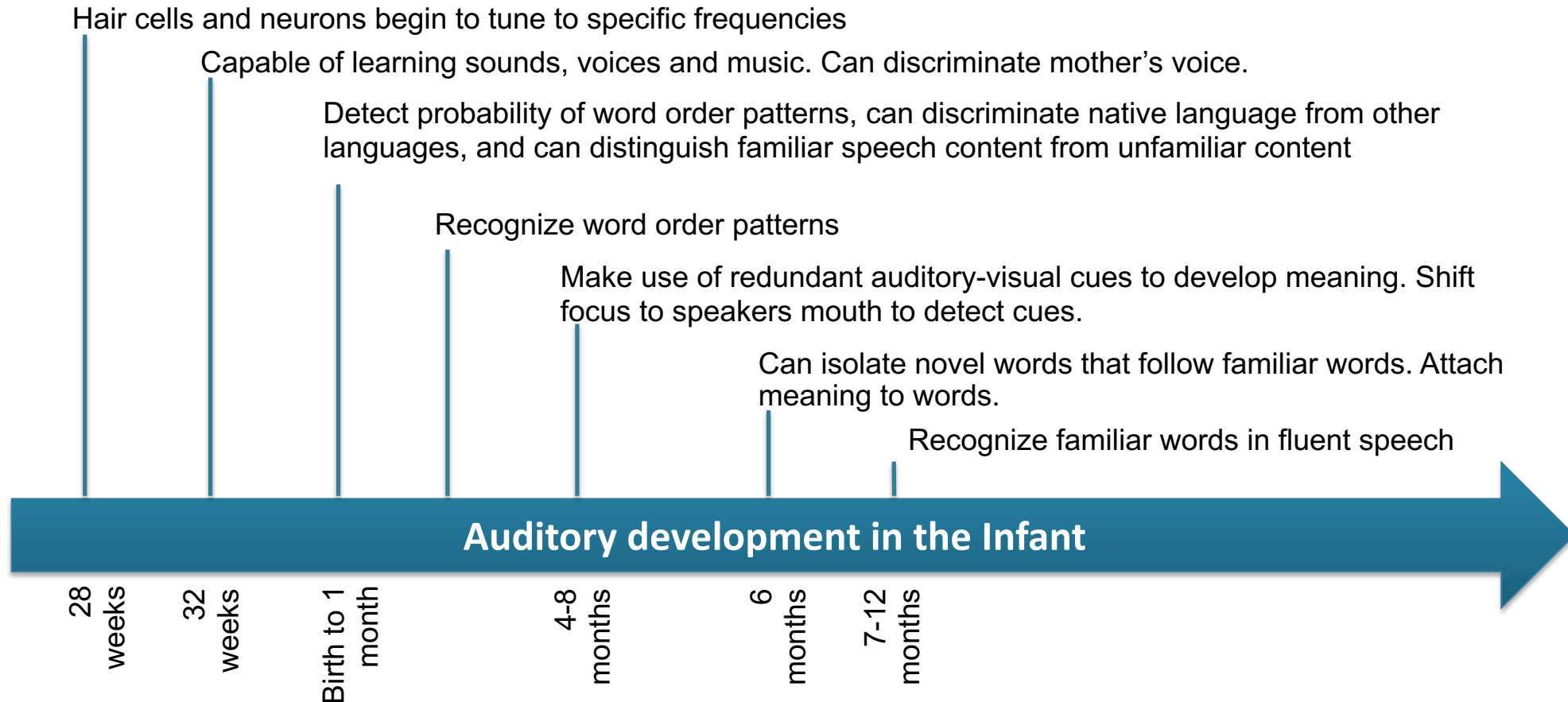
## Children with CI for AHL/SSD

- ❑ Improved **speech perception** in the implanted ear (Deep 2020, Rauch 2021)
- ❑ Improved speech perception in spatially separated speech (Deep 2020, Arras 2022, Benchetrit 2021)
- ❑ No detriment to performance compared to acoustic ear alone (Arras 2022, Benchetrit 2021)
- ❑ **Improved localization** (Arras 2022, Benchetrit 2021)
- ❑ Improved **subjective hearing** (Benchetrit 2021, Arras 2022, Rauch 2021)
- ❑ **Low rate of non-use** (Deep 2020, Arras 2022)
- ❑ Improved cognitive performance (Rauch 2021)
- ❑ Improved **language development** (Rauch 2021)
- ❑ CI promotes normalization of central auditory processing in children with SSD/AHL of both congenital and later onset (Lee 2020, Polonenko 2017)

# Conclusions

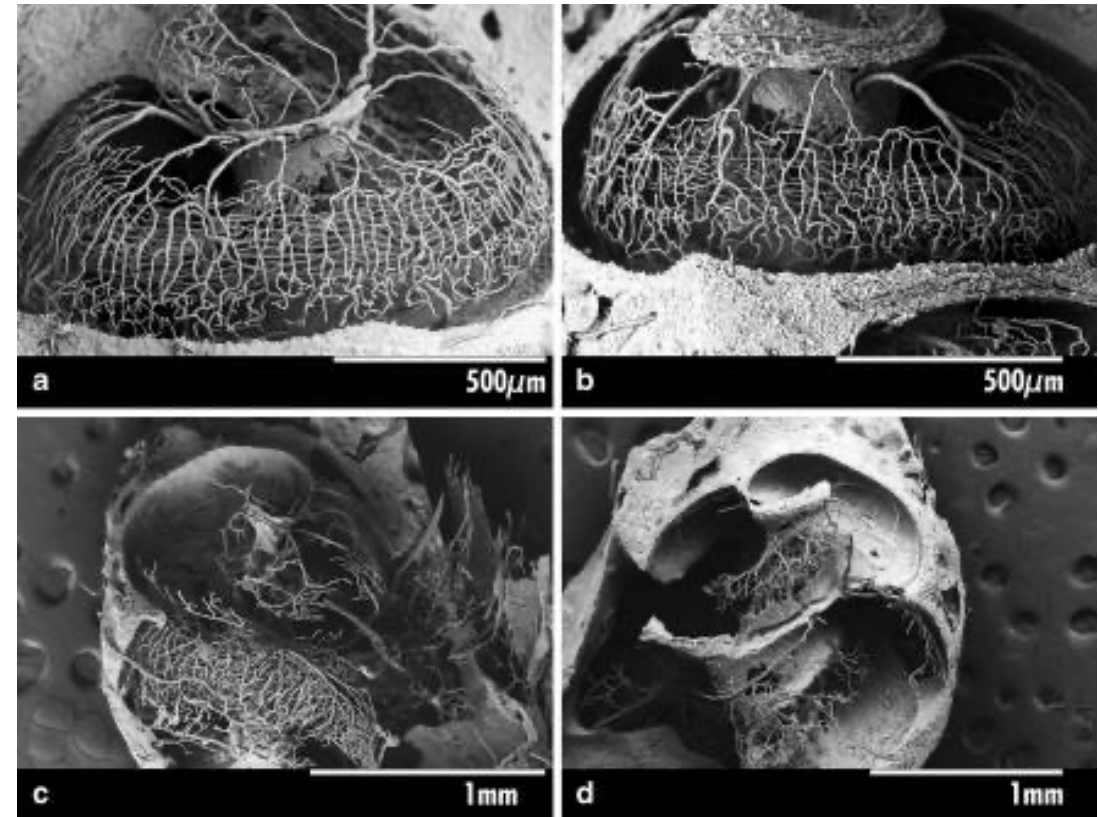


- Children with congenital CMV can be successful with cochlear implantation
- Children with single sided deafness can be successful with cochlear implantation
- Earlier implantation improves outcomes



## Pathophysiology of cCMV HL

- ❑ Virus seems to accumulate in the bone marrow of the cochlear apex but has been demonstrated throughout the inner ear and CNVIII
- ❑ Early dysfunction of stria vascularis and impairment in maintaining endocochlear potential
- ❑ Degeneration of cochlear vasculature progresses from apex to base



Carraro M, Almishaal A, Hillas E, Firpo M, Park A, Harrison RV. Cytomegalovirus (CMV) Infection Causes Degeneration of Cochlear Vasculature and Hearing Loss in a Mouse Model. *J Assoc Res Otolaryngol*. 2017;18(2):263-273.

## Workup for infant and pediatric hearing loss

### CMV negative

- Diagnostic audiologic evaluation
- Medical evaluation
  - Birth and health history
  - EKG
  - Exam for syndromic features
  - Ophthalmology evaluation
  - Genetic testing
  - CT of Temporal bone or
  - MRI of IACs without contrast (R/O Auditory Neuropathy)

### CMV screen positive

- Confirmation of congenital CMV
- Diagnostic audiological evaluation
- Medical Evaluation
  - Developmental/Neurology evaluation
  - Ophthalmology evaluation
  - CBC and LFTs
  - Ultrasound of head or
  - MRI brain and IAC with and w/o contrast

## Congenital CMV is the most common cause of non-genetic childhood HL

- ❑ Toxoplasmosis (10/100,000)
- ❑ Rubella (0.5/100,000)
- ❑ Syphilis (10/100,000)
- ❑ Herpes (10/100,000)
- ❑ **CMV (600/100,000)**
- ❑ Prematurity
- ❑ Low birth weight
- ❑ Jaundice
- ❑ Ototoxic drugs

