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**PEDIATRIC  
OTOTOXICITY**



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**TODAY'S SESSION**

- Pediatric Ototoxicity Monitoring
- Personal Wellness Practices and Mini Health Break
- Hearing Loss in the Context of Childhood Cancer

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## OTOTOXICITY: MONITORING VS MANAGEMENT

### MONITORING

- Has an adverse effect occurred?
- Is treatment protocol impacted by audiology findings?
- For example
  - dose reduction
  - dose elimination
  - take off study
- Long term follow up

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### MANAGEMENT

- What is child's hearing status?
- Effect on communication?
- Compensatory communication strategies
- Management of tinnitus
- Management of hypersensitivity
- Consideration of assistive hearing equipment
- Audiological counselling for child and family
- Networking with care team

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## ILLNESSES OFTEN REQUIRING OTOTOXIC MEDICATIONS

### INFECTIONS

- Multidrug resistant tuberculosis (MDR-TB)
- Lung infections accompanying cystic fibrosis (CF) e.g. pseudomonas
- Gram-positive infections sensitive to aminoglycoside antibiotics

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### CANCER

- Especially specific grade 4 solid tumours especially in the brain, bone tumours (osteosarcoma), liver tumours (hepatoblastoma), germ cell tumours, eye tumours (retinoblastoma), neuroblastoma; testicular tumours, ovarian tumours

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## OTOTOXIC MEDICATIONS

### INFECTIONS

- Aminoglycoside antibiotics
  - Tobramycin
  - Gentamycin
  - Amikacin
  - Streptomycin

### CANCER

- Chemotherapy
  - Cisplatin
  - Carboplatin
  - Oxaliplatin

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## HOW OFTEN TO CHECK HEARING

### ESTABLISH BASELINE PRE-TREATMENT

#### AMINOGLYCOSIDE ANTIBIOTICS

- Work with Infectious Diseases physicians to determine frequency
  - For example:
    - CF, once per hospital admission for 14 day course IV tobramycin
    - MDR-TB, weekly while on amikacin
    - NICU, gentamycin only if additional risk factor provided stable dose levels

#### PLATINUM CHEMOTHERAPY

- Work with Oncology Team; consider treatment protocol
  - Some "On Study" treatment protocols indicate timing of hearing assessments
  - For example:
    - Cisplatin and oxaliplatin, following each cycle of chemo including cisplatin
    - Carboplatin, end of treatment course or after high dose

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## BASELINE ASSESSMENT

- Include both physiologic and behavioural measures
- Use data collection techniques suitable for the child's developmental age
- Prioritize hearing thresholds in the high (2-8 kHz) and extended high (9-16 kHz) frequencies
- Determine any additional etiologies to hearing loss

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## PHYSIOLOGICAL MEASURES

- DPOAEs 1.5-10 kHz
  - 2 runs in each ear if well tolerated
  - Check stability of input signal calibration
- Acoustic reflexes (if well tolerated)
  - e.g. Ipsilateral at 1 & 2 kHz at 85 dB and BBN at 65 dB
- Immittance
  - Tympanograms
- ABR
  - Babies <6months old
  - Prioritize 4kHz, 2kHz plus 6 and/or 8 kHz if available; record down to 15 dB nHL
  - Bone conduction at 4kHz and 2 kHz if AC thresholds are elevated

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## BEHAVIOURAL MEASURES

- Create a positive listening experience in the soundbooth
  - The soundbooth is a very unique acoustic environment that may feel particularly alien to a child (and parent) who has already experienced many unpleasant hospital procedures. Take extra care to make their time with audiology gentle and enjoyable.
  - Encourage parents/caregivers to stay with the child during procedures

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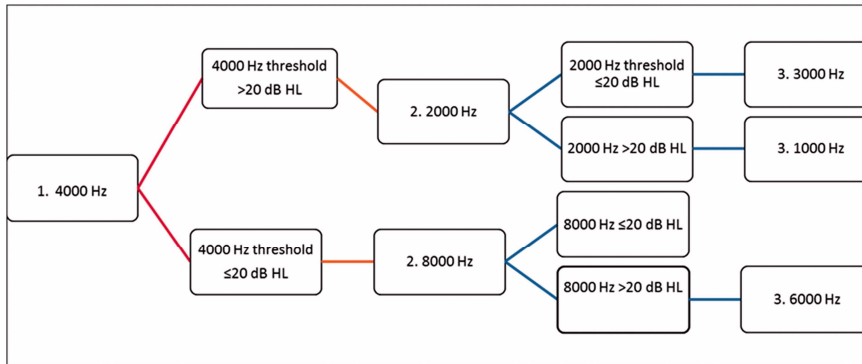
## BEHAVIOURAL MEASURES

- Pure tone thresholds (500-16,000 Hz)
  - Prioritize high frequencies
  - Include intraoctave 3 and 6 kHz to find knee point, inform grading and assist in precision hearing aid programming
  - Reliable soundfield data is more valuable than questionable ear-specific data
  - Include bone conduction
  - Note if you did not test below 10, 15 or 20 dB
  - Use developmentally appropriate activities

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## SIOP MINIMAL TEST BATTERY ALGORITHM



**Decision matrix for a minimal test battery when the clinician feels a complete evaluation is unlikely. If hearing is normal or if hearing status is unknown, begin testing at 4000 Hz. Establish threshold in each ear (or in sound field if the earphones are not tolerated); if threshold is ≤20 dB HL, test 8000 Hz; if threshold is >20 dB HL, test 2000 Hz. Continue testing, as indicated.**

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Brooks & Knight (2018) Ototoxicity monitoring in children treated with platinum chemotherapy, *International Journal of Audiology*, 57:sup4, S62S68  
DOI: [10.1080/14992027.2017.1355570](https://doi.org/10.1080/14992027.2017.1355570)

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## SPEECH PERCEPTION

- SRT/SAT monaural and SF; for SAT consider Ling or LMH phonemes
- WRS consider using a soft presentation level e.g. 35 dB
- Use speech perception materials likely to demonstrate change as child acquires HFSNHL
  - e.g. Gardner's high consonant frequency list (JSHD 1971. 36(3):354-355)
- Consider SF presentation in quiet and with background noise e.g. Auditec 4 talker complex

### COMPARE SPEECH PERCEPTION AT BASELINE VS END OF TREATMENT

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## CHARACTERISTICS OF CISPLATIN OR AMINOGLYCOSIDE INDUCED HEARING LOSS

- Bilateral and sensorineural
- Hearing threshold shift beginning in the EHF's
- Progressively affecting more of the frequency range stepwise
- Progressively more severe in degree
- Corresponding loss of DPOAEs, beginning in the high frequencies
- Hearing thresholds in the lower frequencies are typically preserved at baseline levels

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## BUT WHAT DOES IT MEAN?

### ACTIVITY:

What are the expected effects of acquired HFSNHL on everyday function?

- Toddlers
- Preschoolers
- 5-10 year olds
- 12-18 year olds

### Discuss

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## IS THERE ANYTHING I CAN DO?

- Compensatory communication strategies
- Role of hearing aids and other assistive technology

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## CONCOMITANT ETIOLOGIES MAY OCCUR

- Head and neck cancers
  - Disease/surgery related hearing loss on the affected side
  - Conductive/sensorineural/mixed
- Brain tumours
  - Disease/surgery related hearing loss on the affected side
  - Sensorineural/retrocochlear/ auditory pathway
- Transient middle ear dysfunction
  - Abnormal tympanograms, conductive hearing loss
  - May obscure OAEs

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## REPORTING AND COUNSELLING

- Clear and concise
- Separate effects of ototoxicity from other etiologies
- Indicate stable vs change in hearing status
- Implications for communication
- Plans for audiology follow up

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## MINI HEALTH BREAK

- 10-15 minutes
- Engage in a personal wellness practice
  - For example:
    - Deep breath
    - Stretch
    - Walk around
    - Chat with others
- Prepare to learn more about childhood cancer and ototoxicity

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## CHILDHOOD CANCER AND OTOXICITY

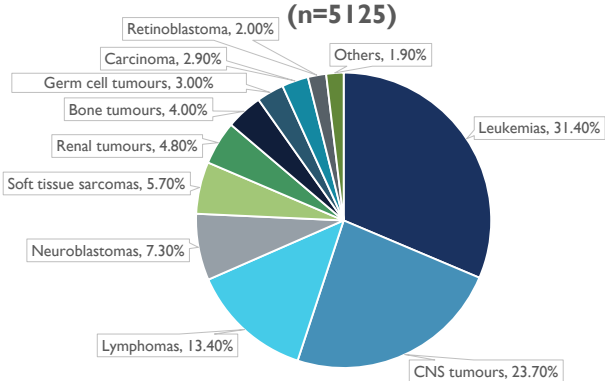


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## PROPORTION OF TYPES OF CANCER IN CHILDREN AGED 0-14 YEARS

**Age 0-14 years  
(n=5125)**



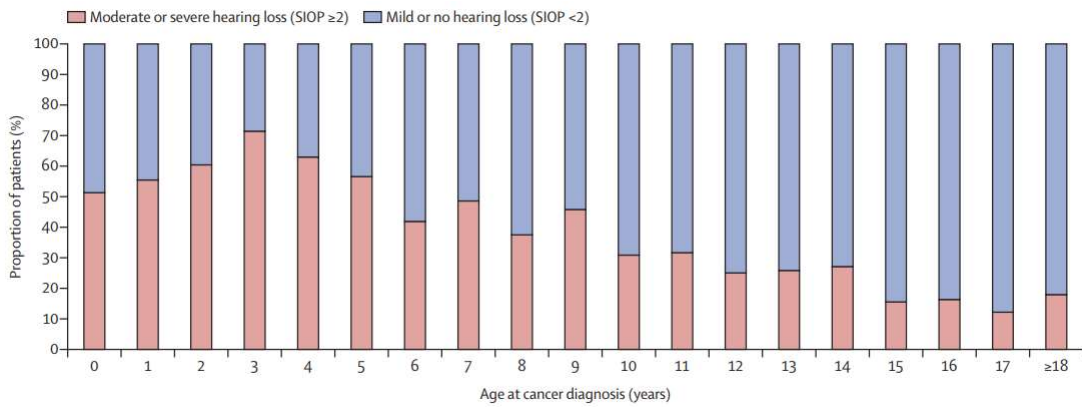
Cancer Type	Percentage
Leukemias	31.40%
CNS tumours	23.70%
Lymphomas	13.40%
Neuroblastomas	7.30%
Soft tissue sarcomas	5.70%
Renal tumours	4.80%
Bone tumours	4.00%
Germ cell tumours	3.00%
Carcinoma	2.90%
Retinoblastoma	2.00%
Others	1.90%

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<https://www.canada.ca/en/health-canada/services/publications/science-research-data/cancer-young-people-canada-surveillance-2017.html#a9>

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## PREVALENCE OF MODERATE OR SEVERE CISPLATIN-INDUCED HEARING LOSS BY AGE

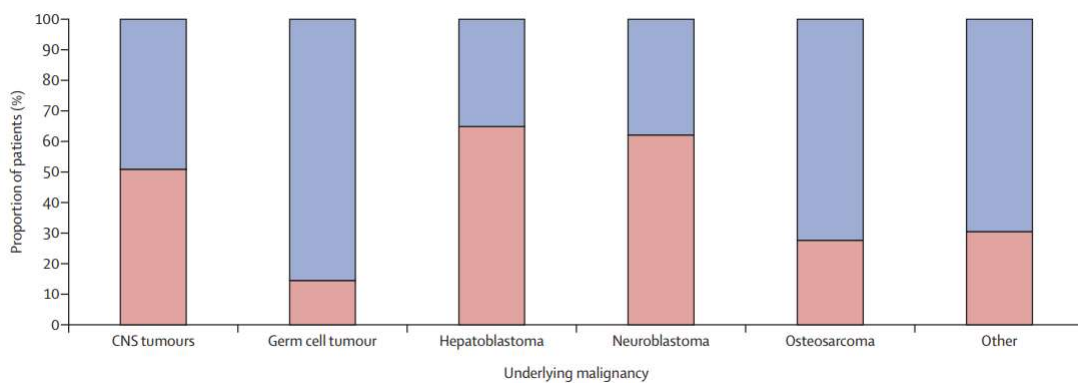


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Moke et al. Lancet Child Adolesc Health. 2021 Apr; 5(4): 274–283.

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## PREVALENCE OF MODERATE OR SEVERE CISPLATIN-INDUCED HEARING LOSS BY UNDERLYING MALIGNANCY



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Moke et al. Lancet Child Adolesc Health. 2021 Apr; 5(4): 274–283.

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## CASE EXAMPLE

### Patient 1 – just under 2-yr old

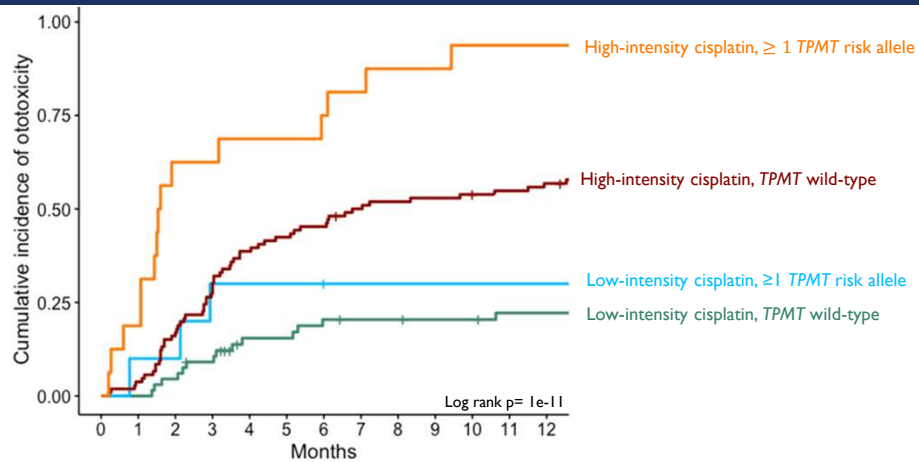
- Treated for Germ Cell tumour on protocol CCG 8882
  - Cumulative dose 400mg/m<sup>2</sup>
- Tolerated full-course of cisplatin therapy without hearing loss
  - Normal bilateral hearing 3-years following cisplatin treatment (tested in high frequencies up to 12kHz).
- Cisplatin given as 20mg/m<sup>2</sup> per day x 5 days x 4 cycles

### Patient 2 – just over 1-yr old

- Treated for Hepatoblastoma on protocol POG 9645
  - Cumulative dose 400mg/m<sup>2</sup>
- After 3 cycles of cisplatin, developed grade 3 ototoxicity
  - Audiogram results: 250/35, 500/20, 1000/30, 2000/70, 3000/80. No response beyond. Impression: Normal to borderline normal hearing to 1000 Hz sloping to severe loss in the high frequencies for at least the better ear (as no ear specific responses obtained).
- Cisplatin given as 100mg/m<sup>2</sup> per day x 1 day x 4 cycles

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## Cumulative incidence of cisplatin-induced ototoxicity by dose intensity and TPMT carrier status



Red; wildtype TPMT:	106	89	65	58	50	48	44
Red; ≥ 1 TPMT variant:	16	6	5	4	2	1	1
Green; ≥ 1 TPMT variant:	10	9	7	7	6	6	6
Green; wildtype TPMT:	66	63	51	48	47	46	44

Siemens et al. Ther Drug Monit 2023;00:1-9

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## HAS OTOTOXICITY OCCURRED?

### ASHA criteria

Change in hearing sensitivity is always computed relative to baseline measures. Criteria to indicate hearing decrease during ototoxicity monitoring are defined here as (a) • 20 dB decrease at any one test frequency, (b) • 10 dB decrease at any two adjacent test frequencies, or (c) loss of response at three consecutive test frequencies where responses were previously obtained (the third criterion refers specifically to the highest frequencies tested, where earlier responses are obtained close to the limits of audiometric output and later responses cannot be obtained at the limits of the audiometer). Finally, change must be confirmed by repeat testing.

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Audiologic Management of Individuals Receiving Cochleotoxic Drug Therapy doi:10.1044/policy.GLI994-00003

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## GRADING SYSTEMS

Adverse drug effects are quantified by degree of impairment

Several grading systems are in the literature

- CTCAE
- SIOP
- Brock
- Chang
- Muenster

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## COMMON TERMINOLOGY CRITERIA FOR ADVERSE EVENTS: CTCAE

- Standardized definitions of adverse events (AEs)
- Also called “common toxicity criteria”
- Established in the United States by the National Cancer Institute (NCI) of the National Institutes of Health (NIH)
- Most recent version (version 5.0) published in November 2017
- Grades 0-5 with grade 0 implying no AE and grade 5 reflecting a lethal event.

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[https://ctep.cancer.gov/protocoldevelopment/electronic\\_applications/docs/ctcae\\_v5\\_quick\\_reference\\_5x7.pdf](https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5x7.pdf)

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## SIOP (INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY) BOSTON

**Table 2.** SIOP Boston Ototoxicity Scale

Grade	Parameters
0	≤ 20 dB HL at all frequencies
1	> 20 dB HL (ie, 25 dB HL or greater) SNHL above 4,000 Hz (ie, 6 or 8 kHz)
2	> 20 dB HL SNHL at 4,000 Hz and above
3	> 20 dB HL SNHL at 2,000 Hz or 3,000 Hz and above
4	> 40 dB HL (ie, 45 dB HL or more) SNHL at 2,000 Hz and above

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Brock et al. J Clin Oncol 30:2408-2417. 2012  
DOI: 10.1200/JCO.2011.39.1110

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## TINNITUS

- Very common with cisplatin
- Young children may ask “What’s that bee in my ear?”
- Often matched to 4 or 6 kHz pure tone in soundfield at various levels
- May interfere with ability to give hearing threshold responses; consider switching stimulus to intermittent or warbled tone
- Helpful to give reassurance that the tinnitus is an expected side effect of the chemo
- Provide simple management strategies

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## HYPERSENSITIVITY

- Very common with chemotherapy; may be accompanied by hypersensitivity to other sensory stimuli eg light, smell, touch
- Often accompanied by tinnitus
- E.g. cannot tolerate sound of a granola bar wrapper; voices may sound like a “spoon banging on a pot”
- Reassure that this can happen with chemo and it typically eases over time
- Provide simple management strategies eg providing acoustically calm environment, soothing sounds

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## TAKING CARE OF OURSELVES

- Become part of the child's Oncology Circle of Care
  - Be prepared to represent Audiology to the care team
  - Reach out to Audiology colleagues in pediatric acute care
  - Reach out to partners in family's home community e.g. TDHH, SLP
  - T8 Psychosocial Team at BCCH hosts
    - Wellness Wednesdays
    - Tea at 3
- T8 is the Oncology Floor in Acute Care Building

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## CONCLUDING THOUGHTS

- Remind yourself what you have done to help
- Plan and pivot
- Shift our Audiology professional perspective from ototoxicity monitoring to ototoxicity management

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QUESTIONS?

**Contact**

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