

Antibiotics and Hearing Loss in Children

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Agenda

- Background
- Implicated antibiotics
- Pathogenesis of antibiotics associated hearing loss
- Prevention strategies and evidence
- Q&A

Background

- Hearing loss is one of the most common sensory disabilities worldwide, affecting around 34 million children.*
- Early-onset hearing loss → Major effects on a child's development.
- Antibiotics-induced ototoxicity is potentially preventable.

Estimated numbers of incident DR-TB cases, treated cases, and preventable cases of ototoxic hearing loss.

Year	n, incident DR-TB cases A	n, treated cases (with second-line regimen)B	n, likely treated with oral regimensC	n, estimated deathsD	n, preventable cases of ototoxic hearing loss=(B-C-D)*40.62%
2019	465,000	177,099	15,884	25,872	54,976
2018	484,000	156,205	n/a	22,820	54,181
2017	558,000	139,144	n/a	20,327	48,263
2016	600,000	130,924	n/a	19,746	45,161
2015	580,000	122,726	n/a	18,939	42,158
Sum	2,687,000	726,098	—	107,703	244,739

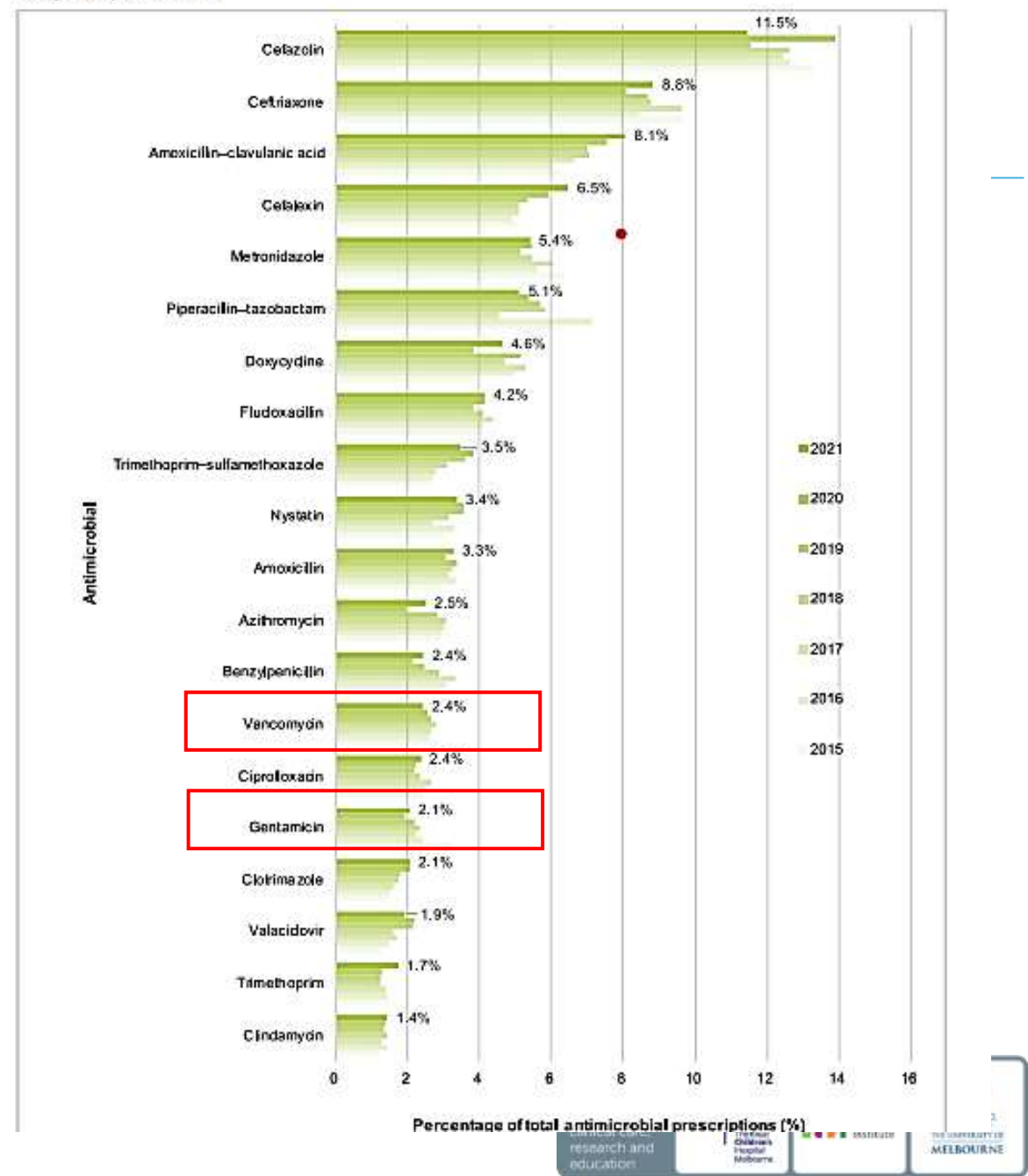
* <https://www.who.int/publications/i/item/world-report-on-hearing>.

Implicated Antimicrobials

The most common Antibiotics

- Vancomycin
- Aminoglycoside antibiotics(AG)
(e.g.gentamycin, streptomycin,
tobramycin, amikacin)

Figure 11: The 20 most common antimicrobials prescribed by Hospital NAPS contributor hospitals, 2015-2021



Hearing Loss with AG and Vancomycin Use

Drug class	Mechanism of Ototoxicity	Type	Incidence
Aminoglycosides	Hair cell damage	Irreversible	40.6%
Vancomycin	Unknown ?vestibular/cochlear damage	Reversible *	8%

*Cases of irreversible hearing loss reported.



Aminoglycoside Ototoxicity

Mechanism:

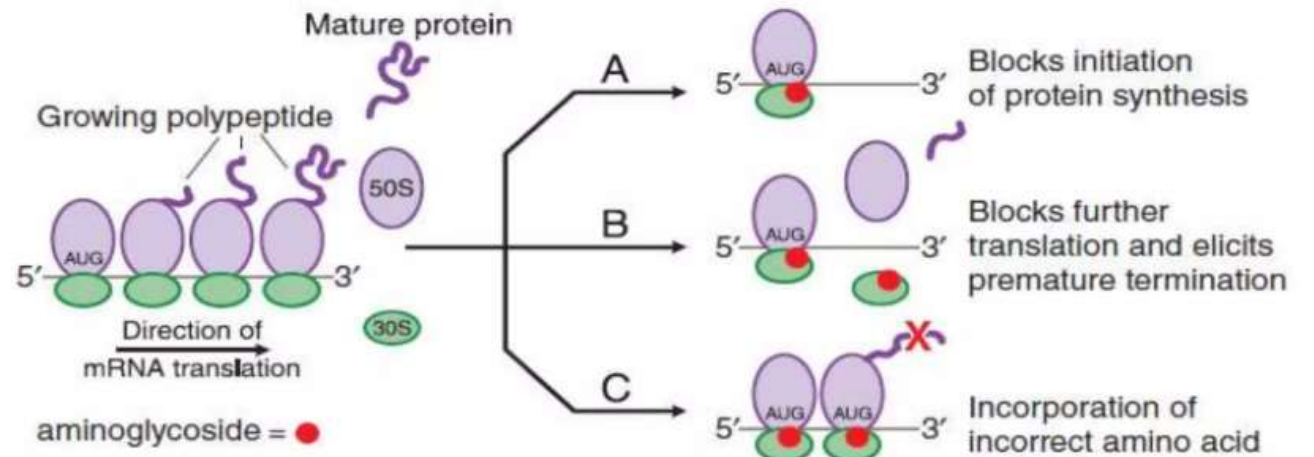
- The loss of hair cells results in permanent hearing loss

Type and Degree:

- Severe to profound SNHL, irreversible.

Risk Factors:

1. Drug-related factors:
 - High cumulative dose
 - Prolonged duration
 - Use of ototoxic drugs
2. Genetic susceptibility



Vancomycin Ototoxicity

Mechanism:

Presumed direct damage of the auditory branch of the eighth cranial nerve, although the mechanism is not fully understood.

Type and Degree:

High-frequency SNHL. The spectrum of transient to permanent hearing loss.

Risk Factors

- High dosage and prolonged use
- Concurrent use of other ototoxic drugs
- Impaired renal function
- Age
- High trough levels

Prevention Strategies and Evidence

Identifying High-Risk Populations

- Genetic Screening: Screen for mitochondrial mutations to identify susceptibility.
- Pre-Exposure Audiometric Testing: Baseline hearing tests before high-risk antibiotic use, especially in long-term treatments.

Minimising Exposure

- Dosing and Duration Control using precision dosing modelling.
- Combination Therapy Caution: Avoid concurrent use of other ototoxic agents.

Does carrying certain genetic variants increase the risk of developing hearing loss after exposure to aminoglycosides in humans?

Article Contents

Abstract

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JOURNAL ARTICLE

Pharmacogenetics of aminoglycoside-related ototoxicity: a systematic review

D Gaafar ✉, N Baxter, N Cranswick, J Christodoulou, A Gwee

Journal of Antimicrobial Chemotherapy, dkae106,

<https://doi.org/10.1093/jac/dkae106>

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Summary of Evidence

Mitochondrial variant	N of Studies	Level of Evidence	SNHL with AG exposure*	SNHL without AG exposure*
m.1555 A>G	17	L 2-4	63-100%	0-40%
m. 1494 C>T	9	L 3-4	21-40%	0-14%
m. 1095 T>C	3	L3-4	NR	NR
m. 1005 T>C	2	L4	NR	NR

Pros and Cons of Genetic Testing

Pros	Cons
Potentially prevent hearing loss	False positive results.
Help to inform treating decision	Use of alternative antibiotics and emerging drug resistance.
	A negative result doesn't eliminate the risk of hearing loss.
	Cost vs benefit – no enough data.

Vancomycin Induced Ototoxicity

- The incidence of possible hearing impairment in neonates receiving Vancomycin is 22% (9/41) compared to 7% in neonates not receiving vancomycin or aminoglycosides (assessed through OAE).
- German Neonatal Network data links vancomycin to dose-dependent risks for abnormal hearing at discharge and age 5.
- Most audiogram changes are mild to moderate; only 3% moderate to severe hearing loss on vancomycin.
- Ototoxicity onset varied from 2 to 5 weeks of vancomycin exposure

How to Prevent it?

- Precision Dose Modelling is essential in children, as their variable renal maturation and pharmacokinetics can make standard dosing guidelines less reliable.
- Individualized intermittent vancomycin dosing using a model-based online calculator resulted in 75% and 83% of infants achieving target concentrations (trough and AUC0-24, respectively).



Take Home Message

- Certain mitochondrial mutations (m.1555A>G and m.1494C>T) increase susceptibility to aminoglycoside-induced ototoxicity, though further research is needed.
- Individualized, model-based dosing to reach target levels is essential for minimising ototoxicity risk while maintaining effective treatment.

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