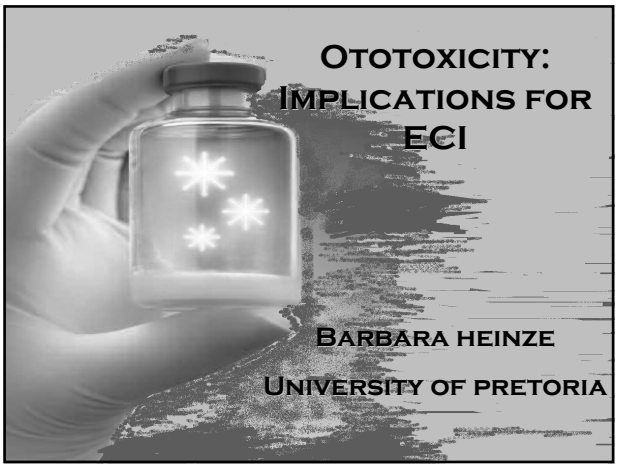


Ototoxicity: Implications for ECI

Barbara Heinze

University of Pretoria

What is ototoxicity?

- ***"… tendency of certain substances to cause functional impairment and cellular damage to the tissues of the inner ear***
- ***… especially to the end organs of the cochlear and vestibular divisions of N. VIII that can occur from systemic or topical administration."***

Rhatican, Mandel and Rutka (2004) in Roland and Rutka:198-206

What is ototoxicity? (cont)

"Therapeutic drug regimes including some medications used to treat cancer and infectious diseases can be toxic to inner ear tissues..."

Fausti et al. (2007) in Campbell:230-251

"Ear Poisoning"

- **Cochleotoxicity**
  - **Hearing loss**
  - **Tinnitus**
  - **Hyperacusis**
  - **Speech discrimination difficulties**
- **Vestibulotoxicity**
  - **Vertigo**
  - **Disequilibrium/imbalance**
  - **Instability of visual field**

Black et al. (2004); Halmagyi et al. (1994)

"Ear Poisoning" agents

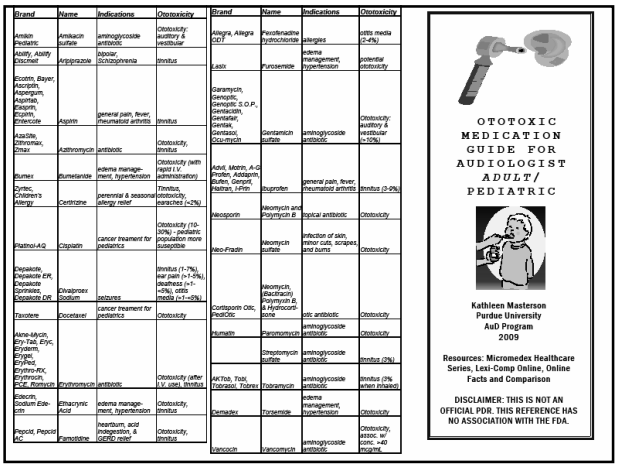
- **Treatments for HIV/AIDS: ARV**
- **Treatments for HIV-related opportunistic infections**
- **Certain chemotherapeutic agents**
- **Diuretics**
- **Quinine**
- **Salicylates**

Ototoxic medication guide

"We need to know about the many agents that can damage our ears"

This handy guide is a resource for Audiologists and Speech-Language therapists

See handout



Brand	Name	Indications	Ototoxicity
Amikin Pediatric	Amikacin sulfate	aminoglycoside antibiotic	Ototoxicity; auditory & vestibular
Abilify, Abilify Discmelt	Aripiprazole	bipolar, Schizophrenia	tinnitus
Ecotrin, Bayer, Ascriptin, Aspergum, Aspirtab, Easprin, Ecprin, Entercote	Aspirin	general pain, fever, rheumatoid arthritis	tinnitus
AzaSite, Zithromax, Zmax	Azithromycin	antibiotic	Ototoxicity, tinnitus
Bumex	Bumetanide	edema management, hypertension	Ototoxicity (with rapid I.V. administration)
Zyrtec, Children's Allergy	Certirizine	perennial & seasonal allergy relief	Tinnitus, ototoxicity, earaches (<2%)
Platinol-AQ	Cisplatin	cancer treament for pediatrics	Ototoxicity (10-30%) - pediatric population more susceptible
Depakote, Depakote ER, Depakote Sprinkles, Depakote DR	Divalproex Sodium	seizures	tinnitus (1-7%), ear pain (>1-5%), deafness (>1-<5%), otitis media (>1-<5%)
Taxotere	Docetaxel	cancer treament for pediatrics	Ototoxicity
Ilene-Mycin, Ery-Tab, Ery, Erysterm, Erygel, EryPed, Erythro-RX, Erythrocin, PCE, Romycin	Erythromycin	antibiotic	Ototoxicity (after I.V. use), tinnitus
Edecrin, Sodium Edecrin	Ethacrynic Acid	edema management, hypertension	Ototoxicity, tinnitus
Pepcid, Pepcid AC	Famotidine	heartburn, acid indegestion, & GERD relief	Ototoxicity, tinnitus

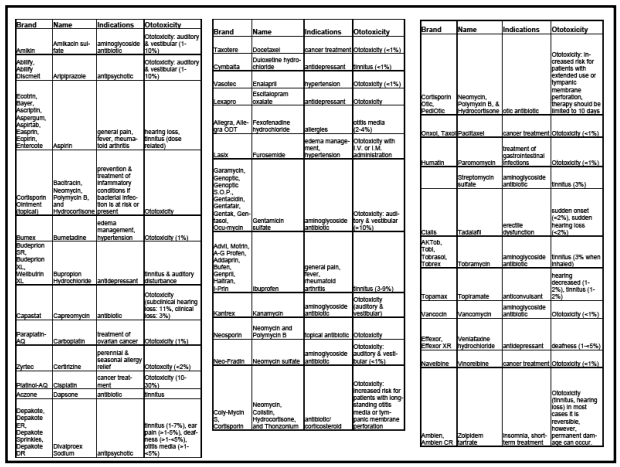
Brand	Name	Indications	Ototoxicity
Allegra, Allegra ODT	Fexofenadine hydrochloride	allergies	otitis media (2-4%)
Lasix	Furosemide	edema management, hypertension	potential ototoxicity
Garamycin, Genoptic, Genoptic S.O.P., Gentacidin, Gentafair, Gentak, Gentasol, Ocu-mycin	Gentamicin sulfate	aminoglycoside antibiotic	Ototoxicity; auditory & vestibular (>10%)
Advil, Motrin, A-G Profen, Addaprin, Buflex, Genpril, Haltran, I-Prin	Ibuprofen	general pain, fever, rheumatoid arthritis	tinnitus (3-9%)
Neosporin	Neomycin and Polymycin B	topical antibiotic	Ototoxicity
Neo-Fradin	Neomycin sulfate	infection of skin, minor cuts, scrapes, and burns	Ototoxicity
Cortisporin Otic, PediOtic	Neomycin, (Bacitracin) Polymycin B, & Hydrocortisone	otic antibiotic	Ototoxicity
Humatin	Paromomycin	aminoglycoside antibiotic	Ototoxicity
	Streptomycin sulfate	aminoglycoside antibiotic	tinnitus (3% when inhaled)
AKTob, Tobi, Tobrasol, Tobrex	Tobramycin	aminoglycoside antibiotic	tinnitus (3% when inhaled)
Demadex	Torsemide	edema management, hypertension	Ototoxicity
Vancocin	Vancomycin	aminoglycoside antibiotic	Ototoxicity, assoc. w/ conc. >40 mcg/mL

OTOTOXIC MEDICATION GUIDE FOR AUDIOLOGIST *ADULT/* PEDIATRIC

Kathleen Masterson
Purdue University
AuD Program
2009

Resources: Micromedex Healthcare Series, Lexi-Comp Online, Online Facts and Comparison

DISCLAIMER: THIS IS NOT AN OFFICIAL PDR. THIS REFERENCE HAS NO ASSOCIATION WITH THE FDA.



Brand	Name	Indications	Ototoxicity
Amikin	Amikacin sulfate	aminoglycoside antibiotic	Ototoxicity; auditory & vestibular (1-10%)
Abilify, Abilify Discmelt	Aripiprazole	antipsychotic	Ototoxicity; auditory & vestibular (1-10%)
Ecotrin, Bayer, Ascriptin, Aspergum, Aspirtab, Easprin, Ecprin, Entercote	Aspirin	general pain, fever, rheumatoid arthritis	hearing loss, tinnitus (dose related)
Cortisporin Ointment (topical)	Bacitracin, Neomycin, Polymycin B, and Hydrocortisone	prevention & treatment of inflammatory conditions if bacterial infection is at risk or present	Ototoxicity
Bumex	Bumetanide	edema management, hypertension	Ototoxicity (1%)
Budeprion SR, Budeprion XL, Wellbutrin XL	Bupropion Hydrochloride	antidepressant	tinnitus & auditory disturbance
Capastat	Capreomycin	antibiotic	Ototoxicity (subclinincal hearing loss: 11%, clinical loss: 3%)
Paraplatin-AQ	Carboplatin	treatment of ovarian cancer	Ototoxicity (1%)
Zyrtec	Certirizine	perennial & seasonal allergy relief	Ototoxicity (<2%)
Platinol-AQ	Cisplatin	cancer treatment	Ototoxicity (10-30%)
Aczone	Dapsone	antibiotic	tinnitus
Depakote, Depakote ER, Depakote Sprinkles, Depakote DR	Divalproex Sodium	antipsychotic	tinnitus (1-7%), ear pain (>1-5%), deafness (>1-<5%), otitis media (>1-<5%)

Brand	Name	Indications	Ototoxicity
Taxotere	Docetaxel	cancer treatment	Ototoxicity (<1%)
Cymbalta	Duloxetine hydrochloride	antidepressant	Tinnitus (<1%)
Vasotec	Enalapril	hypertension	Ototoxicity (<1%)
Lexapro	Escitalopram oxalate	antidepressant	Ototoxicity
Allegra, Allegra ODT	Fexofenadine hydrochloride	allergies	otitis media (2-4%)
Lasix	Furosemide	edema management, hypertension	Ototoxicity with I.V. or I.M. administration
Garamycin, Genoptic, Genoptic S.O.P., Gentacidin, Gentafair, Gentak, Gentasol, Ocu-mycin	Gentamicin sulfate	aminoglycoside antibiotic	Ototoxicity; auditory & vestibular (>10%)
Advil, Motrin, A-G Profen, Addaprin, Buflex, Genpril, Haltran, I-Prin	Ibuprofen	general pain, fever, rheumatoid arthritis	Tinnitus (3-9%)
Kantrex	Kanamycin	aminoglycoside antibiotic	Ototoxicity (auditory & vestibular)
Neosporin	Neomycin and Polymycin B	topical antibiotic	Ototoxicity
Neo-Fradin	Neomycin sulfate	aminoglycoside antibiotic	Ototoxicity; auditory & vestibular (<1%)
Coly-Mycin S, Cortisporin	Neomycin, Colistin, Hydrocortisone, and Thonzonium	antibiotic/ corticosteroid	Ototoxicity; increased risk for patients with long-standing otitis media or tympanic membrane perforation

Brand	Name	Indications	Ototoxicity
Cortisporin Otic, PediOtic	Neomycin, Polymycin B, & Hydrocortisone	otic antibiotic	Ototoxicity; increased risk for patients with extended use or tympanic membrane perforation, therapy should be limited to 10 days
Onxol, Taxol	Paclitaxel	cancer treatment	Ototoxicity (<1%)
Humatin	Paromomycin	treatment of gastrointestinal infections	Ototoxicity (<1%)
	Streptomycin sulfate	aminoglycoside antibiotic	tinnitus (3%)
Cialis	Tadalafil	erectile dysfunction	sudden onset (<2%), sudden hearing loss (<2%)
AKTob, Tobi, Tobrasol, Tobrex	Tobramycin	aminoglycoside antibiotic	tinnitus (3% when inhaled)
Topamax	Topiramate	anticonvulsant	hearing decreased (1-2%), tinnitus (1-2%)
Vancocin	Vancomycin	aminoglycoside antibiotic	Ototoxicity (<1%)
Effexor, Effexor XR	Venlafaxine Hydrochloride	antidepressant	deafness (1-<5%)
Navelbine	Vinorelbine	cancer treatment	Ototoxicity (<1%)
Ambien, Ambien CR	Zolpidem tartrate	insomnia, short-term treatment	Ototoxicity (tinnitus, hearing loss) In most cases it is reversible, however, permanent damage can occur.

Infectious disease: HIV

- **Global pandemic**
- **1st reported pediatric case: 1982 (Rogers, 1988)**
- **UNAIDS (2007): globally number of children living with HIV/AIDS increased – 1.5 million in 2001 to 2.5 million in 2007**

Layton & Hao (2010) in Swanepoel & Louw:135-172

Number of children living with HIV/AIDS globally in 2005
(WHO, 2006)

Area	Number of children	% of cases
Sub-Saharan Africa	2 000 000	87.8%
Asia & Pacific	170 000	7.5%
Latin America	32 000	1.4%
North Africa & Middle East	31 000	1.4%
Caribbean	22 000	0.9%
North America & Europe	15 000	0.7%
Eastern Europe & Central Asia	6 9000	0.3%
TOTAL	2 276 900	

HIV/AIDS and ototoxicity: cause for SNHL

- **HIV treatment: ARV regimes**
  - **Zidovudine**
  - **Didanosine**
  - **Stavudine**
  - **Lamivudine**
  - **Nevirapine**
- **Opportunistic infection treatment**
  - **Antibiotics (aminoglycosides, macrolides, co-trimoxazole)**
  - **Antifungal and –viral agents**

Stearn & Swanepoel (2010) in Swanpoel & Louw:243-288

Ototoxic agents for HIV-related opportunistic infections

Agent	Examples	Opportunistic infection
Aminoglycosides	Amikacin Streptomycin	Mycobacterium tuberculosis
Macrolides	Azithromycin Clarithromycin Erythromycin	Mycobacterium avium-intercellulare complex; Toxoplasma gondii
Co-trimoxasole		
Antifungal	Amphotericin	Cryptococcus
Antiviral	Cidofovir	CMV

Newton (2006) in Stearn & Swanepoel (2010)

Cancer: A life threatening disease

- **Cancer affects millions of people world wide**
- **10 million new diagnoses annually**
- **WHO estimates 15 million by 2020**
- **12500 pediatric diagnoses annually (National Cancer Institute)**
- **After cardiovascular disease the 2nd largest cause of death**

Cancer in Africa and SA

- **More than 60% of all cancer cases occur in developing countries (International Network for Cancer Treatment and Research)**
- **Occurrence of cancer increasing**
  - **Nutrition**
  - **Public health issues**
  - **HIV/AIDS risk factor**
  - **Poor infection control**

Ototoxic chemotherapies: Antineoplastic agents*

- **In some cases life-threatening diseases need to be treated with powerful medication**
- **Cisplatin (most common agent used today)**
- **Carboplatin (2nd generation, less toxic)**
- **Nitrogen mustard**
- **Bleomycin**
- **Dactinomycin**
- **Vincristine**

***All have ototoxic potentail, especially when given in combination**

Use of Antineoplastic agents in treating cancers

- **Bone**
- **Connective tissue and muscles**
- **Brain and nerve tissues**
- **Head and neck**
- **Lungs**
- **Eyes**
- **Kidneys**
- **Adrenal glands**
- **Lymph tissues**
- **Liver**
- **Reproductive organ tissues**

Source: CureSearch, National Childhood Cancer Foundation & Children's Oncology Group, 2008; Mayo Clinic, 2008.

Auditory characteristics of ototoxicity

- **Bilateral and often symmetrical SNHL**
- **Starts above 8000Hz, but may later spread to frequencies important for understanding conversational speech**
- **May occur soon after first dose and may continue several months after final dose**
- **Parents should recognize early signs/symptoms**

Early recognition of childhood ototoxicity

- **Difficulty communicating needs**
- **Ask for repetition**
- **Covers ears**
- **Change in speech/language development**
- **Difficulty hearing in a group eg. small play group, hearing teacher in class**
- **Put TV louder**
- **Have more difficulty hearing female voices than male voices**
- **Inattentive and problems in school**

Early recognition of childhood ototoxicity

The "Pediatric Assessment of Hearing" questionnaire is developed by Jamie M. Baum (2008) as a *tool* to both screen and counsel for a high frequency sensorineural hearing loss (characteristic of ototoxicity)

See handout

Consequences of ototoxicity

- **Difficulty hearing/discriminating high frequency speech sounds (s, f, th, k, p, h, sh, ch).**
- **Difficulty hearing speech over distance and in noise.**
- **Difficulty hearing morphological markers of speech (plurals, tense).**
- **Delay in speech and language development in young children.**
- **Increased risk for difficulty in school.**
- **Auditory processing difficulties**

Stelmachowicz et al, Archives Otolaryngology Head & Neck Surgery, 2004.

Managing ototoxicity: early detection and intervention

*"**Ototoxic hearing loss, particularly in the pediatric population, may be tolerated in favor of survival"***

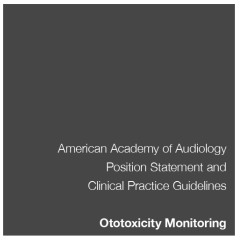
Konrad-Martin et al. (2005) ASHA Leader, 1-14

Managing ototoxicity: early detection and intervention

Yes, but…

Undetected and/or uncorrected hearing loss in early childhood can interfere with children's normal speech and language development

Ototoxicity monitoring



Ototoxicity monitoring

Main purposes:

- **Early detection of changes in hearing**
- **Early intervention when hearing loss has occurred**

Ototoxicity monitoring: suggested procedures

- **Tympanometry**
- **Pure tone audiometry**
  - **VRA (6-30 months)**
  - **play audiometry (24 months–6 years)**
- **DPOAE's (ototoxicity protocol – up to 10kHz)**
- **Extended high frequency audiometry (above 8kHz)**
- **ABR and HF ABR (sedation contra-indicated with other meds)**

Ototoxicity monitoring: challenges

- **Cooperation, attention, poor response reliability when child is ill**
- **Difficulty measuring HF audiometry in children younger than 5 years**
- **Middle ear pathology (immune compromised)**
- **Need for sedation to measure threshold ABR's (sedation may be contra-indicated)**
- **Need for quiet child when measuring DPOAE's.**

Early detection

- **Counseling / education of family of possibility of ototoxicity and consequences**
- **Why monitor? Inform treating physician of hearing changes to**
  - **Alternative Rx protocol**
  - **Reduce Rx dose**
  - **Change time of dosage schedule**
  - **Allow time for ear to "rest"**

Early intervention

Purposes:

- **Maintain effective communication**
- **Speech and language development**
- **Social-emotional development**
- **Academic success**

Management of hearing loss

- **Hearing aids**
- **Cochlear implants**
- **Assistive listening devices**
- **Educational and school support**
- **Parental/family support prior, during and beyond final treatment**

Conclusion

- **Survival rates for childhood cancers are improving**
- **Children under age 5 are 21x more susceptible to ototoxic hearing loss**
- **Priority is disease, but permanent hearing loss can be a traumatic discovery for family**
- **Early detection and intervention through monitoring may prepare family and help set realistic expectations**

QUESTIONS?

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