

**THE COMBINED EFFECT OF NOISE AND
AMINOGLYCOSIDE ANTIBIOTIC
EXPOSURE ON THE AUDITORY SYSTEM
OF THE FULL-TERM INFANT**

Thesis

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Hala Zaki

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

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List of Abbreviations

Abb.	Full term
aABR	Automated Auditory Brain stem Response
ABR	Auditory brain stem response
AIDS	Acquired Immune Deficiency Syndrome
AR	Autosomal Recessive
AUC	Area Under Curve
BAER	Brainstem Auditory Evoked Response
CF	Cystic Fibrosis
CFTR	Cystic Fibrosis Transmembrane conductance Regulator
CHL	Conductive Hearing Loss
CMV	Cytomegalovirus
CN	Cranial Nerve
dB	Decibels
DFN	Indicates X-linked loci
DFNA	Indicates autosomal dominant gene loci
DFNB	Indicates autosomal recessive loci
DNA	Deoxyribonucleic Acid
DPOAE	Distortion Product Otoacoustic Emission
EHDI	Early Hearing Detection and Intervention
EP	Endolymphatic Potential
EPA	Environmental Protection Agency
HIV	Human Immune deficiency Virus
HL	Hearing loss
HPCSA	Health Professions Context of South Africa
HRR	High Risk Register
Hz	Hertz (The number of cycles per second)
JCIH	Joint Committee on Infant Hearing
LBW	Low Birth Weight (<2.5 kg)
NASA	National Aeronautics and Space Administration
NF2	Neurofibromatosis type 2
nHL	non Hearing loss

List of Abbreviations (Cont...)

Abb.	Full term
NICU.....:	Neonatal Intensive Care Unit
NITS.....:	Noise-Induced Threshold Shift
NPV.....:	Negative Predictive Value
OAEs.....:	Otoacoustic emissions
OM.....:	Otitis Media
OME.....:	Otitis Media with Effusion
OSHA.....:	Occupational Safety & Health Administration
Pa.....:	Pascal (level sonorous pressure)
PCV.....:	Pneumococcal Conjugate Vaccine
PK.....:	Pharmako Kientics
PPV.....:	Positive Predictive Value
RNA.....:	Riponucleotide Acid
ROS.....:	Reactive Oxygen Species
RP.....:	Retinitis Pigmentosa
rRNA.....:	Ribosomal Riponucleotide Acid
SABR.....:	Screening Auditory Brainstem Response
SNHL.....:	SensoriNeural Hearing Loss
TEOAE.....:	Transient Evoked Otoacoustic Emission
TM.....:	Tympanic Membrane
TORCH.....:	Toxoplasmosis, Rubella, Cytomegalovirus and Herpes
tRNA.....:	Transfer Riponucleotide Acid
UNHS.....:	Universal Neonatal Hearing Screening
WHO.....:	World Health Organization

INTRODUCTION

Acoustic exposure to high intensity noise causes temporary or permanent threshold shifts in auditory perception, reflected by reversible or irreversible damage in the cochlea. Exposure to damaging levels of sound occurs in two major forms. Firstly, impulse noise that produce high intensity sound that physically damage hair cell stereocilia and produces discrete lesions in the sensory epithelia of the cochlea. Secondly, long-term exposure to lower (but still high) intensity noise generates high levels of reactive oxygen species (ROS), coupled with physiological changes in the blood-labyrinth barrier that result in temporary auditory dysfunction and often permanent hearing loss. Noise also induces a variety of cochlear pathologies, ranging from physical disruption of hair cell stereocilia and organ of Corti integrity to increased endocytosis, vacuolation, mitochondrial lesions, elevation of intracellular calcium concentrations and the generation of reactive oxygen species. These phenomena can lead to apoptotic and/or necrotic cell death processes that may continue for up to 30 days after exposure (*Henderson, 2006*).

Aminoglycosides are antibiotics that are highly effective in treating life-threatening gram negative bacterial infections, such as neonatal sepsis. However, aminoglycosides also induce cytotoxicity in the cochlea. Commonly-used aminoglycosides in the neonatal intensive care unit (NICU) include amikacin,

garamycin, gentamicin, and tobramycin. They are administered in doses based on body weight and their toxicity is dose-related, therefore newborns that receive sufficiently high doses of aminoglycosides experience both functional and/or morphological damage in the cochlea. Aminoglycoside-induced hair cell death processes may continue for up to 4 weeks after cessation of drug administration (*Forge, 2000*).

Many other known ototoxins, such as loop diuretics and noise, can synergistically interact with aminoglycosides and damage the cochlea, when either insult alone appears harmless (*Forge, 2000*). Combined noise and aminoglycoside exposure, particularly in NICU, can lead to auditory threshold shifts greater than simple summation of the two insults. The synergistic toxicity of acoustic exposure and aminoglycoside antibiotics is not limited to simultaneous exposures. Prior acoustic insult which does not result in permanent threshold shifts potentiates aminoglycoside ototoxicity. In addition, exposure to sub-damaging doses of aminoglycosides aggravates noise-induced cochlear damage (*Ward, 2002*).

AIM OF THE WORK

This study aimed to examine the impact of aminoglycosides antibiotics and/or noise exposure on neonatal hearing screening outcome.

HEARING LOSS

Unidentified hearing loss at birth can adversely affect speech and language development as well as academic achievement and social-emotional development (*Kibby et al., 2009*).

Historically, moderate-to-severe hearing loss in young children was not detected until well beyond the neonatal period, and it was not unusual for diagnosis of milder hearing loss and unilateral hearing loss to be delayed until children reached school age (*Lima et al., 2006*).

In its 2007 position statement, the Joint Committee on Infant Hearing (JCIH) endorsed the goal of universal detection of infants with hearing loss and encouraged continuing research and development to improve methods for identification of and intervention for hearing loss (*JCIH, 2007*).

The goal of early hearing detection and intervention (EHDI) is to maximize linguistic competence and literacy development for children who are deaf or hard of hearing. Without appropriate opportunities to learn language, these children will fall behind their hearing peers in communication, cognition, reading, and social-emotional development (*JCIH, 2007*).

Such delays may result in lower educational and employment levels in adulthood. To maximize the outcome for infants who are deaf or hard of hearing, the hearing of all infants should be screened at no later than 1 month of age (*JCIH, 2007*).

Those who do not pass screening should have a comprehensive audiological evaluation at no later than 3 months of age. Infants with confirmed hearing loss should receive appropriate intervention at no later than 6 months of age from health care and education professionals with expertise in hearing loss and deafness in infants and young children (*Flynn et al., 2004*).

All providers of pediatric health care need to recognize children who are at risk of hearing loss or who suffer from congenital or acquired hearing loss be prepared to screen their hearing, and assist the family and arrange for proper referral and treatment by identifying available hearing resources within their communities (*Allen and Bower, 2009*).

Regardless of previous hearing-screening outcomes, all infants with or without risk factors should receive ongoing surveillance of communicative development beginning at 2 months of age during well-child visits (*American Academy of Pediatrics, 2002*).