

**A NOVEL SCREENING PROTOCOL FOR THE DIFFERENTIATION OF
TYPE OF HEARING LOSS IN NEONATAL INTENSIVE CARE UNIT
(NICU) INFANTS**

by

Tara Pamela Millman

Honours B.Sc., Concordia University, 2008

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF
THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

in

The Faculty of Graduate Studies

(Audiology and Speech Sciences)

THE UNIVERSITY OF BRITISH COLUMBIA

(Vancouver)

July 2011

© Tara Pamela Millman, 2011

Abstract

Objective: The current screening protocol of the British Columbia Early Hearing Program for neonatal intensive care unit infants is unable to differentiate between conductive and sensorineural hearing losses at the time of detection. A critical need exists for developing standardized screening procedures for differentiating conductive, sensory, and neural loss in early infancy to provide an appropriate course of intervention and to avoid later consequences on health and the development of speech and language.

Design: The current study examined a novel protocol for the hearing screening of neonatal intensive care unit (NICU) infants that involved the measures of 1000 Hz tympanometry, transient evoked otoacoustic emissions (TEOAE), and ipsilateral broadband middle-ear muscle reflex (MEMR) at a 1 kHz probe tone frequency. The GN Otometrics Accuscreen device was used for automated auditory brainstem response (AABR) and TEOAE screening and the GN Otometrics Otoflex diagnostic immittance meter recorded 1000 Hz tympanometry and the MEMR. A total of 90 infants (180 ears) from the NICU of the Royal University Hospital in Saskatoon, Saskatchewan was recruited, of which 78 infants (143 ears) met the inclusion criteria. The participants mean chronological age was 31.38 days. The novel protocol was examined for three components: 1) if it generated equivalent results with the current two-stage AABR hearing screening protocol for NICU infants; 2) for testing length; and 3) for challenges encountered during testing.

Results: Results revealed that 70.6% of infants passed both the current AABR and novel protocols. TEOAE accounted for most of the referrals for infants who passed the current AABR screening protocol and referred on the novel protocol (70%) and for infants who referred on both protocols (83.3%).

Conclusion: The novel protocol might provide more information regarding the reason for a screening referral, including the identification of middle-ear dysfunction and the detection of mild hearing impairment.

Preface

Ethical approval for this study was obtained from the Clinical Research Ethics Board of the University of British Columbia (UBC CREB # H09-03237) and from the Biomedical Research Ethics Board of the University of Saskatchewan (Bio # 10-03).

Table of Contents

Abstract.....	ii
Preface.....	iii
Table of Contents.....	iv
List of Tables	viii
List of Figures.....	ix
List of Abbreviations	x
Acknowledgements.....	xi
CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW	1
1.1 Missing Elements of Current Hearing Screening Protocols	2
1.2 The NICU Population and Otitis Media with Effusion	5
1.3 The Need for Detection and Treatment of Otitis Media with Effusion	7
1.4 Auditory Neuropathy/Dyssynchrony and the NICU Population	10
1.5 Multi-Frequency Tympanometry.....	12
1.6 Developmental Changes to the Ear in Infancy	13
1.7 1000 Hz Tympanometry	15
1.8 Transient-Evoked Otoacoustic Emissions (TEOAE).....	19
1.9 Broadband Noise Middle-Ear Muscle Reflex (BBN MEMR).....	21
1.10 Automated Auditory Brainstem Response (AABR).....	25
1.11 Minimal and Mild Hearing Loss in Children.....	27

1.12	Noise Levels in the NICU.....	30
1.13	Efficacy of a Screening Protocol	32
1.14	Summary and Rationale for the Study	33
CHAPTER 2: METHODS.....		34
2.1	Participants.....	34
2.2	Inclusion and Exclusion Criteria.....	34
2.2.1	Inclusion Criteria	34
2.2.2	Exclusion Criteria	36
2.3	Instrumentation	38
2.4	Calibration.....	40
2.5	Survey of Background Noise in the NICU	40
2.6	Procedures.....	41
2.6.1	Consent	41
2.6.2	General Procedures	41
2.6.3	Transient-Evoked Otoacoustic Emissions (TEOAE) and Automated Auditory Brainstem Response (AABR).....	42
2.6.4	Tympanometry and Middle-Ear Muscle Reflex (MEMR)	43
2.6.5	Timing of Measures	44
2.6.6	Quantification of Tympanometry	47
2.6.7.	Reasons for Invalid TEOAE, BBN MEMR, and AABR Results	49
2.6.8	Rescreening and Follow-Up	49
CHAPTER 3: RESULTS.....		51

3.1	Normative Tympanometric Data	51
3.2	Screening Outcome	53
3.2.1	First Screening Group	56
3.2.2	Rescreened Group	60
3.2.3	Meshed Group	60
3.3	Analysis of Different Patterns in Screening Outcome	61
3.3.1	Pass Result on Both AABR Protocol and Novel Protocol	61
3.3.2	Pass Result on AABR Protocol and Refer Result on Novel Protocol	64
3.3.3	Refer Result on Both AABR and Novel Protocols	64
3.3.4	Refer Result on AABR Protocol and Pass Result on Novel Protocol	64
3.4	Length of Time for Test Administration	65
CHAPTER 4: DISCUSSION		67
4.1	Reliability of 1000 Hz Tympanograms	67
4.2	Classification of Groups	68
4.3	Screening Outcomes for Each Group	69
4.3.1	First Screening Group	69
4.3.2	Rescreened Group	76
4.3.3	Meshed Group	77
4.4	Analysis of Different Patterns in Screening Outcome	78
4.5	Challenges Encountered During the Screening Protocols	79
4.5.1	Current AABR Protocol	79
4.5.2	Novel Protocol	80

4.6	Effects of Invalid Results on Screening Protocols.....	83
4.7	Length of Time for Test Administration.....	85
4.8	Cost Effectiveness of Test Administration	87
4.9	Future Directions and Overall Conclusions	89
	REFERENCES	92
	APPENDIX A: INVITATION LETTER.....	126
	APPENDIX B: CONSENT FORM	129
	APPENDIX C: 1000 HZ TYMPANOGRAMS CLASSIFIED AS NORMAL AND INCLUDED BASED ON SHAPE OF Y AND BG CURVES THAT DID NOT MEET PRELIMINARY INCLUSION CRITERIA DUE TO SA < 0.10 MMHO.....	134

List of Tables

TABLE 1. NORMATIVE DATA FOR THE USE OF 1000 HZ TYMPANOMETRY WITH A WELL-BABY INFANT POPULATION	18
TABLE 2. CRITERIA FOR A VALID AND INVALID TEST MEASURE	35
TABLE 3. MEAN, STANDARD DEVIATION (SD), AND 90% RANGE (5TH–95TH PERCENTILE) FOR PEAK-COMPENSATED ADMITTANCE MAGNITUDE (Y_{TM} ; MMHO) OBTAINED AT A 1000 HZ PROBE-TONE FREQUENCY WITH BASELINE COMPENSATION AT +200 DA _{PA} AND FOR EQUIVALENT EAR CANAL VOLUME (V_{EA} ; CM ³) FOR NICU AND WELL-BABY NURSERIES.....	52
TABLE 4. NORMATIVE TYMPANOMETRIC VALUES FROM 1000 HZ TYMPANOGRAMS FROM 101 EARS OF 57 NICU INFANTS TESTED AT 2 -161 DAYS CHRONOLOGICAL AGE.....	54
TABLE 5. SCREENING OUTCOME FOR AABR AND NOVEL PROTOCOLS BY GROUP	58
TABLE 6. REASON FOR REFERRAL ON NOVEL PROTOCOL BY GROUP	59
TABLE 7. PATTERN OF SCREENING OUTCOME BY GROUP	62
TABLE 8. PROPORTION OF INFANTS REFERRING ON INDIVIDUAL MEASURES OF NOVEL PROTOCOL BY PATTERN OF SCREENING OUTCOME.....	63
TABLE 9. AVERAGE LENGTH OF TIME FOR INDIVIDUAL MEASURES AND FOR EACH PROTOCOL ...	66

List of Figures

FIGURE 1. SCHEMATIC DIAGRAM OF PROCEDURE DEPENDING ON SCREENING RESULT OBTAINED..	37
FIGURE 2. EXAMPLES OF TYMPANOGRAM CLASSIFICATION.....	45
FIGURE 3. CRITERION #1 FOR CLASSIFICATION OF A NORMAL TYMPANOGRAM DEMONSTRATING THE PEAK OF THE TYMPANOGRAM ABOVE AN IMAGINARY BASELINE CONNECTING THE NEGATIVE TAIL TO THE POSITIVE TAIL (BALDWIN, 2006).....	48
FIGURE 4. SCHEMATIC DIAGRAM OF PROCEDURE DEPENDING ON SCREENING RESULT OBTAINED. .	57

List of Abbreviations

AABR – Automated Auditory Brainstem Response

ABR – Auditory Brainstem Response

AN/AD – Auditory Neuropathy/Auditory Dys-synchrony

BBN MEMR – Broadband Noise Middle-Ear Muscle Reflex

BCEHP – British Columbia Early Hearing Program

ELBW – Extremely-Low Birthweight

MEMR – Middle-Ear Muscle Reflex

NICU – Neonatal Intensive Care Unit

(E)OAE – Evoked Otoacoustic Emissions

OME – Otitis Media with Effusion

PCHI – Permanent Childhood Hearing Impairment

TEOAE – Transient Evoked Otoacoustic Emissions

Acknowledgements

I would like to extend my sincerest thanks and gratitude to Dr. Navid Shahnaz for his guidance and encouragement throughout my thesis journey. His genuine enthusiasm about research was contagious and I am so grateful to have had the opportunity to work with him. Thank you to my thesis committee, Dr. Susan Small and Ms. Sharon Adelman, for your valuable and insightful feedback. A big thank you to Ms. Charlotte Douglas, my Saskatoon clinical educator, who provided invaluable support during the NICU data collection – I could not have done it without you. Thanks are also extended to Ms. Doreen Wingrove-Burke, Family Liaison Nurse at the Royal University Hospital, who helped facilitate data collection and the implementation of a new hearing screening program. I would like to thank the SASS faculty and staff who have enriched the past two years of my life. To my cherished Audi family – thanks for the endless laughter and support. Last but certainly not least, to my family – thank you for believing in me every step of the way.

CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

The human infant is thought to be born with pre-existing neural wiring that forms the “language organ”, enabling the development of speech and language (Chomsky, 1995). Auditory stimulation of these neuronal connections is critical in order for them to strengthen (Chugani, 1997). A lack of auditory stimulation from hearing loss during the first 2 or 3 years of life can place a child at a significant disadvantage in terms of their best outcome for language development (Carney, 1999). The most common causes of congenital hearing loss are hereditary in nature, which can account for 50-60% of childhood hearing losses in developed countries (Morton & Nance, 2006). Furthermore, medical histories of prematurity, pre- and post-natal infections, subarachnoid hemorrhage, head trauma, severe birth asphyxia, assisted ventilation, pharmacologic ototoxicity, and noise can also place infants and young children at risk for hearing loss (DePaul & Chambers, 1995; Hille et al., 2007; Morton & Nance, 2006). A lack of auditory stimulation due to a prelingual hearing loss can thus interfere with the normal development of speech and language (Huizing & Pollack, 1951).

In a literature review of prevalence studies, statistics have estimated that 1-3 infants per 1000 in a well-baby nursery are born with a significant bilateral hearing loss every year, increasing to 2-4 infants per 100 in the neonatal intensive care unit (NICU) (Erenberg et al., 1999). For example, Attias and colleagues (2006) found an overall congenital hearing loss prevalence rate of 0.5% among 8400 Israeli infants. In addition, they noted a prevalence rate of 1.37% among 8251 Jordanian infants. Hille and colleagues (2007) found a prevalence rate for hearing loss of 3.2% among 2186 high-risk NICU infants, whereas Prieve et al. (2000) found prevalence rates for mild or greater hearing impairment in any ear of 1.2 per 1000 live births in

the well-baby nursery and 11.2 per 1000 live births in the NICU. Similarly, Vohr and colleagues (1998) noted hearing losses for every 1.27 per 1000 infants in the well-baby nursery and 9.8 per 1000 infants in the NICU. In addition, 5 infants in every 1000 have been estimated to have lesser degrees of hearing loss (McMurray, 2000). Fortnum and colleagues (2001) found that the prevalence of confirmed permanent childhood hearing impairment increases until the age of 9 years, from 0.91 for three-year-olds to 1.65 for children aged 9-16 years. This research suggests that hearing loss is the most common congenital birth defect (Low, Pang, Ho, Lim, & Joseph, 2005).

The goal of the newborn hearing screening program is the early detection and treatment of hearing loss in children (Joint Committee on Infant Hearing (JCIH), 2007). Successful screening programs ultimately avoid delayed speech and language development, academic difficulties and social and emotional problems that might become apparent at a later age (JCIH, 2007). The Joint Committee on Infant Hearing (JCIH, 2007) recommends that infants are screened no later than 1 month of age, with required follow up including a complete audiological evaluation occurring no later than 3 months of age, and appropriate intervention for confirmed hearing loss implemented by 6 months of age. A critical finding from a study by Yoshinaga-Itano (2003) indicated that infants with hearing loss who received intervention by six months of age had language skills and socio-emotional development that were appropriate for their physical development; this finding was not seen among infants with a hearing loss that was detected after six months of age (Yoshinaga-Itano, 2003).

1.1 Missing Elements of Current Hearing Screening Protocols

Current hearing screening protocols must identify infants with and without hearing loss with a high degree of accuracy and in an efficient and cost-effective manner. The most common

target disorder for screening protocols is congenital permanent childhood hearing impairment (PCHI), which can be bilateral or unilateral (Hyde, 2005; JCIH, 2007). PCHI is a disorder originating in the inner ear or neural pathway to higher cortical areas, i.e., of “sensorineural” origin, or it may involve a structural issue in the external or middle ear that causes a conductive impairment (Hyde, 2005). Current screening protocols for well-baby nurseries in Canada, including the British Columbia Early Hearing Program (BCEHP) involve the measures of evoked otoacoustic emissions (OAE) and automated auditory brainstem response (AABR). The first stage of the current BCEHP protocol for well babies involves the OAE; if infants pass this measure and do not have any risk factors for progressive or late-onset hearing loss, they pass and exit the screening program (BC Early Hearing Program, 2008). If infants obtain a refer result on the first stage of OAE, they proceed to the second stage of the screening, the AABR (BC Early Hearing Program, 2008). As a unit, these measures are sensitive to middle ear, cochlear, and neural status and are non-invasive and objective (Shahnaz, Miranda, & Polka, 2008). Furthermore, they provide ear-specific information in infants who are typically difficult to test behaviourally (Shahnaz, Miranda, & Polka, 2008).

The current BCEHP screening protocol for NICU infants differs in that it involves a two-stage AABR in which the infant must refer on the first AABR to receive the second (BC Early Hearing Program, 2008). The purpose of the two-stage AABR/AABR instead of the two-stage OAE/AABR protocol used in well-baby nurseries is to identify auditory neuropathy/dyssynchrony (AN/AD) among NICU infants who are at increased risk of developing AN/AD (Starr, Picton, Sininger, et al., 1996). AN/AD is usually characterized by normal OAEs, absent or abnormal auditory brainstem response (ABR) and middle-ear muscle reflexes (MEMR), and a normal tympanogram with variable pure-tone sensitivities ranging from

normal to profound; hence, it cannot be detected by OAE alone and requires the use of AABR (Berlin, Hood, Morlet, et al., 2005; Hood & Berlin, 2001).

A critical factor that both well-baby and NICU protocols are missing is that they are unable to differentiate between conductive and sensorineural hearing losses at the time of detection (Hunter & Margolis, 1992). Although both AABR and OAE screening devices can detect hearing loss of cochlear origin, both can be affected by a dysfunction in the outer or middle ear that could be of a transient or permanent nature (Norton et al., 2000; Zhao et al., 2000). Therefore, both AABR and OAE screening devices might provide a “refer” result following a screening despite normal cochlear and neural function in the presence of a conductive problem. Consequently, they are insensitive to the source of the screening failure (Doyle et al., 1997; 2000). Middle-ear dysfunction can confound the interpretation of test results of current screening protocols.

The identification of type of hearing loss might only occur when audiological assessments are performed at an age of 3 or 6 months, at which time the infant is at risk for negative consequences on their health and on the development of their speech and language. Although utilized following a screening for audiological follow-up, the use of behavioural tests such as behavioural observation audiometry (BOA) has been shown to be ineffective due to poor sensitivity, specificity, and reliability, and is therefore inappropriate for the screening of newborn infants (Durieux-Smith et al., 1985; Gravel, 2000). There is a critical need for developing standardized screening procedures for differentiating conductive, sensory, and neural loss in early infancy with the use of physiologic measures in order to provide an appropriate course of medical and audiological intervention (JCIH, 2007). By focusing on the cause of an identified hearing loss versus simply its detection, additional benefits of implementing a hearing screening

program can be reaped (Schimmenti, Martinez, Fox, et al., 2004). Such benefits might include disease prevention, improved therapy, improved interpretation of the results of early intervention, and psychological benefits of understanding the true etiology of a hearing loss (Schimmenti, Martinez, Fox, et al., 2004).

1.2 The NICU Population and Otitis Media with Effusion

An important characteristic that is lacking in current screening protocols is their ability to identify the presence of otitis media with effusion (OME) in neonates. Otitis media is the most common cause of conductive hearing loss in children, being the most common infectious disease of childhood (Uhari, Mäntysaari, & Niemelä, 1996). During their first year of life, more than 50% of children will experience OME – a value that increases to more than 60% by two years of age (Stool et al., 1994; Tos, 1984). For most children, OME has been shown to resolve spontaneously within three months (The Otitis Media Guideline Panel, 1994). Although often transient in nature, OME that is not resolved in children can place them at developmental risk (The Otitis Media Guideline Panel, 1994). Specifically, these children are at high risk for persistent or fluctuant mild-to-moderate hearing loss (Hanks, Adamovich, & Buethe, 2009). Almost all children will experience a period of temporary hearing loss associated with otitis media during the period from birth to 10 years of age (DeLuzio, 2003). The incidence of OME within the first two months of life has been reported to be 33%, and its prevalence has been shown to be 20 per 1000 births (Maxon et al., 1993; Rosenfeld et al., 2004). Furthermore, Roland and colleagues (1989) found that 73.5% of their sample of 483 normal infants had at least one episode of OME between the ages of 6 and 18 months.

Infants in the neonatal intensive care unit (NICU) are of specific interest due to their greater risk for hearing loss, with at least 1 in 174 infants demonstrating a significant hearing

loss (Davis & Wood, 1992). Eavey et al. (1995) reported a prevalence of sensorineural hearing loss in NICU graduates of up to 50 times higher than in normal neonates, while Davis, Bamford, Wilson, Ramkalawan, Forshaw and Wright (1997) found a prevalence for sensorineural hearing loss of 4.4 -7.1 times greater than healthy newborns. Furthermore, NICU infants are at greater risk for developing late-onset or progressive hearing losses (Eavey et al., 1995).

NICU infants might also exhibit a greater susceptibility to otitis media. Among infants in the neonatal intensive care unit (NICU), Berman, Balkany and Simmons (1978) found that 30.5% of the 125 infants they examined had OME. Interestingly, they also found that the duration of nasotracheal intubation that the infants received was correlated with abnormal movement of the tympanic membrane, visualized through pneumatic otoscopy, which is indicative of otitis media. Engel and colleagues (2001) found that NICU infants who were treated with nasal ventilatory tubes appeared to have a 3-4 times greater risk of developing OME than NICU infants who did not require intubation. Intubation might cause mucosal damage in the nasopharynx, which may lead to inflammation around the eustachian tube and hence dysfunction, causing an infant to become more susceptible to OME (Engel et al., 2001). In addition, the higher incidence of OME among premature NICU infants might be related to an immature immune system (Engel, Anteunis, Hendriks, & Marres, 1996). Furthermore, neuromotor impairment has been demonstrated to be associated with a slight increased risk of OME (Engel et al., 2001). Specifically, impairment due to either psychomotor retardation or cerebral palsy may be associated with eustachian tube dysfunction due to related swallowing difficulties (Engel et al., 2001). Interestingly, among their sample of 117 preterm and 29 full-term infants, Wallace, Gravel, McCarton, and Ruben (1996) did not find that premature very-low birth weight infants had an increased risk of developing OME in comparison with healthy

full-term infants. The authors attributed this finding to the use of intubation and oral tubes for feeding instead of nasotracheal tubes. Furthermore, all preterm infants had received antibiotics, regardless of a confirmed episode of sepsis, which might have influenced susceptibility to OME during the infant's stay in the NICU and in the months following discharge (Wallace et al., 1996). However, it is important to highlight the unequal sample size between the two groups of infants, which may have influenced the results.

1.3 The Need for Detection and Treatment of Otitis Media with Effusion

Due to the fact that OME can be recurrent, middle-ear effusion in newborns can continue to attenuate the signal being delivered to their cochlea; in other words, without proper diagnosis and management, these infants can acquire a long-term hearing loss that varies in severity over time (Maxon et al., 1993). Fluid in the middle ear due to OME can decrease mobility of the tympanic membrane and ossicles, creating a mild-to-moderate hearing loss (Alaerts, Luts, & Wouters, 2007). The degree and configuration of an infant's hearing loss can be influenced by the amount and viscosity of the fluid in the infant's ears at a certain time point (Gravel & Wallace, 2000). Gravel and Rubin (1996) suggest that the temporary conductive hearing loss often seen in children with OME is a form of auditory deprivation, which can be detrimental to their speech and language development. Children with untreated conductive hearing loss experience fluctuating changes in their hearing and hence receive inconsistent or conflicting information about language, thus interfering with the acquisition of oral language (Friel-Patti, Finitzo, Meyerhoff, & Hieber, 1986).

Extensive research has demonstrated negative consequences of untreated conductive hearing loss secondary to otitis media (e.g., Luotonen et al., 1996; Petinou, Schwartz, Gravel, & Raphael, 2001; Rach et al., 1988; Roland et al., 1989, Sak & Ruben, 1982; Winskel, 2006).

Luotonen and colleagues (1996) found that at age nine, students who had more than four episodes of OME during their first three years of life had impaired linguistic competence; specifically, they were among the poorest readers. Similarly, Petinou and colleagues (2001) found that children with a history of OME had poorer speech perception skills at two years of age, and suggested that these deficits in perception were the result of auditory deprivation during an infant's first year of life. Having a history of OME has also been seen to have a negative effect on expressive language skills, verbal ability, auditory decoding, spelling skills, phonological awareness, and reading fluency and comprehension (Rach et al., 1988; Sak & Ruben, 1982; Winskel, 2006).

Furthermore, children with chronic histories of otitis media have been shown to have hearing loss at extended high frequencies (Ahonen & McDermott, 1984; Hunter, Margolis, Rykken, Le, Daly, & Giebink, 1996; Lopponen, Sorri, Pekkala, & Penna, 1992; Margolis, Saly, & Hunter, 2000; McDermott, Fausti, & Frey, 1986). The definition of extended high frequencies are those above 8000 Hz, whereas conventional frequencies, tested during routine audiometric evaluations, involve the measurement of thresholds between 250 and 8000 Hz (Filipo, De Seta, & Bertoli, 1988). Margolis et al. (2000) compared a group of children with a history of OME with a control group of children with no history of OME. While both groups had very similar audiometric thresholds at conventional frequencies, the group with a history of OME had significantly poorer thresholds at extended high frequencies than the control group (Margolis et al., 2000). Hearing loss at extended high frequencies has been proposed to be due to a mechanism in which certain toxins related to otitis media are transmitted through the round window membrane, resulting in damage at the base of the cochlea (Margolis, Saly, & Hunter,

2000). This mechanism has been demonstrated in studies of human temporal bones and in animal models (see Hunter et al., 1996, for a review).

There exists a belief that extended high frequencies are less important than conventional frequencies in the perception of speech (Filipo, De Seta, & Bertoli, 1988). However, recent research on psychoacoustic effects of extended high frequencies suggests otherwise. Extended high frequencies are important in the perception of sound quality, music quality, speech, loudness, and spatial awareness (e.g. Moore & Tan, 2003; Pittman, 2008; Ricketts, Dittberner, & Johnson, 2008; Soeta & Nakagawa, 2008; Stelmachowitz, Lewis, Choi, & Hoover, 2007).

The aforementioned studies have shown that a history of chronic OME can result in extended high-frequency hearing loss, which could potentially lead to a negative psychoacoustic impact on speech perception. Research has demonstrated that infants who experience their first episode of OME before the age of two months might be more prone to developing bilateral chronic OME (Marchant et al., 1984; Teele, Klein, & Rosner, 1980). A recent study by Doyle and colleagues (2004) found that infants who have OME 30 to 48 hours after birth are at greater risk for developing chronic OME at a later age than newborns born without OME. Furthermore, the Joint Committee on Infant Hearing 1994 Position Statement specified recurrent or persistent OME for at least three months as a risk factor associated with conductive hearing loss for infants aged 29 days to three years (JCIH, 1994).

These studies highlight the need for early detection and treatment of OME. However, Marchant et al. (1984) found that 46% of infants in their study had an initial episode of OME that was asymptomatic; i.e., with the absence of fever, irritability, and otorrhea. Despite the gold standard for the detection of OME being the finding or absence of visible fluid in myringotomy, it is only justified for use in older infants with recurrent or prolonged (more than three months)

OME (Marchant et al., 1984). Therefore, OME likely goes undetected until infants are examined by their physician for an acute respiratory tract infection, which has similar symptoms as acute otitis media (Kontiokari, Niemela, & Uhari, 1998; Niemela, Uhari, Jounio-Ervasti, Luotonen, Alho, & Vierimaa, 1994). Similarly, Marchant and colleagues (1984) noted that if otoscopic examinations were not performed by physicians, chronic OME would go undetected.

Given this high prevalence of outer or middle-ear dysfunction among NICU infants, a transient dysfunction could result in a “refer” screening result despite normal cochlear and neural function (Doyle, Burggraaff, Fujikawa, Kim, & MacArthur, 1997). Research has demonstrated that middle-ear disease seems to play a role in the amount of screening failures in newborn hearing screening programs (Kenworthy, 1990; McKinley et al., 1997; Rhodes et al., 1999; Sutton et al., 1996). Kenworthy (1990) demonstrated that more than half of newborns with OME failed on their initial hearing screening, yet passed on re-test. It is important for a successful screening program to minimize the number of false positives in order to avoid unnecessary testing, parental stress, and associated costs. As the status of the external and middle ear can influence false positive screening outcomes, measures that can identify middle-ear dysfunction are warranted (Margolis, 2002). However, despite a common occurrence of OME, the current NICU protocol involves a two-stage AABR, which is susceptible to middle-ear status and more importantly, cannot differentiate between the status of the middle and inner ear (Norton, Gorga, Widen, Folsom, Sininger, Cone-Wesson, et al., 2000).

1.4 Auditory Neuropathy/Dyssynchrony and the NICU Population

The two-stage AABR is implemented due to a high rate of auditory neuropathy/dyssynchrony (AN/AD) in the NICU population, which has been shown to be present in 10% of infants with permanent hearing loss, many of whom are graduates of NICU nurseries (Starr,

Picton, Sininger, et al., 1996). Dowley and colleagues (2009) found an annual AN/AD incidence of 0.27 per 1000 neonates, all of whom had been admitted to NICUs. The authors noted that this result suggests that neonatal illness from complications of preterm delivery might play a causative role for the development of auditory neuropathy. Such preterm complications included respiratory failure requiring mechanical ventilation, hypoxia, sepsis, hyperbilirubinemia, and intracranial haemorrhage (Dowley et al., 2009). Furthermore, the four risk factors that were most common among the NICU population included ototoxic medications, very low birth weight, assisted ventilation for longer than 5 days, and low APGAR scores at 1 or 5 minutes (Dowley et al., 2009). Similarly, Rea and Gibson (2003) found that more than 40% of NICU infants may demonstrate audiological result patterns of AN/AD, likely caused by hypoxia. Previous research has found that loss of inner hair cells is associated with hyperbilirubinemia and ototoxic medication (Harrison, 1998; Salvi, Wang, Ding, Stecker, & Arnold, 1999). This can result in the absence of an ABR response and MEMR with the presence of OAEs.

In a study of infants admitted to the NICU over a five-year period, Xoinis and colleagues (2007) found that 2.1% of the 4250 infants screened developed hearing loss. Of this 2.1%, 25.3% displayed electrophysiological test results of having AN/AD. Interestingly, two-thirds (62.5%) of infants with test results suggestive of AN/AD were of extremely-low birth weight (ELBW, < 1000g). These results suggest that ELBW infants might be at greater risk for AN/AD (Xoinis et al., 2007). Furthermore, infants in NICU with AN/AD who are not identified early are at high risk for negative consequences on their language and cognitive development (Xoinis et al., 2007), further emphasizing a critical need for the identification of AN/AD in this population.

1.5 Multi-Frequency Tympanometry

The current well-baby screening protocol of OAE and AABR has been shown to have a refer rate of 2 to 5%, possibly as a result of certain referral cases being due to transient or permanent middle-ear dysfunction which can lead to a conductive hearing loss (Thomson, 1997; Sininger et al., 2000). Watkin and Baldwin (1999) examined infants who had returned for a follow-up diagnostic assessment of ABR following a refer result on a two-stage OAE screening and found that 77% of those who had elevated ABR thresholds were found to have a transient conductive hearing loss. Furthermore, while the median age for ABR follow-up was 9 or 10 weeks of age, there was a delay of several months before the type of hearing loss was identified, with an average of 26 weeks being necessary to determine the absence of a permanent congenital hearing loss (Watkin & Baldwin, 1999). This study highlights the need for a screening protocol capable of differentiating between conductive and sensorineural hearing loss.

A measure that can aid in the differentiation of conductive and sensorineural hearing loss is multi-frequency tympanometry (MFT). Tympanometry is a method of assessing the status of the middle ear, including compliance of the tympanic membrane and estimation of middle-ear pressure (Paradise, Smith, & Bluestone, 1976). It involves a measurement of acoustic energy transferred into the middle ear, while the air pressure in the ear canal is varied (Kei et al., 2007). These results are plotted on a tympanogram which demonstrates the change in acoustic admittance against ear canal pressure (Kei et al., 2007).

Standard tympanometry with the use of a low-frequency probe-tone of 220 or 226 Hz was first used with infants under 6 months of age in 1973 (Keith, 1973). Conventional tympanometry using a 226 Hz probe-tone has been previously shown to be effective in identifying middle-ear dysfunction in preschool and school-aged children (Nozza et al., 1992,

1994). In England, current hearing screening protocols involve the use of the click-ABR and tympanometry using a 226 Hz probe-tone (Baldwin, 2006). However, certain physiological differences exist between adult and infant middle ears which warrant the use of a different probe-tone frequency when obtaining tympanometric measures (Margolis & Hunter, 2000; Sprague, Wiley, & Goldstein, 1985; Shahnaz et al., 2008).

Acoustic properties of infant ear canal and middle ear are different than those of adults due to these physiological differences; for example, the mastoid bone continues to develop after birth, with the mastoid process developing by one year of age (Kenna, 1990). Furthermore, the bony wall of the ear canal is not fully formed until 1 year of age, resulting in a greater mobility of the ear canal walls in early infancy (Eby & Nadol, 1986; Holte et al., 1991; Kenna, 1990). Hence, unlike infant ears, at low probe-tone frequencies, the adult middle ear is a stiffness-dominated system, while the middle ear of infants is mass-dominated and has a lower resonant frequency (Holte et al., 1991; Keefe and Levi, 1996; Meyer, Jardine, & Deverson, 1997; Shahnaz & Polka, 1997; Shahnaz et al., 2008). The infant's non-rigid ear canal has been proposed to play a role in the irregular shape of tympanograms obtained with a low frequency probe-tone due to a change in diameter of up to 70% as a result of pressure changes (Holte, Cavanaugh, & Margolis, 1990; Keefe, Bulen, & Arehart, 1993). However, research has demonstrated that this greater mobility of infant ear canals is not the only reason for the irregular tympanometric shapes seen with low-frequency tympanometry (Holte, Cavanaugh, & Margolis, 1990; Keefe, Bulen, & Arehart, 1993).

1.6 Developmental Changes to the Ear in Infancy

Unlike standard 226 Hz tympanograms, those obtained at 1000 Hz are able to account for physiological differences that exist between infant and adult ears (Margolis & Hunter, 2000).

These developmental effects can also influence TEOAE results in the screening of newborn infants, though for a lesser degree than tympanometry (Margolis, 2002). Unlike the inner ear, for which development is completed at birth, the outer and middle ear continue to develop during the first year of life (Margolis, 2002). Changes to the characteristics of the ear canal and middle ear that occur in the first year of life have been shown to affect the vibration of the ear canal and the input impedance of the middle ear, altering sound transmission to the cochlea (Holte et al., 1991; Keefe et al., 1993; Shahnaz et al., 2008). These changes include an increase in size of the external ear, middle-ear cavity and mastoid; resorption of mesenchyme; pneumatization of the middle ear and mastoid; change in the position of the eardrum; decrease in overall mass of the middle ear resulting from changes in bone density and loss of amniotic fluid in the middle ear; tightening of the joints of the middle-ear bones; development of the osseous portion of the ear canal; and the fusion of this portion of the ear canal with the tympanic ring (Anson & Donaldson, 1981; Eby & Nadol, 1986; Ikui et al., 2000; Paparella, Shea, Meyerhoff, & Goycoolea, 1980; Saunders et al., 1993).

The presence of mesenchyme, or embryonic connective tissue, in an infant's middle ear can influence impedance results, and hence tympanometric findings (Holte et al., 1991). Furthermore, it can affect the forward and backward transmission of a stimulus, hence affecting TEOAE measurement (Margolis, 2002). Although mesenchyme is resorbed following the completion of development, it has been found to be present in the temporal bones of infants (De Sa, 1973; Eavey, 1993). If mesenchyme remains in the middle ear following the completion of development, it can change vibratory patterns of the ossicular chain and tympanic membrane by filling air spaces (Eby & Nadol, 1986).

Similarly, the vibration of the tympanic membrane will also be affected by the air enclosed in the middle ear through the pneumatization of the temporal bone (Margolis, 2002). Poor pneumatization will result in a smaller volume of air with greater impedance that is in contact with the tympanic membrane, ultimately leading to less efficient forward and backward transmission of a signal (Margolis, 2002). An abnormally dense temporal bone due to poor pneumatization could result from an interruption in the pneumatization process, possibly due to a developmental defect (Margolis, 2002).

In addition, the position of the infant tympanic membrane changes from horizontal at birth to a nearly vertical position as the ear undergoes development (Eby & Nadol, 1986). This change is thought to likely affect forward and backward transmission of a stimulus (Margolis, 2002). Moreover, the bony portion of the infant ear canal has only been partially formed at birth, resulting in a more flaccid ear canal wall for infants (Anson et al., 1955). Research has been mixed on the influence of this neonatal anatomical factor on tympanometric patterns (Holte et al., 1990; Paradise et al., 1976); however it seems to have an effect on the measurement of OAEs (Margolis, 2002).

1.7 1000 Hz Tympanometry

These maturational physiological differences can alter expected patterns in standard 226 Hz tympanometry, resulting in normal or bell-shaped/notched tympanograms for infants with both healthy ears and ears with surgically confirmed OME (Marchant et al., 1986; Paradise et al., 1976; Shahnaz et al., 2008). In contrast, tympanograms obtained for a 1000 Hz probe-tone frequency have been shown to be sensitive and specific to abnormal and normal middle ear conditions in newborns (Alaerts, Luts, and Wouters, 2007; Baldwin, 2006; Kei et al., 2003; Margolis et al., 2003; Purdy & Williams, 2000; Shahnaz et al., 2008; Williams et al., 1995). In

addition, tympanometry at 1000 Hz has been shown to be a good predictor of presence or absence of OAEs, providing support for their combined use (Swanepoel et al., 2007; Kei et al., 2003; Shahnaz et al., 2008).

Previous research has examined different classification methods for 1000 Hz tympanograms (Alaerts, Luts, & Wouters, 2007; Baldwin, 2006; Calandruccio, Fitzgerald, & Prieve, 2006; Kei et al., 2003; Kei et al., 2007; Marchant et al., 1986; Margolis et al., 2003; Mazlan et al., 2007; Mazlan, Kei, & Hickson, 2009a; Mazlan, Kei, Hickson, Khan, Gavranich, & Linning, 2009b; McKinley et al., 1997; Sprague et al., 1985; Sutton et al., 1996; Swanepoel et al., 2007; Williams et al., 1995). A visual admittance classification system was utilized by Alaerts, Luts, and Wouters (2007), who obtained 1000 Hz Type 1 tympanograms in 91% of infants younger than three months of age. Type 1 tympanograms were defined as having a single peak and a tympanometric peak pressure (TPP) of 0 daPa, and was based on the Liden/Jerger classification (Alaerts, Luts, and Wouters, 2007; Jerger, 1970; Linden, 1969). Various researchers (e.g., Calandruccio, Fitzgerald, & Prieve, 2006; McKinley et al., 1997; Sprague et al., 1985) have utilized the model by Vanhuyse and colleagues (1975) which describes four patterns of immittance tympanograms that are formed according to the number of combined minima and maxima in susceptance (B) and conductance (G) tympanograms at a 660-Hz probe-tone frequency. However, McKinley and colleagues (1997) could not classify the majority of tympanograms obtained at 1000 Hz with the use of the Vanhuyse et al. (1975) model, which was originally devised for use with a probe-tone frequency of 660 Hz (Vanhuyse et al., 1975). Baldwin (2006) examined a group of infants with transient middle-ear dysfunction using a classification system modified from Marchant et al. (1986). A baseline was drawn between -400 and +200 daPa, followed by a vertical line drawn from the peak of the tympanogram to the

baseline (Baldwin, 2006). A positive peak (above the baseline) signified a normal tympanogram, while a negative peak (below the baseline) indicated an abnormal tympanogram; if both a positive and negative peak were present, the tympanogram was considered to be normal (Baldwin, 2006). As shown in Table 1, normative data for the use of 1000 Hz tympanometry with an infant population has been collected, though research in this area is still limited (Alaerts, Luts, and Wouters, 2007; Calandruccio, Fitzgerald, & Prieve, 2006; Kei et al., 2003; Margolis et al., 2003; Mazlan et al., 2007; Shahnaz et al., 2008; Swanepoel et al., 2007).

Normative data for 1000 Hz tympanometry includes the variables of ear canal volume (V_{ea}), tympanometric peak pressure (TPP), tympanometric width (TW), and peak-compensated static acoustic admittance magnitude (Y_{tm}). V_{ea} has been shown to be a better estimate of ear canal volume when calculated from the susceptance tympanogram (B) than the conductance tympanogram (G) (Shanks & Lilly, 1981). Shanks and Lilly (1981) disproved two previous assumptions about V_{ea} : that it does not change when ear canal pressure is varied, and that V_{ea} at +200 daPa is solely representative of V_{ea} (and not V_{ea} and middle-ear volume combined) due to this pressure driving the impedance of the middle-ear system to infinity. In fact, their study revealed that V_{ea} changes when ear canal pressure is varied between ± 400 daPa (Shanks & Lilly, 1981). Furthermore, the authors did not find that an ear canal pressure of +200 daPa drives the impedance of the middle-ear system to infinity (Shanks & Lilly, 1981). Therefore, V_{ea} is only an estimate of ear canal volume (Shanks & Lilly, 1981).

Y_{tm} is the most common measure of middle-ear admittance and is widely used as a screening measure of middle-ear function (American Speech-Language-Hearing Association (ASHA), 1997). The measurement of static admittance was not measured with the use of rectangular components in the current study, as there are no data showing a better clinical

Table 1. Normative Data for the Use of 1000 Hz Tympanometry with a Well-Baby Infant Population

Previous Research	Age Group	Ear	N (ears)	Y _{tm} (mmho)			TPP (daPa)			TW (daPa)			V _{ea} Y _{a+} (cm ³)		
				Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD
Kei et al., 2003	1 - 6 days	Right	106	1.16	N/A	0.58	N/A			107.6***	N/A	28.0	3.06	N/A	1.07
		Left		1.04	N/A	0.51				97.7	N/A	30.1	3.20	N/A	1.11
Margolis et al., 2003	2-4 wks	N/A	46	1.3	N/A	1	-10	N/A	68	N/A			1.4	N/A	0.4
Mazlan et al., 2007	Birth GA = 39.5 wks	N/A	42	0.78	N/A	0.40	12.46	N/A	44.76	N/A			1.07	N/A	0.44
Shahnaz et al., 2008	3 wks	Right	16	0.78	0.50	0.61	N/A			129.2	131.6	44.2	1.63*	1.60	0.44
		Left	16	0.70	0.65	0.54				142.2	133.9	37.9	1.70	1.60	0.28
		Overall	32	0.74	0.60	0.56				135.7	131.6	41	1.62	1.60	0.38
Swanepoel et al., 2007	< 1 wk	N/A	73	2.2**	N/A	0.9	-10	N/A	48	N/A			N/A		

Note. * Values for V_{ea} for the study by Shahnaz et al. (2008) were determined from the positive tail at +250 daPa.

** Uncompensated peak admittance.

*** TW in the study by Kei et al. (2003) was determined from 57 ears for the left ear value and 62 ears for the right ear value.

See text below for definitions of abbreviations.

outcome for this method; moreover, the peak compensated approach is more commonly used by clinicians in older children and adults and is easier to calculate automatically (Shahnaz et al., 2008). In the current study, the positive tail was chosen for use in calculating Y_{tm} as it has been shown to have greater test-retest reliability and lower intersubject variability among adults (Margolis & Goycoolea, 1993). Shahnaz and colleagues (2008) found no difference in mean values of Y_{tm} and TW between positive and negative tail compensation. Mean changes in infant ear canal diameter have been shown to be larger with the use of negative vs. positive pressure, likely due to ear canal collapse at a high negative pressure (Holte et al., 1990; Shahnaz et al., 2008).

As research has demonstrated that the distensible infant ear canal has an effect on the tails of tympanograms used to estimate V_{ea} in the measurement of Y_{tm} , Shahnaz and colleagues (2008) suggest the use of positive compensation. This method of using the positive tail in the calculation of static admittance is typically performed in clinics to measure Y_{tm} (Shahnaz et al., 2008). The values of tympanometric peak pressure (TPP, in daPa) and tympanometric width (TW, in daPa) are also often calculated from the 1000 Hz tympanograms.

1.8 Transient-Evoked Otoacoustic Emissions (TEOAE)

Otoacoustic emissions (OAEs) were first reported by Kemp in 1978 as a form of acoustic energy emitted by the inner ear, and produced by the active contraction of outer hair cells in the Organ of Corti as a result of normal cochlear function (Brienesse et al., 1998; Kemp, 1978; Probst, Lonsbury-Martin, & Martin, 1991). However, Gold (1948) had hypothesized about a reverse transduction process in the form of an electrical-to-mechanical conversion mechanism 30 years prior to Kemp. Evidence of active mechanical mechanisms within the cochlea was provided by the presence of these evoked sound-pressure oscillations in the external ear canal

(Probst, Lonsbury-Martin, & Martin, 1991). Named for the brief acoustic stimuli that can elicit its response, transient-evoked otoacoustic emissions (TEOAEs) can provide an objective, non-invasive screening for normal cochlear and middle-ear function in that it is very sensitive to cochlear hearing loss of 30 dB HL or more (Bonfils & Uziel, 1989; Kemp, Bray, Alexander, & Brown, 1986; Probst, Lonsbury-Martin, & Martin, 1991; Zorowka, 1993), and is also quite sensitive to mild middle-ear impairment (Koivunen et al., 2000; Naeve, Margolis, Levine, & Fournier, 1992; Owens, McCoy, Lonsbury-Martin, & Martin, 1993).

Although middle-ear effusion can affect both the forward and backward transmission of TEOAE stimulus through the middle ear, previous research has demonstrated that TEOAEs can still be present in ears with middle-ear dysfunction, and should be supplemented with 1000 Hz tympanometry in order to verify middle-ear status (Amedee, 1995; Van Cauwenberge et al., 1996; Doyle et al., 1997; Driscoll et al., 2000; Margolis, 2002; Taylor & Brooks, 2000; Zhao et al., 2000). TEOAEs have been demonstrated to accurately identify infants with moderate, severe, and profound hearing losses and have been shown to be reliably obtained in a population of infants with very low birth weights (Korres et al., 2007; Norton et al., 2000). In addition, when combined with a measure that can assess retrocochlear function, such as ABR or MEMR, TEOAEs can distinguish between a cochlear and retrocochlear hearing loss (Zorowka, 1993). Certain limitations of the TEOAE exist; in comparison with the AABR, it is more susceptible to transient conditions of the external and middle ear, and is limited to identifying cochlear pathologies that involve the outer hair cells (Norton et al., 2000). Furthermore, the TEOAE screening device tests a limited range of frequencies; therefore low- and high-frequency hearing losses might not be detected (GN Otometrics, 2010a). In addition, recording of TEOAE might be affected by the level of noise in the testing environment (Jacobson & Jacobson, 1994).

Although it can serve as a quick and simple screening measure, the use of TEOAE in hearing screening can involve referral rates of 5% to 20% when screening is performed in the first 24 hours following birth, as a result of lingering amniotic fluid, mesenchyme, or debris in the infant's outer or middle ear (Erenberg et al., 1999; Kok et al., 1992; Takahara et al., 1986). Similarly, Chang et al. (1993) found that vernix caseosa, a waxy substance that covers the skin of a neonate, may have been a cause for up to 15% of "refer" results of an OAE screening.

1.9 Broadband Noise Middle-Ear Muscle Reflex (BBN MEMR)

The middle-ear muscle reflex (MEMR) is a contraction of the stapedius muscle, located in the middle ear, which results in a change in acoustic admittance with the presentation of an intense acoustic signal (Wiley & Fowler, 1997). This change in acoustic admittance of sound results from a stiffening of the ossicular chain caused by the stapedius muscle's contraction (Wiley & Fowler, 1997). The change in acoustic admittance is measured with a small probe tip that is placed in the infant's ear canal (Wiley & Fowler, 1997). The MEMR involves the inner hair cells, eighth nerve and brain stem pathways (Berlin, Hood, Morlet, et al., 2005). It has been previously used in site-of-lesion testing to differentiate conductive, cochlear, and retrocochlear pathologies (Ferguson et al., 1996); in the estimation of hearing threshold levels (Niemeyer & Sesterhenn, 1974); and in the evaluation of facial nerve dysfunction (Citron & Adour, 1978). The MEMR can support a suspicion of a conductive hearing loss secondary to middle-ear dysfunction if the reflex is absent or obtained at an elevated intensity (Gelfand, 2009). In addition, the threshold of a MEMR, or the lowest stimulus intensity that could create a recordable change in admittance, will often remain constant with increasing sensorineural hearing loss, up to approximately 50 to 60 dB HL (Gelfand, 2009; Mazlan et al., 2009a). MEMR threshold will then become higher with further increases in magnitude of hearing loss (Gelfand,

2009). This could assist in the prediction of hearing levels in patients who are difficult to test behaviourally due to cognitive or physical factors (Silman & Gelfand, 1982).

BBN MEMR can be effectively used to screen for conductive and sensorineural hearing loss (Hirsch, Margolis, & Rykken, 1992; Plinkert, Sesterhenn, Arnold, & Zenner, 1990). With the use of a BBN stimulus, lower MEMR thresholds can be obtained than those traditionally obtained with tonal stimuli, resulting in less risk of overstimulation (Bennett & Weatherby, 1982; Keefe et al., 2009; Mazlan, Kei, & Hickson, 2009a; Niemeier & Sesterhenn, 1974). Moreover, due to its broadband spectrum, a BBN stimulus is more likely to tax the neural system due to a recruitment of more neurons (Bao, Chang, Davis, Gobeske, & Merzenich, 2003). Therefore, the use of a BBN stimulus might result in a greater detection of pathology, such as AN/AD, than pure-tone stimuli.

The ipsilateral MEMR test with the use of a 1000 Hz probe-tone at an intensity of 105 dB SPL was initially included in the American Speech-Language-Hearing Association middle-ear screening guidelines (ASHA, 1979). However, it was removed in 1990 due to research providing evidence for a high rate of false positives, with normal infant ears providing absent reflexes, leading to a high rate of over-referrals (ASHA, 1990; Gelfand, 2009; Lucker, 1980; Roush & Tait, 1985). Interestingly, Sells and colleagues (1997) found that the instrumentation being used to elicit the MEMR does not produce equivalent results. Specifically, the authors found that the “screening” mode of their middle-ear analyzer produced inconsistent results over multiple trials and differed from results obtained with the “diagnostic” mode (Sells, Hurley, Morehouse, and Douglas, 1997). Hence, the validity of an MEMR protocol appeared dependent upon the operating system used to measure and quantify the MEMR (Sells et al., 1997). For an optimal MEMR screening protocol, they recommended the use of a pulsed elicitation immittance

system involving a multiplexing circuit, with a maximum intensity level of 105 dB HL (Sells et al., 1997). The authors found that 91% of ears in their study had a MEMR at this intensity level and noted that the use a multiplexing circuit would result in a greater control of artifacts (Sells et al., 1997).

To date, neither the pure-tone nor the BBN MEMR has been widely used in protocols for the screening of newborn infants due to this controversy surrounding its use (Gelfant, 2009; Mazlan, Kei, & Hickson, 2009a). However, previous research has demonstrated the effectiveness of the pure-tone MEMR with an infant population (McMillan, Marchant, & Shurin, 1985; Weatherby & Bennett, 1980). Weatherby and Bennett (1980) found that all neonates in their study demonstrated a clear MEMR with probe-tones above 800 Hz, with the exception of 2 ears at 2000 Hz. Furthermore, McMillan and colleagues (1985) observed MEMRs in 95% of normal ears in infants 2-weeks to 12-months of age. Mazlan and colleagues (2007) found a significant increase in mean MEMR threshold among infants from birth to 6 weeks of age, possibly a result of rapid growth of the infant's auditory system during this period. Moreover, Swanepoel and colleagues (2007) found present MEMR in 94% of ears with normal 1000 Hz tympanograms. Similarly to the recording of 1000 Hz tympanometry in neonates, the use of a higher probe-tone frequency is warranted for recording MEMRs (McMillan et al., 1985; Sprague et al., 1985). Previous research has demonstrated that MEMRs are most likely to be absent at lower probe-tone frequencies due to physiological differences between infant and adult outer and middle ears (McMillan et al., 1985; Sprague et al., 1985).

Mazlan et al. (2009a) have shown that ipsilateral BBN MEMR with the use of a 1000 Hz probe-tone frequency can be reliably obtained in 100% of healthy newborns who passed AABR, and who had single peaked tympanograms with present TEOAE, making it useful as a screening

measure for hearing status in infants. Of importance, the authors found that 8.7% of a cohort of 219 infants who passed AABR had absent MEMR and that all of these infants had weak or absent TEOAE and flat tympanograms, providing support for the use of MEMR in the detection of possible middle-ear pathology when paired with AABR (Mazlan et al., 2009a). Furthermore, Mazlan and colleagues (2009a) found that BBN MEMR threshold had good test-retest reliability with the use of a broadband stimulus. Moreover, a recent study by Keefe et al. (2009) demonstrated that a BBN MEMR can be obtained with infants as young as one day of age with a clinically feasible short testing time.

BBN MEMR are also an important test in the detection of AN/AD (Starr, 1996). AN/AD is usually characterized by normal OAEs, absent or abnormal ABR and MEMR, and normal tympanograms with variable pure-tone sensitivities ranging from normal to profound; consequentially, it cannot be detected by EOAE alone and requires the use of AABR and MEMR (Berlin, Hood, Morlet, et al., 2005; Hood & Berlin, 2001; Dowley, Whitehouse, Mason, Cope, Grant, & Gibbon, 2009). The source of generation of an EOAE is the outer hair cells of the cochlea; hence it cannot provide information regarding neural status (Norton et al., 2000). EOAEs are therefore not susceptible to conditions of the auditory nerve and will generally not detect AN/AD (Morton & Nance, 2006). Conversely, both the AABR and the MEMR are sensitive to AN/AD as they are able to assess the inner hair cells (IHCs) including their afferent connections at the auditory nerve and neural pathways to the brainstem (Norton et al., 2000). However, the MEMR is more rapid and less costly than the AABR (Hirsh et al., 1992; Mazlan et al., 2009a). Furthermore, as an efferent reflex, the MEMR also provides an indication of the functioning of the efferent pathway to the stapedius muscle in the middle ear (Berlin, Hood, Morlet et al., 2005). With a dysfunction of the IHCs or auditory nerve, the MEMR is not seen at

the expected hearing level of 95 dB HL or below (Berlin, Hood, Morlet, et al., 2005; Starr, 1996). For example, Berlin, Hood, Morlet, and colleagues (2005) found that none of the 136 patients with confirmed AN/AD in their study displayed a normal pattern of MEMR thresholds at all frequencies of 500, 1000, 2000, and 4000 Hz. Taken together, this research demonstrates that the MEMR might serve as an important measure for the identification of an increased risk of neural hearing loss, such as AN/AD.

1.10 Automated Auditory Brainstem Response (AABR)

The auditory brainstem response (ABR) is the gold standard for the estimation of infant hearing sensitivities and for neonatal hearing screening (Cox, 1984; Durieux-Smith, Picton, Bernard, MacMurray, & Goodman, 1991; Galambos, Hicks, & Wilson, 1984; Joint Committee on Infant Hearing, 2007; Kenworthy, 1990). The diagnostic ABR assessment is administered following a screening referral with the use of a tone-pip stimulus that is frequency specific. Conversely, the automated auditory brainstem response (AABR) was developed for use in current screening protocols. The AABR measures electrical potentials that are generated in the auditory nerve and brainstem in response to a click stimulus through the use of three electrodes that are placed on the infant's forehead, cheek, and nape of the neck, and is recommended for use from 34 weeks gestation (Erenberg et al., 1999; Moller, Jannetta, & Moller, 1981; Moller & Jannetta, 1981, van Straaten, 1999). As it is sensitive to both internal and external noise sources, use of the AABR requires that the infant is in a quiet state; however, it is not affected by sleep, attention or sedation (Erenberg, 1999; Starr, Amlie, Martin, & Sanders, 1977). External noise sources that might interfere with AABR recording in the NICU might include electrical equipment such as IVs and monitors (Cox, 1984). Unlike the OAE, AABR is less affected by external or middle-ear debris (Erenberg, 1999). However, similarly to the OAE, AABR is

susceptible to middle-ear effusion (MEE) in neonates, and hence infants might obtain a refer result on an initial AABR screen (Kenworthy, 1990). Kenworthy (1990) suggested the use of a measure of middle-ear function in conjunction with AABR screening in order to reduce the over-referral rate as a consequence of infants who have MEE that resolves before ABR follow-up. When the AABR screening is performed within 24-48 hours after birth, the AABR has a referral rate of < 3% (Erenberg, 1999). Hyde, Riko, and Malizia (1990) found that with the use of a 30 dB nHL screening level, sensitivity of the AABR was 1.0, and specificity was 0.91. Furthermore, Hyde et al. (1990) found that the ABR was a better predictor of sensorineural hearing loss than conductive hearing loss.

Similar to the measure of the TEOAE, the AABR can serve to evaluate cochlear function. However, the AABR differs from the TEOAE in that it is more labour-intensive, takes longer, and is more costly due to the involvement of more equipment (Gorga & Neely, 2003; White et al., 1994). Although both AABR and OAE screening devices require disposable materials including probe tips and electrodes which are “single-use” for infection control, AABR electrodes range from \$4-8 per set, versus \$1-2 for OAE probe tips (Gorga & Neely, 2003; Norton et al., 2000). Norton and colleagues (2000) note that due to electrode application, AABR usually requires more time than the OAE; Barsky-Firkser and Sun (1997) determined a mean testing time of 9.0 minutes, while Norton and colleagues (2000) determined a mean testing time of 2.05 minutes per ear for OAE screening. Furthermore, Barsky-Firkser and Sun (1997) found AABR cost to be \$29.95 per infant, versus \$25.00 per infant for OAE (Johnson, Mauk, Takekawa, Simon, Sia, & Blackwell, 1993). In addition, the OAE is more sensitive to conductive hearing loss than the ABR (Doyle et al., 2000; Smurzynski et al., 1992). However,

similar to TEOAE, the AABR is unable to differentiate between conductive and mild sensorineural hearing loss (Naeve et al., 1992, Hunter & Margolis, 1992, Zhao et al., 2000).

For the differentiation of conductive and sensorineural hearing loss, the diagnostic ABR, involving the comparison of air- and bone-conduction, has been shown to be an effective measure (Stapells, 2000). However, if air-conduction thresholds were within the normal range (≤ 30 dBnHL), diagnostic ABR would not identify the presence of a conductive component as bone conduction ABR would not be performed (BC Early Hearing Program, 2008). Diagnostic ABR requires the tester to have a greater level of skill and expertise than what is necessary for the AABR screening, and involves a greater amount of analysis time, resulting in a more expensive measure that is not suitable for screening (Shahnaz et al., 2008).

Current neonatal screening protocols present a click stimulus level of 35 dBnHL for the AABR (Johnson et al., 2005). However, the notation of “dB nHL” indicates a level that is referenced to the adult ear, and does not imply that a hearing loss of 35 dB HL or greater will be detected in the infant (Hyde, 2005; Johnson et al., 2005). The actual sound pressure level that is being delivered to the tympanic membrane will vary among infants, depending on the physical volume of the closed ear canal (Stevens et al., 2004). Therefore, in reality, the specific hearing level of 35 dBnHL might be higher for an individual infant; this can increase the possibility of missing a mild hearing loss if the infant passes the AABR (Johnson et al., 2005).

1.11 Minimal and Mild Hearing Loss in Children

An awareness of minimal hearing loss, defined as a pure-tone average (PTA) ≥ 15 and ≤ 25 dB HL has existed since the 1980s, when researchers began to document its negative effect on child development (Bess & Tharpe, 1986; Tharpe, 2010). The term of a “minimal” hearing loss

continues to be controversial today, as it suggests that this degree of loss is inconsequential (Bess, 2004).

However, minimal and mild hearing loss (defined as a PTA ≥ 25 and ≤ 40 dB HL) has been shown to affect child development and school performance (Bess, Dodd-Murphy, & Parker, 1998; Holstrum et al., 2008). Children with minimal to mild hearing loss have been found to experience more difficulty than normal hearing children on educational and functional test measures (Bess, Dodd-Murphy, & Parker, 1998). Specifically, they have been found to have poorer scores on tests involving reading vocabulary, language mechanics, phonologic short-term memory, phonologic discrimination, word analysis, spelling, and science (Bess, Dodd-Murphy, & Parker, 1998; Blair, Peterson, & Viehweg, 1985; Davis, Elfenbein, Schum, & Bentler, 1986; Mckay et al., 2008; Most, 2004; Ross et al., 2005; Yoshinaga-Itano, Johnson, Carpenter, and Brown, 2008). Children with minimal to mild hearing loss might also have higher levels of dysfunction in a classroom setting (Bess, Dodd-Murphy, & Parker, 1998; Dodd-Murphy & Murphy, 2007; Most, 2004; Tharpe, Ricketts, & Sladen, 2004). However, research is mixed as some studies exist that show no negative academic outcomes for these children (Briscoe, Bishop, & Norbury, 2001; Norbury, Bishop, & Briscoe, 2001; Wake et al., 2006).

Despite research demonstrating the negative effects of minimal to mild hearing loss, no evidence exists to determine which children will experience unfavourable outcomes and which children will benefit from early intervention and amplification (Holstrum et al., 2008; Mckay et al., 2008). Current recommendations include decisions made on a child-by-child basis, including regular monitoring of hearing status and speech and language development and provision of resources to parents and educators (Mckay et al., 2008). Amplification might be a good option

for some children and consideration should always be made for the use of an FM system (AAA, 2003).

Due to improvements in health care, audiologists are encountering milder degrees of hearing loss than what was seen decades ago (Tharpe, 2010). Suggested etiologies for minimal and mild hearing loss include noise-related hearing impairment; increased survival rates of at-risk premature NICU infants; enlarged vestibular aqueduct syndrome; atresia or microtia; viral or bacterial causes; sudden idiopathic hearing loss; auditory neuropathy/dys-synchrony; genetic causes; and a history of otitis media, which has been speculated to involve a transmission of bacterial products through the round window, resulting in damage at the base of the cochlea (Hunter et al., 1996; Mills, 1975; Tharpe & Sladen, 2008; Walton & Hendricks-Munoz, 1991).

Current estimate of prevalence of minimal to mild hearing loss in newborns range from 0.36 to 1.3 per 1000 (Johnson et al., 2005; Watkin & Baldwin, 1999); however, this estimate varies due to differences in defining specific audiometric categories (Tharpe, 2010). This prevalence has been noted to increase with age, with 2.4 per 100 school-aged children estimated to have permanent minimal to mild bilateral hearing loss (Bess, Dodd-Murphy, & Parker, 1998).

Detection of minimal or mild hearing loss does not occur through the current protocol for newborn hearing screening, which only identifies hearing losses ≥ 35 dB HL; therefore, these degrees of hearing loss are only identified at a later age (Gravel, 2005; Tharpe, 2010). If the target degree of hearing loss in a screening program were to be lowered, this might result in a greater amount of false positives and hence a more costly program (Tharpe, 2010). As minimal or mild hearing loss is not identified in the current newborn hearing screening program, physiological and behavioural tests are used when a suspicion of hearing loss arises. However, parental suspicion is usually unlikely given a lack of obvious speech and language deficits

associated with this degree of hearing loss (Tharpe, 2010). In addition, variability exists in the methods currently used for the differentiation of minimal or mild hearing loss from normal hearing (Tharpe, 2010). Although a behavioural assessment such as visual reinforcement audiometry (VRA) with the use of insert earphones can be a reliable component in a pediatric test battery, young children with normal hearing often respond to signals at a suprathreshold level between 15-30 dB HL (Tharpe, 2010). Moreover, TEOAEs are absent for hearing loss \geq 30 dB HL; therefore, minimal to mild hearing loss might be missed with its use (Norton, 1993; Tharpe, 2010). In addition, MEMR can be present for individuals with minimal to mild hearing losses (Tharpe, 2010). Therefore, audiological uncertainty can exist regarding the identification of a minimal or mild hearing impairment.

Although there has been an increase in awareness over the past decade on the management of minimal and mild hearing loss, studies continue to demonstrate that students with this degree of hearing loss are still experiencing academic challenges (Tharpe, 2010). In order to determine the benefit and necessity of intervention, it is imperative to first accurately identify children with this degree of hearing loss. As current methods for detection involve an element of variability, research is required for the effective identification of minimal and mild hearing loss.

1.12 Noise Levels in the NICU

Previous research has examined noise levels in the NICU and its influence on neonates. High noise levels in the NICU might interfere with the efficient recording of results for a newborn hearing screening protocol, and have also been suspected of contributing to neonatal hearing impairment. Studies examining an association between high levels of noise in the NICU and sensorineural hearing loss in preterm and very-low birthweight (< 1500 grams) infants have

revealed opposing findings (Darcy, Hancock, & Ware, 2008; DePaul & Chambers, 1995; Levy, Woolston, & Browne, 2003; Zahr & Balian, 1995). Zahr and Balian (1995) noted that premature infants might be more susceptible to high noise levels in the NICU due to physiologic immaturity. Similarly, Surenthiran and colleagues (2003) suggested that NICU noise might play a causative role in sensorineural hearing loss. However, Roizen (2003) noted that no studies have been able to determine a link between NICU noise and hearing loss in neonates.

Nevertheless, the American Academy of Pediatrics (1997) reports that noise levels above 45 dBA are a concern for neonatal hearing impairment. Similarly, current guidelines in the Recommended Standards for Newborn ICU Design (White, 2007) state that overall continuous sound in any NICU must not be above an hourly loudness equivalent (Leq) sound level of 45 dBA or a maximum sound level (Lmax) (one second in duration) of 65 dBA. However, a recent study by Matook and colleagues (2010) found that the decibel level in their NICU ranged from 49.5-89.5 dBA, thereby exceeding the recommended Leq level. In addition, the authors found an average Lmax of 100.81 dBA, also exceeding the recommended Lmax. Alarmingly, 28.2 percent of the readings taken in the NICU had average peak levels of greater than 110 dBA (Matook et al., 2010).

Previous research has noted *in utero* protection of the fetus from high noise levels through sound reduction around 23 to 24 weeks gestation (Gerhardt & Abrams, 2000). Infants born preterm lose these uterine protective effects against high noise levels, resulting in a greater amount of auditory stimulation in the NICU (Matook et al., 2010). High levels of sound in the NICU must therefore be recognized by NICU staff as a cause for concern (Matook et al., 2010). Although no data are available regarding maximum noise levels that can inhibit the function of hearing screening devices, high levels of sound can mask and therefore interfere with the

screening process. The monitoring of high noise levels in the NICU would therefore facilitate hearing screening protocols by reducing sources of error that might interfere with administration of the tests.

1.13 Efficacy of a Screening Protocol

In order for a screening protocol to be deemed effective, it must involve objective, non-invasive physiological tests that can be administered by non-professional personnel and have the ability to influence the educational outcomes of infants with hearing loss through its implementation (Hayes, 2003; Yoshinaga-Itano, Sedey, Coulter, & Mehl, 1998). Furthermore, as noted by the Task Force on Newborn and Infant Hearing, the protocol must lie within an acceptable cost-effective range and consist of tests that are easy to use and that have high sensitivity and specificity in order to minimize referrals (Erenberg et al., 1999). Specifically, the false positive rate, or the number of infants incorrectly deemed to have a significant hearing loss, should be $\leq 3\%$, and the referral rate for follow-up audiological testing following screening should not exceed 4% (Barsky-Firsker & Sun 1997; Downs, 1995; Mason & Herrmann, 1998; Mehl & Thomson, 1998; Vohr, Carty, Moore, & Letourneau, 1998). Ideally, the screening protocol should have a false negative rate of zero, implying that it should not miss any infants with a significant hearing loss (Vohr, Carty, Moore, & Letourneau, 1998; Watkin, 1996). In addition, it should be capable of detecting, at a minimum, infants with significant bilateral hearing impairment (i.e., infants with a hearing loss of ≥ 35 dB HL in the better ear (Barsky-Firsker & Sun 1997; Mason & Herrmann, 1998)). While the Task Force on Newborn and Infant Hearing recognized that currently accepted methodologies for physiological screening include evoked otoacoustic emissions (EOAE) and automated auditory brainstem response (AABR), they deferred recommendation as to a preferred method (Erenberg et al., 1999).

1.14 Summary and Rationale for the Study

The goal of this study is to compare screening results from the current two-stage AABR protocol used for NICU babies with results of a novel protocol, involving the measures of 1000 Hz tympanometry, TEOAE, and ipsilateral BBN MEMR at 1000 Hz probe-tone frequency. These measures of the novel protocol will be assessed as a unit in terms of testing length, challenges encountered while testing, and whether they generate equivalent results with the current protocol for NICU infants. If comparable, this novel protocol might enable early identification of the type of hearing loss in neonates, ideally in a more timely and cost-effective manner than the currently existing protocol.

CHAPTER 2: METHODS

2.1 Participants

A total of 90 infants (180 ears) from the neonatal intensive care unit (NICU) of the Royal University Hospital in Saskatoon, Saskatchewan, were recruited for the present study, of which 78 infants (143 ears) met the inclusion criteria. Participants ranged in chronological age between 0 and 161 days old at the time of testing ($M = 31.38$ days, $SD = 33.01$). Gestational age (GA) at the time of testing was not readily accessible. GA was obtained through a sub-sample of 12 infants who were randomly selected and representative of the larger sample ($M = 37.18$ weeks GA; range = 35 – 40 weeks GA). Participants were recruited through information letters placed in their files (Appendix A) and through word of mouth among the nursing staff.

2.2 Inclusion and Exclusion Criteria

2.2.1 Inclusion Criteria

In order to be included in the study, infants were required to be in stable medical condition at their initial screening date, as determined by the nursing staff. If a second screening was necessary, it was to occur no later than four to six weeks following the date of the initial screening in order for the infant to be included. Furthermore, infants were required to have a valid result (pass or refer) on each of the four screening measures (AABR, TEOAE, BBN MEMR, and 1-kHz tympanometry) during at least one of the screening dates, i.e., initial screening or follow-up. Please refer to Table 2 for valid test criteria for each of the four measures. For the purpose of this study, the terms “rescreening” and “follow-up” are operationally defined. If an infant obtained an invalid result for at least one test at their initial screening, they were scheduled for a second screening date, entitled a *rescreening*. If an infant

Table 2. *Criteria for a Valid and Invalid Test Measure*

<u>Measure</u>	<u>Valid Criteria</u>	<u>Invalid Criteria</u>
1000 Hz Tympanometry	<p>Classified as a pass or refer.</p> <ul style="list-style-type: none"> • <u>For a pass:</u> <ol style="list-style-type: none"> 1) Peak is above a baseline drawn from -400 to +200 daPa (Baldwin, 2006; Marchant et al., 1986). 2) $Y_{tm} \geq 0.10$ mmho (Shahnaz et al., 2008) • <u>For a refer:</u> <p>Flat line with an ear canal volume that is ≤ 0.10 mmho and ≥ 0.04 mmho.</p> 	<p>Flat line with ear canal volume ≤ 0.04 mmho.</p>
BBN MEMR	<ul style="list-style-type: none"> • <u>For a pass:</u> <p>Positive or negative deflection of ≥ 0.04 mmho.</p> • <u>For a refer:</u> <p>Positive or negative deflection ≤ 0.04 mmho.</p> 	<p>Incomplete test or could not test.</p>
TEOAE	<p>“Pass” or “Refer” as per operational definition of the Accuscreen.</p>	<p>Incomplete test or could not test.</p>
AABR	<p>“Pass” or “Refer” as per operational definition of the Accuscreen.</p>	<p>Incomplete test or could not test.</p>

obtained a refer result on any test at the first screening date, they were scheduled for a second screening date entitled a *follow-up* (see Figure 1). Infants meeting inclusion criteria were divided into three groups: included based on *first screening*, included based on *rescreening*, and included based on *meshed results*. It was possible for one infant to have an ear in two different groups (e.g., left ear in *first screening* and right ear in *rescreening* groups).

Infants included based on their *first screening* had a successful first screening (either in the NICU or in the Audiology department following discharge from the hospital, if they were missed in the NICU), with valid results for each of the four screening measures for at least one ear. Infants included based on *rescreening* had invalid results for at least one test measure at their first screening for at least one ear, yet had valid results for all test measures at their second screening date. Infants included based on *meshed results* had invalid results for at least one of the screening measures at both of their first and second screening dates; however, when valid results obtained on each day were combined, the infant had a complete set of valid results that enabled them to be included in the study.

2.2.2 Exclusion Criteria

From the total number of infants recruited, 12 infants (24 ears) had both ears excluded from the sample. Furthermore, 13 infants (13 ears) had one ear excluded and one ear included, for a total of 37 ears excluded. Among ears excluded, 62.2% (N = 23 ears) were excluded due to an invalid result on at least one measure of the novel protocol; 21.6% (N = 8 ears) were excluded due to an invalid AABR; and 16.2% (N = 6 ears) were excluded due to measures from

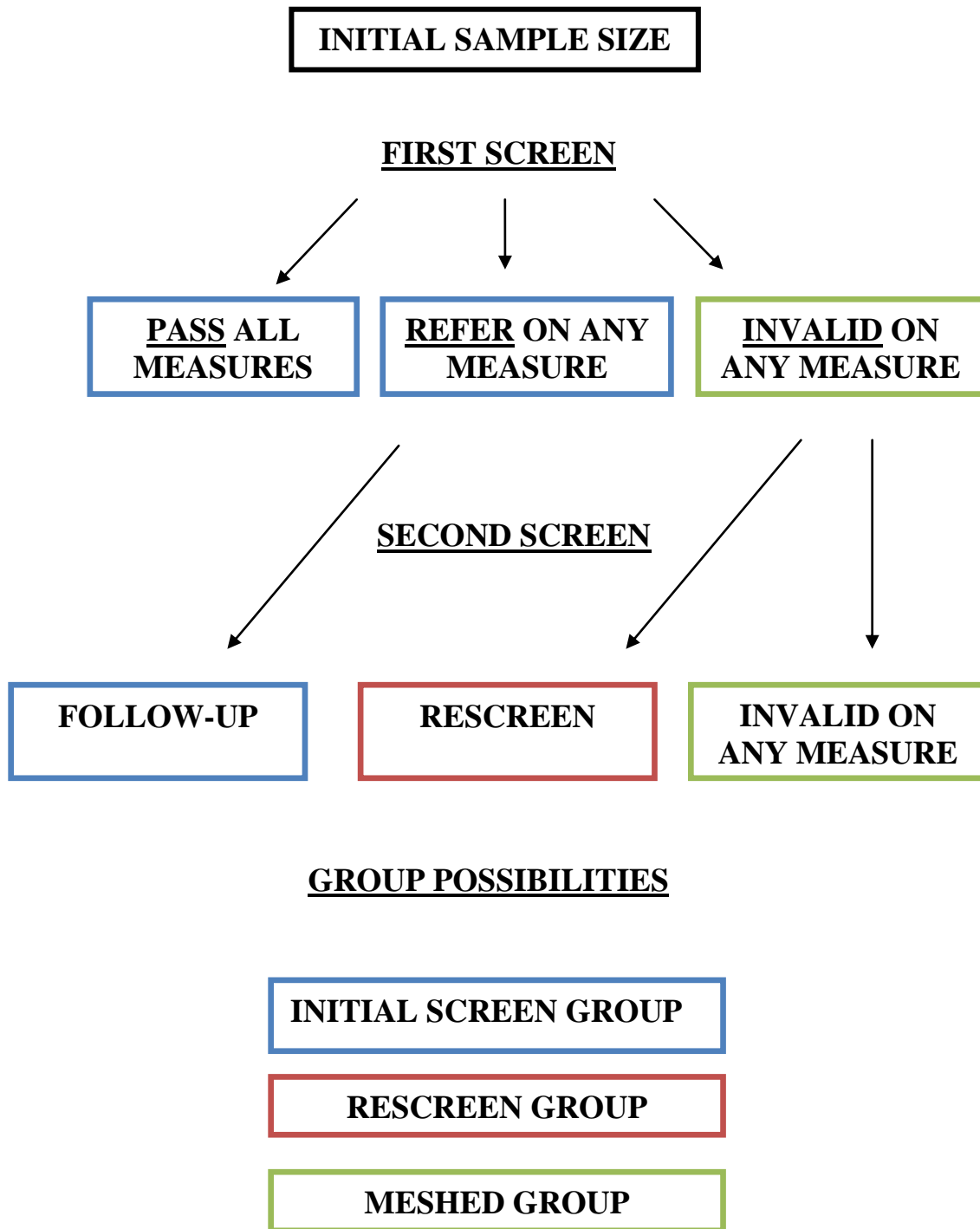


Figure 1. Schematic diagram of procedure depending on screening result obtained. The three possible groups of infants are indicated by the blue, red, and green colours.

both protocols. Of the ears that were excluded due to at least one measure the novel protocol, including the ears excluded due to inability of obtaining valid results using both protocols (N = 29 ears), 89.7% (N = 26 ears) were excluded due to invalid 1000 Hz tympanometry; 31.0% (N = 9 ears) were excluded due to invalid BBN MEMR; and 10.3% (N = 3 ears) were excluded due to invalid TEOAE.

Of the 37 ears that were excluded, 9 ears (7 infants) had an attempted rescreening; however, both their first and second screening results contained invalid measures. Specifically, at their second screening, 66.7% of ears (N = 6) could not be tested on AABR; infants were often alert and/or upset when they returned for a rescreening appointment in the Audiology department. Furthermore, 33.3% of ears (N = 3) obtained invalid results for 1000 Hz tympanometry, and one ear could not be tested for BBN MEMR. The remaining 28 ears that were excluded did not return for a rescreening appointment in the Audiology department. Please refer to section 2.6.7 for reasons for invalid test results.

2.3 Instrumentation

The GN Otometrics Accuscreen was used as the screening device to measure TEOAEs and AABR. The Accuscreen assesses the presence of TEOAEs (a pass result) through noise-weighted averaging with the counting of significant signal peaks (GN Otometrics, 2010a). A non-linear click sequence stimulus is used at a level of 45-60 dB HL, which self-calibrates depending on ear canal volume (GN Otometrics, 2010a). The Accuscreen has a click rate of approximately 60-Hz, with a frequency range of 1500 to 3500-Hz and uses a binomial statistics algorithm (GN Otometrics, 2010a; Natus Medical Inc., 2005). The presence of AABR (a pass result) was assessed by the Accuscreen through noise-weighted averaging and template matching through binomial statistics signal detection, with a click stimulus of 35 dB nHL at a rate of

approximately 80-Hz (GN Otometrics, 2010a). The Accuscreen had a testing frequency range of 2000 to 4000-Hz (GN Otometrics, 2010a). Impedance is measured both prior to and during the test, and the impedance sense signal is a 1000 Hz square wave (GN Otometrics, 2010a). Furthermore, the Accuscreen contained an artifact rejection system that distinguished between external noise and an actual response from the infant (GN Otometrics, 2010a).

The GN Otometrics Otoflex diagnostic impedance meter was used as the screening device to measure 1000 Hz tympanometry and BBN MEMR. Tympanometry was performed with the use of a 1000 Hz probe-tone and pressure was varied from +200 to -400 daPa in a positive to negative sweep direction and was delivered at a pump speed setting of “as fast as possible, ‘AFAP’” or > 500 daPa per second (GN Otometrics, 2010b). Pump speed did not vary at the tails or peak of the tympanogram (A. Mroz, GN Otometrics Clinical Project Liaison, personal communication, August 17, 2010). BBN MEMR was tested with a probe-tone of 1000 Hz with pressure compensation from the tympanometric peak pressure (TPP) of the most recently recorded tympanogram at the same probe-tone (GN Otometrics, 2010b). The stimulus was a broadband noise (BBN) in the ipsilateral mode at an intensity of 85 dB HL. The Otoflex registered a BBN MEMR when the change in admittance, in either the upward (increase) or downward (decrease) direction exceeded 0.04 mmho, based on operation manual of the system and as per Mazlan, Kei, and Hickson (2009a). Weatherby and Bennett (1980) noted a change from an increase to a decrease in impedance (or an increase in admittance) around a 1200-Hz probe-tone in neonatal ears. This was attributed to a reduction in reactance and resistance close to the resonant frequency of the infant middle ear (Weatherby & Bennett, 1980). Hence, in recording neonatal MEMR at a probe-tone of 1000 Hz, which is close to the resonant frequency, a decrease in impedance (increase in admittance) might be observed by an upward deflection in

reflex tracing (Mazlan, Kei, & Hickson, 2009a; Weatherby & Bennett, 1980). Therefore, both upward and downward changes in admittance were accepted as a MEMR in the current study.

2.4 Calibration

Calibration of both the GN Otometrics Accuscreen and Otoflex were performed daily or whenever a change in calibration was suspected, with the use of an external 2 cc probe test cavity, or a built-in 2 mL cavity, respectively. In addition, the Accuscreen performed a calibration check prior to testing TEOAE automatically (Natus Medical Inc., 2005).

2.5 Survey of Background Noise in the NICU

Noise levels in the NICU were assessed by Dan Black from dB Special Instruments Inc. with the use of a Quest model 155 Sound Level Meter (SN DL4080010) that included an octave band filter set. In order to exclude low frequency rumble, C weighting was used which includes frequencies from 100 Hz to 8000 Hz (-3dB). Sources of noise within the three areas of the NICU ward included bassinets, foot traffic, voices, telephones, monitor alarms, refrigerator pumps, sink faucets, and crying babies. Area 1 of the NICU was a separate room with a door to access the other two areas. Areas 2 and 3 were one large room that was divided by the bassinette stations between. Data collection was performed in all three areas.

The mean ambient noise level in Area 1 was found to be 55 dBC, assessed during a relatively quiet time in the ward to provide a good base measure. The most significant sources of noise noted in Area 1 were crying babies (up to 75 dBC across the room and 80+ dBC within one meter) and monitor alarms (up to 75 dBC across the room and 80+ dBC within one meter). The ambient background noise of Areas 2 and 3 was 63 dBC due to a greater amount of activity including paper rustling, chatting, and general movement of people. Areas 2 and 3 also had

significant noise sources of crying babies and monitor alarms that were similar in levels as Area 1. Moreover, constant telephone ringing exceeded 75 dBC throughout Areas 2 and 3.

2.6 Procedures

2.6.1 Consent

Parents first signed a consent form entitled, “Comparison of Screening Protocol for the Differentiation of Type of Hearing Loss in Neonatal Intensive Care Unit (NICU) Infants”, which was approved by the Clinical Research Ethics Board of the University of British Columbia (H09-03237) and by the Biomedical Research Ethics Board of the University of Saskatchewan (Bio # 10-03).

2.6.2 General Procedures

The current study coincided with the start of a newborn hearing screening program in Saskatchewan; therefore, education was provided to the nursing staff regarding its purpose and to provide an understanding of the screening procedures. For initial screenings, testing was performed in the NICU, most often in the morning or middle afternoon in an effort to avoid testing during rounds, which contributed to the increased noise level. Noise level was not objectively monitored during testing; however testing was paused if levels became subjectively too high (i.e., increased activity in the NICU such as family visitors or external medical staff). Infants were tested in order of priority of date or time of discharge from the hospital. Permission was verified with the nursing staff prior to the commencement of testing. Once an infant was identified as being a priority, the tester (a trained research assistant or audiologist) verified with the nursing staff that they were in stable medical condition. The equipment was thoroughly sterilized before and after the testing of each infant and a towel was placed underneath the

equipment when it was rested on the infant's crib or on the top of their isolette as a further sanitary precaution.

The test protocol for infants who passed the novel screening in the current study was a strict parallel protocol; infants were required to obtain a pass on every measure in the protocol in order to receive a pass outcome (Turner, Robinette, & Bauch, 1999). In addition, the test protocol for infants who referred on the novel screening was a loose parallel protocol; infants required a refer result on any one measure to receive a refer outcome on the protocol (Turner, Robinette, & Bauch, 1999).

2.6.3 Transient-Evoked Otoacoustic Emissions (TEOAE) and Automated Auditory Brainstem Response (AABR)

Identifying information for each infant was entered into the Accuscreen (for TEOAE and AABR testing) and Otoflex (for 1000 Hz tympanometry and BBN MEMR testing) and a new probe tip was used for each new infant and with each device. Once the devices were ready for use, electrode application began with three disposable hydrogel electrodes being applied to the infant's high forehead (vertex; white clip), cheek (common; black clip), and centered on the back of the neck (nape; red clip) following a brief, gentle scrub with a cotton ball and a pea-sized amount of NuPrep mild abrasive gel (Natus Medical Inc., 2005). The electrodes were applied prior to the start of the testing as the testers found that impedances improved with time elapsed since application.

Once the electrodes were applied to the infant's skin, nondiagnostic otoscopy was performed to ensure a clear ear canal, although no infants were excluded based on otoscopic findings. The first ear to be tested depended on the infant's orientation; efforts were made to ensure minimal disturbance of the infant, therefore, the ear closest to the tester was chosen as the

first to be tested. Testing then began with the Accuscreen, which was chosen as the first device for use due to the possibility of being short on time with the infant and being able to obtain the TEOAE and AABR at a minimum. For placement of the probe tips for both devices, the infant's pinna was gently pulled back and down in order to straighten the ear canal and ensure an optimal fit. The TEOAE test was run followed by the AABR. The Accuscreen verified impedances prior to beginning the AABR test and if any impedance was higher than 8 k Ω a new electrode was applied. Throughout measurement of the TEOAEs and AABRs, probe stability and extraneous noise levels were monitored to ensure optimal recording conditions. At times, during the recording of the AABR, the Accuscreen noted "interference" of surrounding electrical equipment. When this occurred, testing was restarted and the tester attempted to change the position of where they were standing for the recording, as well as the orientation of the electrode cables.

2.6.4 Tympanometry and Middle-Ear Muscle Reflex (MEMR)

Following the TEOAE and AABR tests, the Otoflex device was used to obtain 1000 Hz tympanometry and BBN MEMR. In some cases if the infant was fidgeting, tympanometry was attempted several times until recording was successful. Furthermore, a very low ear canal volume (< 0.04 mmho) with a flat tympanogram often indicated that the probe tip was against the wall of the infant's ear canal and needed to be repositioned. Obtaining the correct fit of the probe tip was a challenge with certain infants as the smallest size probe tip available from GN Otometrics was often too large for the infant's ear. Once a seal was obtained, the pressure sweep took approximately 5 seconds. The pressure sweep involved a decrease in air pressure of the external ear canal from +200 daPa to -400 daPa while the probe-tone was held constant at 1000 Hz. Descending pressure changes are preferred as they have been shown to result in fewer seal

problems in infants (Holte et al., 1991; Sprague et al., 1985). Furthermore, with the use of high-frequency probe signals, pressure changes in this direction result in more consistent tympanogram morphology (Margolis et al., 1985; Wilson et al., 1984).

Tympanograms were classified as a “pass” if there was a clear peak above an imaginary baseline drawn from -400 to +200 daPa (Baldwin, 2006; Marchant et al., 1986) and if the Y_{tm} was ≥ 0.10 mmho (Shahnaz et al., 2008). Tympanograms that did not meet this criteria were classified as a “refer”. Tympanograms were classified as invalid if a recording was incomplete, if multiple peaks existed above and below the imaginary baseline, if the tympanogram was a simple straight horizontal line with a very small ECV (i.e., ≤ 0.04 ml), or if it was unclassifiable as a pass or refer (e.g., in the case of a noisy baby; for examples, see Figure 2).

The BBN MEMR was run in succession with tympanometry at a level of 85 dB HL. The pass criterion for a reflex to be present was a deflection of greater than 0.04 mmho from baseline, in either the upward or downward direction. The BBN MEMR was run up to a maximum of three times if a reflex was not obtained at the first trial as an attempt to avoid an absent BBN MEMR due to a problem with probe fit.

2.6.5 Timing of Measures

Timing of the individual measures was performed with the use of a stopwatch. Timing began when the start button was pressed for the measure, and was stopped when a result was obtained. If interference occurred during measurement of the AABR, timing was uninterrupted and continued despite restarting the test. Timing was not performed for the initial recording of the infant’s data into the two devices. Once the testers had gained sufficient experience with the testing (approximately 1 month from the start of the study), preparation time for AABR was recorded for the application of electrodes. Essentially no preparation time was required for the

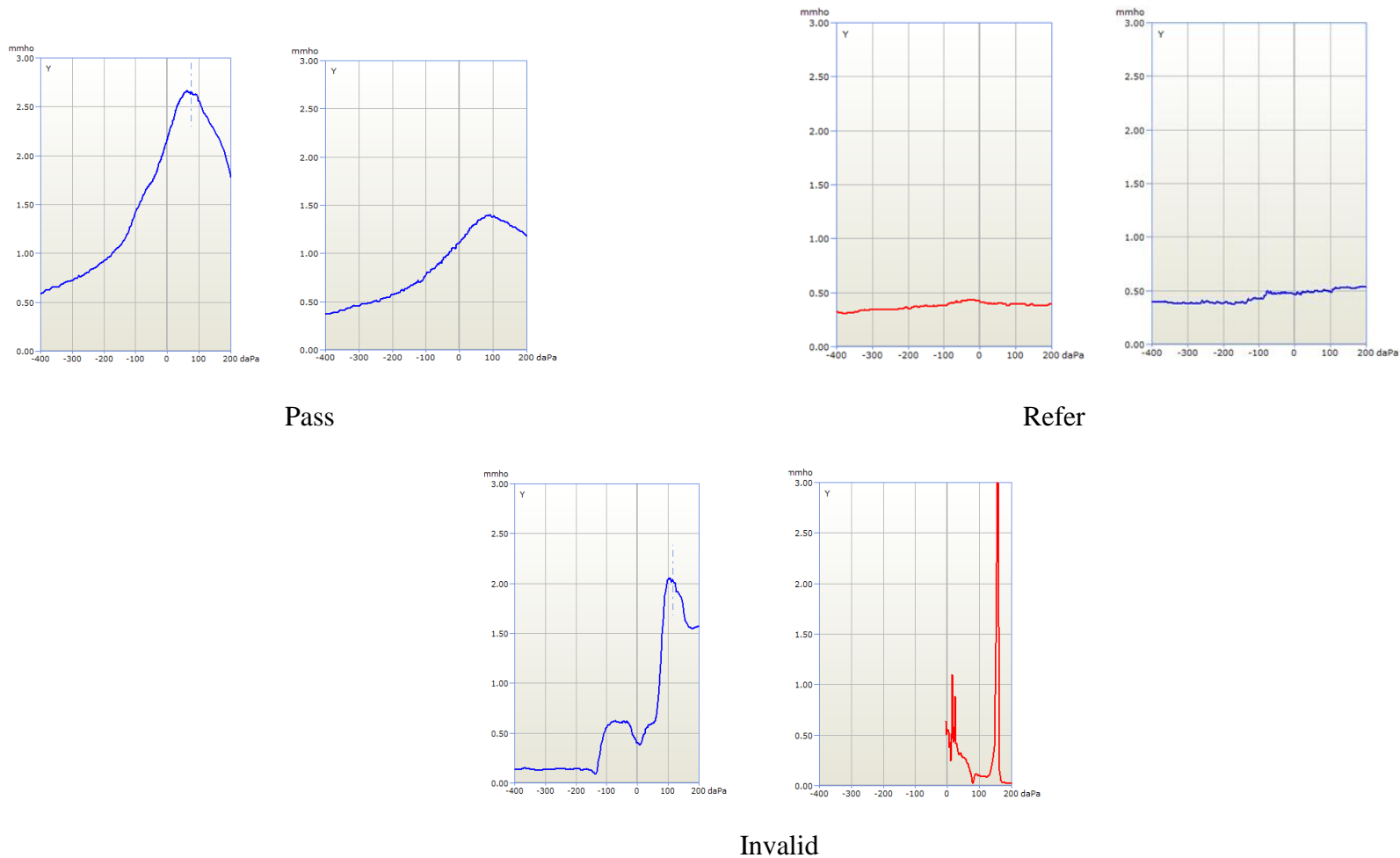


Figure 2. Examples of tympanogram classification. For classification of a pass, tympanograms required a clear peak above an imaginary baseline drawn from -400 to +200 daPa (Baldwin, 2006; Marchant et al., 1986) and an SA of ≥ 0.10 mmho (Shahnaz et al., 2008). Possible reasons for an invalid classification included a tympanogram having an incomplete recording; having multiple peaks above and below the imaginary baseline; being a simple straight horizontal line with a very small ECV (i.e., ≤ 0.04 ml); or being unclassifiable as pass or refer (e.g., in the case of a noisy baby).

measures of TEOAE, 1000 Hz tympanometry, and BBN MEMR as it simply involved a placement of appropriate probe tip.

Times for the three measures consisting of the novel protocol (1000 Hz tympanometry, TEOAE, and BBN MEMR) were combined to obtain a total length of time for the novel protocol. In addition, the total length of time for administration of both the AABR and novel protocols was found. This total length of time was measured from the very beginning of the first measure until very end of the last measure and included any preparation time required (e.g., electrode application for AABR, changing size of probe tips, repositioning of probe tip, restarting recording due to high noise conditions). This value of total length of time for administration of both protocols represented the test time for both ears. For the purpose of this study, this total length of time was labelled, “Total Time – With Prep”.

The total length of time for test administration could not be obtained for every infant in the study; therefore a second form of “total length of time” was calculated for infants who had times available for all of the individual measures of the protocols. Specifically, times for the three measures of the novel protocol were summed with time for the AABR measure of the AABR protocol and a total length of time was obtained. However, as this second form of total length of time was composed of individual test measures, it did not include any preparation time. For the purpose of this study, this second form of total length of time was labelled, “Total Time – No Prep”.

2.6.6 Quantification of Tympanometry

The infant obtained a pass for 1000 Hz tympanometry if the tympanogram satisfied two criteria that enabled the tympanogram to be classified as normal: 1) the peak of the tympanogram was above an imaginary baseline connecting the negative tail to positive tail as shown in Figure 3 (Baldwin, 2006) and 2) the baseline compensated static acoustic admittance was greater than 0.10 mmho (Shahnaz et al., 2008) (Table 2). Six tympanograms did not meet the second criterion as SA was < 0.10 mmho; however were deemed to be normal in shape based on observation by the principal investigators who have ample experience with tympanometric shapes in newborns (Appendix C).

Although the GN Otometrics Otosuite software that accompanied the Otoflex device provided a value for tympanometric variables on certain tympanograms, preliminary analyses revealed unreliable values for the variable of equivalent ear canal volume (V_{ea} , in cm^3); hence, the measurement of all tympanometric variables was performed manually. The V_{ea} was measured from both the positive (+200 daPa) and negative (-400 daPa) tails of the admittance (Y) tympanogram, and from the B (susceptance) tympanograms. Peak-compensated static acoustic admittance magnitude (Y_{tm}) was calculated by subtracting the V_{ea} obtained from the positive tail from the peak or notch on the admittance tympanogram. If a notch was present, it was chosen instead of one of the two maxima on either side of the notch (Shahnaz et al., 2008). The values of tympanometric peak pressure (TPP, in daPa) and tympanometric width (TW, in daPa) were also calculated from the 1000 Hz tympanograms.

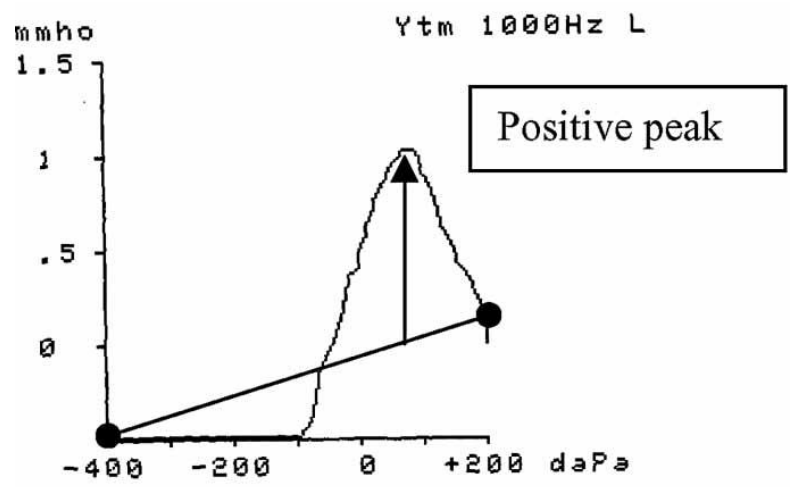


Figure 3. Criterion #1 for classification of a normal tympanogram demonstrating the peak of the tympanogram above an imaginary baseline connecting the negative tail to the positive tail (Baldwin, 2006).

2.6.7. Reasons for Invalid TEOAE, BBN MEMR, and AABR Results

As previously mentioned in Table 2, infants obtained a valid result for AABR and TEOAE if a “pass” or “refer” result was obtained, as per the operational definition of the Accuscreen. An invalid AABR result was obtained when the testing could not be completed due to interference with other electrical equipment, which was noted on the device. In addition, testing could not be completed for infants who were noisy due to movement or sucking, and often for those in isolettes, for whom high electrode impedances were often present. Despite thorough skin preparation, high impedance values might also have occurred for unknown reasons. An invalid TEOAE result was obtained if an infant was very noisy or aroused/upset, or if probe fit was not adequate. In these scenarios, the test could not be completed as the system would take a lengthy amount of time to record or would stop during the testing due to high noise levels.

Infants obtained a valid result for BBN MEMR if their reflex demonstrated a positive or negative deflection of ≥ 0.04 mmho, preset on the Otoflex to indicate a “pass”, or a positive or negative deflection of ≤ 0.04 mmho, preset on the Otoflex to indicate a “refer”. Infants might have obtained an invalid result for BBN MEMR if they were too noisy or if a flat line with a volume of 0.00 mmho was obtained, indicating that the probe tip was against the ear canal wall. Although repositioning of the probe tip was always attempted, in certain cases the very small ear canals of the infants made the recording of a valid result challenging.

2.6.8 Rescreening and Follow-Up

If an infant was discharged before they were able to be screened, or if an invalid or incomplete test result was obtained at the first screening in the NICU, the infant was scheduled to return to the Audiology department of the Royal University Hospital for a second screening

date. If a cochlear hearing loss was suspected based on the pattern of screening test results (e.g., normal tympanogram with absent TEOAE, AABR, and/or MEMR) the infant was scheduled to return 4 weeks following the initial screening date; however, if a conductive loss was suspected (e.g., abnormal tympanometry), the infant was scheduled to return 6-8 weeks later to provide time for possible OME to clear. The infant's second screening date was entitled a "rescreening" if invalid results were obtained on the first screening date, or entitled a "follow-up" if valid results that included a refer on any measure were obtained at the first screening. If an infant had one ear that passed and one ear that referred at their first screening, both ears were screened again at their second screening.

CHAPTER 3: RESULTS

3.1 Normative Tympanometric Data

Descriptive statistics were initially conducted in order to verify the reliability of the 1000 Hz tympanograms that were classified as a pass, and to compare normative values on NICU babies obtained in this study with those of previous researchers (e.g., Margolis et al., 2003; Shahnaz et al., 2008). Normative data are reported for 101 ears of 57 NICU infants who ranged in chronological age from 2 to 161 days at the time of testing. Results for peak-compensated admittance magnitude (Y_{tm}) and equivalent ear canal volume (V_{ea}) from the current study are presented in comparison with previous studies in Table 3. To obtain the value of Y_{tm} , the V_{ea} for each infant was subtracted from the value of uncompensated admittance magnitude (Y_a) from their tympanogram. Values for V_{ea} are included in Table 3 for informational purposes only, versus the values of Y_{tm} which were compared with those obtained in previous studies. All infants passed both the novel (TEOAE, 1000 Hz tympanometry and BBN MEMR) and AABR protocols; 60 ears at their first screening, 17 ears at rescreening, 13 ears at follow-up, and 4 ears were meshed. In addition, 7 out of the 60 ears that passed both protocols at their first screening also passed both protocols when they were seen for a second screening, to bring the total ears with normative tympanometric data to 101. As mentioned in the Methods section, if an infant had one ear pass and one ear refer at their first screening, both ears were screened again at their second screening (entitled “follow-up”). If an infant had one ear pass and one ear had an invalid result (see Table 2), both ears were screened again their second screening (entitled “rescreening”).

Table 3. Mean, Standard Deviation (SD), and 90% range (5th–95th percentile) for Peak-Compensated Admittance Magnitude (Y_{tm} ; mmho) obtained at a 1000 Hz Probe-Tone Frequency with Baseline Compensation at +200 daPa and for Equivalent Ear Canal Volume (V_{ea} ; cm^3) for NICU and Well-Baby Nurseries

Nursery	Study	N	System Used	Y_{tm} (mmho)			V_{ea} (cm^3)		
				Mean	SD	90% Range	Mean	SD	90% Range
NICU	Current Study 37 weeks CGA*	101 ears	Otometrics Otoflex	0.59	0.43	0.10-1.43	1.26	0.62	0.44-2.5
	Margolis et al., 2003 32.8 weeks GA	105 ears	Grason-Stadler Incorporation - GSI-33 version 2	0.80	0.50	0.20-1.60	1.40	0.30	0.90-1.90
	Shahnaz et al., 2008 32 weeks CGA	54 ears	Grason-Stadler Incorporation -GSI- 33 version 2	0.77	0.52	0.10-1.50	1.24	0.25	0.87-1.70
Well- Baby	Mazlan et al., 2007 39.5 weeks GA	42 ears	Otometrics Otoflex	0.78	0.40	0.15-1.86	1.07	0.44	0.44-2.56
	Mazlan et al., 2010 36-42 weeks GA	273 ears	Otometrics Otoflex	0.65	0.34	N/A	0.97	0.38	N/A

*Note. CGA obtained for N = 12 infants. Mean CGA or GA is indicated below each study.

The mean, standard deviation (SD), and 90% range (5th to 95th percentile) for the positive tail (+200 daPa), the negative tail (-400 daPa), TW, TPP, and Y_{tm} at a 1000 Hz probe-tone frequency are shown in Table 4.

Reliability of the TEOAE and AABR measures were not questioned due to the objective nature of a pass result as determined by the screening device. As previously noted in the Methods section, the BBN MEMR was run up to a maximum of three times if a reflex was not obtained at the first trial as an attempt to avoid an absent BBN MEMR due to a problem with probe fit.

3.2 Screening Outcome

As described in the Methods section, all infants with valid results were divided into three groups depending on reason for inclusion: first screening (N = 115 ears or 65 infants, $M = 16.37$ days, range = 0 – 65 days); rescreened (N = 20 ears or 13 infants, $M = 69.3$ days, range = 28 – 161 days); and meshed (N = 8 ears or 5 infants, $M = 74.6$ days*, range = 57 – 102 days).

Following the first screening appointment, there were two possible outcomes for infants that obtained valid results: either the infant passed every measure on the screening and follow-up was not required, or the infant obtained a “refer” result on one of the screening measures and required follow-up (Table 2). Twenty-one ears (N = 15 infants, $M = 62.4$ days, range = 25 – 107 days) out of the 115 ears that obtained valid results with a “refer” outcome at their first screen returned for follow-up and again obtained valid results for all four screening measures at this second screening time.

Follow-up data were obtained for these 21 ears regardless of whether they passed or referred on their first screening. An ear that passed on a first screening might have been screened again at a second screening if it had returned due to a refer on the infant’s other ear. No

*Age obtained at date of second screening, at which time all test measures had a valid result.

Table 4. *Normative Tympanometric Values from 1000 Hz Tympanograms from 101 Ears of 57 NICU Infants Tested at 2 -161 Days Chronological Age*

	TPP (daPa)	Y_{tm} (mmho)	TW (mmho)	$V_{ea}Y_{a-}$ (cm ³)	$V_{ea}B_{a-}$ (mmho)	$V_{ea}B_{a+}$ (mmho)	$V_{ea}Y_{a+}$ (cm ³)
Mean	37.12	0.59	138.42	0.48	0.26	1.26	0.95
Median	50.0	0.49	136.40	0.40	0.21	1.18	0.86
SD	66.68	0.43	48.58	0.33	0.30	0.62	0.50
90% Range	-76-133.3	0.09-1.43	77.74-210	0.14-1.13	-0.10-0.83	0.44-2.5	0.24-1.79

follow-up data were available for ears in the first screening group that did not show for or who received an invalid screening result at their second screening appointment.

Infants in the rescreened group (N = 20 ears or 13 infants) obtained an invalid result on at least one screening measure at their first screening. However, when the infants returned for a second screening, valid results on all four measures were obtained. These infants were therefore included in the study based on their second screening results. Specifically, at their first screening, 14 out of 20 ears in this group (70%) had an AABR that could not be obtained due to poor conditions in the NICU (e.g., excessive noise, electrical interference, or a restless baby). Furthermore, 7 out of 20 ears (35%) had invalid 1000 Hz tympanometry. Possible reasons for this were excessive movement or crying that prohibited the measurement of tympanometry; tympanograms that did not meet criteria as being valid; or tympanograms that were not available for analysis due to technical difficulties with storing and recording the result. Three out of 20 ears (15%) had BBN MEMRs which could not be tested. There were only 2 out of 20 ears (10%) in which TEOAE could not be recorded.

Infants in the meshed group (N = 8 ears or 5 infants) obtained an invalid result for at least one screening measure at both of their first and second screenings. Specifically, all 8 ears in the group (100%) obtained an invalid result on AABR at their second screening but a valid result at their first screening. An invalid AABR was obtained when an infant was awake or too noisy for the measure to run successfully. Similarly, all 8 ears (100%) obtained an invalid result on 1000 Hz tympanometry at their first screening date but a valid result at their second screening. Furthermore, 3 out of 8 ears (37.5%) obtained an invalid result on BBN MEMR, which occurred at the first screening for 1 ear and at the second screening for 2 ears. Moreover, 1 out of 8 ears (12.5%) obtained a valid result on TEOAE (registered as a pass or refer on the Accuscreen

device) at their first screening and an invalid result at their second screening due to excessive noise from fussing or crying. Therefore, when results from both screenings were combined for these 8 ears, a valid result existed for each screening measure. Please refer to Figure 4 for an illustration of the groupings.

Results of screening outcomes for the AABR and novel protocols are described below for each of the three groups and are summarized in Table 5. Please note that it was possible for one ear to obtain a refer result on more than one measure in the novel protocol. Specific reasons for referral on the novel protocol are displayed in Table 6 for each of the three groups.

3.2.1 First Screening Group

For the group that was included based on their first screening (N = 115 ears or 65 infants), most ears (77.4%; 55 infants) passed the AABR protocol, while 57.4% (45 infants) passed the novel protocol. Specifically, most ears that referred on the novel protocol referred on TEOAE (79.6%), while a little over half (55.1%) referred on 1000 Hz tympanometry, and 23 ears (46.9%) referred on BBN MEMR. In terms of screening measures of the novel protocol that were often referred on together, most of the ears (40.8%) referred for both 1000 Hz tympanometry and TEOAE and 26.5% referred for all three measures of 1000 Hz tympanometry, TEOAE and BBN MEMR. In addition, approximately half of the ears in the group (52.2%; 40 infants) passed both the AABR and novel protocols, while a smaller percentage (17.4%; 16 infants) referred on both protocols. Furthermore, of the 21 ears in this group (15 infants) that had a valid follow-up screening, all passed both protocols except for one ear (4.8%) that referred on the novel protocol for all three measures. Please refer to Table 5 for a summary of results of screening outcomes on the AABR and novel protocols and to Table 6 for specific reasons for referral on the novel protocol for this group.

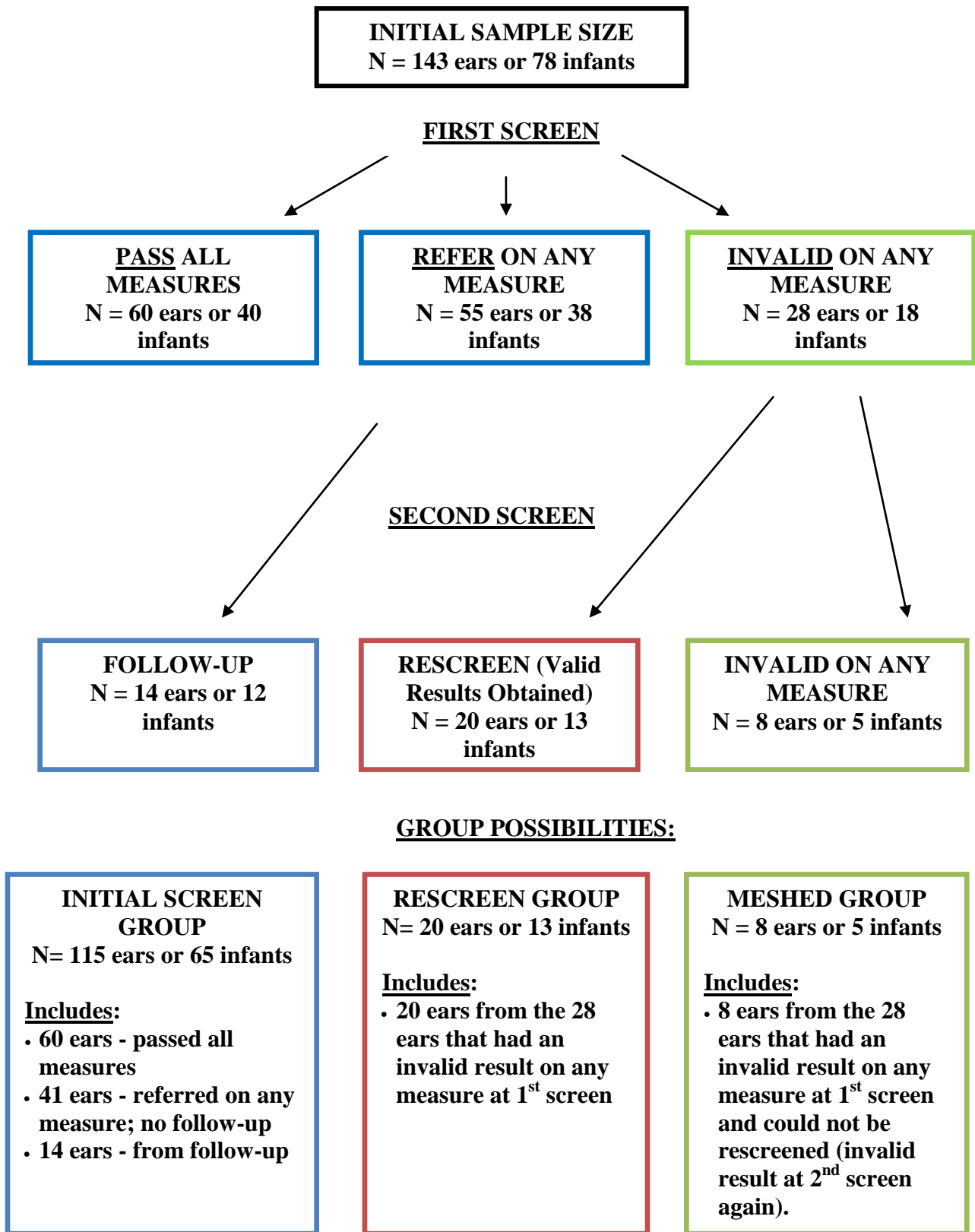


Figure 4. Schematic diagram of procedure depending on screening result obtained. The three possible groups of infants are indicated by the blue, red, and green colours.

Table 5. *Screening Outcome for AABR and Novel Protocols by Group*

Group	AABR Protocol		Novel Protocol		Both Protocols	
	Pass (%)	Refer (%)	Pass (%)	Refer (%)	Pass (%)	Refer (%)
First Screening (115 ears)	77.4 (89)	22.6 (26)	57.4 (66)	42.6 (49)	52.2 (60)	17.4 (20)
Rescreened (20 ears)	90 (18)	10 (2)	85 (17)	15 (3)	85 (17)	10 (2)
Meshed (8 ears)	75 (6)	25 (2)	50 (4)	50 (4)	50 (4)	25 (2)

Note. Number of ears is indicated in brackets.

Table 6. Reason for Referral on Novel Protocol by Group

Group	Reason for Referral						
	TEOAE (%)	1000 Hz tympanometry (%)	BBN MEMR (%)	TEOAE & 1000 Hz tympanometry	TEOAE & BBN MEMR	1000 Hz tympanometry & BBN MEMR	All three measures
First Screening (115 ears)	79.6 (39)	55.1 (27)	46.9 (23)	40.8 (20)	32.7 (16)	34.7 (17)	26.5 (13)
Rescreened (20 ears)	33.3 (1)	66.7 (2)	33.3 (1)	0 (0)	0 (0)	33.3 (1)	0 (0)
Meshed (8 ears)	50 (2)	100 (4)	50 (2)	50 (2)	25 (1)	50 (2)	25 (1)

Note. Number of ears is indicated in brackets.

3.2.2 Rescreened Group

Infants with invalid results for their first screening who obtained valid results for their second screening were included in the rescreened group (N = 20 ears or 13 infants). As shown in Table 5, almost all of the ears (90%; 12 infants) passed the AABR protocol, with 2 ears referring (10%; 2 infants) on the AABR protocol. Most of the ears (85%; 12 infants) passed the novel protocol, with 3 ears referring (15%; 3 infants) on the novel protocol (Table 5). The 1000 Hz tympanometry was the most common reason for referral on the novel protocol (66.7 % of ears) (Table 6). In addition, most ears in the group (85%; 12 infants) passed both the AABR and novel protocols, with a small percentage (10%; 2 infants) referring on both (Table 5).

3.2.3 Meshed Group

Infants who obtained invalid results for certain measures at both of their first and second screenings but who had a complete set of valid results when the screenings were combined were included in the meshed group (N = 8 ears or 5 infants). Results revealed that most of the ears in this group (75%; 3 infants) passed the AABR protocol (Table 5). In terms of the novel protocol, half of the ears passed and half referred (2 and 3 infants, respectively) (Table 5). Specifically, all ears that referred on the novel protocol had a refer result on 1000 Hz tympanometry, with half referring on TEOAE and BBN MEMR, respectively (Table 6). Moreover, half of the ears (4 ears or 2 infants) passed both the AABR and novel protocols and 2 ears (2 infants) referred on both protocols (Table 5).

Future follow-up data are not available for ears in the rescreened or meshed groups that obtained a refer result on a screening measure. Data from the present study were not collected beyond the second screening appointment.

3.3 Analysis of Different Patterns in Screening Outcome

Four patterns of screening outcomes were possible: obtaining a pass result on both the AABR and novel protocols; obtaining a pass result on the AABR protocol and a refer result on the novel protocol; obtaining a refer result on both the AABR and novel protocols; and obtaining a refer result on the AABR protocol and a pass result on the novel protocol. Results of patterns of screening outcome for each group of infants are illustrated in Table 7. Reasons for referrals for the novel protocol are displayed in Table 8.

3.3.1 Pass Result on Both AABR Protocol and Novel Protocol

One hundred and one ears, or 57 infants, obtained a pass result on both protocols. These infants passed all four measures of the AABR, TEOAE, BBN MEMR, and 1000 Hz tympanometry. Most of the ears obtaining this pattern of results (59.4%) were from the first screening group. The sum of the ears in these groups does not add up to 101 ears; 7 ears of the 60 that were from the first screening group also passed both protocols when they were screened again at follow-up. Thirteen ears passed both protocols for the first time when they were screened at follow-up. Therefore, an additional 20 ears passed both protocols based on their follow-up screening (Table 7).

Table 7. *Pattern of Screening Outcome by Group*

Pattern of Screening Outcome	Total		Proportion of Infants in Each Group		
	Ears	Infants	First Screen % (# ears)	Rescreened % (# ears)	Meshed % (# ears)
Pass on Both Protocols	101*	57	59.4 (60)	16.8 (17)	4 (4)
Pass on AABR Protocol, Refer on Novel Protocol	33**	25	87.9 (29)	3.0 (1)	6.1 (2)
Refer on Both Protocols	24	19	83.3 (20)	8.3 (2)	8.3 (2)
Pass on Novel Protocol, Refer on AABR Protocol	6	6	100 (6)	0 (0)	0 (0)

Note. *The total of 101 ears that obtained a pass on both protocols includes 60 ears from the first screen group, 17 ears from the rescreened group, 4 ears from the meshed group, and an additional 20 ears (not displayed) that obtained this screening outcome at their follow-up screening. These 20 ears include 7 ears that obtained this screening outcome at both their first and second screenings, and 13 ears that received this screening outcome for the first time at their follow-up screening.

**The total of 33 ears that obtained a pass on the AABR protocol and refer on the novel protocol includes 29 ears from the first screen group, 1 ear from the rescreened group, 2 ears from the meshed group, and an additional ear (not displayed). This additional ear was an ear from the 29 ears of the first screen group, but had a follow-up appointment at which time it obtained this screening outcome.

Table 8. *Proportion of Infants Referring on Individual Measures of Novel Protocol by Pattern of Screening Outcome*

Pattern of Screening Outcome	Total		Reason for Referral						
	Ears	Infants	TEOAE % (# of ears)	1000 Hz tympanometry % (# of ears)	BBN MEMR % (# of ears)	TEOAE & 1000 Hz tympanometry % (# of ears)	TEOAE & BBN MEMR % (# of ears)	1000 Hz tympanometry & BBN MEMR % (# of ears)	All three measures % (# of ears)
Pass on AABR Protocol, Refer on Novel Protocol	33	25	70 (23)	54.5 (18)	27.3 (9)	30.3 (10)	12.1 (4)	21.2 (7)	12.1 (4)
Refer on Both Protocols	24	19	83.3 (20)	66.7 (16)	75 (18)	54.2 (13)	58.3 (14)	58.3 (14)	45.8 (11)

3.3.2 Pass Result on AABR Protocol and Refer Result on Novel Protocol

Thirty-three ears (25 infants) obtained a pass result on the AABR protocol and a refer result on the novel protocol (Table 7). Of those infants who referred on the novel protocol, most of the ears (70.0%) referred on TEOAE; 54.5% of ears referred on 1000 Hz tympanometry; and 27.3% of ears referred on BBN MEMR (Table 8). Furthermore, the most frequent pattern was a referral on both 1000 Hz tympanometry and TEOAE (30.3% of ears), with only 12.1% referring on all three measures of the novel protocol (Table 8). Most of the ears (87.9%) obtaining this screening outcome of a pass on the AABR protocol and a refer on the novel protocol were from the first screening group, which included one ear that obtained this pattern of screening outcome at their follow-up screen (Table 7).

3.3.3 Refer Result on Both AABR and Novel Protocols

Twenty-four ears (19 infants) obtained a refer result on both the AABR and novel protocols (Table 7). Specifically, most of the ears (83.3%) referred on TEOAE, with 75% referring on BBN MEMR (Table 8). A significant number of ears (66.7%) referred on 1000 Hz tympanometry (Table 8). Moreover, equal number of ears (58.3%) referred on both 1000 Hz tympanometry and BBN MEMR and also on both TEOAE and BBN MEMR (Table 8). 54.2% of the ears referred on both 1000 Hz tympanometry and TEOAE, with 45.8% referring on all three measures of the novel protocol (Table 8). The majority of ears (83.3%) obtaining this screening outcome were from the first screening group (Table 7).

3.3.4 Refer Result on AABR Protocol and Pass Result on Novel Protocol

Six ears, or 6 infants, obtained a refer result on the AABR protocol, and a pass result on the novel protocol. Six ears (100%) obtaining this screening outcome were from the first screening group (Table 7).

3.4 Length of Time for Test Administration

The test times for each individual measure for *both* ears was determined as a sum of the average test times for the right and left ears. As shown in Table 9, the average length of time for the AABR protocol for both ears was 6.84 minutes (SD = 1.98 minutes). It should be noted that this involved a 1-stage AABR protocol (a single administration of the AABR), which differed from the current 2-stage BCEHP AABR protocol for NICU infants. Therefore, administration time for a 2-stage AABR protocol would likely be longer. Conversely, the average length of time for the novel protocol was 4.04 minutes (SD = 1.37 minutes). The total test time for both protocols including any preparation time (Total Time – With Prep) could only be obtained for 10 infants in the included sample and was 23.6 minutes.

As described above, preparation time involved the application of electrodes for AABR prior to starting all of the recordings in order to maximally reduce impedances, as mentioned in the Methods section. This time measure was only obtained for a random sub-sample of five infants and was found to be 9.8 minutes. Preparation time could only be obtained from infants who had a measure for both “Total Length of Time – With Prep” and “Total Length of Time – No Prep”, as each time variable was subtracted from one another to obtain preparation time.

Time measures could not be obtained for every infant as screening was performed by a single researcher and the simultaneous measurement with time recording often proved to be challenging. It is important to note that the five infants for whom preparation time was available had a wide range of time recordings (55.2 – 1250.4 seconds). Longer preparation times often occurred during noisy rounds due to frequent pausing in testing; therefore, this sub-sample of 5 infants may not be representative of the preparation time required for the larger sample.

Table 9. Average Length of Time for Individual Measures and for Each Protocol

Ear	Protocol	Included Infants (N = 78)		Excluded Infants (N = 12)		All Infants (N = 90)	
		Time (minutes)	# Infants	Time (minutes)	# Infants	Time (minutes)	# Infants
Right	TEOAE	1.25	71	0.90	7	1.22	78
	TYMP/BBN	0.87	68	1.06	5	0.89	73
	Novel Protocol	2.12	*	1.96		2.11	
	AABR Protocol	3.46	66	4.43	6	3.54	72
Left	TEOAE	1.16	71	1.16	7	1.16	78
	TYMP/BBN	0.76	68	0.71	6	0.76	74
	Novel Protocol	1.92		1.87		1.92	
	AABR Protocol	3.38	69	4.95	6	3.51	75
Both	TEOAE	2.41	71	2.06	**	2.38	
	TYMP/BBN	1.63	68	1.77		1.65	
	Novel Protocol	4.04		3.83		4.03	
	AABR Protocol	6.84		9.38		7.05	
	Total Time - With Prep	23.6	10	24.5	2	23.8	12
	Total Time - No Prep	10.9	63	13.68	5	11.1	68
	Prep Time	9.80	5	N/A	N/A	9.80	5

Note. *Not every infant obtained a time length for each measure in the novel protocol. The # of infants is not presented here because the value of 2.12 minutes (time of the novel protocol) was obtained from 71 infants who had TEOAE times and 68 who had Tympanometry/Behavioral Nursery Noise (TYMP/BBN) times (i.e., different numbers of infants with times for each measure). This applies for every instance where # of infants is blank next to the time of the novel protocol.

**Times available for right and left ears were not from equal numbers of infants; e.g., some infants had a time for right TEOAE and not left, or for right AABR protocol and not left. Times for both ears for certain measures are therefore not displayed if unequal # of infants for right and left ears were obtained.

CHAPTER 4: DISCUSSION

The current study sought to examine a novel protocol for the hearing screening of NICU infants that involved the measures of 1000 Hz tympanometry, TEOAE, and ipsilateral BBN MEMR at a 1000 Hz probe-tone frequency. This novel protocol was examined for three components: equivalency with the current two-stage AABR hearing screening protocol for NICU infants; testing length; and challenges encountered during testing. Unlike the current AABR screening protocol, the proposed novel protocol has the potential to provide information regarding the type of a hearing loss based on different result patterns that could emerge from the screening protocol. These different result patterns were examined to understand possible reasons for a screening referral.

4.1 Reliability of 1000 Hz Tympanograms

To verify the reliability of the 1000 Hz tympanograms that were classified as a pass in this study, normative tympanometric data from the current study were compared with normative data obtained from previous studies with NICU neonates (Table 3). The current study revealed a peak-compensated admittance (Y_{tm}) mean value of 0.59 mmho ($SD = 0.43$). This value was smaller than values obtained by previous researchers examining a sample of NICU infants (Margolis et al., 2003; Shahnaz et al., 2008). However, the current study was the first to use the GN Otometrics Otoflex in a screening protocol with NICU infants in comparison with previous studies that utilized the Grason-Stadler Incorporation (Tymptstar version 2) middle-ear analyzer for the measurement of 1000 Hz tympanograms. Therefore, differences in Y_{tm} values might be attributed to variations in equipment. Mazlan and colleagues (2007) also used the GN Otometrics

Otoflex in testing 1000 Hz tympanometry and BBN MEMR for 42 normal hearing infants at birth and similar to the findings of Margolis et al. and Shahnaz et al., found a higher Y_{tm} of 0.78 mmho (SD = 0.40). However, a recent study by Mazlan and colleagues (2010) examined high-frequency tympanometric results from a larger sample of 273 healthy newborn infants with normal TEOAEs and single-peak tympanograms. Results revealed a Y_{tm} value of 0.65 mmho (SD = 0.34) with the use of the Otoflex, which is comparable with the Y_{tm} value of 0.59 mmho obtained in the present study. Additional studies of NICU infants using the GN Otometrics Otoflex are warranted to develop normative values for Y_{tm} in this population.

One of the Otoflex parameters for the recording of 1000 Hz tympanometry examined in the current study was pump speed. Pump speed in the current study (> 500 daPa/sec) was faster than the speed used in previous studies with NICU infants. As previous research has shown that an increase in pump speed will result in an increase in peak admittance (Y_a) (Koebsell & Margolis, 1985), implying an increase in peak-compensated admittance (Y_{tm}), we expected a larger Y_{tm} in the current study (0.59 mmho) than in previous studies. However, Shahnaz et al. (2008) obtained a larger mean Y_{tm} value of 0.77 mmho with the use of a slower pump speed of +200 daPa/sec. Furthermore, Margolis and colleagues (2003) obtained a larger mean Y_{tm} value of 0.80 mmho with two different pump speeds of +600 daPa/sec at the tail and +200 daPa/sec at the peak. Therefore, an increase in Y_{tm} with an increase in pump speed was not noted with the sample of the current study.

4.2 Classification of Groups

Three groups of infants were created based on outcomes obtained at the time of screening: first screening group (N = 115 ears), rescreened group (N = 20 ears), and meshed group (N = 8 ears). Infants classified into the first screening group obtained valid results on

every screening measure at their initial screening. Infants classified into the rescreened group obtained an invalid result on at least one screening measure at their first screening. However, when these infants returned for a second screening, valid results on all four measures were obtained. These infants were included in the study based on results from their second screening. Infants classified into the meshed group obtained an invalid result for at least one screening measure at both of their first and second screenings. However, when results from the first and second screenings were combined, a valid result existed for each screening measure.

4.3 Screening Outcomes for Each Group

4.3.1 First Screening Group

Screening outcome (pass or refer) for the AABR and novel protocols were examined for each of the three groups of infants. For the first screening group, results revealed that 77.4% of infants passed the AABR protocol and 57.4% passed the novel protocol. Although 20% more infants passed the AABR protocol, the two protocols differed in their criteria for a pass outcome. The test protocol for the novel protocol was strict parallel for a pass, i.e., infants were required to obtain a pass result on every test measure in order to receive a pass outcome. However, the pass outcome for AABR was based on the single measure. As the novel protocol comprised of three test measures compared to the single test measure of the AABR protocol, the novel protocol might have been inherently more sensitive to hearing loss due to transient conductive components than the latter. Previous research has demonstrated that the measure of OAE, which was included in the novel protocol of the current study, may be more sensitive to milder hearing losses than AABR (Johnson et al., 2005).

Interestingly, the majority (79.6%) of the ears from the first screening group who referred on the novel protocol referred on the measure of TEOAE. TEOAEs have been demonstrated to

be more susceptible to transient conditions of the external and middle ear, in comparison with the AABR (Norton et al., 2000). TEOAEs are quite sensitive to mild middle-ear impairment (Koivunen et al., 2000; Naeve et al., 1992; Owens, McCoy, Lonsbury-Martin, & Martin, 1993) and can be utilized to verify normal middle-ear status in addition to their utility in screening for normal cochlear function (Kemp, Bray, Alexander, & Brown, 1986). Moreover, previous research has revealed referral rates for OAEs as high as 20% for hearing screening performed within the first 24 hours of birth, possibly as a result of residual amniotic fluid, mesenchyme, or debris in the infant's outer or middle ear (Erenberg et al., 1999; Kok et al., 1992; Takahara et al., 1986). Although infants in the present study were tested at a mean age of 31.38 chronological days, many infants were born prematurely. As such, lingering fluid or debris might have been present in the ears of these infants, resulting in a higher referral rate. An additional contribution to a higher referral rate might have been the use of nasotracheal tubes for ventilation, which has been associated with a prevalence of 30% for otitis media with effusion (OME) in NICU infants (Berman et al., 1978; Pestalozza, 1984; Salamy et al., 1989). Furthermore, although specific ethnicity data could not be obtained, discussions with the NICU nurses revealed that many of the infants tested were of First Nations descent. Research has revealed a high prevalence of otitis media among First Nations children (Ayukawa et al., 2003). Although high prevalence rates have been associated with environmental factors, genetic predisposition for increased susceptibility might also exist (Todd & Bowman, 1985). The investigation of ethnicity data is warranted for future studies.

Another source for a higher referral rate among the measures of the novel protocol in the first screening group was due to 1000 Hz tympanometry (55.1% of ears). Tympanograms obtained at 1000 Hz probe-tone frequency have been shown to be sensitive and specific to

abnormal and normal middle-ear conditions in newborns (Alaerts, Luts, and Wouters, 2007; Baldwin, 2006; Kei et al., 2003; Margolis et al., 2003; Purdy & Williams, 2000; Shahnaz et al., 2008; Williams et al., 1995). Given the aforementioned possibility of lingering fluid or debris in the neonate ear canal and/or middle ear, this referral result is unsurprising. Tympanometry at 1000 Hz has also been demonstrated to be a good predictor of the presence or absence of OAE (Swanepoel et al., 2007; Kei et al., 2003; Shahnaz et al., 2008). Similarly, results from the current study indicated that 40.8% of the ears who referred on the novel protocol from the first screening group referred for both 1000 Hz tympanometry and TEOAE, providing further support for their conjoint use.

A third source of referral on the novel protocol in the first screening group was due to the absence of BBN MEMR (46.9%). Such a result might have been obtained with the existence of a conductive hearing loss secondary to middle-ear dysfunction (Gelfand, 2009); with a sensorineural loss of greater than 50 to 60 dB HL (Gelfand, 2009; Mazlan et al., 2009a); or simply with an issue regarding probe fit. Given the aforementioned percentages of infants who referred on each of the measures of TEOAE and 1000 Hz tympanometry, it is likely that the primary cause for referral was due to residual fluid or debris or true OME. Furthermore, at the time of the follow-up screening, occurring six to eight weeks following the date of the first screening, all but one of the 15 ears that returned for follow-up obtained a pass result on the novel protocol. As OME has been shown to resolve spontaneously within three months for most children (The Otitis Media Guideline Panel, 1994), it is possible that by the time of the follow-up appointment, any residual fluid or debris that was present at the time of the first screening had cleared. This finding might have implications for the modification of future screening protocols; current two-stage AABR protocols require a diagnostic audiological assessment following a

referral result. However, if a likely reason for referral is due to a transient middle-ear problem, a follow-up screening appointment following the administration of the novel protocol might be a less costly way of verifying an infant's screening outcome at a later date. At this follow-up appointment, all measures of the novel protocol would be repeated to rescreen for a dysfunction in the conductive pathway or possible sensorineural pathology.

4.3.1.1 Comparability of Screening Protocols for the First Screening Group

The current study also examined if comparable results between the two protocols were obtained; i.e., if infants who passed the AABR protocol also passed the novel protocol. Results revealed that 52.2% of infants in the first screening group passed both protocols, and 17.4% referred on both. This implies that 69.6% of infants obtained comparable results on the two protocols, while 30.4% of infants obtained different screening outcomes for each of the AABR and novel protocols.

One pattern of results that occurred for infants obtaining different screening outcomes for each of the protocols was a pass result for AABR and a refer result for the novel protocol (25.2%). A potential reason for different screening outcomes between AABR and the novel protocols has been explored by Johnson and colleagues (2005) and Ross and colleagues (2008). They examined the critical issue of infants with mild hearing losses being missed by the current screening protocol for infants in the well-baby nursery. This protocol includes a first-stage TEOAE, followed by a second-stage AABR if a refer result is obtained on the TEOAE. Johnson and colleagues (2005) found that approximately 23% of infants with permanent hearing loss of ≥ 25 dB HL at nine months of age were missed by their screening at birth. They found that of those infants not identified, >70% had a mild hearing loss (defined as 25-40 dB HL across the frequency range). These infants had referred on the initial TEOAE, yet passed the subsequent

AABR and did not receive follow-up. This research is comparable to the present study as infants might have referred on the novel protocol due to the measure of TEOAE, while passing the current AABR protocol.

There are important issues regarding the stimuli used with the GN Otometrics Accuscreen device that need to be discussed in light of this pattern of results of passing the AABR protocol and referring on the novel protocol. Firstly, a notable difference between the TEOAE and AABR stimuli of the Accuscreen device is that the TEOAE stimulus level of 45-60 dB HL self-calibrates depending on the size of the infant ear canal to maintain a constant stimulus level; however, although an electrode impedance check is run prior to the recording, no such ear size calibration exists for the AABR (A. Moroz, GN Otometrics Clinical Project Liaison, personal communication, November 8, 2010). Therefore, the level of the AABR click stimulus might vary at the tympanic membrane depending on the size of the infant ear canal, often being a higher level than 35 dB nHL given the small size (Stevens et al., 2004). This might provide evidence as to why some infants with mild hearing loss might refer on TEOAE and pass AABR. Moreover, there are no agreed-upon ANSI standards for the calibration of OAE and AABR equipment among screening devices being used in universal hearing screening programs; therefore differences might exist in stimulus levels among devices (Johnson et al., 2005).

It is also important to note that the initial goal of the universal screening program when it began in the early 1990s was to identify infants with congenital moderate or greater bilateral hearing loss, and equipment was therefore designed to address this need (Johnson et al., 2005). Davis and colleagues (1997) discuss how although epidemiological data exists for moderate or greater degrees of hearing loss, it does not exist for milder degrees. Milder degrees of hearing loss might go undetected, creating challenges in the identification of affected individuals (Davis

et al., 1997). Evidence that does exist has been shown to be poorly controlled and subject to various interpretations (Davis et al., 1997). As a result, screening programs have not included minimal or mild hearing loss as their target disorder due to a lack of data regarding the effectiveness of interventions (Davis et al., 1997; Fitzpatrick, Durieux-Smith, & Whittingham, 2008). Despite this, the World Health Organization (Strong, 2005) lists requirements for medical screening as involving a well-defined, medically important disorder for which a remedy exists, comprising of screening tests that are simple and safe. The novel protocol examined in the current study follows these requirements and may have the ability to detect mild degrees of hearing loss that can go undetected with the current well-baby screening protocol.

Previous research has highlighted the impact of minimal and mild hearing losses on educational performance and psychosocial development (e.g., Bess, Dodd-Murphy, & Parker, 1998; Gravel, Wallace, & Ruben, 1996; Holstrum et al., 2008). Bess and colleagues (1998) noted that children with minimal sensorineural hearing loss experienced greater challenges than normal hearing children on various educational and functional test measures. Similarly, Gravel and colleagues (1996) found that mild conductive hearing loss secondary to otitis media early in life might have an effect on auditory abilities including speech in noise, auditory memory, and binaural processing at a later age. However, some studies have shown that no negative academic outcomes exist for children with minimal to mild degrees of hearing loss (Briscoe, Bishop, & Norbury, 2001; Norbury, Bishop, & Briscoe, 2001; Wake et al., 2006).

Although research on the negative outcomes of minimal to mild hearing loss is mixed, the detection of such degrees of hearing loss at birth might optimize future academic, psychosocial, and auditory processing outcomes. With the use of a protocol that could detect minimal hearing loss, appropriate interventions (e.g., routine monitoring of hearing loss;

educational support; FM systems in the classroom) would need to be implemented in order for the protocol to be maximally beneficial for the future outcomes of children identified. The use of the novel protocol might enable the early detection of children with minimal to mild hearing loss, which could assist in the documenting the justification for early detection and intervention (Davis et al., 1997).

An additional pattern of results was that infants might have passed the novel protocol and referred on the AABR protocol (5.2%). This result was less expected and only occurred for 6 infants in the first screening group. This finding was slightly surprising; it was thought that the novel protocol was more sensitive than the AABR protocol due to its strict parallel test protocol and greater number of screening measures. A possible reason for a referral on AABR for these 6 infants was high noise levels in the NICU, which might have interfered with test recordings. Specific noise levels were not recorded for these 6 infants; however, 2 of the infants had AABR times of 8:25 minutes and 9:09 minutes. The screeners noted that long AABR test times such as these often occurred with high environmental and/or internal body noise, which might have contributed to the AABR screening result. However, a reason for AABR referral for the other 4 infants remains unclear. Only one of these 6 infants returned for follow-up, at which time a pass result was obtained for both protocols. Unfortunately, the reason for AABR referral for the other 5 infants could not be determined as they did not return for follow-up. For a pass on the novel protocol, an infant must not have had significant middle-ear dysfunction; a refer result on the AABR might therefore signify a sensorineural pathology. However, it was expected that a refer result on AABR would have been mirrored by the TEOAE result if the pathology was cochlear in origin and by the BBN MEMR result, as both AABR and BBN MEMR measures assess the pathway up to the level of the brainstem (Berlin, Hood, Morlet, et al., 2005; Erenberg et al.,

1999). It is important to note that the Otoflex device recorded a BBN MEMR as being present on certain occasions when an infant had a flat tympanogram. It is possible that in these cases the BBN MEMR was recorded erroneously by the system, which might lead to suspicions regarding the validity of the Otoflex device. This issue will be discussed below in the “Challenges Encountered during the Screening Protocols” section.

4.3.2 Rescreened Group

Results for screening outcomes for the AABR and novel protocols for infants in the rescreened group revealed that 90% of ears passed the AABR protocol and 85% of ears passed the novel protocol. The 5% difference in passing rates could again be attributed to the difference in test protocols, with the novel protocol being more sensitive than the AABR protocol to mild degrees of hearing loss and to transient losses secondary to middle-ear dysfunction. The majority of ears from the rescreened group that referred on the novel protocol (N = 3) referred on the measure of 1000 Hz tympanometry (66.7%). As previously mentioned, 1000 Hz tympanograms have been demonstrated to be sensitive and specific to normal and abnormal middle-ear conditions in newborns (Baldwin, 2006; Kei et al., 2003). These infants might have had a compromised middle-ear system at the time of their screening. Previous research has highlighted that NICU infants might have a greater susceptibility to otitis media, with increased risk in comparison to infants from the well-baby nursery (Berman, Balkany, & Simmons, 1978; Engel, Anteunis, Hendriks, & Marres, 1996; Engel et al., 2001). Furthermore, as revealed through discussions with NICU staff, the known high prevalence of otitis media among First Nations children might have contributed to this result (Ayukawa et al., 2003).

4.3.2.1 Comparability of Screening Protocols for the Rescreened Group

In evaluating the comparability of screening results from both protocols, results revealed that 85% of ears passed both the AABR and novel protocols and 10% referred on both protocols. Therefore, 95% of the infants in the rescreened group obtained comparable screening results from each of the screening protocols. Infants in this group obtained valid results at their second screening, and therefore were older at the time of screening than infants in the first screening group. These infants might have had more time for residual fluid or debris to clear and hence present with normal middle ears at the time of screening; therefore, increasing the chances for a pass outcome on the novel protocol. Furthermore, with increased age, a better fit of the probe tip might have occurred with the increased size of the infant's ear canal at the second screening.

4.3.3 Meshed Group

Results for screening outcomes for the AABR and novel protocols for infants in the meshed group revealed that 75% of ears passed the AABR protocol and 50% of ears passed the novel protocol. Interestingly, all of ears from this group that referred on the novel protocol (N = 4) referred on the measure of 1000 Hz tympanometry (100%), with 50% of ears referring on TEOAE and 50% on BBN MEMR. This result lends further support to the possibility that infants might have had middle-ear dysfunction at the time of screening, as evidenced by a refer result on the measure of 1000 Hz tympanometry.

4.3.3.1 Comparability of Screening Protocols for the Meshed Group

In terms of comparability, 50% of ears passed both of the AABR and novel protocols, and 25% referred on both protocols. Therefore, 75% of ears in the meshed group (N = 6 ears) obtained comparable results on the two protocols, while 25% of infants (N = 2 ears) obtained different screening outcomes for each of the AABR and novel protocols. The 2 ears obtaining

different outcomes each passed the AABR protocol and referred on the novel protocol; specifically, both ears referred on 1000 Hz tympanometry and one ear referred on BBN MEMR. This result provides further evidence for the comparability of the two screening protocols and the increased sensitivity of the novel protocol to middle-ear dysfunction.

4.4 Analysis of Different Patterns in Screening Outcome

Regardless of the group that they were classified into, each infant could obtain one of four patterns of screening outcomes when tested with the AABR and novel protocols: obtaining a pass result on both protocols; obtaining a pass result on the AABR protocol and a refer result on the novel protocol; obtaining a refer result on both protocols; and obtaining a refer result on the AABR protocol and a pass result on the novel protocol. A pass result on both protocols was obtained by most infants in the sample (57 infants; 101 ears; 70.6%), of whom the majority (59.4%, 60 ears) had been classified into the first screening group. This result provides support for the comparability of results between the current AABR protocol and the novel protocol.

Of the infants who passed the current AABR screening protocol and referred on the novel protocol (25 infants; 33 ears), most referred due to TEOAE (70%, 23 ears). This is consistent with the above discussion of the possibility of lingering middle-ear debris or fluid at the time of screening and with the increased sensitivity of TEOAE to milder degrees of hearing loss. The majority of infants obtaining this pattern of screening outcome were from the first screening group (87.9%, 29 ears) which comprised of the group with the youngest infants at the time of screening. Infants who obtained this pattern of screening outcome might have had middle-ear dysfunction that was not detected by the AABR protocol.

Nineteen infants (24 ears) referred on both screening protocols and once again TEOAE was the screening measure that resulted in the highest referral rate among the measures of the

novel protocol (83.3%, 20 ears). Interestingly, a substantial percentage of infants also referred on BBN MEMR (75%, 18 ears). This finding provides support for the consistency of results between the measures of AABR and BBN MEMR, both of which provide information regarding the integrity of the auditory pathway up to the level of the brainstem (Berlin, Hood, Morlet, et al., 2005; Erenberg et al., 1999). Results revealed that 45.8% of ears (N = 11) referred on all three measures of the novel protocol. Similarly, support for the use of BBN MEMR in the detection of possible middle-ear pathology was noted by Mazlan and colleagues (2009a), who found that a cohort of their sample that passed AABR and referred on BBN MEMR also had elevated or absent TEOAEs and flat tympanograms. Infants who referred on both screening protocols most likely had middle-ear dysfunction; however, a sensorineural component cannot be ruled out.

Six infants (6 ears) passed the novel protocol yet referred on the AABR protocol. All six of these infants were from the first screening group, and were discussed above under the subheading of “4.3.1.1 Comparability of Screening Protocols for the First Screening Group”.

4.5 Challenges Encountered During the Screening Protocols

4.5.1 Current AABR Protocol

With greater testing experience, the researchers became more adept at successfully running the screening protocols; however, certain challenges were noted throughout the course of data collection. The four screening measures of AABR, 1000 Hz tympanometry, TEOAE, and BBN MEMR all had instances of invalidity; however, most notably, 70% of ears in the rescreened group and all ears in the meshed group had an invalid result for AABR at their first screening. A valid AABR result could not be obtained for these ears due to unfavourable conditions in the NICU; at times, noise levels reached from 75 dBC to more than 80 dBC, which

hindered clear recordings. There was often a large amount of activity in the NICU, including general movement and discussions of staff and visitors, telephones ringing, infants crying, beeping of monitors, and paper rustling. Furthermore, there were certain instances of electrical interference between the Accuscreen device and surrounding electrical equipment that prevented any recordings. In addition, the AABR was sensitive to any movement, and therefore, was not possible to complete when the infant was fussing and moving.

The measure of AABR often ran for very long periods of time; in certain cases up to 8 minutes. Testing time increased when the infant was noisy (e.g., sucking, moving) and when there was a possible presence of pathology. It ran most quickly in cases of a normal screening result. Furthermore, infants in isolettes were noted to have high electrode impedances, likely due to the warm temperatures of their skin. Lower electrode impedances have been shown to reduce testing time and increase the pass rate for AABR screening (Norton et al., 2000). Moreover, the electrodes would often need to be reapplied. Consequentially, the researchers attempted to prioritize infants who were not in isolettes in order to save valuable screening time.

4.5.2 Novel Protocol

4.5.2.1 1000 Hz Tympanometry

A lesser, though still noteworthy, percentage of ears in the rescreened group (35%) obtained an invalid tympanometric result at their first screening. Moreover, all ears in the meshed group obtained an invalid tympanometric result at their first screening. Tympanograms could not be recorded for infants with excessive movement or who were crying. In addition, at times the recorded tympanogram would have an ear canal volume (V_{ea}) of 0.04 ml or less, indicating that the probe tip was resting against the ear canal wall of the infant. For this reason, tympanograms with V_{ea} of ≤ 0.04 mL were considered invalid. A possible contribution to this

challenge included size of the available probe tips, which might have been too large for the very small infant ear canal. With time, increased screening experience of the testers proved to lessen the frequency of obtaining these invalid tympanograms due to improvements in probe tip positioning.

Furthermore, the Otosuite software that accompanied the GN Otometrics Otoflex had certain inefficient characteristics that are still being worked out by the manufacturer. There were instances that tympanometric data could not be saved due to deficiencies in the software. Moreover, preliminary analyses revealed that values generated by the Otosuite software were unreliable for the V_{ea} of the Y tympanogram; therefore manual calculations were performed for each variable instead of relying on software-generated values. Given these inconveniences, it is evident that the Otosuite software still requires attention before it is utilized in larger-scale screening protocols.

4.5.2.2 BBN MEMR

Challenges were also noted in the recording of BBN MEMR with the GN Otometrics Otoflex device. Like the recording of 1000 Hz tympanometry, the probe tip was at times against the ear canal wall and needed to be readjusted. A measurement against the canal wall was noted by the researchers as a volume of < 0.04 ml and a straight line. Furthermore, at times a reflex might have been present, yet wasn't recorded during the first test; therefore, the test was run for approximately three trials to ensure that a reflex was captured if it was present. Often, this seemed to be associated with probe fit and resolved once the probe was readjusted. As the probe tips were the same ones used in the recording of 1000 Hz tympanometry, their size did not always seem ideal as they were often too large for the infant's small ear canal. Similar challenges in the recording of BBN MEMR with the Otoflex were noted by Mazlan, Kei, and Hickson

(2009a); specifically, they noted difficulty in maintaining the probe seal due to the small, soft nature of the neonate's external ear.

The present study revealed an important issue with the GN Otometrics Otoflex device in the recording of BBN MEMR. As briefly mentioned above, certain infants had a present BBN MEMR in the case of an abnormal tympanogram and/or in the case of absent TEOAE.

Specifically, 13 ears had a present BBN MEMR and an abnormal tympanogram; 25 ears had a present BBN MEMR and absent TEOAE; and 8 ears had a present BBN MEMR with both an abnormal tympanogram and absent TEOAE. Any conductive pathology demonstrated by an abnormal tympanogram can inhibit a change in tympanic membrane compliance that is required for the recording of a MEMR (Jerger, Burney, Mauldin, et al., 1974). Hence, BBN MEMR would not be expected in cases with abnormal tympanometry. In addition, as TEOAEs are quite sensitive to mild middle-ear impairment (Koivunen et al., 2000; Naeve et al., 1992; Owens, McCoy, Lonsbury-Martin, & Martin, 1993), BBN MEMR would also not be expected in cases with absent TEOAEs. However, for a BBN MEMR to be recorded as present, the GN Otometrics Otoflex device might have noted either an upwards (increase in admittance; decrease in impedance) or downwards (decrease in admittance; increase in impedance) deflection of the reflex tracing of at least 0.04 mmho. Similarly, this decrease in impedance, or upwards deflection with the GN Otometrics Otoflex device was noted for 4% of normal ears with the use of both 2 kHz pure tone and BBN stimuli in a study by Mazlan, Kei, and Hickson (2009a).

Previous research has demonstrated that the direction of the reflex tracing changes at around 1200 Hz in newborn infants, when an upwards deflection is noted (Weatherby & Bennett, 1980). This can occur as a result of a decrease in impedance (increase in admittance) due to a reduction of resistance and reactance at this high probe-tone frequency, which is close to the

resonant frequency of the infant middle ear (Mazlan, Kei, & Hickson, 2009a; Weatherby & Bennett, 1980). In the present study, it is possible that infants obtaining a reflex with an abnormal tympanogram or with absent TEOAE had a reflex tracing with an upwards deflection, an unexpected direction that often does not qualify as a reflex in children and adults. Although the appearance of an upwards deflection can signify an increase in admittance in normal ears, this might not be the case for infants with abnormal middle-ear status due to their unique disease process. Future research should investigate this unexpected reflex deflection direction. This would help to further understand this phenomenon, and to differentiate a possible true characteristic of the reflex in the GN Otometrics Otoflex.

4.5.2.3 TEOAE

TEOAE was the easiest measure to run; if a refer result was obtained on the first attempt a second test was always administered to verify the result. The TEOAE test was less sensitive to noise than the AABR and a pass result was usually obtained on the second attempt if it wasn't recorded for the first.

4.6 Effects of Invalid Results on Screening Protocols

The original sample of infants from whom data were collected for the present study included infants who obtained invalid test results. It is important to compare the number of ears obtaining invalid results for each screening protocol, as a protocol with a low number of invalid results might be more feasible in implementing than a protocol with a larger number of invalid results. Thirty-seven ears were excluded from the sample for either obtaining an invalid test result at their first screening and not returning to the Audiology department for a second screening (28 ears), or for coming back for a second screening and obtaining an invalid test result once again that could not be meshed with valid results from their first screening (9 ears).

As previously mentioned in section 2.2.2 describing exclusion criteria, most of these ears (62.2%; 23 ears) were excluded due to at least one measure on the novel protocol, while 21.6% (8 ears) were excluded due to the AABR measure of the AABR protocol, and 16.2% (6 ears) were excluded due to measures from both protocols. For the nine ears that returned for a second screening, 66.7% (6 ears) could not be tested on AABR and 33.3% of ears (3 ears) obtained invalid results for the novel protocol. Although most of the 37 excluded ears were excluded due to an invalid result on at least one measure of the novel protocol, there was a greater likelihood of obtaining an invalid result due to the greater number of measures. Furthermore, due to the administration of two screening protocols as described in Section 2.6, with TEOAE and AABR preceding the recording of 1000 Hz tympanometry and BBN MEMR, it is possible that by the time those last two novel protocol measures were recorded, the infant had woken up or become agitated. Future research might further examine this possibility by reordering the administration of the two protocols to avoid any order effects. At the second screening, most ears remained excluded due to obtaining an invalid result on AABR at this time. When infants returned for a second screening, the novel protocol therefore appeared to have a better rate of success in obtaining valid results than did the AABR protocol.

An additional 28 ears obtained invalid results at their first screening, but were included in the study due to the rescreened and meshed groups. Twenty of these ears returned for a rescreening and were hence included in the rescreened group. From this group, 70% (14 ears) had an AABR that could not be obtained while 60% (12 ears) had at least one invalid measure on the novel protocol. For the 8 ears included in the meshed group, all 8 ears obtained an invalid result on the novel protocol at their first screening; however, when they returned for a second screening, all 8 ears obtained an invalid result on the AABR measure as they could not be tested.

These similar values demonstrate that the number of invalid results obtained for each protocol is comparable for the ears that were included in the study.

4.7 Length of Time for Test Administration

The length of time for test administration was compared for the AABR and novel protocols. Results revealed that the average length of time for the AABR protocol for both ears was 6.84 minutes, and 4.04 minutes for the novel protocol. These time lengths did not include preparation time (e.g., applying electrodes, changing probe tips). Preparation time for the entire length of administration for both protocols was 9.80 minutes (N = 5), although this was likely not representative of the total sample. Much of this preparation time was for the AABR, which involved the application of electrodes and/or the pausing of testing during high levels of noise in the NICU (e.g., during rounds). Despite the novel protocol comprising of a greater number of screening measures, it was 2.80 minutes shorter in length of administration time than the AABR protocol. Therefore, the length of testing for whole sample of 143 ears in the current study with the use of the AABR protocol would have taken a total of 8.2 hours (using an average of 3.42 minutes per ear), and with the novel protocol would have taken a total of 4.8 hours (using an average of 2.02 minutes per ear). It must be noted that this length of testing time accounted for the first screening only; additional time would be required for the administration of a second screening in the case of a refer result on an initial screening. Future studies should examine the length of time recorded at both the initial and follow-up screenings to have a more exact indication of the time required for the implementation of the novel protocol.

Barsky-Firkser and Sun (1997) used the Nicolet Compass ABR System (Natus Medical Inc., San Carlos, CA) and found that testing time, calculated from the start of preparation of the infant's skin for electrode placement to the end of the test after the electrodes were removed, was

at its shortest time 4 minutes and 20 seconds and longest time 25 minutes and 2 seconds, with a mean time of 9 minutes and 1 second (SD = 2 minutes and 55 seconds). Isolated preparation time was not included in this study. Another study by van den Berg, Deiman, and van Straaten (2010) compared the ALGO portable (Natus Medical Inc., San Carlos, CA) with the MB11 BERAphone (Maico Diagnostic, Germany) for AABR screening in a Dutch NICU. Similarly to the Otoflex used in the current study, the ALGO portable uses three disposable electrodes to measure EEG activity. However, unlike the Otoflex and ALGO systems, the MB11 BERAphone consists of a handheld headphone unit containing three fixed electrodes. This avoids the need to apply and remove the electrodes from the infants' skin; however, it requires that the screener maintains a hold on the headphone unit against the infants' skin (van den Berg, Deiman, & van Straaten, 2010). Length of time for each of the two systems was recorded in minutes, from the beginning of the infant positioning and skin preparation. The mean total testing time for the MB11 BERAphone was 11.4 minutes (SD = 6.6 minutes) and for the ALGO portable 13.9 minutes (SD = 8.1 minutes). Dort and colleagues (2000) examined the Intelligent Hearing System's Smart Screener unit and found a mean total test time for both ears of 18:50 minutes, including any preparation time. Meier and colleagues (2004) compared test times of the Echoscreen-TDA, ALGO 3, and BERAphone MB 11 AABR screening devices and found median preparation times of 2.75 (with ear probe), 3, and 2.33 minutes, respectively. Furthermore, they found median total testing times of 3.97, 7.8, and 5.17 minutes. It should be noted that the testing time for the ALGO 3 involved the length of simultaneous binaural testing (Meier, Narabayashi, Probst, & Schmuziger, 2004). In terms of time length for TEOAE recording, Briennesse and colleagues (1998) used the ILO88 Otoacoustic Emission Analyser device (Otodynamics, London UK: version 3.94) in the testing of 19 preterm infants (38 ears)

and found a range of 1 minute 53 seconds to 15 minutes and 26 seconds per ear, with a median of 5 minutes. In addition, they found that the mean total test time, including the equipment setup and probe placement, was approximately 15 minutes (Briennesse et al., 1998). Norton and colleagues studied a sample of 4478 NICU infants and found a mean total test time of 2.05 minutes per ear (SD = 2.02), which included time for probe fit, in-the-ear stimulus calibration, and response recording.

The mean TEOAE time obtained in the Norton and colleagues study is comparable to the mean time obtained in the current study of 2.41 minutes for both ears. In addition, preparation time for the AABR protocol in the current study likely resembled times in the study by Meier and colleagues; however, these values were not reflected in the present study due to the small number of ears for which preparation time was available. Future studies might examine length of preparation time for the administration of the current AABR and novel protocols for a larger sample to obtain a better representation. For the purpose of research studies, it might also be useful to have a time measure built into the screening devices, thereby eliminating the need for simultaneous time and device checking by the researchers.

4.8 Cost Effectiveness of Test Administration

An effective hearing screening protocol would also be cost efficient. Screening devices that are used solely for the testing of AABR are typically more costly than OAE devices (Gorga & Neely, 2003). Previous researchers have noted the cost of AABR and TEOAE screening devices in their studies. Dort and colleagues (2000) found that based on 1000 infants and including the equipment, disposables, and staffing, their Intelligent Hearing System's Smart Screener unit for AABR cost an average of \$25.55 per infant, while the ILO88 TEOAE system cost \$15.70 per infant. Moreover, Meier and colleagues (2004) noted that the unit cost for the

AABR devices of the BERAprone MB11 was € 7590 and for ALGO 3 € 21 666 (including printer, cart, and laptop). Furthermore, Meier and colleagues found that Echoscreen-TDA, with functions for TEOAE and AABR, cost €7690 (€ 1 = CDN\$ 1.35; November 28, 2010). Supply costs for the Echoscreen-TDA, which most closely mirrored those required for the Accuscreen device, were € 4.20 per child (for ear probes and disposable electrodes) and € 8.60 for the ALGO 3 (for ear couplers and disposable electrodes). There were no supply costs for the BERAprone MB11 other than the cost of conductive gel for the handheld headphone unit. Furthermore, Johnson and colleagues (1993) found the cost of OAE screening to be less than \$25.00 per infant.

The cost of the Accuscreen device used in the current study for the testing of both AABR and TEOAE was \$16.00 per infant, based on 1000 infants (A. Mroz, GN Otometrics Clinical Project Liaison, personal communication, November 30, 2010). Supply costs for the Accuscreen (ear tips and disposable electrodes) were \$3.36 per infant (A. Mroz, GN Otometrics Clinical Project Liaison, personal communication, November 30, 2010). The cost of the Otoflex device was \$8.45 per infant, based on 1000 infants, with a supply cost of \$1.20 per infant for ear tips (A. Mroz, GN Otometrics Clinical Project Liaison, personal communication, November 30, 2010). Although the Otoflex device was less costly than the Accuscreen, it would be interesting to examine the cost of a device that assessed the TEOAE separately from the AABR to have a better understanding of the cost of the novel protocol.

Beyond the operating expenses, including staffing and disposable supplies, and the capital expenses, including the purchase of necessary equipment that are required for the start-up of a new screening protocol, it is also important to consider the cost of follow-up testing (Gorga & Neely, 2003). Although the novel protocol in the current study had a higher referral rate than

the AABR protocol, this referral rate led to a second screening appointment, which ultimately served to avoid any unnecessary, more costly diagnostic ABR assessments. The implementation of the novel screening protocol would require sufficient staff for the follow-up screening appointments, which would contribute to the cost of implementing the protocol; however, it might reduce the number of infants requiring a diagnostic ABR assessment. A diagnostic ABR assessment might still be indicated following a refer result on a follow-up screening with the novel protocol, and costs for this occurrence would need to be taken into consideration. Future studies should examine the costs of setting up the novel protocol in a clinical setting in greater detail.

4.9 Future Directions and Overall Conclusions

The present study demonstrated that the novel protocol for the hearing screening of NICU infants involving the measures of 1000 Hz tympanometry, TEOAE, and ipsilateral BBN MEMR at a 1000 Hz probe-tone frequency is comparable to the current AABR protocol. Furthermore, the novel protocol might provide more information regarding the reason for a screening referral, which is paramount given the high prevalence of middle-ear dysfunction in NICU infants. Specifically, the current study suggests that the novel protocol might be more sensitive to middle-ear dysfunction than the current AABR protocol. In addition, the novel protocol might be more sensitive for the detection of mild hearing impairment than the current AABR protocol. Although research is mixed on the benefit of providing intervention for children with minimal or mild degrees of hearing loss, the novel protocol might enable its early detection in infants. This first step in detection can assist in providing information to further understand the implications of providing intervention at a later age. Furthermore, results from the current study have shown that administration of the novel protocol is more rapid than the

current AABR protocol when administered in the NICU. Moreover, challenges that were encountered with the novel protocol can likely be resolved with increased screener experience and with updates to the software used for screening (i.e., Otosuite).

In the future, data from follow-up visits for a larger sample of NICU infants is warranted in order to better understand hearing screening results obtained at birth with the use of the novel protocol. If the novel protocol is better able to detect mild hearing impairment than the current AABR protocol, it might be worth investigating a new gold standard for the confirmation of mild hearing impairment in infants over the course of their first year of life. As the diagnostic ABR might not detect mild degrees of hearing loss, the use of visual reinforcement audiometry (VRA) at 6, 9, and 12 months of age might provide more information regarding the confirmation of a mild hearing loss detected by the novel protocol.

In addition, it would be interesting to apply the novel protocol to a sample of infants from the well-baby nursery in order to obtain normative values. Furthermore, the use of another device for the measurement of 1000 Hz tympanometry and BBN MEMR, for example the Grason-Stadler Incorporation (Tymptstar version 2) middle-ear analyzer, would be a valuable asset for evaluating the validity and comparability of the GN Otometrics Otoflex device. To further assess the length of time required for the administration of the novel protocol, preparation time should be examined for a larger sample. Furthermore, future studies might examine the use of the middle-ear analysis technique of wideband reflectance (WBR) in a newborn hearing screening protocol (Shahnaz, 2008). WBR might provide additional insight into the middle-ear status of NICU infants, hence further improving existing hearing screenings in newborns (Shahnaz, 2008). Finally, although this study is the first step in assessing the feasibility of the implementation of a novel screening protocol for NICU infants, it is imperative that the novel

protocol undergoes a thorough cost-benefit analysis to fully understand its sensitivity and specificity.

Despite the novel screening protocol's potential utility in the identification of reasons for screening referrals, families and medical practitioners must be continually reminded that a pass on a newborn hearing screening does not rule out the possibility of late-onset or fluctuating hearing loss, and that children must be continually monitored for hearing loss as they develop speech and language (Johnson et al., 2005). Continued research on the most effective and efficient protocols for hearing screening will enable earlier detection and treatment of hearing loss in infants to optimize their future outcomes in the areas of speech and language, social and emotional development, and academic achievement.

REFERENCES

- AAA. American Academy of Audiology Pediatric Amplification Protocol. *American Academy of Audiology*. 2003.
- Ahonen, J. E., & McDermott, J. C. (1984). Extended high-frequency hearing loss in children with cleft palate. *Audiology : Official Organ of the International Society of Audiology*, 23, 467-476.
- Alaerts, J., Luts, H., & Wouters, J. (2007). Evaluation of middle-ear function in young children: Clinical guidelines for the use of 226- and 1000 Hz tympanometry. *Otology & Neurotology : Official Publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*, 28(6), 727-732.
- Amedee, R. G. (1995). The effects of chronic otitis media with effusion on the measurement of transiently evoked otoacoustic emissions. *The Laryngoscope*, 105(6), 589-595.
- American Academy of Pediatrics Committee on Environmental Health. (1997). Noise: A hazard for the fetus and newborn. *Pediatrics*, 100, 724-727.
- American Speech-Language-Hearing Association. (1979). Guidelines for acoustic immittance screening of middle-ear function. *ASHA*, 21, 282-288.
- American Speech-Language-Hearing Association. (1990). Guidelines for screening for hearing impairments and middle-ear disorders. *ASHA*, 32 (Suppl. 2), 17-24.
- Anson, B. J., & Donaldson, J. A. (1981). The temporal bone. In B. J. Anson, & J. A. Donaldson (Eds.), *Surgical anatomy of the temporal bone*. (pp. 3). Philadelphia, PA: W.B. Saunders.

Anson, B. J., Bast, T. H., & Richany, S. F. (1955). The fetal and early postnatal development of the tympanic ring and related structures in man. *The Annals of Otology, Rhinology, and Laryngology*, 64, 802-823.

Attias, J., Al-Masri, M., Abukader, L., Cohen, G., Merlov, P., Pratt, H., Othman-Jebara, R., Aber, P., Raad, F., & Noyek, A. (2006). The prevalence of congenital and early-onset hearing loss in Jordanian and Israeli infants. *International Journal of Audiology*, 45, 528-536.

Ayukawa, H., Bruneau, S., Proulx, J. F., Macarthur, J., & Baxter, J. (2004). Otitis media and hearing loss among 12-16-year-old Inuit of Inukjuak, Quebec, Canada. *International Journal of Circumpolar Health*, 63 Suppl 2, 312-314.

Balbani, A. P., & Montovani, J. C. (2003). Impact of otitis media on language acquisition in children. [Impacto das otites medias na aquisicao da linguagem em criancas] *Jornal De Pediatria*, 79, 391-396.

Baldwin, M. (2006). Choice of probe-tone and classification of trace patterns in tympanometry undertaken in early infancy. *International Journal of Audiology*, 45(7), 417-427.

Barsky-Firkser, L., & Sun, S. (1997). Universal newborn hearing screenings: A three-year experience. *Pediatrics*, 99, E4.

BC Early Hearing Program (2008). Section 2: Protocols. In *Screening Training Manual*.

Retrieved from

<http://www.phsa.ca/AgenciesAndServices/Services/BCEarlyHearing/ForProfessionals/Resources/Training-Materials.htm>

Bennett, M. J., & Weatherby, L. A. (1982). Newborn acoustic reflexes to noise and pure-tone signals. *Journal of Speech and Hearing Research, 25*, 383-387.

Berlin, C. I., Hood, L. J., Morlet, T., Wilensky, D., St John, P., Montgomery, E., & Thibodaux, M. (2005). Absent or elevated middle-ear muscle reflexes in the presence of normal otoacoustic emissions: A universal finding in 136 cases of auditory neuropathy/dys-synchrony. *Journal of the American Academy of Audiology, 16*, 546-553.

Berman, S. A., Balkany, T. J., & Simmons, M. A. (1978). Otitis media in the neonatal intensive care unit. *Pediatrics, 62*, 198-201.

Bess, F. H. (2004, May). *Children with minimal sensorineural hearing loss*. Paper presented at Children with Hearing Loss Workshop, Casper, WY.

Bess, F. H., Dodd-Murphy, J., & Parker, R. A. (1998). Children with minimal sensorineural hearing loss: Prevalence, educational performance, and functional status. *Ear and Hearing, 19*, 339-354.

Bess, F.H., & Tharpe, A.M. (1986). Case history data on unilateral sensorineural hearing loss in children. *Ear and Hearing, 7*, 14-19.

Blair, J., Peterson, M. E., & Viehweg, S. H. (1985). The effects of mild sensorineural hearing loss on academic performance of young school-age children. *Volta Review, 93*, 87-93.

- Bonfils, P., & Uziel, A. (1989). Clinical applications of evoked acoustic emissions: Results in normally hearing and hearing-impaired subjects. *The Annals of Otology, Rhinology, and Laryngology*, 98(5 Pt 1), 326-331.
- Brienesse, P., Maertzdorf, W. J., Anteunis, L. J., Manni, J. J., & Blanco, C. E. (1998). Click-evoked oto-acoustic emission measurement in preterm infants. *European Journal of Pediatrics*, 157, 999-1003.
- Briscoe, J., Bishop, D. V., & Norbury, C. F. (2001). Phonological processing, language, and literacy: A comparison of children with mild-to-moderate sensorineural hearing loss and those with specific language impairment. *Journal of Child Psychology and Psychiatry*, 42, 329-340.
- Calandruccio, L., Fitzgerald, T. S., & Prieve, B. A. (2006). Normative multifrequency tympanometry in infants and toddlers. *Journal of the American Academy of Audiology*, 17, 470-480.
- Carlson, L. H., & Fall, P. A. (1998). Otitis media: An update. *Journal of Pediatric Health Care : Official Publication of National Association of Pediatric Nurse Associates & Practitioners*, 12(6 Pt 1), 313-319.
- Carney, A. (1999). Auditory system development and dysfunction: What do we really know about childhood hearing loss? *Trends in Amplification*, 4, 32-38.

- Casselbrant, M. L., & Mandel, E. M. (2003). Epidemiology. In R. M. Rosenfeld, & C. D. Bluestone (Eds.), *Evidence-based otitis media* (2nd ed., pp. 147-162). Hamilton, Ontario: BC Decker Inc.
- Chang, K. W., Vohr, B. R., Norton, S. J., & Lekas, M. D. (1993). External and middle-ear status related to evoked otoacoustic emission in neonates. *Archives of Otolaryngology--Head & Neck Surgery*, *119*, 276-282.
- Chomsky, N. (1995). Chimp talk debate: Is it really language? *The New York Times*.
- Chugani, H. (1997). How to build a baby's brain. *Newsweek, Special Edition*, 29-30.
- Citron, D., 3rd, & Adour, K. K. (1978). Acoustic reflex and loudness discomfort in acute facial paralysis. *Archives of Otolaryngology (Chicago, Ill.: 1960)*, *104*, 303-306.
- Cox, L. C. (1984). The current status of auditory brainstem response testing in neonatal populations. *Pediatric Research*, *18*, 780-783.
- Darcy, A. E., Hancock, L. E., & Ware, E. J. (2008). A descriptive study of noise in the neonatal intensive care unit. ambient levels and perceptions of contributing factors. *Advances in Neonatal Care : Official Journal of the National Association of Neonatal Nurses*, *8*, 165-175.
- Davis, A., Bamford, J., Wilson, I., Ramkalawan, T., Forshaw, M., & Wright, S. (1997). A critical review of the role of neonatal hearing screening in the detection of congenital hearing impairment. *Health Technology Assessment (Winchester, England)*, *1*, i-iv, 1-176.

- Davis, J. M., Elfenbein, J., Schum, R., & Bentler, R. A. (1986). Effects of mild and moderate hearing impairments on language, educational, and psychosocial behaviors of children. *Journal of Speech and Hearing Disorders, 51*, 53-62.
- Davis, A., & Wood, S. (1992). The epidemiology of childhood hearing impairment: Factors related to planning of services. *British Journal of Audiology, 26*, 77-90.
- DeLuzio, J. (2003). Update on hearing health care for preschool children. *Rehabilitation Medicine, 80*, 256-258.
- DePaul, D., & Chambers, S. E. (1995). Environmental noise in the neonatal intensive care unit: Implications for nursing practice. *The Journal of Perinatal and Neonatal Nursing, 8*, 71-76.
- De Sa, D. J. (1973). Infection and amniotic aspiration of middle-ear in stillbirths and neonatal deaths. *Archives of Disease in Childhood, 48*, 872-880.
- Dodd-Murphy, J., & Murphy, W. (2007, November). *Educational risk and perception of hearing difficulty in school children*. Paper presented at American Speech-Language-Hearing Association National Convention, Boston, MA.
- Dort, J. C., Tobolski, C., & Brown, D. (2000). Screening strategies for neonatal hearing loss: Which test is best? *The Journal of Otolaryngology, 29*, 206-210.
- Dowley, A. C., Whitehouse, W. P., Mason, S. M., Cope, Y., Grant, J., & Gibbin, K. P. (2009). Auditory neuropathy: Unexpectedly common in a screened newborn population. *Developmental Medicine and Child Neurology, 51*, 642-646.
- Downs, M. P. (1970). The

identification of congenital deafness. *Transactions - American Academy of Ophthalmology and Otolaryngology*. *American Academy of Ophthalmology and Otolaryngology*, 74, 1208-1214.

Downs, M. P. (1995). Universal newborn hearing screening--the colorado story. *International Journal of Pediatric Otorhinolaryngology*, 32, 257-259.

Doyle, K. J., Burggraaff, B., Fujikawa, S., Kim, J., & MacArthur, C. J. (1997). Neonatal hearing screening with otoscopy, auditory brain stem response, and otoacoustic emissions. *Otolaryngology--Head and Neck Surgery : Official Journal of American Academy of Otolaryngology-Head and Neck Surgery*, 116(6 Pt 1), 597-603.

Doyle, K. J., Kong, Y. Y., Strobel, K., Dallaire, P., & Ray, R. M. (2004). Neonatal middle-ear effusion predicts chronic otitis media with effusion. *Otology & Neurotology : Official Publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*, 25, 318-322.

Doyle, K. J., Rodgers, P., Fujikawa, S., & Newman, E. (2000). External and middle-ear effects on infant hearing screening test results. *Otolaryngology--Head and Neck Surgery : Official Journal of American Academy of Otolaryngology-Head and Neck Surgery*, 122, 477-481.

Driscoll, C., Kei, J., & McPherson, B. (2000). Transient evoked otoacoustic emissions in 6-year-old school children: A normative study. *Scandinavian Audiology*, 29, 103-110.

Durieux-Smith, A., & Jacobson, J. T. (1985). Comparison of auditory brainstem response and behavioral screening in neonates. *The Journal of Otolaryngology. Supplement*, 14, 47-53.

- Durieux-Smith, A., Picton, T. W., Bernard, P., MacMurray, B., & Goodman, J. T. (1991). Prognostic validity of brainstem electric response audiometry in infants of a neonatal intensive care unit. *Audiology : Official Organ of the International Society of Audiology*, 30, 249-265.
- Early identification of hearing impairment in infants and young children. (1993). *NIH Consensus Statement*, 11, 1-24.
- Eavey, R. D. (1993). Abnormalities of the neonatal ear: Otoscopic observations, histologic observations, and a model for contamination of the middle-ear by cellular contents of amniotic fluid. *The Laryngoscope*, 103(1 Pt 2 Suppl 58), 1-31.
- Eavey, R. D., Bertero Mdo, C., Thornton, A. R., Herrmann, B. S., Joseph, J. M., Gliklich, R. E., Krishnamoorthy, K. S., & Todres, I. D. (1995). Failure to clinically predict NICU hearing loss. *Clinical Pediatrics*, 34, 138-145.
- Eby, T. L., & Nadol, J. B., Jr. (1986). Postnatal growth of the human temporal bone. implications for cochlear implants in children. *The Annals of Otology, Rhinology, and Laryngology*, 95(4 Pt 1), 356-364.
- Engel, J. A. M., Anteunis, L. J. C., Hendriks, J. J. T., & Marres, E. H. M. A. (1996). Epidemiologic aspects of otitis media with effusion in infancy. In D. J. Lim, C. D. Bluestone, M. Casselbrant, J. O. Klein & P. L. Ogra (Eds.), *Proceedings of the sixth international symposium recent advances in otitis media* (pp. 47). B.C. Decker, Ontario:

- Engel, J., Mahler, E., Anteunis, L., Marres, E., & Zielhuis, G. (2001). Why are NICU infants at risk for chronic otitis media with effusion? *International Journal of Pediatric Otorhinolaryngology*, *57*, 137-144.
- Erenberg, A., Lemons, J., Sia, C., Trunkel, D., & Ziring, P. (1999). Newborn and infant hearing loss: Detection and intervention. American Academy of Pediatrics Task Force on Newborn and Infant Hearing, 1998- 1999. *Pediatrics*, *103*, 527-530.
- Erenberg, S. (1999). Automated auditory brainstem response testing for universal newborn hearing screening. *Otolaryngologic Clinics of North America*, *32*, 999-1007.
- Ferguson, M. A., Smith, P. A., Lutman, M. E., Mason, S. M., Coles, R. R., & Gibbin, K. P. (1996). Efficiency of tests used to screen for cerebello-pontine angle tumours: A prospective study. *British Journal of Audiology*, *30*, 159-176.
- Filipo, R., De Seta, E., & Bertoli, G. A. (1988). High-frequency audiometry in children. *Scandinavian Audiology*, *17*, 213-216.
- Fitzpatrick, E. M., Durieux-Smith, A., & Whittingham, J. (2010). Clinical practice for children with mild bilateral and unilateral hearing loss. *Ear & Hearing*, *31*, 392-400.
- Fortnum, H.M., Summerfield, A.Q., Marshall, D.H., Davis, A.C., & Bamford, J.M. (2001). Prevalence of permanent childhood hearing impairment in the United Kingdom and implications for universal neonatal hearing screening: questionnaire based ascertainment study. *British Medical Journal*, *323*, 1-5.

Friel-Patti, S., Finitzo-Hieber, T., Meyerhoff, W., & Heiber, J. P. (1986).

Speech-language learning and early middle-ear disease: A procedural report. In J. F.

Kavanagh (Ed.), *Otitis media and child development*. (pp. 60). Parkton, MD: York Press.

Galambos, R., Hicks, G. E., & Wilson, M. J. (1984). The auditory brain stem response reliably predicts hearing loss in graduates of a tertiary intensive care nursery. *Ear and Hearing*, 5, 254-260.

Gelfand, S. A. (2009). The acoustic reflex. In: Katz, J., Medwetsky, L., Burkhard, R., Hood, L. J. (Eds.), *Handbook of Clinical Audiology, sixth ed.* Lippincott Williams & Wilkins, Baltimore, pp. 189-221 (Chapter 10).

Gerhardt, K. J., & Abrams, R. M. (2000). Fetal exposures to sound and vibroacoustic stimulation. *Journal of Perinatology : Official Journal of the California Perinatal Association*, 20(8 Pt 2), S21-30.

GN Otometrics (2010a). Madsen Accuscreen Technical Specifications. Retrieved from http://www.bsure4balance.com/7-26-8100-en_00_std.pdf

GN Otometrics (2010b). Madsen Otoflex Product Brochure. Retrived from <http://www.otometrics.com/SiteCollectionDocuments/Product%20brochures/otoflex%20brochure.pdf>

Gold, T. (1948). Hearing II: The physical basis of the action of the cochlea. *Proceedings of the Royal Society B: Biological Sciences*, 135, 492-498.

- Gorga, M. P., & Neely, S. T. (2003). Cost-effectiveness and test-performance factors in relation to universal newborn hearing screening. *Mental Retardation and Developmental Disabilities Research Reviews*, 9, 103-108.
- Gravel, J. S. (2000). Audiologic assessment for the fitting of hearing instruments: Big challenges from tiny ears. In: Seewald RC, editor. *A Sound Foundation Through Early Amplification*. Phonak AG; 2000. p. 33-46.
- Gravel, J. S. (2005). Prevalence and screening in newborns. *Proceedings of a National Workshop on Mild and Unilateral Hearing Loss*. Breckenridge, CO. Retrieved from http://www.cdc.gov/ncbddd/ehdi/documents/unilateralhl/Mild_Uni_2005%20Workshop_Proceedings.pdf
- Gravel, J. S., & Ruben, R. J. (1996). Auditory deprivation and its consequences: From animal models to humans. In R. Fay, A. Popper & T. Van De Water (Eds.), *Clinical aspects of hearing: Springer series in auditory research*. (pp. 86-115). New York: Springer-Verlag.
- Gravel, J. S., Roberts, J. E., Roush, J., Grose, J., Besing, J., Burchinal, M., Neebe, E., Wallace, I. F., & Zeisel, S. (2006). Early otitis media with effusion, hearing loss, and auditory processes at school age. *Ear and Hearing*, 27, 353-368. Gravel, J. S., & Wallace, I. F. (2000). Effects of otitis media with effusion on hearing in the first 3 years of life. *Journal of Speech, Language, and Hearing Research : JSLHR*, 43, 631-644.
- Gravel, J. S., Wallace, I. F., & Ruben, R. J. (1996). Auditory consequences of early mild hearing loss associated with otitis media. *Acta Oto-Laryngologica*, 116, 219-221.

- Hanks, W. D., Adamovich, S., & Buethe, P. (2009). *1000 Hz tympanometry and EMDI programs*. Unpublished manuscript.
- Harrison, R. V. (1998). An animal model of auditory neuropathy. *Ear and Hearing, 19*, 355-361.
- Hayes, D. (2003). Screening methods: Current status. *Mental Retardation and Developmental Disabilities Research Reviews, 9*, 65-72.
- Hille, E. T., Weisglas-Kuperus, N., van Goudoever, J. B., Jacobusse, G. W., Ens-Dokkum, M. H., de Groot, L., Wit, J. M., Geven, W. B., Kok, J. H., de Kleine, M. J., Kollee, L. A., Mulder, A. L., van Straaten, H. L., de Vries, L. S., van Weissenbruch, M. M., Verloove-Vanhorick, S. P., & Dutch Collaborative POPS 19 Study Group. (2007). Functional outcomes and participation in young adulthood for very preterm and very low birth weight infants: The dutch project on preterm and small for gestational age infants at 19 years of age. *Pediatrics, 120*, e587-95.
- Hirsch, J. E., Margolis, R. H., & Rykken, J. R. (1992). A comparison of acoustic reflex and auditory brain stem response screening of high-risk infants. *Ear and Hearing, 13*, 181-186.
- Holte, L., Cavanaugh, R. M., Jr, & Margolis, R. H. (1990). Ear canal wall mobility and tympanometric shape in young infants. *The Journal of Pediatrics, 117*(1 Pt 1), 77-80.
- Holte, L., Margolis, R. H., & Cavanaugh, R. M., Jr. (1991). Developmental changes in multifrequency tympanograms. *Audiology : Official Organ of the International Society of Audiology, 30*, 1-24.

- Holstrum, W.J., Gaffney, M., Gravel, J.S., Oyler, R.F., and Ross, D.S. (2008). Early intervention for children with unilateral and mild bilateral degrees of hearing loss. *Trends in Amplification, 12*, 35-41.
- Hood, L. J., & Berlin, C. I. (2001). Auditory neuropathy (auditory dis-synchrony) disables efferent suppression of otoacoustic emissions. In Y. Sininger, & A. Starr (Eds.), *Auditory neuropathy: A new perspective on hearing disorders* (pp. 183). San Diego, CA: Singular.
- Huizing, H.C., & Pollack, D. (1951). Effects of limited hearing on the development of speech in children under three years of age. *Pediatrics, 8*, 53-58.
- Hunter, L. L., & Margolis, R. H. (1992). Multifrequency tympanometry: Current clinical application. *American Journal of Audiology, 1*, 33-43.
- Hunter, L. L., Margolis, R. H., Rykken, J. R., Le, C. T., Daly, K. A., & Giebink, G. S. (1996). High frequency hearing loss associated with otitis media. *Ear and Hearing, 17*, 1-11.
- Hyde, M. L. (2005). Newborn hearing screening programs: Overview. *The Journal of Otolaryngology, 34 Suppl 2*, S70-8.
- Hyde, M. L., Riko, K., & Malizia, K. (1990). Audiometric accuracy of the click ABR in infants at risk for hearing loss. *Journal of the American Academy of Audiology, 1*, 59-66.
- Ikui, A., Sando, I., Haginomori, S., & Sudo, M. (2000). Postnatal development of the tympanic cavity: A computer-aided reconstruction and measurement study. *Acta Oto-Laryngologica, 120*, 375-379.

- Jacobson, J. T., & Jacobson, C. A. (1994). The effects of noise in transient EOAE newborn hearing screening. *International Journal of Pediatric Otorhinolaryngology*, 29, 235-248.
- Jerger, J., Burney, P., Mauldin, L., et al. (1974). Predicting hearing loss from the acoustic reflex. *Journal of Speech and Hearing Disorders*, 39, 11-22.
- Jerger, J. (1970). Clinical experience with impedance audiometry. *Archives of Otolaryngology (Chicago, Ill.: 1960)*, 92, 311-324.
- Joint Committee on Infant Hearing (JCIH): American Academy of Pediatrics (1994). Year 1994 position statement. *International Journal of Pediatric Otorhinolaryngology*, 32, 265-274.
- Joint Committee on Infant Hearing (JCIH): American Academy of Pediatrics (2007). Year 2007 position statement: Principles and guidelines for early hearing detection and intervention programs. *Pediatrics*, 120, 898-921.
- Johnson, J. L., White, K. R., Widen, J. E., Gravel, J. S., James, M., Kennalley, T., Maxon, A. B., Spivak, L., Sullivan-Mahoney, M., Vohr, B. R., Weirather, Y., & Holstrum, J. (2005). A multicenter evaluation of how many infants with permanent hearing loss pass a two-stage otoacoustic emissions/automated auditory brainstem response newborn hearing screening protocol. *Pediatrics*, 116, 663-672.
- Johnson, J. J., Mauk, G. W., Takekawa, K. M., Simon, P. R., Sia, C. J., Blackwell, P. M. (1993). Implementing a statewide system of service for infants and toddlers with hearing disabilities. *Seminars in Hearing*, 14, 105-119.

- Keefe, D. H., Bulen, J. C., Arehart, K. H., & Burns, E. M. (1993). Ear-canal impedance and reflection coefficient in human infants and adults. *The Journal of the Acoustical Society of America*, *94*, 2617-2638.
- Keefe, D. H., & Levi, E. (1996). Maturation of the middle and external ears: Acoustic power-based responses and reflectance tympanometry. *Ear and Hearing*, *17*, 361-373.
- Keefe, D. H., Schairer, K. S., Ellison, J. C., Fitzpatrick, D. F., & Jesteadt, W. (2009). Use of stimulus-frequency otoacoustic emissions to investigate efferent and cochlear contributions to temporal overshoot. *The Journal of the Acoustical Society of America*, *125*, 1595-1604.
- Kei, J., Allison-Levick, J., Dockray, J., Harrys, R., Kirkegard, C., Wong, J., Maurer, M., Hegarty, J., Young, J., & Tudehope, D. (2003). High-frequency (1000 Hz) tympanometry in normal neonates. *Journal of the American Academy of Audiology*, *14*, 20-28.
- Kei, J., Mazlan, R., Hickson, L., Gavranich, J., & Linning, R. (2007). Measuring middle-ear admittance in newborns using 1000 Hz tympanometry: A comparison of methodologies. *Journal of the American Academy of Audiology*, *18*, 739-748.
- Keith, R. W. (1973). Impedance audiometry with neonates. *Archives of Otolaryngology (Chicago, Ill.: 1960)*, *97*, 465-467.
- Kemp, D. T. (1978). Stimulated acoustic emissions from within the human auditory system. *The Journal of the Acoustical Society of America*, *64*, 1386-1391.

- Kemp, D. T., Bray, P., Alexander, L., & Brown, A. M. (1986). Acoustic emission cochleography--practical aspects. *Scandinavian Audiology.Supplementum*, 25, 71-95.
- Kenna, M. A. (1990). Embryology and developmental anatomy of the ear. In C. D. Bluestone, S. E. Stool & M. D. Sheetz (Eds.), *Pediatric otolaryngology* (2nd ed., pp. 77-87). Philadelphia: Saunders.
- Kenworthy, O. T. (1990). Screening for hearing impairment in infants and young children. *Seminars in Hearing*, 11, 315-332.
- Koebshell, K. A., & Margolis, R. H. (1986). Tympanometric gradient measured from normal preschool children. *Audiology : Official Organ of the International Society of Audiology*, 25, 149-157.
- Koivunen, P., Uhari, M., Laitakari, K., Alho, O. P., & Luotonen, J. (2000). Otoacoustic emissions and tympanometry in children with otitis media. *Ear and Hearing*, 21, 212-217.
- Kok, M. R., van Zanten, G. A., & Brocaar, M. P. (1992). Growth of evoked otoacoustic emissions during the first days postpartum. A preliminary report. *Audiology : Official Organ of the International Society of Audiology*, 31, 140-149.
- Kontiokari, T., Niemela, M., & Uhari, M. (1998). Middle-ear effusion among children diagnosed and treated actively for acute otitis media. *European Journal of Pediatrics*, 157, 731-734.
- Korres, S. G., Balatsouras, D. G., Gkoritsa, E., Kandiloros, D., Korres, G. S., & Ferekidis, E. (2007). The effect of very low birth weight on otoacoustic emissions. *B-Ent*, 3, 15-20.

- Levy, G. D., Woolston, D. J., & Browne, J. V. (2003). Mean noise amounts in level II vs. level III neonatal intensive care units. *Neonatal Network*, 22, 33-38.
- Lindén, G., Peterson, J. L., & Björkman, G. (1970). Tympanometry. *Archives of Otolaryngology (Chicago)*, 92, 248.
- Lopponen, H., Sorri, M., Pekkala, R., & Penna, J. (1992). Secretory otitis media and high-frequency hearing loss. *Acta Oto-Laryngologica. Supplementum*, 493, 99-107.
- Low, W. K., Pang, K. Y., Ho, L. Y., Lim, S. B., & Joseph, R. (2005). Universal newborn hearing screening in singapore: The need, implementation and challenges. *Annals of the Academy of Medicine, Singapore*, 34, 301-306.
- Lucker, J. R. (1980). Application of pass-fail criteria to middle-ear screening results. *ASHA*, 22, 839-840.
- Luotonen, M., Uhari, M., Aitola, L., Lukkaroinen, A. M., Luotonen, J., Uhari, M., & Korkeamaki, R. L. (1996). Recurrent otitis media during infancy and linguistic skills at the age of nine years. *The Pediatric Infectious Disease Journal*, 15, 854-858.
- Marchant, C. D., McMillan, P. M., Shurin, P. A., Johnson, C. E., Turczyk, V. A., Feinstein, J. C., & Panek, D. M. (1986). Objective diagnosis of otitis media in early infancy by tympanometry and ipsilateral acoustic reflex thresholds. *The Journal of Pediatrics*, 109, 590-595.

- Marchant, C. D., Shurin, P. A., Turczyk, V. A., Wasikowski, D. E., Tutihasi, M. A., & Kinney, S. E. (1984). Course and outcome of otitis media in early infancy: A prospective study. *The Journal of Pediatrics*, *104*, 826-831.
- Margolis, R. H., Bass-Ringdahl, S., Hanks, W. D., Holte, L., & Zapala, D. A. (2003). Tympanometry in newborn infants--1000 Hz norms. *Journal of the American Academy of Audiology*, *14*, 383-392.
- Margolis, R. H., & Goycoolea, H. G. (1993). Multifrequency tympanometry in normal adults. *Ear and Hearing*, *14*, 408-413.
- Margolis, R. H., Saly, G. L., & Hunter, L. L. (2000). High-frequency hearing loss and wideband middle-ear impedance in children with otitis media histories. *Ear and Hearing*, *21*, 206-211.
- Mason, J. A., & Herrmann, K. R. (1998). Universal infant hearing screening by automated auditory brainstem response measurement. *Pediatrics*, *101*, 221-228.
- Matook, S. A., Sullivan, M. C., Salisbury, A., Miller, R. J., & Lester, B. M. (2010). Variations of NICU sound by location and time of day. *Neonatal Network : NN*, *29*, 87-95.
- Maxon, A. B., White, K. R., Vohr, B. R., & Behrens, T. R. (1993). Using transient evoked otoacoustic emissions for neonatal hearing screening. *British Journal of Audiology*, *27*, 149-153.
- Mazlan, R., Kei, J., & Hickson, L. (2009a). Test-retest reliability of the acoustic stapedial reflex test in healthy neonates. *Ear and Hearing*, *30*, 295-301.

Mazlan, R., Kei, J., Hickson, L., Gavranich, J., & Linning, R. (2010). Test-retest reproducibility of the 1000 Hz tympanometry test in newborn and six-week-old healthy infants.

International Journal of Audiology, 49, 815-822.

Mazlan, R., Kei, J., Hickson, L., Khan, A., Gavranich, J., et al. (2009b). High frequency (1000 Hz) tympanometry findings in newborns: Normative data using a component

compensated admittance approach. *Australian and New Zealand Journal of Audiology, 31*, 15 – 24.

Mazlan, R., Kei, J., Hickson, L., Stapleton, C., Grant, S., Lim, S., Linning, R., & Gavranich, J. (2007). High frequency immittance findings: Newborn versus six-week-old infants.

International Journal of Audiology, 46, 711-717.

McDermott, J. C., Fausti, S. A., & Frey, R. H. (1986). Effects of middle-ear disease and cleft palate on high-frequency hearing in children. *Audiology : Official Organ of the*

International Society of Audiology, 25, 136-148.

McKay, S., Gravel, J. S., & Tharpe, A. M. (2008). Amplification considerations for children with minimal or mild bilateral hearing loss and unilateral hearing loss. *Trends in Amplification,*

12, 43-54.

McKinley, A. M., Grose, J. H., & Roush, J. (1997). Multifrequency tympanometry and evoked otoacoustic emissions in neonates during the first 24 hours of life. *Journal of the American*

Academy of Audiology, 8, 218-223.

- McMillan, P. M., Marchant, C. D., & Shurin, P. A. (1985). Ipsilateral acoustic reflexes in infants. *The Annals of Otolaryngology, Rhinology, and Laryngology*, 94, 145-148.
- McMurray, J. S. (2000). Hearing screening in the newborn. *Current Opinion in Otolaryngology & Head and Neck Surgery*, 8, 465-468.
- Mehl, A. L., & Thomson, V. (1998). Newborn hearing screening: The great omission. *Pediatrics*, 101, E4.
- Meier, S., Narabayashi, O., Probst, R., & Schmuziger, N. (2004). Comparison of currently available devices designed for newborn hearing screening using automated auditory brainstem and/or otoacoustic emission measurements. *International Journal of Pediatric Otorhinolaryngology*, 68, 927-934.
- Meyer, S. E., Jardine, C. A., & Deverson, W. (1997). Developmental changes in tympanometry: A case study. *British Journal of Audiology*, 31, 189-195.
- Mills, J. H. (1975). Noise and children: A review of literature. *Journal of the Acoustical Society of America*, 58, 768-779.
- Moller, A. R., & Jannetta, P. J. (1981). Compound action potentials recorded intracranially from the auditory nerve in man. *Experimental Neurology*, 74, 862-874.
- Moller, A. R., Jannetta, P. J., & Moller, M. B. (1981). Neural generators of brainstem evoked potentials. results from human intracranial recordings. *The Annals of Otolaryngology, Rhinology, and Laryngology*, 90, 591-596.

- Moore, B. C., & Tan, C. T. (2003). Perceived naturalness of spectrally distorted speech and music. *The Journal of the Acoustical Society of America*, *114*, 408-419.
- Morton, C. C., & Nance, W. E. (2006). Newborn hearing screening--a silent revolution. *The New England Journal of Medicine*, *354*, 2151-2164.
- Naeve, S. L., Margolis, R. H., Levine, S. C., & Fournier, E. M. (1992). Effect of ear-canal air pressure on evoked otoacoustic emissions. *The Journal of the Acoustical Society of America*, *91*, 2091-2095.
- Most, T. (2004). The effects of degree and type of hearing loss on children's performance in class. *Deafness and Education International*, *6*, 154-166.
- National Institutes of Health (1993). Early identification of hearing impairment in infants and young children. *NIH Consensus Statement*, *11*, 1-24.
- Natus Medical Inc. (2005). Echoscreen Brochure. Retrieved from <http://www.natus.com/documents/051624C.pdf>
- Niemela, M., Uhari, M., Jounio-Ervasti, K., Luotonen, J., Alho, O. P., & Vierimaa, E. (1994). Lack of specific symptomatology in children with acute otitis media. *The Pediatric Infectious Disease Journal*, *13*, 765-768.
- Niemeyer, W., & Sesterhenn, G. (1974). Calculating the hearing threshold from the stapedius reflex threshold for different sound stimuli. *Audiology : Official Organ of the International Society of Audiology*, *13*, 421-427.

- Norbury, C. F., Bishop, D. V. M., & Briscoe, J. (2001). Production of English finite verb morphology: A comparison of SLI and mild moderate hearing impairment. *Journal of Speech, Language, Hearing Research, 44*, 165-178.
- Norton, S.J. (1993). Applications of transient evoked otoacoustic emissions to pediatric populations. *Ear and Hearing, 14*, 64-73.
- Norton, S. J., Gorga, M. P., Widen, J. E., Folsom, R. C., Sininger, Y., Cone-Wesson, B., Vohr, B. R., & Fletcher, K. A. (2000). Identification of neonatal hearing impairment: Summary and recommendations. *Ear and Hearing, 21*, 529-535.
- Nozza, R. J., Bluestone, C. D., Kardatzke, D., & Bachman, R. (1992). Towards the validation of aural acoustic immittance measures for diagnosis of middle-ear effusion in children. *Ear and Hearing, 13*, 442-453.
- Nozza, R. J., Bluestone, C. D., Kardatzke, D., & Bachman, R. (1994). Identification of middle-ear effusion by aural acoustic admittance and otoscopy. *Ear and Hearing, 15*, 310-323.
- Owens, J. J., McCoy, M. J., Lonsbury-Martin, B. L., et al. (1993). Otoacoustic emissions in children with normal ears, middle-ear dysfunction, and ventilating tubes. *American Journal of Otology, 14*, 34-40.
- Paap, C. M. (1996). Management of otitis media with effusion in young children. *The Annals of Pharmacotherapy, 30*, 1291-1297.

- Paparella, M. M., Shea, D., Meyerhoff, W. L., & Goycoolea, M. V. (1980). Silent otitis media. *The Laryngoscope*, *90*, 1089-1098.
- Paradise, J. L., Rockette, H. E., Colborn, D. K., Bernard, B. S., Smith, C. G., Kurs-Lasky, M., & Janosky, J. E. (1997). Otitis media in 2253 pittsburgh-area infants: Prevalence and risk factors during the first two years of life. *Pediatrics*, *99*, 318-333.
- Paradise, J. L., Smith, C. G., & Bluestone, C. D. (1976). Tympanometric detection of middle-ear effusion in infants and young children. *Pediatrics*, *58*, 198-210.
- Pestalozza, G. (1984). Otitis media in newborn infants. *International Journal of Pediatric Otorhinolaryngology*, *8*, 109-124.
- Petinou, K. C., Schwartz, R. G., Gravel, J. S., & Raphael, L. J. (2001). A preliminary account of phonological and morphophonological perception in young children with and without otitis media. *International Journal of Language & Communication Disorders / Royal College of Speech & Language Therapists*, *36*, 21-42.
- Pittman, A. L. (2008). Short-term word-learning rate in children with normal hearing and children with hearing loss in limited and extended high-frequency bandwidths. *Journal of Speech, Language, and Hearing Research : JSLHR*, *51*, 785-797.
- Plinkert, P. K., Sesterhenn, G., Arnold, R., & Zenner, H. P. (1990). Evaluation of otoacoustic emissions in high-risk infants by using an easy and rapid objective auditory screening method. *European Archives of Oto-Rhino-Laryngology : Official Journal of the European Federation of Oto-*

Rhino-Laryngological Societies (EUFOS) : Affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery, 247, 356-360.

Prieve, B., Dalzell, L., Berg, A., Bradley, M., Cacace, A., Campbell, D., DeCristofaro, J., Gravel, J., Greenberg, E., Gross, S., Orlando, M., Pinheiro, J., Regan, J., Spivak, L., & Stevens, F. (2000). The new york state universal newborn hearing screening demonstration project: Outpatient outcome measures. *Ear and Hearing, 21*, 104-117.

Probst, R., Lonsbury-Martin, B. L., & Martin, G. K. (1991). A review of otoacoustic emissions. *The Journal of the Acoustical Society of America, 89*, 2027-2067.

Purdy, S., & Williams, M. J. (2000). High frequency tympanometry: A valid and reliable immittance test protocol for young infants? *New Zealand Audiological Society Bulletin, 10*, 9-24.

Rach, G. H., Zielhuis, G. A., & van den Broek, P. (1988). The influence of chronic persistent otitis media with effusion on language development of 2- to 4-year-olds. *International Journal of Pediatric Otorhinolaryngology, 15*, 253-261.

Ramakrishnan, K., Sparks, R. A., & Berryhill, W. E. (2007). Diagnosis and treatment of otitis media. *American Family Physician, 76*, 1650-1658.

Rea, P. A., & Gibson, W. P. (2003). Evidence for surviving outer hair cell function in congenitally deaf ears. *The Laryngoscope, 113*, 2030-2034.

Rhodes, M. C., Margolis, R. H., Hirsch, J. E., & Napp, A. P. (1999). Hearing screening in the newborn intensive care nursery: Comparison of methods. *Otolaryngology--Head and Neck Surgery : Official Journal of American Academy of Otolaryngology-Head and Neck Surgery*, 120, 799-808.

Ricketts, T. A., Dittberner, A. B., & Johnson, E. E. (2008). High-frequency amplification and sound quality in listeners with normal through moderate hearing loss. *Journal of Speech, Language, and Hearing Research : JSLHR*, 51, 160-172. Roizen, N. J. (2003). Nongenetic causes of hearing loss. *Mental Retardation and Developmental Disabilities Research Reviews*, 9, 120-127.

Roland, P. S., Finitzo, T., Friel-Patti, S., Brown, K. C., Stephens, K. T., Brown, O., & Coleman, J. M. (1989). Otitis media. incidence, duration, and hearing status. *Archives of Otolaryngology--Head & Neck Surgery*, 115, 1049-1053.

Rosenfeld, R. M., Culpepper, L., Doyle, K. J., Grundfast, K. M., Hoberman, A., Kenna, M. A., Lieberthal, A. S., Mahoney, M., Wahl, R. A., Woods, C. R., Jr, Yawn, B., American Academy of Pediatrics Subcommittee on Otitis Media with Effusion, American Academy of Family Physicians, & American Academy of Otolaryngology--Head and Neck Surgery. (2004). Clinical practice guideline: Otitis media with effusion. *Otolaryngology--Head and Neck Surgery : Official Journal of American Academy of Otolaryngology-Head and Neck Surgery*, 130, S95-118.

- Rosenfeld, R. M., Culpepper, L., Yawn, B., Mahoney, M. C., & AAP, AAFP, AAO-HNS Subcommittee on Otitis Media with Effusion. (2004). Otitis media with effusion clinical practice guideline. *American Family Physician*, *69*, 2776, 2778-9.
- Ross, D. S., Visser, S., Holstrum, J., & Kenneson, A. (2005). Minimal hearing loss and cognitive performance in children: Brief update. *Proceedings from a National Workshop on Mild and Unilateral Hearing Loss*, Breckenridge, CO. Retrieved from:
http://www.cdc.gov/ncbddd/ehdi/documents/unilateralhl/Mild_Uni_2005%20WorkshopProceedings.pdf
- Roush, J., & Tait, C. A. (1985). Pure-tone and acoustic immittance screening of preschool-aged children: An examination of referral criteria. *Ear and Hearing*, *6*, 245-250.
- Sak, R. J., & Ruben, R. J. (1982). Effects of recurrent middle-ear effusion in preschool years on language and learning. *Journal of Developmental and Behavioral Pediatrics : JDBP*, *3*, 7-11.
- Salamy, A., Eldredge, L., & Tooley, W. H. (1989). Neonatal status and hearing loss in high-risk infants. *The Journal of Pediatrics*, *114*, 847-852.
- Salvi, R. J., Wang, J., Ding, D., Stecker, N., & Arnold, S. (1999). Auditory deprivation of the central auditory system resulting from selective inner hair cell loss: Animal model of auditory neuropathy. *Scandinavian Audiology. Supplementum*, *51*, 1-12.

- Saunders, J. C., Doan, D. E., & Cohen, Y. E. (1993). The contribution of middle-ear sound conduction to auditory development. *Comparative Biochemistry and Physiology.Comparative Physiology*, *106*, 7-13.
- Schimmenti, L. A., Martinez, A., Fox, M., Crandall, B., Shapiro, N., Telatar, M., Sininger, Y., Grody, W. W., & Palmer, C. G. (2004). Genetic testing as part of the early hearing detection and intervention (EHDI) process. *Genetics in Medicine : Official Journal of the American College of Medical Genetics*, *6*, 521-525.
- Sells, J. P., Hurley, R. M., Morehouse, C. R., & Douglas, J. E. (1997). Validity of the ipsilateral acoustic reflex as a screening parameter. *Journal of the American Academy of Audiology*, *8*, 132-136.
- Shahnaz, N. (2008). Wideband reflectance in neonatal intensive care units. *Journal of the American Academy of Audiology*, *19*, 419-429.
- Shahnaz, N., Miranda, T., & Polka, L. (2008). Multifrequency tympanometry in neonatal intensive care unit and well babies. *Journal of the American Academy of Audiology*, *19*, 392-418.
- Shanks, J. E., & Lilly, D. J. (1981). An evaluation of tympanometric estimates of ear canal volume. *Journal of Speech and Hearing Research*, *24*, 557-566.
- Shekelle, P., Takata, G., Chan, L. S., & et al. (2003). *Diagnosis, natural history and late effects of otitis media with effusion. evidence report/technology assessment no. 55*. No. AHRQ Publication No. 03-E023). Rockville, MD: Agency for Healthcare Research and Quality.

- Silman, S., & Gelfand, S. A. (1982). The acoustic reflex in diagnostic audiology. *II. Audiology: Journal of Continuing Education*, 7, 125-138.
- Sininger, Y. S., Cone-Wesson, B., Folsom, R. C., Gorga, M. P., Vohr, B. R., Widen, J. E., Ekelid, M., & Norton, S. J. (2000). Identification of neonatal hearing impairment: Auditory brain stem responses in the perinatal period. *Ear and Hearing*, 21, 383-399.
- Soeta, Y., & Nakagawa, S. (2008). The effects of pitch and pitch strength on an auditory-evoked N1m. *Neuroreport*, 19, 783-787.
- Sprague, B. H., Wiley, T. L., & Goldstein, R. (1985). Tympanometric and acoustic-reflex studies in neonates. *Journal of Speech and Hearing Research*, 28, 265-272.
- Starr, A., Amlie, R. N., Martin, W. H., & Sanders, S. (1977). Development of auditory function in newborn infants revealed by auditory brainstem potentials. *Pediatrics*, 60, 831-839.
- Starr, A., Picton, T. W., Sininger, Y., Hood, L. J., & Berlin, C. I. (1996). Auditory neuropathy. *Brain : A Journal of Neurology*, 119, 741-753.
- Stelmachowicz, P. G., Lewis, D. E., Choi, S., & Hoover, B. (2007). Effect of stimulus bandwidth on auditory skills in normal-hearing and hearing-impaired children. *Ear and Hearing*, 28, 483-494.
- Stool, S. E., Berg, A. O., Berman, S., & et al. (1994). *Otitis media with effusion in young children*. (Clinical Practice Guideline, Number 12 No. AHCPR Publication No. 94-0622.). Rockville, MD: Agency for Health Care Policy and Research, Public Health Service, US Department of Health and Human Services.

- Strong, K., Wald, N., Miller, A., & Alwan, A. (2005). Current concepts in screening for non-communicable disease: World Health Organisation Consultation Group Report on methodology of non-communicable disease screening. *Journal of Medical Screening*, 12, 2-9.
- Surenthiran, S. S., Wilbraham, K., May, J., Chant, T., Emmerson, A. J., & Newton, V. E. (2003). Noise levels within the ear and post-nasal space in neonates in intensive care. *Archives of Disease in Childhood. Fetal and Neonatal Edition*, 88, F315-8.
- Sutton, G. J., Gleadle, P., & Rowe, S. J. (1996). Tympanometry and otoacoustic emissions in a cohort of special care neonates. *British Journal of Audiology*, 30, 9-17.
- Swanepoel de, W., Werner, S., Hugo, R., Louw, B., Owen, R., & Swanepoel, A. (2007). High frequency immittance for neonates: A normative study. *Acta Oto-Laryngologica*, 127, 49-56.
- Takahara, T., Sando, I., Hashida, Y., & Shibahara, Y. (1986). Mesenchyme remaining in human temporal bones. *Otolaryngology--Head and Neck Surgery : Official Journal of American Academy of Otolaryngology-Head and Neck Surgery*, 95, 349-357.
- Taylor, C. L., & Brooks, R. P. (2000). Screening for hearing loss and middle-ear disorders in children using TEOAEs. *American Journal of Audiology*, 9, 50-55.
- Teele, D. W., Klein, J. O., & Rosner, B. A. (1980). Epidemiology of otitis media in children. *The Annals of Otology, Rhinology & Laryngology. Supplement*, 89, 5-6.

- Teppo, H., & Revonta, M. (2007). Comparison of old, professional and consumer model acoustic reflectometers in the detection of middle-ear fluid in children with recurrent acute otitis media or glue ear. *International Journal of Pediatric Otorhinolaryngology*, *71*, 1865-1872.
- Tharpe, A.M. (2010). Permanent minimal and mild bilateral hearing loss in children: implications and outcomes. In R. Seewald, A. M. Tharpe (Eds.), *Comprehensive handbook of pediatric audiology* (pp. 193-202). Plural Publishing Inc.
- Tharpe, A.M., Ricketts, T., & Sladen, D.P. (2004). FM systems for children with minimal to mild hearing loss. In D. Fabry, C.D. Johnson (Eds.), *Access conference proceedings* (pp. 191-197). Chicago, IL: Phonak AG.
- Tharpe, A.M., & Sladen, D.P. (2008). Causation of permanent unilateral and mild bilateral hearing loss in children. *Trends in Amplification*, *12*, 17-25.
- The Otitis Media Guideline Panel: American Academy of Pediatrics (1994). Managing otitis media with effusion in young children. *Pediatrics*, *94*, 766-773.
- Todd, N. W., Jr, & Bowman, C. A. (1985). Otitis media at Canyon Day, Ariz. A 16-year follow-up in Apache Indians. *Archives of Otolaryngology (Chicago, Ill.: 1960)*, *111*, 606-608.
- Tos, M. (1984). Epidemiology and natural history of secretory otitis. *The American Journal of Otology*, *5*, 459-462.

- Turner, R.G., Robinette, M.S., & Bauch, C.D. (1999). *Clinical Decisions*. In Musiek, F. & Rintelmann, W.F. (Eds.), *Contemporary Perspectives in Hearing Assessment* (pp 437-463). Boston: Allyn and Bacon.
- Uhari, M., Mäntysaari, K., & Niemelä, M. (1996). A meta-analytic review of the risk factors for acute otitis media. *Clinical Infectious Diseases*, 22, 1079-1083.
- van den Berg, E., Deiman, C., & van Straaten, H. L. (2010). MB11 BERA(Phone) hearing screening compared to ALGO(Portable) in a dutch NICU: A pilot study. *International Journal of Pediatric Otorhinolaryngology*, 74, 1189-1192.
- van Straaten, H. L. (1999). Automated auditory brainstem response in neonatal hearing screening. *Acta Paediatrica (Oslo, Norway : 1992).Supplement*, 88, 76-79.
- Vanhuyse, V. J., Creten, W. L, Van Camp. K. J. (1975). On the W-notching of tympanograms. *Scandinavian Audiology*, 4, 45-50.
- Vohr, B. R., Carty, L. M., Moore, P. E., & Letourneau, K. (1998). The rhode island hearing assessment program: Experience with statewide hearing screening (1993-1996). *The Journal of Pediatrics*, 133, 353-357.
- Wake, M., Tobin, S., Cone-Wesson, B., Hans-Henrik, D., Gillam, L., McCormick, L., Williams, J., et al. (2006). Slight/mild sensorineural hearing loss in children. *Pediatrics*, 118, 1842-1851.

- Wallace, I. F., Gravel, J. S., McCarton, C. M., & Ruben, R. J. (1996). Incidence and correlates of otitis media during the first year of life in premature infants: A comparison study. In D. J. Lim, C. D. Bluestone, M. Casselbrant, J. O. Klein & P. L. Ogra (Eds.), *Proceedings of the sixth international symposium recent advances in otitis media* (pp. 47). B.C. Decker, Ontario.
- Walton, J. P., & Hendricks-Munoz, K. (1991). Profile and stability of sensorineural hearing loss in persistent pulmonary hypertension of the newborn. *Journal of Speech and Hearing Research, 34*, 1362-1370.
- Watkin, P. M. (1996). Outcomes of neonatal screening for hearing loss by otoacoustic emission. *Archives of Disease in Childhood. Fetal and Neonatal Edition, 75*, F158-68.
- Watkin, P. M., & Baldwin, M. (1999). Confirmation of deafness in infancy. *Archives of Disease in Childhood, 81*, 380-389.
- Weatherby, L. A., & Bennett, M. J. (1980). The neonatal acoustic reflex. *Scandinavian Audiology, 9*, 103-110.
- White, R. D. (2007). Recommended standards for the newborn ICU. *Journal of Perinatology : Official Journal of the California Perinatal Association, 27 Suppl 2*, S4-S19.
- White, K. R., Behrens, T. R. (1993). The Rhode Island hearing assessment project: implications for universal newborn hearing screening. *Seminars in Hearing, 14*, 1-119.

- White, K. R., Vohr, B. R., Maxon, A. B., Behrens, T. R., McPherson, M. G., & Mauk, G. W. (1994). Screening all newborns for hearing loss using transient evoked otoacoustic emissions. *International Journal of Pediatric Otorhinolaryngology*, 29, 203-217.
- Wiley, T. L., & Fowler, C. G. (1997). *Acoustic Immittance Measures in Clinical Audiology: A Primer*. Singular, San Diego.
- Williams, M. J., Purdy, S. C., & Barber, C.S. (1995). High-frequency probe-tone tympanometry in infants with middle-ear effusion. *Australian Journal of Otolaryngology*, 2, 169-173.
- Williamson, I. (2007). Otitis media with effusion in children. *Clinical Evidence*, 2007, 0502.
- Winkel, H. (2006). The effects of an early history of otitis media on children's language and literacy skill development. *The British Journal of Educational Psychology*, 76(Pt 4), 727-744.
- Xoinis, K., Weirather, Y., Mavoori, H., Shaha, S. H., & Iwamoto, L. M. (2007). Extremely low birth weight infants are at high risk for auditory neuropathy. *Journal of Perinatology : Official Journal of the California Perinatal Association*, 27, 718-723.
- Yoshinaga-Itano, C. (2003). Early intervention after universal neonatal hearing screening: Impact on outcomes. *Mental Retardation and Developmental Disabilities Research Reviews*, 9, 252-266. Yoshinaga-Itano, C., Sedey, A. L., Coulter, D. K., & Mehl, A. L. (1998). Language of early- and later-identified children with hearing loss. *Pediatrics*, 102, 1161-1171.

- Yoshinaga-Itano, C., Johnson, C. D., Carpenter, K., & Brown, A. S. (2008). Outcomes of children with mild bilateral hearing loss and unilateral hearing loss. *Seminars in Hearing, 29*, 196-211.
- Zahr, L. K., & Balian, S. (1995). Responses of premature infants to routine nursing interventions and noise in the NICU. *Nursing Research, 44*, 179-185.
- Zhao, F., Wada, H., Koike, T., & Stephens, D. (2000). The influence of middle-ear disorders on otoacoustic emissions. *Clinical Otolaryngology and Allied Sciences, 25*, 3-8.
- Zorowka, P. G. (1993). Otoacoustic emissions: A new method to diagnose hearing impairment in children. *European Journal of Pediatrics, 152*, 626-634.

APPENDIX A: INVITATION LETTER



Newborn Hearing Screening Project
A Collaborative Research Project between:
UBC School of Audiology
and the Royal University Hospital

Invitational Letter for NICU Babies at Royal University Hospital in Saskatoon

Project Title:

A Novel Screening Protocol for the Differentiation of Type of Hearing Loss in Neonatal Intensive Care Unit (NICU) Infants

Principal Investigator:

Dr. Navid Shahnaz
Associate Professor,
School of Audiology & Speech Sciences
University of British Columbia

Local Investigator:

Charlotte Douglas, M.Sc., Aud(C), Reg SK
Senior Audiologist
Audiology Department
Royal University Hospital
Saskatoon, SK

Student Researcher:

Tara Millman, B.Sc.
Graduate Student
U.B.C. School of Audiology &
Speech Sciences

Sub-Investigator:

Laurie Usher, M.S.
Audiologist
BC Children's Hospital

Dear Parent,

Normal hearing during the first three years of life is essential for normal development of the child's ability to speak, to do well in school, and to contribute productively in society. Hearing problems are often invisible to parents, because the child with a hearing problem is generally healthy-looking and develops other skills normally during the first year of life. However, listening and language develop very rapidly during the first year of life, therefore, the longer a child has an undetected hearing problem, the more difficult it will be for the child to learn to talk normally.

This project is interested in exploring the most efficient method for early identification of the type of hearing loss in neonates in a more timely and cost-effective manner. The School of Audiology & Speech Sciences at University of British Columbia and the Royal University Hospital in Saskatoon are carrying out a joint research project to improve our ability to distinguish conductive and sensorineural hearing loss in early infancy. Sensorineural hearing loss is a permanent type of hearing loss which is caused by impairment in the inner ear. Conductive hearing loss is a typically a temporary form of hearing loss which, in infants, is most commonly caused by middle ear fluid associated with middle ear infection (otitis media). When present early in life, each of these types of hearing loss can have serious consequences for the health and development of your child. Distinguishing conductive hearing loss from sensorineural hearing loss is vital since the course of medical and hearing intervention is quite different for these two types of hearing problems. The good news is that many of the negative effects of these hearing problems can be prevented or substantially lessened if intervention comes early. Therefore, hearing loss must be detected and correctly diagnosed as early as possible for intervention to be most successful. Presently, there is a need to improve our ability to distinguish between types of hearing loss in newborn infants that are part of the neonatal intensive care unit (NICU). This is the objective of the present study.

If you agree to be part of the project, your baby's test results from the routine hearing screening program that is currently being administered on all NICU babies at Royal University Hospital in Saskatoon will be collected for this study. All of these tests are part of a routine hearing screening program that is currently being conducted on NICU babies at Royal University Hospital. We are not asking your baby to devote any additional time beyond the time that is required to conduct these tests. The outcome of these tests will be compared to each other to explore the most efficient method for early identification of the type of hearing loss in neonates in a more timely and cost-effective manner. All the screening is done in natural sleep. There are no known risks with these procedures. The screening does not hurt your baby in any way.

By including your baby's screening results in the current study and for later diagnostic follow-up, this will provide more information regarding the efficacy of the screening protocol in terms of its ability for the early identification of the type of hearing loss in neonates.

Thank you for considering participation in this research project. If you are interested in participating, please inform the NICU nursing staff or contact any of the investigators listed above for more information at any time.

Dr. Navid Shahnaz, Principal Investigator

APPENDIX B: CONSENT FORM



Newborn Hearing Screening Project
A Collaborative Research Project between:
UBC School of Audiology & Speech Sciences
and the Royal University Hospital



Consent Form for NICU Babies at Royal University Hospital in Saskatoon

Project Title:

Comparison of Screening Protocol for the Differentiation of Type of Hearing Loss in Neonatal Intensive Care Unit (NICU) Infants

Principal Investigator:

Dr. Navid Shahnaz
Associate Professor,
School of Audiology & Speech Sciences
University of British Columbia

Local Investigator:

Charlotte Douglas, M.Sc., Aud(C), Reg SK
Senior Audiologist
Audiology Department
Royal University Hospital
Saskatoon, SK

Student Researcher:

Tara Millman, B.Sc.
Graduate Student
U.B.C. School of Audiology &
Speech Sciences

Sub-Investigator:

Laurie Usher, M.S.
Audiologist
BC Children's Hospital

Introduction:

Your baby is being invited to take part in this study which is investigating hearing and middle-ear status of babies in the Neonatal Intensive Care Unit (NICU). The procedure explained in this consent form is already a standard protocol for screening the hearing of the neonatal intensive care unit (NICU) babies at Royal University Hospital.

Purpose:

Your baby has been invited to participate in this research project because we are studying a method of hearing screening in newborn infants that are part of the neonatal intensive care unit (NICU). Our objective is to improve our ability to distinguish between conductive and sensorineural hearing loss. Sensorineural hearing loss is a permanent type of hearing loss which is caused by impairment in the inner ear. Conductive hearing loss is typically a temporary form of hearing loss which, in infants, is most commonly caused by middle ear fluid associated with middle ear infection (otitis media). When present early in life, each of these types of hearing loss can have serious consequences for the health and development of your baby. Distinguishing conductive hearing loss from sensorineural hearing loss is vital since the course of medical and hearing intervention is quite different for these two types of hearing problems. The good news is that many of the negative effects of these hearing problems can be prevented or substantially lessened if intervention comes early. Therefore, hearing loss must be detected and correctly diagnosed as early as possible for intervention to be most successful.

If you agree for your baby to participate in the project, results from his/her routine hearing screening and later diagnostic follow-up (if any) at Royal University Hospital in Saskatoon will be included in the current study. Each of the tests used in the screening protocol are commonly used in infants and young children for the detection of middle ear problems and assessment of hearing, and poses no risk to your baby's ear or to your baby's hearing. All the screening is done in natural sleep. There are no known risks with these procedures. The screening does not hurt your baby in any way.

Your baby's participation in this study is voluntary. If they do not take part, their care will continue normally and they will still have the routine hearing screening. If you choose for your baby to be a subject, you may withdrawal from the study at any time and no reason needs to be given to withdraw from this study. Withdrawal will not change your baby's care.

Study Procedures:

If you do choose for your baby to be a subject to participate in this research study, results from his/her routine hearing screening and later diagnostic follow-up (if any) at Royal University Hospital in Saskatoon will be included in the current study for further data analysis. Should there be any findings from this study that may be useful to your baby's doctor; this information will be communicated to him/her with your permission.

The results of the following standard screening tests will be used for this research study:

- 1) Transient-evoked otoacoustic emissions (TEOAE)
- 2) High-frequency tone tympanometry (HFT)

- 3) Broadband Noise (BBN) acoustic stapedial reflex at 1 kHz probe tone frequency
- 4) Automated auditory brainstem response (AABR)

In each of the tests, a small earphone will be placed into the entrance of your baby's ear canal using a soft and delicate plastic or sponge tip. It is designed not to cause any allergic reactions. All of these tests are part of a routine hearing screening program that is currently being conducted on NICU babies at Royal University Hospital. We are not asking your baby to devote any additional time beyond the time that is required to conduct these tests. The outcome of these tests will be compared to each other to explore the most efficient method for early identification of the type of hearing loss in neonates in a more timely and cost-effective manner.

Advantages:

It is hoped that the information obtained will help refine our ability to distinguish between conductive and sensorineural hearing loss, and hence provide early detection and treatment. There are no direct benefits to your baby for participating in this research, but in the long run the results may improve the accuracy and earlier detection and treatment of specific types of hearing loss in newborns.

Disadvantages:

We are not asking your baby to have any additional tests beyond the tests that is required to conduct standard hearing screening test protocol that is currently being conducted on NICU babies at Royal University Hospital. We are simply comparing the outcome of these tests against each other to explore the most efficient method. Therefore, there is no risk involved in participating in this project.

How your baby's information will be used:

Your baby's test results from the four screening measures will be compared to each other. We will find out which of these measures are better for providing more information regarding their hearing status.

Confidentiality:

In Saskatchewan, *the Health Information Protection Act (HIPA)* protects the privacy of your personal health information. Your baby's identity will be coded using a code known only to the researchers, and all information that is collected from your baby will remain confidential. Only group results or coded individual results will be given in any reports about the study. Coded results only (no personal information) will be kept in computer files on a password protected hard drive. Your baby's confidentiality will be respected. No information that discloses your baby's identity will be released or published without your specific consent to the disclosure. However, research records and medical records identifying your baby may be inspected in the presence of the Investigator or his designate by the University of Saskatchewan Research Ethics Board for the purpose of monitoring the research. However, no records which identify your child by name or initials will be allowed to leave the Investigators' offices.

Compensation for Injury:

Signing this consent form in no way limits or restricts your legal rights against the investigators, or anyone else.

Consent:

I, _____, have read the above study consent form and I consent to permit my child to participate in this study. The researcher assures me that my baby's participation in this data collection is completely voluntary and that I may withdraw him/her from this research at any time without consequences.

If you have any questions or desire further information about this study before or during participation, you can contact *Charlotte Douglas, M.Sc.* at 306-655-1327.

If you have any concerns about your rights as a research subject and/or your experiences while participating in this study, contact the Chair of the University of Saskatchewan Research Ethics Board, at 306-966-4053. The Research Ethics Board is a group of individuals (scientists, physicians, ethicists, lawyers and members of the community) that provide an independent review of human research studies. This study has been reviewed and approved on ethical grounds by the University of Saskatchewan and the University of British Columbia Research Ethics Boards.

I have received a signed and dated copy of this consent form for my records.

Parent signature

Date

Parent name (please print)

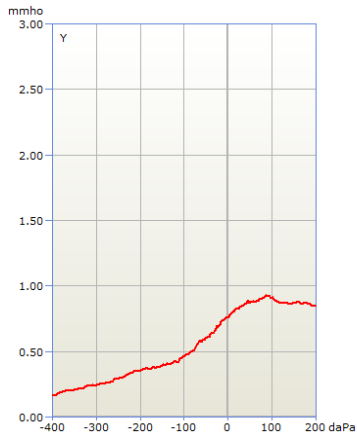
Signature of principal/co- investigator

Date

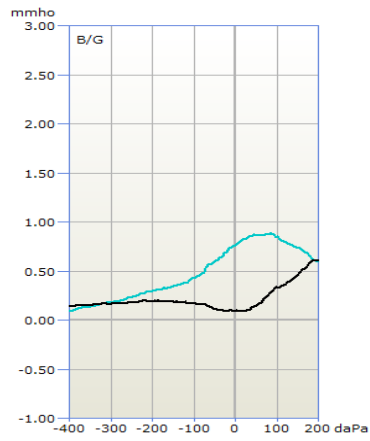
Name of principal/co-investigator (please print)

APPENDIX C: 1000 HZ TYMPANOGRAMS CLASSIFIED AS NORMAL AND INCLUDED BASED ON SHAPE OF Y AND BG CURVES THAT DID NOT MEET PRELIMINARY INCLUSION CRITERIA DUE TO SA < 0.10 MMHO. THESE INFANTS PASSED ALL SCREENING MEASURES.

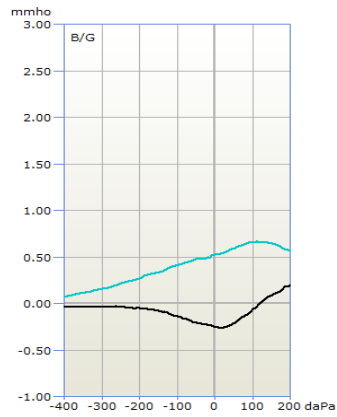
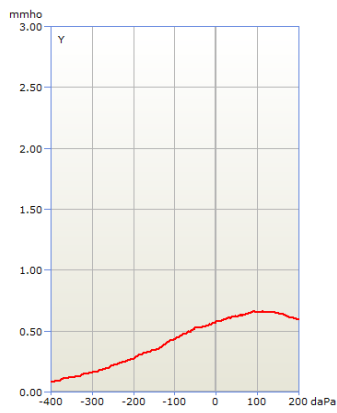
Infant #1: Y



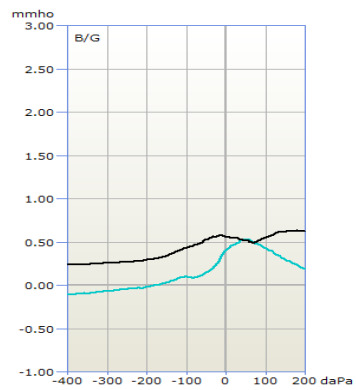
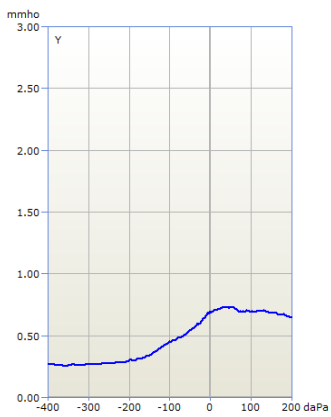
B/G



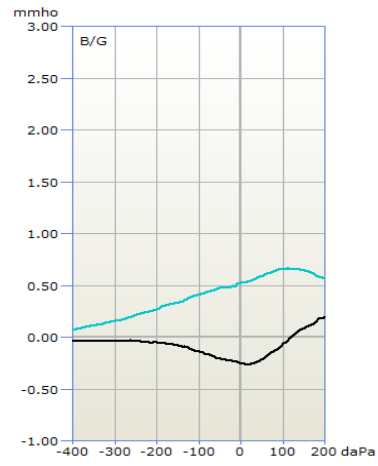
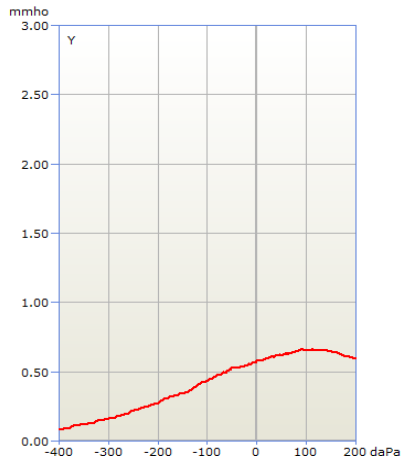
Infant #2:



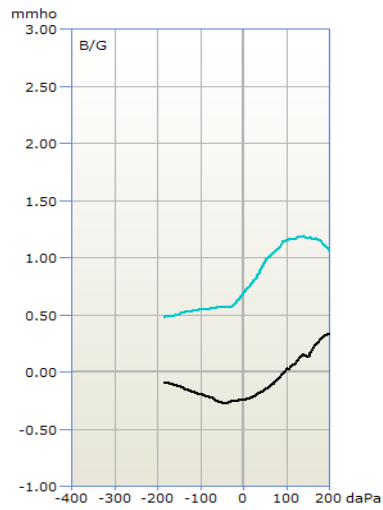
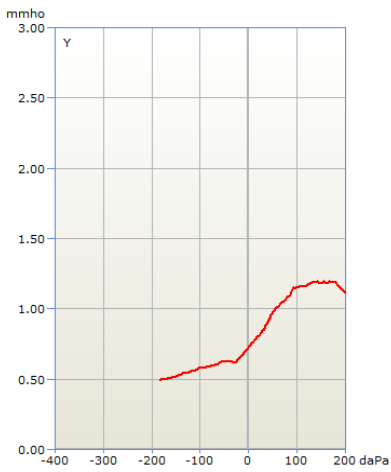
Infant #3:



Infant #4:



Infant #5:



Infant #6:

