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**A Profile of the Auditory Function of Children with TB Receiving Ototoxic
Medication at Brooklyn Chest Hospital**

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GHFNAZ001

Submitted in fulfilment of the requirements for the degree MSc. Audiology

In the Division of Communication Sciences and Disorders

Faculty of Health Sciences

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February 2012

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Declaration

I, Nazanin Ghafari, hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Signature

Date

Acknowledgements

I would like to acknowledge Prof Shajila Singh, my supervisor, for her tireless dedication, expertise and guidance which made this journey possible. For that I am sincerely thankful. I would also like to thank Christine Rogers and Lucretia Peterson, my co-supervisors, for their encouragement and constructive comments. I would also like to thank Brooklyn Chest hospital and its staff specially Dr Marianne Willemse, the paediatrician, and Kayleen Jacobs, senior audiologist, for their kind clinical assistance.

A special dedication to my family, my mom Nasrin, my dad Dariush and my sister Nastaran, I love you all. Amir, my dearest husband, without your support and editorial work, I would not have been able to complete my thesis. This work is dedicated to you, my love.

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Glossary of Terms

ASSR	Auditory Steady-State Response (ASSR) audiometry is a test which can accurately predict the behavioural pure-tone audiogram (Aoyagi et al., 2007)
Asymmetric hearing loss	Hearing loss of average 15dB at 0.5, 1, 2 kHz or average of 30 dB at 3, 4, 6 kHz between two ears (American Academy of Otolaryngology-Head and Neck Surgery, 1997)
Disseminated TB	One of the complications of primary TB that has spread from the lungs to other parts of the body through the blood stream or lymphatic system (Jeyapaul, 2007).
Extensively drug-resistant TB (XDR-TB)	"Resistance to at least isoniazid, rifampin, fluoroquinolones, and either aminoglycosides or capreomycin" (Young, Chick, Kormos & Goroll, 2010, p.145)
Multidrug-resistant TB	"Resistance to at least isoniazid, rifampin" (Young et al., 2010, p.145)
Paucibacillary	Having or made up of few bacilli (The American Heritage Medical Dictionary, 2007)
Pre extensively drug-resistant TB	Disease caused by a strain resistant to isoniazid and rifampin and either a fluoroquinolone or a second-line injectable drug, but not both (Banerjee et al., 2008).

Abstract

A descriptive survey research design was used to describe the auditory function of children with tuberculosis (TB) receiving ototoxic medication at Brooklyn Chest Hospital. A battery of audiologic tests (otoscopy, immittance, audiometry or OAE and AABR) were conducted on 29 children, aged 0 to 18 years, and the results were analysed using descriptive statistics and Generalized Linear Models. The results suggest that 55% of children had middle ear abnormality and 48% had hearing loss. The degree of hearing loss ranged from mild to profound in 41% of the cases while 59% had hearing within the normal range with their loss restricted to high frequencies. No statistically significant associations were found between sex, duration of hospitalization, comorbid presentation of HIV and TB and middle ear abnormality. There was also no significant relationship between sensorineural hearing loss and comorbid presentation of HIV and TB. The frequency of middle ear abnormality was significantly lower for the age group 3 to 7 years ($\chi^2 = 6.620$, $df = 2$, $p = .038$). Conclusion: (i) An ototoxicity monitoring program should be routinely implemented with all children receiving ototoxic TB medication for early identification of ototoxic hearing loss, in order, to prevent or minimise further loss and provide appropriate audiologic services for this population. (ii) The Northern and Downs's degree of hearing loss classification system, based on average thresholds for speech frequencies may not be suitable for determining severity of ototoxic hearing loss, which initially occurs at high frequencies. It is therefore recommended that for children at risk of ototoxic hearing loss, the Northern and Downs's classification should be based on the average degree of thresholds in high frequencies (4 & 8 kHz).

Keywords: Children, Hearing loss, Hearing monitoring, Ototoxicity, TB.

Introduction

South Africa with 0.46 million TB cases in 2007, ranked fifth among 22 high-burden TB countries (WHO, 2009). About 15-20% of the total number of TB cases in many developing countries are children under 15 years of age (Marais, Schaaf & Donald, 2009). Children account for a significant proportion of TB cases in the Western Cape province, South Africa, where a high prevalence of TB has been reported (Marais, Hesselings, Gie, Schaaf & Beyers, 2006). Children with TB are often hospitalized and medicated with first-line or second-line drugs (WHO, 2006; Espinal et al., 2000), some of which are ototoxic and may lead to severe, bilateral and permanent hearing loss (Xing, Chen & Cao, 2007). Hospitalization increases the risk of ear infections in children which may also lead to hearing loss (Rizzo, 2002; Garner et al., 1996). Undetected hearing loss can have adverse effects on the child's language, psychosocial and educational development (Copley & Friderichs, 2010; Northern & Downs, 2002). The effects of ototoxicity in adults are well described in the literature and have been discussed since shortly after the introduction of the first aminoglycoside, streptomycin, in the 1940s (Bagger-Sjoberg, 1997). However, there are few studies on children. Such studies are crucial and may help develop an appropriate hearing monitoring programme which can be routinely implemented to facilitate management and planning for service delivery to this population. The present study aimed to describe the auditory function of children hospitalized with TB receiving ototoxic medication at Brooklyn Chest Hospital, the main referral centre for TB in the Western Cape. The possible relationship between sensorineural hearing loss/ middle ear abnormality and parameters such as sex, age and duration of hospitalization were also investigated.

Literature Review

Global and Regional Incidence of Tuberculosis

Each year tuberculosis infects over nine million individuals around the world with a third from African countries (Palitza, 2010). South Africa with 0.46 million TB cases in 2007, ranked fifth among 22 high-burden TB countries (WHO, 2009). The rate of TB in this country was estimated to be 960 cases per 100 000 population in 2008 (WHO, 2010). A high incidence of TB was found in the Western Cape Province with 967 cases per 100 000 population in 2004 (Western Cape Department of Health, 2006). In 2004 and 2005 the incidence in Cape Town was 810 and 874/100 000 populations, respectively (Western Cape Department of Health, 2006).

In 2002, the WHO reported that the prevalence of TB in Africa was increasing after 40 years of decline. Poor health services, the emergence of multidrug-resistant TB and the high incidence of HIV/AIDS have contributed to the disease resurgence (WHO, 2002). In South Africa about 55% of TB cases are HIV positive (Setswe, 2009) rendering the diagnosis and treatment of this disease difficult (Jeena, Pillay, Pillay & Coovadia, 2002; Swaminathan, 2004). Both HIV and TB are more common in impoverished societies, a result of inferior living conditions, such as poor public-health, malnutrition, overcrowding, homelessness and lack of education (Killewo, 2002; Figueroa-Munoz & Ramon-Pardo, 2008). It has been estimated that in South Africa poverty currently affects 40% of the population (Health Systems Trust, 2008) prone to HIV and TB infections. Those who succumb to these infections are often unable to work and become subsequently poor, so the cycle of poverty, HIV and TB continues (Killewo, 2002). Children account for a significant proportion of TB cases, especially in impoverished societies with high prevalence of HIV including South Africa (Marais et al., 2006; Killewo, 2002). Children are

particularly more vulnerable to TB than adults because of their developing immune systems and those who are borne HIV positive or live in poverty are even at higher risk of acquiring this infection (Killewo, 2002; Palitza, 2010).

Incidence of TB in children. The WHO data on the incidence of TB in children focuses only on smear-positive cases. In 2002, 1.8% of the smear-positive cases in Africa were children (Cooreman, 2006). Since smears are rarely positive in children with TB, this report reflects only a minor fraction of the total cases, and thus the true incidence of TB in children is unknown (Cooreman, 2006). It is estimated that about 15-20% of the total TB cases in many developing countries including South Africa are children under 15 years of age (Marais et al., 2009). Nationally, about nine percent of all TB cases occur in children under four years of age (Sigwebela, 2010). There are no detailed statistics available for the number of paediatric TB cases in South Africa (Palitza, 2010) but the abovementioned percentages indicate that, an appreciable proportion of the population with TB are children. The lack of accurate data on childhood TB will negatively influence and limit future research in this area and planning for health service delivery to this population.

Nature of Tuberculosis in Children

Children are more likely to develop TB after infection by *Mycobacterium tuberculosis* (5 to 10% in adults vs 24 to 43% in children) and are significantly more prone to develop extrapulmonary and severe disseminated TB than adults because of their weaker immune systems (Lewinsohn, Gennaro, Scholvinck & Lewinsohn, 2004). All forms of TB are more common in HIV-infected children as a result of their severely compromised immune systems (Palitza, 2010). The severity of TB in an HIV infected child depends on the progression of HIV disease (WHO, 2003). As the

HIV infection progresses and immunity declines, TB tends to spread throughout the body to involve different organs (WHO, 2003). Diagnostic error and delayed diagnosis of TB are common among HIV infected children, since the radiographic manifestations of TB overlap with other lung diseases (Jeena, Pillay, Pillay & Coovadia, 2002; Swaminathan, 2004). Misdiagnosis may lead to development of drug-resistant TB (Davies, 2001). Treatment of TB, especially drug-resistant TB can lead to ototoxicity in children, this will be discussed in full detail under the heading "Side effects & impact of TB drugs".

Management of Tuberculosis in Children

Nature of management. Children who are suspected to have TB or are diagnosed with TB require medical management (Edward & Nardell, 2009). Depending on the nature of the TB and the child's physical status, further management may be required through institutionalization (WHO, 2006 a; Edward & Nardell, 2009).

Medical management. Medical management of TB involves prescription of medication, supervision and patient support programs (Department of Health, 2004). First-line and second-line drugs are used for medical intervention. First line drugs (isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin) are prescribed for children with drug-susceptible TB and may have unpleasant side effects including ototoxicity (Espinal et al., 2000; Kamal, Azeeza, Malik, Shaik & Rao, 2008). Directly observed treatment short-course (DOTS) involves utilization of first-line medication (WHO, 2003). The length of treatment with first-line drugs is about six to eight months (Jindani, Numm & Enarson, 2004). The second line drugs (amikacin, kanamycin, capreomycin, viomycin, ciprofloxacin, moxifloxacin, ofloxacin, ethionamide, prothioamide, cycloserine and *p*-aminosalicylic acid) are used to treat children with multi drug

resistance TB (MDR-TB) and may also have adverse effects including ototoxicity. Treatment with second-line drugs takes 18 to 24 months and DOTS-Plus facilitates the taking of these medications (WHO, 2003). It is estimated that the success rate of DOTS-Plus in 2010 for treatment of patients with MDR-TB (including children) is 73% in African countries, like South Africa, with high incidence of HIV (WHO, 2006 b). The success rate of DOTS for treatment of all South Africans with TB increased from 65 percent in 2001 to 74 percent in 2006 (WHO, 2010).

Side effects & impact of TB drugs. The two most toxic classes of TB drugs are aminoglycosides (streptomycin, kanamycin and amikacin) and polypeptides (capreomycin) with ototoxic and nephrotoxic side effects (Kamal et al., 2008). The nephrotoxicity is often reversible but the ototoxicity is severe, bilateral and permanent (Xing et al., 2007; Guthrie, 2008). Ototoxicity involves vestibulotoxicity and cochleotoxicity (Rybak, Touliatos & Campbell, 2006).

Vestibulotoxicity

Streptomycin is vestibulotoxic (Rybak & Ramkumart, 2007; Peloquin et al., 2004). Vestibulotoxicity is the result of damage to the vestibular sensory neuroepithelium with the most extensive hair cell damage occurring in the apex of the ampullar cristae and the striolar regions of the maculae of the saccule and utricle (Rybak et al., 2006). Vestibulotoxicity can affect equilibrium which in turn may lead to oscillopsia and disequilibrium (Rybak et al., 2006).

Cochleotoxicity

Amikacin, kanamycin and capreomycin are all cochleotoxic (Hain, 2010) however it has been suggested that capreomycin might be less cochleotoxic than the former two drugs (Sturdy et al., 2011). Cochleotoxicity is the result of damage to sensory hair cells and the stria vascularis in the

cochlea (Xing et al., 2007; Guthrie, 2008). Exposure to ototoxic drugs initially affects the base of the cochlea, where the hair cells code for high frequencies. With continued exposure, damage to the apex of the cochlea ensues (the low frequency coding region) (Xing et al., 2007; Guthrie, 2008). The duration of exposure to these drugs may be associated with cochleotoxicity. Some studies have found no significant association between the duration of ototoxic treatment and cochleotoxicity (Sturdy et al., 2011; de Jager and van Altena, 2002; Lima, Lessa, Aguiar-Santos & Medeiros, 2006), while others have come to the conclusion that the risk of cochleotoxicity increases with prolonged duration of treatment (Arbex, Varella, Siqueira, Mello, 2010; Peloquin et al., 2004). Cochleotoxicity may have an impact on hearing and in children can affect the acquisition or further development of speech, language, communication and learning. The impact of hearing loss in children is discussed later, but it is evident that every effort needs to be made to prevent or minimize the effects of cochleotoxic hearing loss in children (Vasquez & Mattucci, 2003).

Susceptibility

In general there are a number of risk factors which predispose TB patients including children to drug-induced ototoxicity, such as serum drug levels; previous sensorineural hearing loss; genotype; simultaneous administration of other known ototoxic agents (loop diuretics, aspirin); concomitant noise exposure; duration of therapy with ototoxic drugs in excess of seven days and the very young (neonates), (Monsell et al., 2007; Kokotas, Petersen & Willems, 2007). While currently there are no studies to determine possible risk factors for drug induced ototoxicity in children with TB, there is some suggestion that children may be at greater risk for ototoxicity than similarly treated adult patients (Schell et al., 1989; Kokotas et al., 2007).

Institutionalization. Hospitalization of children may be necessary for management of TB. The main indications for hospitalization of patients with TB including children are severe forms of the disease, co-infections (e.g. HIV), severe TB drug reactions, the need for diagnostic procedures and social issues which may lead to non-compliance (e.g. homelessness), (Edward & Nardell, 2009). The duration of drug treatment for TB is about 6 months to two years but the exact length of hospitalization is not known (Jindani et al., 2004; WHO, 2003).

Side effects & impact of institutionalization. Ear infection and linguistic deprivation are the most important side effects of institutionalization of children with TB (Ruben, 2003; Rizzo, 2002; Garner, Jarvis, Emori, Horan & Hughes, 1996). Linguistic deprivation and the resultant hearing loss from ear infections may negatively influence speech and language development in children, which is thoroughly discussed in the following section.

Ear Infection

All hospitalized children with TB are susceptible to contracting an ear infection (Rizzo, 2002; Garner et al., 1996) but children with compromised immune systems (e. g. those infected with HIV) and young children are at greater risk than others (Rizzo, 2002). Children in health care institutions are in close contact with other potentially sick children, increasing their risk of upper respiratory tract infections, which can lead to otitis media (Cober & Johnson, 2005). Ear infection or otitis media is common during childhood and affects sound conduction in the middle ear (Silveira Netto, da Costa, Sleifer & Braga, 2009). Untreated otitis media may result in serious complications (Bluestone & Klein, 2003). The infection can spread from the middle ear to nearby structures, including the brain (Racanello & McCabe, 2010). Persistent fluid in the middle ear prevents movement of the tympanic membrane and the ossicles resulting in mild to

moderate conductive hearing loss. When otitis media involves the cochlea, it may cause sensorineural hearing loss which varies from mild to profound (Bluestone & Klein, 2003; Bluestone & Klein, 2007). Untreated otitis media affects the child's hearing ability and thus may lead to speech and language disabilities (Racanello & McCabe, 2010). The impact of hearing loss in children will be discussed in detail later.

Linguistic Deprivation

Children who have been hospitalized for a long time may experience linguistic deprivation (Ruben, 2003), which is particularly true in developing countries including South Africa, where the institutional conditions are quite poor (Ruben, 2003). Shortage of staff and the increasing number of hospitalized children result in inadequate linguistic stimulation (Nelson, 2007). Parental absenteeism and neglect by hospital staff may restrict the child's interaction with nurses/parents with very little language input, both in quantity and quality (Nelson, 2007; Leung, 2010). In addition, in multi-lingual countries such as South Africa staff and patients may not have a common language. Lack of adequate linguistic stimulation may lead to linguistic deprivation which can be deleterious for children's speech and language development (Ruben, 2003).

As mentioned, hospitalized children with TB are at increased risk of both linguistic deprivation and middle ear infections. Linguistic deprivation combined with the hearing loss induced by middle ear infections, can lead to speech and language disorders (Ruben, 2003). Thus, early detection and treatment of otitis media decreases the risk of linguistic disability in this population.

Prevalence of Auditory Dysfunctions in Children with TB

Following extensive search of the literature, using Google Scholar and Pubmed search engines, there were no documented studies which assessed the ototoxicity in children with TB. The only issue investigated was the prevalence of ototoxicity in adult TB patients. This review will therefore focus on the prevalence of ototoxic hearing loss in adults (since it may have some implications for children) and the prevalence of common outer and middle ear abnormalities in children.

In general, outer ear abnormalities do not affect the hearing unless there is blockage of the ear canal e.g. impacted wax (Stach, 2008). Impacted wax is the most common ear problem among school children (Phaneendra Rao, Subramanyam, Nair & Rajashekhar, 2002; Adhikari, 2009), which can result in conductive hearing loss (Subha & Raman, 2006). Minja and Machemba (1996) and Brkic (2010) reported prevalence rates of 15.7% and 24% for impacted wax among school children in Tanzania and Bosnia and Herzegovina respectively, while Phaneendra Rao et al. (2002) and Adhikari (2009) reported much higher prevalence rates of 63% and 62% among rural school children in India and Nepal respectively. The prevalence rates of impacted wax in school children in developing countries indicate a possibly high incidence of this preventable condition in South African school-aged children including those with TB.

Middle ear abnormalities may cause conductive and even sensorineural hearing loss (Bluestone & Klein, 2007). Otitis media is the most common middle ear abnormality in children, which is more prevalent during the cold months of the year (Okur, Yildirim, Akif Kilic, Guzelsoy, 2004; Adhikari, 2009). The prevalence of otitis media with effusion is significantly influenced by the age of the child (Martines, 2010). In general younger children are more

vulnerable to this disease and as they grow older its incidence decreases (Caylan, 2005; Zielhuis et al., 1990). It is not clear whether sex plays a role in the prevalence of otitis media with effusion. Caylan (2005) reported the prevalence of otitis media with effusion to be significantly more in male children in Turkey, while Martines (2010) found the prevalence to be significantly more in female children in Italy. Tong et al. (2006) in China found no real differences between the sexes.

Most of the studies which assessed the middle ear status of school children, have reported on abnormalities of middle ear and tympanic membrane separately. In this review, in order to report on the prevalence of middle ear abnormality in these studies, the number of the tympanic membranes and middle ear abnormalities were added together (when the same child did not present with more than one abnormality). Adhikari (2009), Olusanya, Okolo and Ijaduola (2000), and Sockalingham, Hives and Kel (2003) reported the prevalence rates of middle ear abnormality (combined prevalence rate of middle ear and tympanic membrane abnormalities) to be 15%, 49% and 53% among school children in Nepal, Nigeria and Australia (among Aboriginal school-aged children) respectively. These high prevalence rates of middle ear abnormality in school children together with the vulnerability of hospitalized and younger children to ear infections indicate the need to assess the middle ear status of hospitalized children with TB for the presence of any abnormality.

As mentioned earlier, no study has ever been conducted to determine the prevalence of ototoxic hearing loss in children with TB, while there are numerous reports on the prevalence of ototoxic hearing loss in adults. Thus, it is difficult to estimate the percentage of children with TB who may be at risk of ototoxic hearing loss in South Africa. However, it would be wise to review the studies on ototoxicity in adults, in which the patients received the same ototoxic TB

drugs as the South African children (amikacin, kanamycin, streptomycin or capreomycin), since this may shed some light on the prevalence of ototoxic hearing loss among children with TB in South Africa. The prevalence of ototoxic hearing loss in developed countries such as the Netherlands, UK and USA has been reported to be 18%, 28% and 37% respectively (De Jager & van Altena, 2002; Peloquin et al., 2004; Sturdy et al., 2011) while the prevalence rates in developing countries such as India, Turkey and Brazil were 18.7%, 42% and 64% (Duggal & Sarkar, 2007; Tourn et al., 2005; Lima et al., 2006).

The reported high prevalence rates of ototoxic hearing loss in adults and the fact that children may be more vulnerable to ototoxicity than similarly treated adults (Schell et al., 1989; Kokotas et al., 2007) strongly suggest a possible high prevalence of ototoxic hearing loss in children with TB receiving ototoxic drugs. Ototoxicity is an important health issue, which requires active monitoring and periodic assessment of the hearing status of children receiving ototoxic TB drugs.

Auditory Monitoring in Ototoxicity

The goal of an ototoxicity monitoring programme is to detect early changes in hearing thresholds to preserve hearing before there is damage in the speech frequency range (Jacob, Aguiar, Tomiasj, Tschoeke & Bitencourt, 2006; Kathleen, 2004; Campbell, 2004). The moment early changes of hearing thresholds are detected, the dosage of the offending agent must be limited and an alternative drug should be considered (WHO, 2003; Jacob et al., 2006).

ASHA (1994) presented guidelines for monitoring the hearing of all individuals receiving cochleotoxic medication. According to these guidelines, a baseline hearing evaluation should be obtained before or within the first 72 hours of treatment with aminoglycosides. Follow-up

evaluations also need to be performed at 3 months, 6 months, and 1 year post-treatment intervals to detect ototoxic hearing loss. The baseline evaluation must be a complete audiologic assessment including speech audiometry and acoustic immittance measure (ASHA , 1994). The basic monitoring evaluations, which should be performed weekly throughout the treatment, include otoscopic examination and air-conduction threshold (ASHA, 1994). High frequency audiometry (9 to 20 kHz) is also recommended to provide maximum hearing sensitivity information (Goodman, Fitzpatrick, Ellison, Jesteadt & Keefe, 2009; 2006; ASHA, 1994). Moreover, objective measures, such as evoked otoacoustic emissions and brainstem evoked response audiometry should be carried out when the patient is unable to respond to subjective testing e.g. young children (Stavroulaki et al., 2002; ASHA, 1994). Review of the literature revealed that currently there is no accepted protocol or criteria for monitoring ototoxicity in children, indicating the need to develop a standard monitoring program for this population.

Institutionalization of Children at Brooklyn Chest Hospital for TB

The following information was obtained from Dr M Willemse, the paediatrician at Brooklyn Chest Hospital to help identify suitable patients for the present study (personal communication, August 19, 2010).

Children are admitted to Brooklyn Hospital once they have been diagnosed with TB and have begun TB treatment at a referral hospital. At Brooklyn Chest Hospital a comprehensive assessment confirms the diagnosis and type of TB and the relevant treatment is determined. Unlike drug susceptible TB, the treatment of drug resistant-TB includes ototoxic drugs. Drug-resistant-TB is suspected in a child who fails to respond to treatment despite good documented adherence or if he/she has a history of close household contact with a drug-resistant TB patient.

Drug resistant TB is confirmed by sputum culture and drug susceptibility testing, which is only positive in 30-60% of suspected cases due to the paucibacillary nature of childhood TB. In addition, test results may take up to two months, for these reasons and on the basis of the physician's advice children with high index of suspicion of MDR-TB contacts are treated for drug-resistant TB with amikacin, ofloxacin, isoniazid, pyrazinamide, ethambutol, ethionamide prior to laboratory test results. Once the drug susceptibility test results are available, children with resistance to amikacin or ofloxacin or both of these second-line drugs will receive capreomycin and para-aminosalicylic acid respectively. Drug susceptibility test results may show different forms of drug-resistant TB including mono-rifampicin resistant, multi-drug resistant, pre-extensively drug-resistant and extensively drug-resistant (XDR). Patients with different forms of drug-resistant TB are treated with ototoxic drugs and hence should be closely monitored for ototoxic hearing loss (ASHA, 1994).

When this study was initiated there were no hearing testing protocols for children and the hearing screening tests were not performed routinely at Brooklyn Chest Hospital. It is only during the course of this study that the ototoxicity monitoring has been established at the hospital.

Hearing evaluation. The following protocol was obtained from Dr M Willemse, the paediatrician and Miss K Jacobs, senior audiologist at Brooklyn Chest Hospital in order to get familiar with the hearing evaluation process in this institution (personal communication, August 19, 2010).

Children receiving ototoxic medication are referred to the resident audiologist for hearing evaluation. Hearing screening tests which include otoscopy, tympanometry, otoacoustic

emissions (for younger children) or air conduction audiometry (for older children) are implemented almost every 2 weeks. Since children initially receive the ototoxic medication from the referring hospital/clinic, where hearing tests are not routinely performed, there is no baseline hearing evaluation that could be compared to the test results for earlier detection of ototoxicity. Patients with test results that indicate hearing loss are referred to the attending physician for an alternative treatment with potentially less ototoxic drugs, which may prevent further hearing loss, particularly in speech frequencies. Children who require hearing aids are referred to audiologists at Tygerberg or Red Cross Hospitals, and those with middle ear abnormalities are referred to the attending physician. Children with middle ear abnormalities which require special care (children whose middle ear pathologies persist following the physician's intervention) are referred to an Ear, Nose and Throat specialists at Tygerberg or Red Cross Hospitals.

The current study reports on the nature and frequency of outer and middle ear abnormalities and hearing loss in institutionalized children at Brooklyn Chest Hospital receiving ototoxic medication for TB. The purpose is to alert the relevant health care authorities of the possible effects of ototoxic drugs and institutionalization on hearing of children with TB and to emphasize the need for a routine ototoxicity monitoring programme in this population.

The Impact of Hearing loss in Children

The severity of the impact of hearing loss in children depends on various factors; the most important ones being the degree, laterality, configuration and time of onset of hearing loss (Probst, 2006, Knight, 2008). Childhood hearing loss as it was mentioned earlier has a significant impact on the development of receptive and expressive communication skills (speech and language) (ASHA, 2010). Children with hearing loss have poor vocabulary when compared to

their normal peers and as they grow older the gap between their vocabulary and those with normal hearing increases (Johnson, Benson & Seaton, 1997; Northern & Downs, 2002). In addition, hearing impaired children have difficulty understanding grammar, word order, words with multiple meanings and idioms (Johnson et al., 1997; Northern & Downs, 2002), which adversely influences their academic achievement. Poor academic achievement is seen as early as the first grade and learning problems become more severe when the child enters second or third grade (Khiri Md Daud, Noor, Rahman, Sidek & Mohamad, 2010; Nelson, 1997). Children with hearing loss have difficulty in reading, writing and mathematical reasoning (Khiri Md Daud et al., 2010; ASHA, 2010). Hearing loss can also negatively influence a child's cognitive, social and emotional development (Adams & Rohring, 2004; Ansari, 2004). Children with hearing loss are often unsuccessful in social activities and are usually unhappy in the school environment or other social gatherings (ASHA, 2010; Rall, 2007). Any undetected or unmanaged hearing loss in children could affect their behaviour and quality of life (Olusanya, 2000). Anxiety, depression and attention problems are common behavioural problems in hearing impaired children (Gouma et al., 2011). In adulthood, hearing impaired individuals may face various problems in obtaining, performing and keeping a job (Copley & Friderichs, 2010), thus unemployment rate, low wages and fewer full-time job opportunities are higher among this population (Punch, Hyde & Creed, 2004). In essence, hearing loss in children especially in those who are at the age of speech and language development could have disastrous consequences, since hearing loss may cause delays in speech and language development, schooling difficulties (literacy), social and emotional disorders with resultant poor quality of life (Northern & Downs, 2002; Neuwelt & Brock, 2010).

The negative consequences of childhood hearing loss indicate the need to assess the hearing status of children with TB receiving ototoxic medication, who are at risk of mild to

profound hearing loss and even deafness. Such information will allow early identification of ototoxic hearing loss and the opportunity to prevent or minimize further hearing loss in frequencies critical for speech, by administering an alternative less ototoxic agent (Fausti et al., 2007; ASHA, 1994). Moreover this information will be valuable for planning for service delivery to this population (e.g. provision of hearing aids for those who already have hearing loss to reduce its impact).

University of Cape Town

Methodology

Aim

To describe the auditory function of participants with TB between the ages of 0 (from the time of birth) and 18 years who are receiving ototoxic drugs at Brooklyn Chest Hospital.

Objectives

In participants at Brooklyn Chest Hospital who are receiving ototoxic medication for TB:

1. To determine the prevalence of outer and middle ear abnormalities pre and post medical intervention:

1.1. Outer ear

1.2. Middle ear

1.2.1. Appearance of the tympanic membrane

1.2.2. Function of the middle ear as determined by:

1.2.2.1. Impedance and admittance

1.2.2.2. Ipsilateral acoustic reflexes

1.2.3. Unresolved middle ear abnormalities

2. To describe the prevalence and nature of hearing loss

2.1. Prevalence of hearing loss

2.2. Nature of the hearing loss

2.2.1. Type and Configuration

2.2.2. Degree

2.2.3. Laterality and symmetry

3. To determine the relationship between:

3.1. Middle ear abnormality and sex

3.2. Middle ear abnormality and age

3.3. Duration of hospital stay and middle ear abnormality

3.4. Duration of ototoxic drug exposure and the presence of a sensorineural hearing loss

3.5. Type of ototoxic drug and the presence of a sensorineural hearing loss

3.6. Type of TB and

- Sensorineural hearing loss
- Middle ear abnormality

3.7. Comorbid presentation of HIV and TB and middle ear abnormality

3.8. Comorbid presentation of HIV and TB and sensorineural hearing loss

Research Design

A descriptive survey research design (Polit & Beck, 2004) was used in this study. Such a design examines the situation as it is by identifying the characteristics of the observed phenomena (Polit & Beck, 2004). The aim of descriptive research is to describe the relationship among variables rather than to infer cause and effect relationships, as many research problems are cast in non causal terms (Polit & Beck, 2004). A survey design describes the characteristics of a large population by surveying a sample of that population (Trochim, 2001). Since this study examined

the hearing status of a group of TB children receiving ototoxic medication, a descriptive survey research design best facilitated this process.

Descriptive research is an efficient means of collecting a large amount of data about a problem (Polit & Beck, 2004). The major limitation of descriptive research designs is that they are weak in their ability to reveal causal relationships (Polit & Beck, 2004). It was not the intention of this study to infer any causal relationships and therefore a descriptive design was suitable.

Participants

Selection criteria.

Inclusion criteria. Children who met the following criteria were selected to participate in the study:

- Be between 0 and 17.11 years of age
 - Resident at Brooklyn Chest Hospital
 - Received ototoxic TB medication for a minimum period of 14 days prior to assessment
- Ototoxicity does not generally appear until 5 to 14 days after the start of ototoxic treatment (de Jager & van Altena, 2002).

Exclusion criteria. Children who were excluded from the study:

- Too ill to have hearing tests done (as determined by a physician/nurse).
- Had a congenital hearing loss

Recruitment. Following ethics approval of the study by the University of Cape Town's Faculty of Health Sciences and Human Research Ethics Committee, permission was obtained from the Provincial Department of Health in the Western Cape and the Medical Superintendent at Brooklyn Chest Hospital to:

1. Review the records of all children at the hospital to identify eligible participants.
2. Contact the parents of all eligible participants.

Once permission was granted, the researcher met the parents at the hospital, explained the nature of the study to them and obtained written informed consent for the inclusion of their children in the study.

Sampling method. Non probability purposive sampling (Trochim, 2006) was used for this survey. In purposive sampling, one samples with a *purpose* in mind. The sample includes one or more specific predefined groups. In this method one of the first things to do is to verify that the respondent does in fact meet the criteria for being in the sample (Trochim, 2006). For this study all individuals who met the selection criteria were included in the study. As a result a non probability purposive sampling method best facilitated this study.

Sample size. The size of the sampling frame was estimated to be 50 by the resident audiologist at Brooklyn Chest Hospital. The size of the sample was directly linked to the number of eligible participants who were at Brooklyn Chest Hospital at the time of the study. All eligible participants were included in the study. While a power analysis typically guides the determination of the sample size, this study's sample size was constrained by the size of the sampling frame which reflected the population of children with TB at Brooklyn Chest Hospital

(the only residential facility in the Cape Town metropole for individuals with MDR TB, who would receive ototoxic medication).

The records of the patients at Brooklyn Chest Hospital were reviewed, with 65 children hospitalized for TB from beginning of May to end of August 2010. Of these children, 32 were eligible to participate in the study. Prior to the commencement of the study, one child died and one was discharged from the hospital, which left 30 patients to form the basis of the study. Of 30 children who were recruited, one died, one was discharged and one was referred to Tygerberg Hospital for severe illness before hearing tests could be completed, with only outer and middle ears of these three participants assessed.

Description

Research site description. The following information was obtained from the patient records and Dr M Willemse, the paediatrician at the hospital (personal communication, August 19, 2010).

The Brooklyn Chest Hospital (BCH) is the main referral center for patients with TB diseases from hospitals and clinics across the Western Cape. It is the only facility that treats XDR TB patients in the province and contains 349 beds with 16 children beds and 40 baby cots which are usually filled to capacity. Children treated at BCH may be hospitalized for periods ranging from 6 months to 3 years. The hospital has a school on site with 30 to 40 pupils. The majority of patients admitted to Brooklyn Chest Hospital are poor and are African or Coloured.

Participant description. The mean age of the participants (n=30) was 7 years (85.7 months) and ranged from seven months to 16.6 years. There were nine participants in the 0 to 3 years age group (group I), six participants in the 3 to 7 years age group (group II) and 15

participants in the 7 to 18 years age group (group III). The distribution of the participants between the two sexes was almost equal and there were 16 (53.3%) females and 14 (46.6%) males.

The majority of the participants (n = 25, 83.3%) had pulmonary TB. The frequency of TB meningitis was 10% (n = 3), disseminated TB 3.3% (n = 1) and TB of hip joint 3.3% (n = 1). Forty percent (n = 12) of the participants were HIV-positive.

Drug-resistant-TB was confirmed in 20 participants with a diagnosis of MDR-TB (n=14), XDR-TB (n=4) and mono-rifampicin resistant TB (n=2). Drug-resistant-TB was suspected in 10 participants with a diagnosis of probable MDR-TB (n=8) and XDR-TB (n=2). The TB treatment regimen included, amikacin in 83.3% (n=25), capreomycin in 13.3% (n = 4) and streptomycin in 3.3% (n = 1) of participants. The mean duration of the participants' hospital stay (up to the date of the study) was 28 weeks (with a range of 6 to 92 weeks). The length of treatment with ototoxic drugs before commencement of hearing tests ranged from 6 to 92 weeks, with a mean time of 27 weeks. Participants had TB treatment prior to their stay at Brooklyn Chest Hospital, the duration and nature of which could not be determined since records were not available.

One of the participants in group III (7-18 years) was developmentally delayed with hemiplegia, the hearing status of whom was determined using OAE and AABR. See Appendix A for the participants' characteristics.

Data Collection

Test protocol. The use of a single test for assessing a child's hearing sensitivity is not recommended (Diefendorf, 2009). Based on the complex nature of the auditory mechanism, multiple tests are employed in clinical practice (Diefendorf, 2009). Test battery allows the

audiologist to reach a more confident diagnosis (Diefendorf, 2009). In test battery selection, the researcher selected the most cost effective tests for which validity and reliability are the highest.

Table 1

Illustration of the Test Protocol and Equipment Used to Assess Auditory Function in Different Age Groups

Age groups of participants	Tests	Equipment
All age groups	Test environments	Quest Technologies 2700 -sound level meter
	Otoscopic examination	Heine Minilux 2000- otoscope
	Tympanometric examination	GSI 38- immittance instrument Interacoustic AT 235H
	Acoustic Reflex examination	GSI 38- immittance instrument
	DPOAE examination	GSI audioscreener
Participants ≤ 3yr	AABR examination	GSI audioscreener
	Diagnostic ABR examination	GSI Audera
	ASSR examination	GSI Audera
	3yr < participants ≤ 7yr	Play Audiometric examination
7yr < participants < 18yr	Audiometric examination	MA51- audiometer

Note. DPOAE=Distortion Product Otoacoustic Emissions. AABR=Automated Auditory Brainstem Responses. ABR=Auditory Brainstem Responses. ASSR= Auditory Steady-State Responses.

Equipment. All equipment had been calibrated within the last six months, in accordance with the manufacturer's specifications.

Test Environments

1. Sound treated booth (ANSI S3.1_1999, Audio Sound Rooms)
2. Quiet environment: An acceptable low level of noise is under 50 dB SPL (ANSI standard). A sound level meter is used to determine the ambient noise level. However

since the Participants were examined in a sound proof audiobooth for pure tone audiometric, OAE and AABR examinations there was no need to utilize a sound level meter.

Heine Minilux 2000- otoscope. The otoscope is designed for the visual examination of the external auditory meatus and tympanic membrane (Stach, 2008). This implement was used in the study to visually examine the status of the outer ear and tympanic membrane.

GSI 38-immittance instrument/Interacoustic AT 235H. The immittance instrument is used to determine the mobility and impedance of the tympanic membrane by measuring the sound pressure reflected, thereby providing information on the status of the tympanic membrane, middle ear cavity, Eustachian tube, stapedius muscle and the VII and the VIII cranial nerves. This instrument is used to obtain a tympanogram and to determine the threshold or the presence of an acoustic reflex (Frank & Rosen, 2007).

1. Tympanogram: A tympanogram is a measurement of acoustic admittance at the tympanic membrane as a function of ear canal's air pressure (Frank & Rosen, 2007).

Stimulus characteristics:

1. Probe tone frequency: children < 7 months of age = 1000 Hz,

children > 7 months of age = 226Hz

2. Air pressure: +200 to -400 daPa

Since the GSI 38-Immittance Instrument could not produce a 1000 Hz tone, Interacoustic AT 235H was considered for testing participants under 7 months of age. However, this

instrument was never used in the study, since none of the participants were under 7 months of age.

2. Acoustic Reflex: acoustic reflex is a measure of stapedius muscle contraction to a pure tone stimulus via the probe (Frank & Rosen, 2007).

Stimulus characteristics:

1. Stimulus type: Pure tone
2. Frequencies: 500, 1000, 2000 and 4000 Hz
3. Intensity range: 0 to 105 dB HL

In this study, the immittance instrument was used to accurately assess the status of the middle ear and tympanic membrane. Since GSI 38-Immittance Instrument is only equipped with ipsilateral stimuli, contralateral acoustic reflexes could not be determined.

MA51-audiometer. The audiometer measures the hearing sensitivity and delivers the calibrated suprathreshold stimuli (Stach, 2003).

Pure tone audiometry: It is used to determine the hearing threshold and type of hearing loss (sensorineural or conductive) via air and bone audiometry. With air conduction audiometry the stimulus to the ear canal is delivered via headphones. With bone conduction audiometry the stimulus to the cochlea is delivered by vibrational energy transmitted through the skull from a transducer (vibrator) that is placed on the mastoid (Hinchcliffe, 2003).

Stimulus characteristics:

1. Stimulus type: Pure tone

2. Frequencies: Air conduction = 250, 500, 1000, 2000, 4000, 8000 Hz;

Bone conduction = 250, 500, 1000, 2000, 4000 Hz

3. Intensity range: Air conduction = -10 to 120 dB HL

Bone conduction = 0 to 70 dB HL

GSI audioscreener. The GSI Audioscreener is an effective screening tool in the evaluation of hearing in newborns and small children. The instrument includes two tests:

1. DPOAE (Distortion Product Otoacoustic Emissions): This test is used to assess cochlear integrity by measuring the physiologic response of the outer hair cells to acoustic stimuli. During DPOAE, the audioscreener generates tonal stimuli, and the acoustic energy produced in response to the clicks is detected by a microphone within the probe (Ceranic, 2003).

Stimulus characteristics:

1. Stimulus type: tonal stimuli
2. Test frequency: 2000, 3000 and 4000 Hz (Roeser, Clark, 2004)
3. Intensity range: 45 to 70 db SPL
4. Ratio of f_2/f_1 : 1.2

This study utilized distortion product otoacoustic emissions to assess the integrity of the inner ear because DPOAEs are less sensitive to environmental noise, including the

noise made by the patient, and have a wider frequency range than Transient Evoked Otoacoustic Emissions (Hall, 2000).

2. AABR (Automated Auditory Brainstem Responses): This test is used to measure the integrity of the inner ear and the auditory pathway to the level of the brainstem (Hamilton-Craig, 2003). The click stimulus is presented via an ear canal probe, and the electrophysiological brain-stem responses are detected by scalp electrodes. Average responses from a large number of stimuli are used by automated screener to produce a final result (Hamilton-Craig, 2003).

Stimulus characteristics:

1. Stimulus type: Click
2. Stimulus range: 500-4000 Hz
3. Intensity range: 35-40 dBnHL
4. Stimulus rate: 37 per second

Click stimuli, because of their rapid onset and broadband spectrum, elicit a neural response from a large number of auditory neurons almost synchronously and therefore, are most likely to produce a robust response when measured from the scalp (Sininger & Hyde, 2009). Thus click stimuli have been chosen for this test.

Quest Technologies 2700 -sound level meter. A sound level meter is a basic instrument for determining noise levels (Gelfand, 2009). The presence of ambient noise above 50 dB SPL (ANSI standard) negatively influences the results of any hearing tests. It was therefore

considered to use a sound level meter in the study to determine the level of noise present at hearing assessment sites.

Sound Level Meter characteristic:

1. Unit of measure: dB SPL
2. Frequency weighting networks: A. The 'A' weighting setting emulates the response of the human ear at low levels and is used for most industrial and community noise measurements (Quest Technologies 2700 SLM user manual).
3. Response: Slow (1 second time constraint).
4. Reference frequency: 1 kHz
5. Frequency range: 4 Hz to 50 kHz
6. Accuracy: Within 0.7 dB SPL

GSI Audera. An electrical instrument which provides objective information to estimate hearing sensitivity and to identify neurological abnormalities of auditory nerve and the auditory pathway up to the brainstem (Don & Kwong, 2009). The hearing thresholds of participants younger than 3 years of age who were suspected of having hearing loss (from the results of OAE and AABR tests) were considered to be determined using this instrument which conducts two tests:

1. ABR (Auditory Brainstem Responses): ABR audiometry is detection of an evoked potential generated by a brief click or tone burst transmitted from an acoustic transducer e.g. insert earphone. The elicited waveform response is measured by

surface electrodes placed in the vertex and each ear lobes or mastoid. The output of the electrodes is averaged and charted against the time (millisecond). The resultant waveform is characterized by seven peaks. These waveforms normally occur in a period of 10-millisecond period after the onset of the stimulus (Burkard & Don, 2007; Sininger, 2007).

Stimulus characteristics:

1. Stimulus type: Click stimuli and tone burst
 2. Frequency range for tone burst: 500 to 4000 Hz
 3. Stimulus rate: 33.1 per second (for threshold), 11.1 per second (neurological)
 4. Intensity range: 20 to 90 dBnHL
2. 80-Hz ASSR (Auditory Steady-State Responses): The auditory steady-state response (ASSR) refers to an electrophysiologic response to rapid auditory stimuli which creates an estimated audiogram. Auditory Steady-State Responses are recorded from electrodes taped on the forehead and each mastoid (or ear lobe) while the person listens to tones of varying frequency and intensity via earphones (Aoyagi, Watanabe, Ito & Abe, 2007). 80-Hz ASSR was chosen for this test because 80-Hz ASSR, or high frequency ASSR, is applicable to sleep children (Aoyagi et al., 2007).

Stimulus characteristics:

1. Stimulus type: Tone
2. Frequency range: 250 to 8000 Hz

3. Intensity range: -10 to 127 dB HL

Validity and reliability. The validity and reliability of the tests used in this study are well established in every day practice and further outlined by sensitivity and specificity of the data presented in the table below.

Table 2

The Sensitivity and Specificity of the Tests Used to Assess the Integrity of the Auditory Pathway

Tests	Sensitivity	Specificity	Assessment region	Limitation	Solution	Reference
Tymp	90%	75%	TM problems	Can't be done when wax/discharge present	Refer + repeat once they cleared	Onusko, 2004
AR	95%	50%	ME problems	Lack of contra reflex	Use of test battery	Northern & Downs, 2002
PTA	74.4%	92.1%	Hearing loss	Diagnosis of MEE	Use of test battery	Forster & Kumar, 1997
OAE	>97.5%	94%	Cochlear problems	Diagnosis neural HL	Use of AABR	Steam & Swanepoel, 2007
AABR	100%	96-98%	Hearing loss	Diagnosis of MEE	Use of test battery	Bhattacharya, 2009
ABR	>90%	90%	Hearing loss	Diagnosis of MEE	Use of test battery	Bhattacharya, 2009
ASSR	100%	51%	Hearing loss	Diagnosis of MEE	Use of test battery	Santiago-Rodriguez, et al., 2005

Note. AC=acoustic reflexes. Tymp=tympanometry. PTA=pure tone audiometry. HL= hearing loss. ME= meddle ear. MEE= middle ear effusion. TM=tympanic membrane.

Study personnel. An audiology undergraduate student who was familiar with test procedures and fluent in the English, Afrikaans and IsiXhosa languages was recruited to explain the instructions in the language appropriate to the participant. However, there was no need for the translator, since all of the participants could speak either English or Afrikaans and the resident audiologist at Brooklyn Chest Hospital, who could speak both languages, assisted the researcher in this regard.

Procedure. The researcher registered with the Health Profession Council of South Africa (Appendix B). Ethical approval was obtained from the University of Cape Town's Faculty of Health Sciences Research Ethics Committee (REC Reference Number: 010/2010) and Provincial Health Research Committee (Reference Number: RP40/2010), (Appendix C & D). The Medical Superintendents of Brooklyn Chest Hospital gave verbal permission to the researcher to conduct the research at Brooklyn Chest Hospital. Informed written consent was obtained from parents/legal guardians and assent from participants who were old enough to make decisions, before commencement of the study (Appendix E). The informed consent forms were available in English, Afrikaans and isiXhosa (Appendix F, G & H). A flow diagram of the steps involved in obtaining ethical approval and consent from parents/participants is provided in appendix I.

A hard copy of the tympanometric and acoustic reflex examinations results could not be made due to lack of a compatible printer. Moreover, it was not possible to save the audiometric examination results on the researcher's computer (no compatible cable) and the researcher manually recorded the results of all hearing examinations. In all test procedures, each ear was tested separately and the right ear was tested first.

A real- time analysis and interpretation of the results were provided for each step of the procedure as this had a significant impact on decision making and the next step of the procedure. A flow diagram of the procedure is provided in Appendix J.

Otoscopic examination: A visual inspection of the outer ear, middle ear and tympanic membrane was carried out using the otoscope. Participants with visible dermatological conditions of the pinna, impacted wax in ear canal, tympanic membrane micro-perforations or active middle ear infections were referred to a Physician at Brooklyn Chest Hospital. Upon completion of their treatment, which entailed 2 weeks to 3 months of therapy (depending on the nature of the pathology) the participants' ears were otoscopically examined again. Participants who failed for the second time were referred to Tygerberg/Red Cross Hospital by the physician. Participants who passed the otoscopic examination were then assessed further (Tympanometry).

Tympanometric examination: The status of the middle ear and tympanic membrane was assessed using the immittance instrument. The participant was instructed to keep quiet and sit still during the examination. The test was performed by inserting a clean rubber-tipped probe with suitable size and shape into the ear canal. The GSI 38-immittance instrument changed the pressure (from +200 to -400 daPa) in the ear, produced a pure tone (226 Hz), and measured the tympanic membrane responses to the sound at different pressures. The results were depicted in a tympanogram, which was displayed on the unit's screen (Clark et al., 2007).

The probe frequency for children older than 7 months of age was adjusted to 226 Hz. This value would have been adjusted to 1000 Hz had any of the participants been younger than 7 months of age, which was not the case (Baldwin, 2006). The results were manually recorded and categorized according to the norms outlined infra.

Type A tympanogram ($-100 < \text{peak values} < +100 \text{ daPa}$, $0.3\text{cc} < \text{SC} < 1.6\text{cc}$, $\text{ECV} < 2\text{cc}$) was considered normal (Jerger, 1970; Llieden, 1969, as cited in Shanks & Shohet, 2009), which indicates the presence of a normal pressure in the middle ear with natural mobility of the eardrum and the ossicular chain (Gelfand, 2001). Type B (no peak values, $\text{SC} = 0\text{cc}$, $\text{ECV} = \text{or} > 2\text{cc}$) or C (peak values $< -100 \text{ daPa}$, $0.3\text{cc} < \text{SC} < 1.6\text{cc}$, $\text{ECV} < 2\text{cc}$) tympanograms (Jerger, 1970; Llieden, 1969, as cited in Shanks & Shohet, 2009) may indicate the presence of fluid in the middle ear, scarring of the tympanic membrane, lack of contact between the ossicular chain of the middle ear or a tumor in the middle ear (Gelfand, 2001). If abnormal results (type B or C tympanograms) were obtained, the test was reimplemented for confirmation of the results. The probe tip was removed for cleaning after tympanometric examination of each ear.

Type B tympanogram also occurs when a probe is sealed against the canal wall and type C tympanogram occurs in the presence of a negative middle ear pressure. Since a hermetic seal is required for obtaining acoustic reflexes in ears with middle ear pathology and negative pressure (Shanks & Shohet, 2009), an acoustic reflex test following tympanometry determines the definite type of tympanograms. Moreover, diagnostic information from immittance measures are strengthened when results from both procedures (AR and tympanogram) are interpreted together (Clark et al., 2007). Thus all participants with type A, B and C tympanograms proceed to the next step of the procedure (Acoustic Reflex).

Acoustic Reflex examination: This test was performed using the GSI 38-immittance instrument by inserting a rubber-tipped probe in the ear canal that presented sound stimuli (at intensities of 85 to 105 dB HL) at 500, 1000, 2000 and 4000 Hz for Ipsilateral reflexes. The results were displayed on the unit's screen and were manually recorded by the researcher.

Participants with absent ipsilateral acoustic reflexes but normal tympanograms (Type A) required further audiologic investigations prior to medical referral and proceeded to the next step (hearing assessment). Participants with Type B or C tympanograms, and with absent acoustic reflexes, were referred to the physician at Brooklyn Chest Hospital. Upon completion of their treatment, which entailed 2 weeks to 3 months of therapy depending on the nature of the pathology [e.g. those with chronic otitis media or otitis media with effusions required much longer and more complicated treatment (Margolis & Hunter, 2000)], the participants were retested using the immittance instrument. Participants under 3 years of age, whose condition remained unresolved, were referred to an Ear, Nose and Throat specialist at Tygerberg/Red Cross Hospital by the physician. The rest of the participants proceeded to the next step, in which they were tested with equipment appropriate to their age. They were divided into the following age groups:

A) Participants under 3 years of age:

It should be mentioned that participants with cognitive impairment (who were older than 3 years of age) or who were uncooperative were also assessed using this procedure.

DPOAE examination: In this step the function of the outer hair cells of the inner ear was assessed using distortion product otoacoustic emissions (DPOAE) technology. During DPOAE screening, the audiologist placed a small probe in the ear canal that is designed to deliver the sound stimuli and also to collect a response via a sensitive receiving microphone. In a healthy ear, sound stimuli from the probe are transmitted through the middle ear to the inner ear where outer hair cells of the cochlea respond by producing an emission. This emission was picked up by the microphone, analyzed by the screening unit, and a "pass" or "refer" result was displayed

on the unit's screen (Swanepoel, Ebrahim, Joseph & Friedland, 2007). If a "pass" test result for each frequency was obtained, the overall result was a "pass" too. The results were manually recorded by the researcher.

The test results read "refer" if there was an impaired cochlea that was not responding normally to sound. For purposes of this study, an additional error message, "can't test", was generated by the equipment due to internal noise generated by the participant's movement. If the participant continued to move and did not settle at all, the researcher re-tested him/her later at a more appropriate time.

This test was completed in less than 5 minutes and participants with "pass" or "refer" results proceeded to the next step of the procedure. Participants with refer results would have also proceeded to the next step, AABR examination, in order to obtain more information about their hearing status, prior to referral for audiology services (which was not the case).

AABR examination: Participants who were tested with DPOAE were also tested by automated auditory brain responses (AABR) to assess their auditory function from the eighth nerve through the auditory brainstem. AABR measurements were obtained by placing disposable surface electrodes high on the forehead, and on the mastoids after these anatomical areas were cleaned adequately so that the maximum impedance difference between the two electrodes was less than 5 k Ohms (Maruthy & Mannarukrishnaiah, 2008). The click stimulus (at 35-40 dBnHL) was delivered to the participant's ear via a small earphone designed to attenuate background noise. The AABR system compared a participant's waveform with that of a template developed from normative ABR child data. A "pass" or "fail" response was determined from this

comparison and was displayed on the unit's screen. The results were recorded manually by the researcher.

Participants who did not pass AABR or AOAIE were to be referred for audiology services at Tygerberg/Red Cross Hospital for determination of their hearing thresholds (diagnostic ABR and ASSR tests) by the resident audiologists. However all participants passed the DPOAE and AABR tests and no one was referred for the ABR and ASSR tests.

ASSR examination: 80-Hz ASSR is used to create statistically valid audiograms. ASSR examination is done by placing electrodes taped on the forehead and each mastoid/earlobe, after these anatomical areas are cleaned adequately so that the maximum impedance difference between the two electrodes becomes less than 5 k Ohms (Hatton & Stapells, 2011). This test, 80-Hz ASSR, is performed under sedation or in natural sleep if the participant is under 6 months of age. Stimulation of a repetitive sinusoidal amplitude/frequency (AM/FM)-modulated tone is delivered using earphones. The results are detected objectively using statistical formulas that determine the presence or absence of a true response (Aoyagi et al., 2007).

Diagnostic ABR examination: This test estimates the hearing sensitivity by placing disposable surface electrodes high on the forehead, on the mastoid, and on the nape of the neck after these anatomical areas are cleaned adequately so that the maximum impedance difference between the two electrodes becomes less than 5 k Ohms (Maruthy & Mannarukrishnaiah, 2008). The participant should be sleep for the duration of the test. Participants under the age of six months are not sedated, and the test is performed while the participant is naturally sleeping, following a feeding. Participants over the age of six months are sedated by an anaesthetist with chloral hydrate. As clicks and tone bursts (at 20-90 dBnHL) are delivered through the earphones,

the electrodes measure the electrical activity from the auditory pathway. These electrical responses are analyzed by the computer and produced a waveform. The different peaks on the resulting waveform provide information on the time it takes various structures of the auditory pathway to respond following the stimulus. The results are interpreted by an audiologist to estimate the hearing thresholds (Bhattacharyya, 2009).

These procedures (ABR and ASSR) are in accordance with the routine hearing tests performed at Tygerberg/Red Cross Hospital. The total testing time is approximately 1.5 hours with 30 minutes reserved for sedation recovery time.

B) Participants between 3 and 7 years of age:

Play Audiometric examination: In this step the degree and type of hearing loss (sensorineural or conductive) were determined using pure tone audiometry. In Play audiometric examination a participant's hearing is assessed in decibels (dB HL) with a calibrated audiometer. Both air and bone conduction were tested at frequencies between 250-8000 Hz and 250-4000 Hz respectively in a sound proof audiobooth. During play audiometry the participant is conditioned to engage in an activity, such as putting rings on a spindle or putting together simple puzzles, each time the signal is heard. The participant was then introduced into a sound proof audiobooth and the researcher placed a headphone that was completely centred over the ear canals. The participant was taught to wait, listen and only respond with the play activity when the auditory signal was heard. The initial test frequency was 1000 Hz at 30 dB HL. When the participant failed to indicate the presence of a tone, the sound intensity was increased at 10 dB HL increments until a response was obtained indicating that a tone was heard. The intensity was then decreased by 5 dB. The procedure was repeated and the response to the lowest audible tone at each frequency

was recorded as the threshold. The pure tone thresholds for each ear were obtained, in order of 2000, 3000, 4000, 6000, 8000, 1000, 500 and 250 Hz (American National Standards Institute, 2004). The inter-octave measurements were also made whenever there was a difference of 20 dB or more between two adjacent octave frequencies (ASHA, 2005). The same procedure was used to determine bone conducted thresholds, except that a bone vibrator was placed on the mastoid processes and thresholds were obtained at a frequency range of 250 to 4000 Hz (Diefendorf, 2009). Masking was used for both, air conducted and bone conducted when indicated it was appropriate to do (ASHA, 2005).

In order to minimize habituation, maintain a participant's attention and maximize repeated response behavior, attractive stickers were given to the participants at appropriate times, as a form of reinforcement (social praise). Hearing thresholds at audiometric level of lower than 16 dB HL, at all test frequencies, from 125 Hz to 8000 Hz with air-bone gap of ≤ 10 dB for both ears was considered normal hearing sensitivity (Duggal & Sarkar, 2007; Schlauch & Nelson, 2009). The hearing thresholds were recorded on audiograms by the researcher. Participants who failed this step were referred to the audiologist and the physician at the hospital for further audiological testing and possible alternative less ototoxic treatment.

C) Participants between 7 and 17.11 years of age:

Audiometric examination: In this step the same procedure described in play audiometry was used to determine the air and bone conduction thresholds of the participants, with the exception that the participant engaged in no play activity to indicate the presence of a tone.

Data Analysis

The services of a statistical consultant were utilized in analysing the data. In order to determine the prevalence of outer ear abnormalities, the data obtained from the otoscopic examination of the outer ear were analysed via frequency counts since all the information was categorical data (Howell, 2007). With categorical data, the data consists of totals or frequencies for each category and thus frequency counts were the best statistical method to extrapolate information (Howell, 2007).

The outcomes of the otoscopic, tympanometric and acoustic reflex examinations (Table 3) were analysed via frequency counts to ascertain the prevalence of middle ear abnormalities. The presence of mixed hearing loss or air bone gap was determined in order to confirm abnormal middle ear function of ears with no acoustic reflexes but with normal otoscopic and tympanometric results.

Table 3

Determination of the Normality and Abnormality of Middle Ear

Middle ear	Examination results
Normal	Normal otoscopic result + Type A tymp + present Ipsi AR
	Normal otoscopic result + Type A tymp + Absent Ipsi AR + 7 th nerve injury
Abnormal	Normal otoscopic result + Type A tymp + Absent Ipsi AR + Mixed HL/ABG
	Normal/abnormal otoscopic result + Type B/C tymp + Absent/present Ipsi AR
	Perf/Grommet ^a

Note. ME=middle ear. Perf= perforation. ABG= air-bone gap. HL=hearing loss. AR= acoustic reflexes. Tymp=tympanogram.

^a Tympanometric and acoustic reflex examinations on ears with grommet or perforations of the tympanic membrane were not done.

In order to determine the prevalence of unresolved middle ear abnormalities, the number of ears with middle ear abnormality before and after referral for medical intervention was compared using the Generalized Linear Models. Generalized Linear Models are an extension of the linear modeling process which analyzes dependent variables with non-normal distributions and for many link functions other than identity (Hardin & Hilbe, 2007). Wald Chi-Square is used to test the Generalized Linear Models (Hardin & Hilbe, 2007). The probability distribution was binomial (which was a non-normal distribution), since the dependent variable was middle ear abnormality that could be normal or abnormal, and the link function was logit (not identity). Thus Generalized Linear Models were the best statistical method to extrapolate information with the 0.05 level of significance (Hardin & Hilbe, 2007).

Data obtained from pure-tone audiometric or OAE and AABR examinations (Table 4) were analysed via frequency counts to determine the prevalence of hearing loss. It should be mentioned that, a "Pass" DPOAE or AABR result which is considered normal hearing, means that the hearing thresholds were less than 30 dB HL (Sininger, 2007; Prieve, 2008).

Table 4

Determination of Hearing Status

	Audiometric examination	DPOAE examination (screening test)	AABR examination (screening test)
Normal hearing	Thresholds \leq 15 dB HL (0.25-8 kHz)	Pass	Pass
Abnormal hearing	Thresholds $>$ 15 dB HL (0.25-8 kHz)	Refer	Fail

Note. DPOAE= Distortion Product Otoacoustic Emissions. AABR= Automated Auditory Brainstem Response.

Adapted from "Hearing and deafness" (p.63), by P. V. Paul and G. M. Whitelaw, 2010, Sudbury, MA: Jones and Bartlett Publisher.

Data obtained from the type, configuration (Table 5) and degree (Table 6) of hearing loss were analysed via frequency counts to describe the nature of hearing loss. The degree of hearing loss for participants who passed OAE and AABR was considered within normal limits.

Table 5

Determination of Configuration of Hearing Loss

	High frequency loss	Low frequency loss	Flat loss
Frequency range	4 - 8 kHz	0.125 - 1 kHz	0.25 - 3 kHz & 4 - 8 kHz
AC Threshold	> 15 dB HL	> 15 dB HL	> 15 dB HL

Note. HFL= high frequency loss. LFL= low frequency loss. Flat= flat Hearing loss. AC= air conduction.

Adapted from "Audiologic monitoring of multi-drug resistant tuberculosis patients on aminoglycoside treatment with long term follow-up" by P. Duggal and M. Sarkar. 2007. *BMC Ear, Nose and Throat Disorders*, 7, 1-7.

The degree of hearing loss was determined using the Northern and Downs (2002) classification system based on pure tone averages of 0.5, 1 and 2 kHz. In this classification system, the degree of hearing loss for ears with high frequency loss is considered within the normal range. In the present study a great number of ears with their degree of hearing loss within the normal range (according to the mentioned classification system) had high frequency hearing loss, most likely due to ototoxicity. In order to determine the degree of hearing loss in

this population, the average of the thresholds for high frequencies (4 & 8 kHz) were also calculated (using the same classification system).

Table 6

Determination of the Degree of Hearing Loss Based on the Northern and Downs classification and the adapted proposed Classification

Classification	Normal	Slight	Mild	Moderate	Severe	Profound
Northern & Downs C (PTA of speech F)	0-15	15-25	25-30	30-50	50-70	70+
Proposed C (PTA of high F)	0-15	15-25	25-30	30-50	50-70	70+

Note. PTA of speech F= pure tone average of speech frequencies (0.5, 1 and 2 kHz). PTA of high F= pure tone average of high frequencies (4 and 8 kHz). C= classification.

Adapted from "Hearing in children" by J. L. Northern and M. P. Downs (p. 22). 2002. Philadelphia: Lippincott Williams & Wilkins.

The affect of sex, age and duration of hospitalization on middle ear abnormality were analysed using Generalized Linear Models (Hardin & Hilbe, 2007). It was not possible to assess the relationship between duration of ototoxic drug exposure and sensorineural hearing loss, due to lack of information about the nature of the TB treatment the children received prior to admission to Brooklyn Chest Hospital. Statistical analysis of the relationship between the type of ototoxic drugs and sensorineural hearing loss was not feasible because of the small sample size. It was also impossible to evaluate the link between type of TB and sensorineural hearing loss/ middle ear abnormality, due to low prevalence of different forms of TB other than pulmonary TB. A comparison was made using Generalized Linear Models, between the ears of participants diagnosed with HIV & TB versus those with TB only, to determine the effect of comorbid presentation of HIV and TB on middle ear abnormality (Hardin & Hilbe, 2007). The relationship

between sensorineural hearing loss and comorbid presentation of HIV and TB were also analysed using Generalized Linear Models (Hardin & Hilbe, 2007).

Ethical Considerations

Prior to commencement of the study ethics approval was obtained from the University of Cape Town's Faculty of Health Sciences Human Research Ethics Committee (REC Reference Number: 010/2010, Appendix C) and the Provincial Health Research Committee (Reference Number: RP40/2010, Appendix D). The following ethical principles were considered and adhered to in accordance with the Declaration of Helsinki (World Medical Association, 2008)

Autonomy. Parents/guardians of the children were informed both verbally and in writing about the aims and nature of the study and what was expected of their children. They were given the opportunity to ask questions and seek clarification prior to signing the informed consent form.

Informed consent (written) was obtained from each participant's parent by the researcher (Appendix C & D) prior to including them in the study. Once parental consent was obtained, the researcher sought verbal assent from each participant (if the participant was old enough) and their wishes respected.

All participants and their parents were verbally and in writing informed of their rights to voluntary participation in the study and to withdraw their participation at any time once the study has begun, without their treatment being affected in any way.

Confidentiality. All participants were assigned a research number and data were recorded and analysed using this number and not their names. Information on participants was

treated as confidential by the translators, the researcher and her supervisors. The participant's hospital records and the results of the hearing tests were handled with caution, and were not disclosed to anyone other than the healthcare professionals working with the child. All the parents of participants were informed in the information letter that their child will not be identified in any way in any publications arising from the study.

Non-maleficence. The hearing tests at Brooklyn Chest Hospital were non-invasive, non-painful and part of routine care and did not cause any harm. The study was designed in such a way that there were none/minimal risks involved in participation.

For participants less than three years of age who were considered for referral to Red Cross Hospital for additional audiometric examinations under sedation, there was a potential risk of not recovering from the sedative effect but this is a very rare event and has not occurred in the Cape Town area in the last 20 years (Professor S. Singh, personal communication, September 10, 2009). This test is the usual method to diagnose hearing loss in children less than three years of age. The benefit of early diagnosis and intervention is thought to outweigh possible risks of the procedure. However, the risk is significantly reduced by the presence of experienced physicians/nurses. This information was conveyed in the consent form.

Beneficence. At Brooklyn Chest Hospital the children's auditory status is monitored at monthly intervals, where possible. However, due to the high workload of the resident audiologist, regular testing is not always possible. The participants of the present study received a comprehensive auditory assessment, which could identify peripheral auditory problems. Children received stickers or a pen for their participation in the study.

Justice. All participants were treated fairly during all stages of the study and they were able to benefit from the outcomes of the research as indicated above.

Professional Competence. The researcher is an Audiologist with 3 years of work experience as a paediatric audiologist.

University of Cape Town

Results

The results are described in accordance with the aim and objectives of the study. Since the auditory status of two ears of a participant can be different, in the present study the results of the ears are reported and not of the participants. A summary of the results is presented at the end of each relevant section. The results described the auditory function of children with TB between the age of 0 and 18 years who were receiving ototoxic drugs at Brooklyn Chest Hospital.

1.1. Prevalence of outer ear abnormalities pre and post medical intervention

The results of the otoscopic examination of the 58 ears (29 participants), prior medical intervention, revealed that the participants had no structural abnormalities, foreign objects, growths or infections of the outer ear. Impacted wax was observed in 12% of ears ($n = 7$, 14% of participants) and was successfully cleared following management. Three out of four participants with impacted wax had bilateral presentations.

1.2. Prevalence of middle ear abnormalities pre and post medical intervention

The appearance and function of the tympanic membrane and the middle ear are described in the following sections.

1.2.1. Appearance of the tympanic membrane

Post the removal of impacted wax which had occluded the ear canal, otoscopic examination of the 58 tympanic membranes revealed 14% ($n = 8$, 21% of participants) with abnormal appearance. Four participants had abnormal tympanic membranes unilaterally while two had bilateral presentations. Following medical attention, two ears (which had both bulging tympanic

membrane and abnormal colour) presented as normal but six (which had grommets and perforations) had not improved. Table 7 details the nature and frequency of tympanic membranes which presented with an abnormal appearance (pre and post medical intervention).

Table 7

Nature and Frequency of Tympanic Membranes with Abnormal Appearance (Pre and Post Medical Intervention)

	Perforation	Grommet	Bulging	Retraction	Abnormal colour
Pre-intervention	3	3	2	0	2
Post-intervention	3	3	0	0	0

Note. Two ears presented with bulging and abnormal colour simultaneously. Two of the ears with perforations also presented with otorrhea.

1.2.2. Function of the middle ear

1.2.2.1. Impedance and admittance

Tympanometry was not conducted on six ears as they had grommets in situ or tympanic membrane perforations. Tympanometry on the remaining 52 ears (28 participants), prior to medical intervention, revealed that 73% ($n = 38$) of ears had type A tympanograms, indicating normal middle ear function, 21% of ears ($n = 11$) had type B tympanograms, associated with middle ear fluid or micro-perforation of the tympanic membrane, and 6% of ears ($n = 3$) had type C tympanograms associated with Eustachian tube disorders or middle ear fluid. In essence, 36% ($n = 10$) of participants (14 ears) had abnormal tympanograms, with four presenting bilaterally and six unilaterally. While medical referral for two participants (four of 14 ears) was not possible

(due to the death of one participant and the hospital discharge of the other) the remaining 10 ears presented as normal with type A tympanograms post medical intervention.

1.2.2.2. Ipsilateral acoustic reflexes

Ipsilateral acoustic reflex examination was not conducted on six ears as they had grommets in situ or perforations of the tympanic membrane. The examination on the remaining 52 ears (28 participants), before medical intervention, revealed that 62% ($n = 32$) of ears had ipsilateral acoustic reflexes and 38% ($n = 20$) of ears (54% of participants) had no ipsilateral acoustic reflexes. Six participants had absent acoustic reflexes bilaterally while eight had unilateral presentations. None of the participants were referred to a medical practitioner for the absence of acoustic reflexes as further audiologic investigation was required prior to referral. In all ears with absent ipsilateral acoustic reflexes ($n = 20$) a strong association was observed with middle ear pathology or facial nerve disorder, indicating that there was no auditory neural involvement or idiopathic absence of acoustic reflexes (See Table 8).

Table 8

Conditions which may have Contributed to Participants' Absent Ipsilateral Acoustic Reflexes

Conditions contributory to the absence of an ipsilateral acoustic reflexes	<i>n</i> (ears)	References
Type B tympanogram	11	Campbell, 2009
Type C tympanogram	3	Gelfand, 2009
Facial nerve disorder	1	Gelfand, 2009
Severe - profound hearing loss	2	Campbell, 2009
Air-bone gap	3	Gelfand, 2009
Total	20	

1.2.4. Unresolved middle ear abnormality

The assessment of the middle ear status in 58 ears revealed that 47% ($n = 27$) of ears (55% of participants) had middle ear abnormality. Of the 27 ears, 18 ears were referred for medical attention, 39% ($n = 7$) of which still had unresolved middle ear problems post medical intervention (See Table 9). The results ($X^2 = 7.809$, $df = 1$, $p = .005$) indicated that there were significantly fewer ears with middle ear abnormality post medical intervention suggesting successful resolution following treatment. Of the remaining nine ears which were not referred to a medical practitioner, four ears were lost (two participants were discharged from the hospital or died) and five ears had absent ipsilateral acoustic reflexes with normal otoscopic and tympanometric examination results and required further audiologic investigations prior to medical referral.

Table 9

Frequency and Nature of Middle Ear Abnormality of Ears Referred for Medical Intervention

Middle ear abnormality	Pre intervention (ears)		Post intervention (ears)	
	<i>n</i>	%	<i>n</i>	%
Perforation of TM	3	17	3	17
Grommet	3	17	3	17
Type C tymp & absent Ipsi AR	2	11	1	5
Type B tymp & absent Ipsi AR	8	44	0	0
Bulging & red TM	2	11	0	0
Total	18	100	7	39

Note. TM= tympanic membrane. Tymp=tympanogram. Ipsi AR= ipsilateral acoustic reflexes.

Summary of the Prevalence of the Outer and Middle ear Abnormalities Before and After Medical Intervention

Table 10 reflects the outer and middle ear status in three different age groups (pre and post medical intervention). The outer ear of 14% of the participants had impacted cerumen which was removed following referral to a medical practitioner. The middle ear function in 55% ($n = 16$) of the participants was abnormal, of whom 75% ($n = 12$) were referred for medical intervention and the rest for further audiological evaluation (except two participants who were discharged from the hospital or died). Fifty percent ($n = 6$) of participants still had unresolved middle ear dysfunction following medical intervention.

Table 10

Outer and Middle Ear Status in Three Different Age Groups (pre and post medical intervention)

Assessment	Status	Age Group (in years)					
		I		II		III	
		(≤ 3 yr)		(>3 & ≤ 7 yr)		(>7 & <18 yr)	
		N=18		N=12		N=28	
		<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Otosopic examination of outer ear	Normal	16	89	11	92	24	86
	Impacted wax	2	11	1	8	4	14
	Structural abnormality	0	0	0	0	0	0
	Foreign objects	0	0	0	0	0	0
	Growths	0	0	0	0	0	0
	Infection	0	0	0	0	0	0
Otosopic examination (TM)	Normal	12	67	12	100	24	86
	Abnormal colour	2	11	0	0	0	0
	Perforated	0	0	0	0	3	11
	Grommet	2	11	0	0	1	4
	Bulging	2	11	0	0	0	0
Retraction	0	0	0	0	0	0	
Tympanometric examination	Type A	7	39	11	92	20	71
	Type B	7	39	1	8	3	11

	Type C	2	11	0	0	1	4
	CNT	2	11	0	0	4	14
Ipsilateral AR examination	Present	5	28	11	92	14	50
	Absent	11	61	1	8	10	36
	CNT	2	11	0	0	4	14
Otoscope examination of outer ear	Normal	18	100	12	100	28	100
	Impacted wax	0	0	0	0	0	0
	Structural abnormality	0	0	0	0	0	0
	Foreign objects	0	0	0	0	0	0
	Growths	0	0	0	0	0	0
	Infection	0	0	0	0	0	0
Otoscope examination (TM)	Normal	16	89	12	100	24	86
	Abnormal colour	0	0	0	0	0	0
	Perforated	0	0	0	0	3	11
	Grommet	2	11	0	0	1	4
	Bulging	0	0	0	0	0	0
	Retraction	0	0	0	0	0	0
Tympanometric examination	Type A	12	67	12	100	24	86
	Type B	0	0	0	0	0	0
	Type C	0	0	0	0	0	0
	CNT	2	11	0	0	4	14
	Died or discharged	4	22	0	0	0	0

Note. Tympanometric and acoustic reflex examination of ears with grommet or tympanic membrane perforation was not done. None of the participants were referred to a medical practitioner for the absence of acoustic reflexes as further audiologic investigation was required prior to referral. yr= year. CNT= could not test. N = total number of ears.

2.1. Prevalence of hearing loss

The evaluation of hearing status was only possible in 50 of the 58 ears (one participant died, two participants were discharged and one participant who was under 3 years of age had grommets in both ears). Of 50 ears, in which hearing status was evaluated, 34% ($n = 17$) of ears [48% of participants ($n = 12$)] had hearing loss (threshold greater than 15 dB HL in at least one frequency from 0.25 to 8 kHz). See Table 11 for the hearing status of the ears.

Table 11

Hearing Status of the Ears

Hearing tests	Normal hearing (ears)		Hearing loss (ears)	
	<i>n</i>	%	<i>n</i>	%
DPOAE & AABR (screening tests)	16	32	0	0
Pure tone audiometry	17	34	17	34
Total	33	66	17	34

2.2. Nature of the hearing loss

The type, configuration, degree, laterality and symmetry of the hearing loss are described in detail.

2.2.1. Type and configuration of the hearing loss

Of 12 participants with hearing loss, 75% ($n = 11$) had sensorineural hearing loss (with 65% of ears affected), while 25% ($n = 6$) of hearing impaired participants presented with mixed hearing loss (with 35% of ears affected). In 25% ($n = 6$) of the hearing impaired participants the configuration of hearing loss was flat (with 35% of ears affected) and in 75% ($n = 11$) it was high frequency loss (with 65% of ears affected).

2.2.2. Degree

The results for the degree of hearing loss were influenced by the classification system utilized. When the Northern and Downs (2002) classification system (based on pure tone averages of 0.5, 1 & 2 kHz) was used, 41% of hearing impaired participants (16% of ears) had mild to profound hearing loss [according to this classification system the degree of the rest of hearing impaired

participants (59%) was within the normal range]. However, when the average of the thresholds for the high frequencies of 4, 6 and 8 kHz (instead of the average at 0.5, 1 and 2 kHz) were calculated there was an increase to 66% of hearing impaired participants (28% of ears) with mild to profound hearing loss. See Table 12 for the comparison of the degree of hearing loss between conventional pure tone average and high frequencies pure tone average.

Table 12

Degree of Hearing Loss Based on the Conventional PTA and High Frequencies PTA

Degree of Hearing Loss	Conventional PTA (0.5, 1 & 2 kHz)		High frequencies PTA (4, 6 & 8 kHz)	
	<i>n</i>	%	<i>n</i>	%
Normal (0-15 dB HL)	42	84	36	72
Mild (15-30 dB HL)	5	10	6	12
Moderate (30-50 dB HL)	0	0	4	8
Severe (50-70 dB HL)	1	2	2	4
Profound (70+ dB HL)	2	4	2	4
Total (ears with mild to profound HL)	8	16	14	28

Note. PTA= pure tone average. HL= hearing loss. *n*= number of ears.

2.2.3. Laterality and symmetry

Of the 12 participants (17 ears) with hearing loss, 58% (*n* = 7) presented unilaterally and 42% (*n* = 5) bilaterally. In the five participants with bilateral hearing loss, 80% (*n* = 4) of the losses were symmetrical while 20% (*n* = 1) were asymmetrical.

Summary of the Prevalence and Nature of the Hearing Loss

Table 13 reflects the frequency and nature of hearing loss in the two older age groups (there was no hearing loss in the youngest age group). Forty eight percent of the participants (34% of ears) presented with hearing loss, of which 75% had sensorineural hearing loss while 25% had mixed hearing loss. The degree of hearing loss varied depending on which classification system was utilized. When Northern and Downs (2002) classification system was used, of 12 hearing impaired participants, 41% had mild to profound hearing loss. However, when the average of the thresholds for the high frequencies of 4, 6 and 8 kHz were calculated (using the same classification system), of 12 hearing impaired participants, 66% had mild to profound hearing loss. Thus using the high frequency pure tone average increases the number of participants whose degree of hearing loss is outside the normal range.

Table 13

The Frequency and Nature of Hearing Loss in the Two Older Age Groups

Hearing status (of ears)		Age group			
		II (> 3 yr & ≤ 7 yr) N=10		III (> 7 yr & < 18 yr) N=24	
		<i>n</i>	%	<i>n</i>	%
Normal hearing		8	80	9	37
Hearing loss		2	20	15	62
Type of HL	SNHL	2	100	9	60
	Mixed HL	0	0	6	40
	Conductive HL	0	0	0	0
Configuration of HL	High frequency loss	2	100	9	60
	Flat	0	0	6	40
	Low frequency loss	0	0	0	0
Degree of HL	Normal (0-15 dB HL)	9	90	17	71
	(Average: Mild (15-30 dB HL)	1	10	4	17
	0.5, 1 & 2 kHz) Moderate (30-50 dB HL)	0	0	0	0
	Severe (50-70 dB HL)	0	0	1	4
	Profound (70+ dB HL)	0	0	2	8
	Normal (0-15 dB HL)	9	90	11	46
(Average: Mild (15-30 dB HL)	1	10	5	21	

4 & 8 kHz)	Moderate (30-50 dB HL)	0	0	4	17
	Severe (50-70 dB HL)	0	0	2	8
	Profound (70+ dB HL)	0	0	2	8

Note. There was no hearing loss in the age group I (aged 0 to 3 years); N= total number of ears.

HL= hearing loss; SNHL= sensorineural hearing loss.

3.1. Determination of the relationship between middle ear abnormality and sex

There were 26 ears in the male group and 32 ears in the female group. Fifty four percent of ears ($n = 14$) in the male group had middle ear abnormality compared to 41% of ears ($n = 13$) in the female group with middle ear abnormality. The frequency of ears with middle ear abnormality in male and female groups was not significantly different ($\chi^2 = .575$, $df = 1$, $p = .448$).

3.2. Determination of the relationship between middle ear abnormality and age

Seventy two percent of ears ($n = 13$) in age group 0 to 3 years, 8% of ears ($n = 1$) in age group 3 to 7 years and 46% of ears ($n = 13$) in age group 7 to 18 years had middle ear abnormality. See Table 10 for more details. The frequency of middle ear abnormality was significantly less ($\chi^2 = 6.620$, $df = 2$, $p = .038$) in group 3 to 7 years than in groups 0 to 3 years and 7 to 18 years.

3.3. Determination of the relationship between middle ear abnormality and duration of hospitalization

Sixty six percent of ears ($n = 38$) belonged to participants who were hospitalized for less than six months (group A) and 34% of ears ($n = 20$) belonged to participants who were hospitalized for more than six months (group B). Forty seven percent of ears ($n = 18$) in group A had middle ear abnormality compared to 45% of ears ($n = 9$) in group B with middle ear abnormality. The

frequency of middle ear abnormality in these two groups was not significantly different (Generalized Linear Models, $X^2 = .096$, $df = 1$, $p = .757$).

3.4. Determination of the relationship between duration of ototoxic drug exposure and sensorineural hearing loss

Children admitted to Brooklyn Hospital had previously received TB medication at a referral center, the nature of which could not be determined from the medical records. It was therefore not possible to rule out the use of ototoxic medication prior to hospitalization at Brooklyn Chest Hospital. Thus, the duration of ototoxic drug exposure was unknown and its relationship with sensorineural hearing loss could not be determined.

3.5. Determination of the relationship between type of ototoxic drugs and sensorineural hearing loss

The ototoxic TB drugs used at Brooklyn Chest Hospital are amikacin, capreomycin and streptomycin. Since 86% of the current study's participants received amikacin and the remaining 14% were on capreomycin or streptomycin, the relationship between type of ototoxic drug and sensorineural hearing loss could not be analysed statistically.

3.6. Determination the relationship between type of TB and sensorineural hearing loss/ middle ear abnormality

In the present study the prevalence of pulmonary TB, TB meningitis, disseminated TB and TB of hip joint was 83%, 10%, 3% and 3% respectively. Since most of the participants had pulmonary

TB with the remaining minority having other forms of TB, the relationship between type of TB and sensorineural hearing loss/middle ear abnormality could not be analysed statistically.

3.7. Determination of the relationship between middle ear abnormality and comorbid presentation of HIV and TB

Of 29 participants, 18 participants (36 ears) had TB while 11 participants (22 ears) had both TB and HIV. In the TB group 39% of ears ($n = 14$) had middle ear abnormality as compared to 57% of ears ($n = 13$) in the TB and HIV group. The frequency of middle ear abnormality in these two groups was not significantly different ($X^2 = 1.267$, $df = 1$, $p = .260$).

3.8. Determination of the relationship between sensorineural hearing loss and comorbid presentation of HIV and TB

Of 25 participants (which their hearing status were known), 16 participants (32 ears) had TB while nine participants (18 ears) had both HIV and TB. In the TB group 25% of ears ($n = 8$) had sensorineural (or mixed) hearing loss while in the TB and HIV group 50% of ears ($n = 9$) had sensorineural (or mixed) hearing loss. The frequency of the ears with sensorineural (or mixed) hearing loss in these two groups was not significantly different ($X^2 = 3.351$, $df = 1$, $p = .067$).

Auditory Function of Participants with TB who are Receiving Ototoxic Drugs

In the present study 55% of the participants had middle ear abnormality and 48% had some degree of hearing loss. Forty two percent of hearing impaired participants demonstrated moderate to profound hearing loss in high frequencies (4, 6 & 8 kHz), which are typically affected by ototoxicity.

Discussion

The results of the present study will be discussed in light of the current literature and the implications for clinical practice and future areas of research will be considered. Firstly, the prevalence and nature of outer and middle ear abnormalities will be discussed. Then, the prevalence and nature of the hearing loss will be discussed. Lastly, the relationship between sensorineural hearing loss/middle ear abnormality and other parameters will be discussed.

Prevalence of Outer and Middle Ear Abnormalities

The prevalence rate of impacted wax in participants, who were hospitalized for TB at Brooklyn Chest Hospital, was 14%. Impacted wax is generally a silent condition and can cause tinnitus, vertigo, itching, pain, infection and sometimes hearing loss (Subha & Raman, 2006). The configuration of the hearing loss is nearly flat and the degree varies between 30 and 40 dB (Stach, 2008). In the current study the presence of impacted cerumen was not restricted to any particular age group and its effect on hearing was unknown since the hearing status of participants was determined after removal of the impacted wax. Many studies have addressed the prevalence rate of impacted wax among school children within the last decade, with only few studies in this decade. Minja and Machemba (1996) reported a similar prevalence rate (15.7%) of impacted ear wax among school children in Tanzania, while Phaneendra and Rao et al., 2002; and Adhikari, 2009 reported much higher prevalence rates of 63% and 62% in rural school children in India and Nepal respectively. Both of these studies had a much larger sample size (N=855 and N=2000) and a limited age range (5-6 years and 5-13 years) when compared with the current study's cohort of 29 children whose ages ranged between 0 and 18 years. The current study's prevalence rate (14%) is closer to the prevalence rate of 24% reported by Brkic (2010) in

a study of school children (7 to 10 years) in Bosnia and Herzegovina. The reason for the lower prevalence rate in the present study cannot be determined.

Although the hearing loss associated with impacted cerumen is often mild, it can have a significant impact on school-aged children as well as younger children who are in the process of developing speech and language (Stach, 2008; Northern & Downs, 2002). Thus screening for the presence of impacted wax in children hospitalized for TB with subsequent referral for cerumen management may prevent conductive hearing loss and its negative consequences in this population (Subha & Raman, 2006).

The prevalence rate of middle ear abnormality in participants, who were hospitalized for TB at Brooklyn Chest Hospital, was 55%. Middle ear abnormality causes mild or moderate conductive hearing loss up to 60 dB HL (Bluestone & Klein, 2007). Sensorineural hearing loss can also result from an untreated middle ear abnormality or its complications (Bluestone & Klein, 2007). In the present study, the effect of middle ear abnormality on hearing could not be determined since the hearing status of participants was assessed following medical referral for middle ear problems. The high prevalence of middle ear abnormality (55%) in this study could be explained by the fact that it was conducted during winter, when the prevalence of ear infections has been reported to be much higher (Okur et al., 2004). Moreover, the participants in this study were immunocompromised children living in close quarters with lots of other sick children, which could have contributed to the high prevalence of middle ear infection (Cober & Johnson, 2005).

Comparisons of the current study's results with others on a similar topic cannot be easily made because the present research reports on the prevalence of middle ear abnormality (any

abnormality of the tympanic membrane or middle ear), while others have reported on the abnormalities of middle ear and tympanic membrane separately. In order to compare the result of the present study with others, the numbers of the tympanic membrane and middle ear abnormalities were added together wherever possible (when the same child did not present with more than one pathology).

The prevalence of middle ear abnormality in the present study (55%) is similar to the combined prevalence rate of 53% reported for Aboriginal school-aged children in Australia by Sockalingham et al. (2003). It also closely approximates the combined prevalence rate of 49% reported by Olusanya et al. (2000), in eight randomly selected schools in Nigeria.

Adhikari (2009) found that 15% (combined prevalence rate of middle ear and tympanic membrane abnormalities) of rural school children in Nepal had middle ear abnormality. The low prevalence rate of middle ear abnormality in Adhikari's study when compared with the current study could be due to the high prevalence of unremoved impacted wax (62%) in that study, which rendered the assessment of middle ear status impossible. Thus the figure 15% is not a true reflection of the percentage of children with middle ear abnormality in Adhikari's study.

Middle ear abnormality may lead to conductive and sensorineural hearing loss which can adversely affect the development of speech, language, and cognitive skills in children (Bluestone & Klein, 2007; Northern & Downs, 2002). In the present study more than half of the participants including older children had middle ear abnormality; therefore it is important to monitor the middle ear status of all children hospitalized for TB to prevent hearing loss and its negative consequences in this vulnerable group.

Prevalence and Nature of the Hearing Loss

In the present study, 48% of the participants who were exposed to ototoxic drugs had hearing loss (threshold >15 dB HL), 41% of which had mild to profound hearing loss with the remaining (59%) within the normal range (in 59% of hearing impaired participants the hearing loss was restricted to high frequencies and undetected by Northern and Downs classification system). The type of hearing loss was sensorineural (75%) or mixed (25%) and its configuration was high frequency (75%) or flat (25%). As no baseline audiograms/OAE results were obtained prior to the treatment with ototoxic drugs, the hearing loss cannot be reliably attributed to these drugs. Thus, the term "prevalence rate of sensorineural hearing loss" and not "prevalence rate of ototoxic hearing loss" has been used to describe the percentage of children with hearing loss following administration of ototoxic drugs.

Comparisons of the reported prevalence rates in the literature and the prevalence rate in this study pose a challenge due to differing methodologies, including ages of the participants, hearing loss criteria and the sample size. Following an extensive search of the literature, using Google Scholar and Pubmed search engines, there were no other documented studies which assessed the effects of ototoxic medication on the hearing of children with TB; studies which investigated the ototoxicity were conducted on adults, thus limited inferences can be drawn from them about the impact of these drugs on children's hearing. Moreover, the hearing loss criteria that were used in this study were different from the studies on adults in two ways. First, in the current study the hearing loss criteria was set at 15 dB HL at any one test frequency (Northern & Downs, 2002) while in studies which had baseline audiograms, 10 to 20 dB loss from the baseline was considered as hearing loss (Peloquin et al., 2004; de Jager & van Altena 2002; Sturdy et al., 2011; Duggal & Sarkar, 2007). Second, the frequency range of the audiograms in this study (0.25 to 8 kHz) was more limited than in the study by Lima et al. (2006) (0.25 to 12

kHz). The current study's sample size (N = 25) is smaller than the sample size in other studies, which ranged from 36 to 110 participants (Peloquin et al., 2004; de Jager & van Altena 2002; Sturdy et al., 2011; Duggal & Sarkar, 2007; Lima et al., 2006). Despite these differences, comparisons may be made with caution and the results of studies done in adults are compared with results of the current study.

The prevalence of sensorineural hearing loss is variable, ranging from 18% to 64%, depending on the methods used and the population characteristics (Peloquin et al., 2004; de Jager & van Altena 2002; Sturdy et al., 2011; Duggal & Sarkar, 2007; Lima et al., 2006). In the present study, the prevalence of sensorineural hearing loss in children who received amikacin, streptomycin or capreomycin was 48%. This prevalence rate (48%) is lower than the prevalence rate of 64% reported by Lima et al. (2006) in Brazil. A major difference between the two studies is that Lima et al. used a Damplex audiometer (model 65), which emitted tone in frequency range of 0.25 to 12 kHz, to easier recognize ototoxic alterations at higher frequency, while the current study used a MA51- audiometer with frequency range of 0.25 to 8 kHz.

The current study's hearing loss rate of 48% is higher than that of other studies conducted by Peloquin et al. (2004) in the USA (37%, N=87), de Jager and van Altena (2002) in the Netherlands (18%, N=110), Sturdy et al. (2011) in the UK (28%, N=50) and Duggal and Sarkar (2007) in the India (18.7%, N=64). Irrespective of the different methods used, children may be at greater risk for ototoxicity than similarly treated adult patients (Schell et al., 1989; Kokotas et al., 2007), which could explain the higher prevalence rate of hearing loss reported in the current study. Perhaps, a longer study (from the time of ototoxic drug exposure until 6 months post treatment) with a larger sample size may help to determine the vulnerability for ototoxicity in children when compared to adult patients.

Tourn et al. (2005) assessed disequilibrium and tinnitus in addition to hearing loss in adults in Turkey and reported an ototoxicity prevalence rate of 42%. The vestibulotoxicity and tinnitus were not investigated in the current study (and in no other studies on children with TB) but they need to be addressed in future studies and audiologists need to be aware of the fact that vestibulotoxicity and tinnitus may be complications of ototoxic treatment (Rybak et al., 2006; Tourn et al., 2005) in children.

The present study suggests that a high percentage (48%) of the participants may have ototoxicity. It is also possible that there were participants whose hearing thresholds deteriorated following ototoxic treatment but remained within the normal range. Due to the lack of baseline audiograms, the ototoxic effect in these participants was undetected. Moreover, some of the participants who passed OAE and AABR tests may have had mild ototoxic hearing loss, since a "pass" result means that the hearing thresholds (in tested frequencies) were less than 30 dB HL. Nevertheless, the results of the current study indicate that at least half of the participants in this study had sensorineural hearing loss, the disabling effect of which depends on various factors; particularly its degree, laterality and configuration (Probst, 2006; Knight, 2008).

In the current study the degree of hearing loss varied between mild to profound. Children with mild hearing loss (15-30 dB HL) miss voiceless consonants, short unstressed words and less intense speech sounds which may result in lack of attention, and mild speech and language delays. With moderate hearing loss (31-50 dB HL) speech sounds are heard inaccurately and therefore most of the conversational speech sounds may be missed (Northern & Downs, 2002). These children present speech intelligibility and learning problems. Children with severe hearing loss (50-70 dB HL) can only hear some very loud sounds and the most intense conversational speech at close distance; therefore they will not learn speech and language spontaneously

(Northern & Downs, 2002). Children with profound hearing loss (70+ dB HL) generally cannot hear sounds, which results in severe language retardation as well as learning problems (Northern & Downs, 2002).

The severity of the effect of the hearing impairment is also related to the laterality of hearing loss (Probst, 2006). In the current study, the hearing loss was found to be unilateral in 58% and bilateral in 42% of the participants with hearing loss. Unilateral hearing loss in childhood reduces the auditory stimulation from one ear and may result in speech and language delays (Probst, 2006). School children with unilateral hearing loss may also have learning problems especially where there is background noise, like a noisy classroom (Probst, 2006; Lieu, 2004). Bilateral hearing loss (depending on its severity) may lead to articulation problems, delays in language acquisition, poorly comprehensible speech and absence of spontaneous speech development (Probst, 2006).

In addition, the effect of hearing impairment in children is influenced by the configuration of hearing loss. In high frequency losses (due to ototoxicity), the high-pitched consonant sounds (s, f, th, sh, h, k, p, t) are lost and thus the ability to perceive the range of speech sounds necessary for speech and language development is diminished (Knight, 2008). In summary, even mild unilateral or high frequency hearing loss may have a serious disabling effect in children (Northern & Downs, 2002; Probst, 2006). Therefore the monitoring of hearing status in children with TB receiving ototoxic drugs is recommended, as early detection and intervention may prevent further hearing loss or minimize its progression.

It should be mentioned that the impact of hearing loss in a child who is ill with a potentially life-threatening illness like TB may be greater than in a healthy child. Chronic

hospitalization and shortage of health care personnel and facilities in developing countries like South Africa divest these children from adequate communication with nurses/parents, interaction with their healthy peers, formal schooling and normal socialization which may lead to educational challenges, social and emotional problems and linguistic deprivation (Nelson, 2007; Ruben, 2003). This issue once again emphasizes the need for ototoxicity monitoring in children with TB.

There is a great chance of developing further sensorineural hearing loss in hearing impaired children with TB. Children who have sensorineural hearing loss may be at risk for exacerbating the loss through continuous exposure to ototoxic drugs, re-administration of ototoxic medications (for recurrent TB or the occurrence of other infections) and noise-induced hearing loss (e.g. listening to loud music via earphones). Thus health care providers and parents/guardians should be made aware of these issues to avoid progression of sensorineural hearing loss in this population.

The results of the current study suggest that 42% of the hearing impaired participants would be eligible for hearing aids. They may benefit from personal FM or sound field FM system in the classroom and may require special support for their language development and education (Adams & Rohring, 2004). The rest of the hearing impaired participants (58%) with mild hearing loss or just slight high frequency losses do not necessarily require hearing aids but may need favourable seating in the classroom, counselling and special attention from their teachers and parents (Adams & Rohring, 2004). Therefore, appropriate referral of these children upon discharge from TB centers and provision of suitable services in accordance with their needs at school, community and hospital/clinic levels are necessary to prevent their hearing disablement in the future.

In the current study using Northern and Downs (2002) classification system, which is based on average degree of hearing loss for speech frequencies (0.5, 1 & 2 kHz), 16% of ears had mild to profound hearing loss. Since ototoxic hearing loss affects high frequencies first, the Northern and Downs's classification based on the average degree of thresholds in high frequencies (4, 6 & 8 kHz) was used and a higher percentage (28%) of the ears was found to have mild to profound hearing loss. The observed difference in results (16% vs 28%) suggests that the conventional classification system (Northern and Downs) may not be applicable for patients who receive ototoxic medication (who tend to be more at risk of initially manifesting hearing loss in high frequencies), as the initial degree of hearing loss in a high percentage of these patients will be considered within the normal range. Therefore the criteria for determining the degree of ototoxic hearing loss should be revised. It is recommended that the average of 4, 6 and 8 kHz (instead of the average at 0.5, 1 and 2 kHz) be used to determine the degree of hearing loss in the Northern and Downs (2002) classification system.

Ototoxicity is determined by comparing the baseline results, which is preferably obtained prior to the initiation of treatment with the ototoxic drug, and the results of subsequent monitoring tests (Campbell, 2004). In the current study, due to the lack of baseline audiograms/OAE results, it was not possible to determine the prevalence rate of ototoxicity. The reason for the absence of baseline audiograms/OAE in the current study is that the participants began their ototoxic treatment in referral hospitals (not Brooklyn Chest Hospital) where hearing tests are not routinely performed due to lack of equipment and trained personnel. In 2010, the Department of Health, Republic of South Africa, proposed a new health care service delivery model with a shift from the curative to the cost-effective primary health care model at basic health care level (Department of Health, Republic of South Africa, 2010). In line with the

recently proposed health care service delivery model, it is recommended that auditory monitoring of children receiving ototoxic drugs should be implemented at district hospital/clinic level from the initiation of treatment to detect hearing loss. It is also recommended that future studies should include a larger sample size and a longer period of observation from the time of ototoxic drug exposure to determine the prevalence of ototoxicity in children.

Otoacoustic emissions test (in infants and young children) and high frequency audiometry (in older children and adolescents) have been considered the best methods for early detection of ototoxicity (Stavroulaki et al., 2002; Jacob et al., 2006). One of the limitations of the current study was the lack of a high frequency audiometer. In ototoxicity, higher frequencies (base of cochlea) are affected first before the lower frequencies (apex of the cochlea) are involved, therefore high frequency audiometry is essential for early detection of hearing loss and to prevent communication defects in children (> 3 years) receiving ototoxic TB drugs (Duggal & Sarkar, 2007). Hence, although high frequency audiometer is expensive and has its own limitations e. g. calibration difficulties (Goodman et al., 2009) it is recommended to purchase it for ototoxicity monitoring, given the high prevalence of children with TB at risk of ototoxic hearing loss in South Africa.

The clinical implication of this study is that an ototoxic monitoring program should be implemented for all children with TB receiving ototoxic medication. Such a program must begin prior to commencement of ototoxic medication at the local clinics to obtain baseline data and should be continued at least six months post treatment, as ototoxicity may manifest even after cessation of drugs (ASHA, 1994). Review of the literature revealed that there is no specific protocol for monitoring ototoxicity in children. It is recommended that a standard protocol be developed exclusively for children.

The following ototoxicity monitoring program is proposed which should be managed by an audiologist (but could be performed by an adequately trained health care provider). Baseline testing is the first step of this program and needs to be a complete audiologic evaluation, including otoscopy, immittance, audiometry (preferentially high frequency audiometry) or OAE and AABR (dependent on patient's age). Since middle ear abnormality is common among children and may interfere with the results of the hearing tests, immittance evaluation should be done prior these tests (Silveira Netto, da Costa, Sleifer & Braga, 2009). Baseline data must be obtained prior to ototoxic drug treatment. The next step is basic monitoring evaluation which must be done weekly (ASHA, 1994) and includes otoscopy, OAE and AABR (in young children) or air-conduction thresholds (in older children). The results of the air-conduction thresholds need to be compared with their baseline results to detect threshold shift. The recommended criteria by ASHA (1994) for determination of ototoxic threshold shift from baseline is as follows: (i) 20 dB or greater decrease at any one test frequency, (ii) 10 dB or greater decrease at any two adjacent frequencies, or (iii) loss of response at three consecutive frequencies where responses were previously obtained.

Children who show any significant increase in their thresholds (according to ASHA's criteria, 1994) or fail the OAE or AABR may have middle ear abnormality, so they must be assessed by immittance and if applicable bone-conduction. Children with middle ear abnormality need to be referred to a medical practitioner (for medical care). Children with normal middle ear function may have sensorineural hearing loss and must be retested for their hearing, those who fail OAE or AABR again, should be referred to tertiary hospitals (for further diagnostic tests including diagnostic ABR and ASSR) and those with a change in threshold must be reported to their physician. This early identification of hearing threshold shift provides the physician with

the opportunity to adjust the therapy to be potentially less ototoxic, and the audiologists the opportunity to perform appropriate rehabilitation during and after treatment (Stavroulaki et al., 2002).

Determination of the Relationship between Sensorineural Hearing Loss/ Middle Ear Abnormality and other Parameters

There is a difference between the objectives of the current study, pertaining to the middle ear abnormality, and the issues reported in the literature. In the present study the middle ear abnormality and its relationship with other parameters (e.g. sex, age, duration of hospitalization) were assessed, while otitis media with effusion in particular, which is the case in the literature was not addressed, so comparisons of the results of this study with those reporting on otitis media with effusion (OME) were made with caution.

The current results suggest no sex differences in middle ear abnormalities in boys (44%) and girls (41%). These findings are supported by Tong (2006). In Turkey, Caylan (2005) reported that male children had significantly more otitis media with effusion than females (13.8% versus 8.2%) while Martines (2010) in Italy found the opposite (8.6% female versus 4.6% male). The discrepancies in results of the above mentioned studies indicate the need for further research to ascertain if there are any significant differences between genders regarding prevalence of middle ear abnormality. The results of the present study indicate that both male and female children are equally at risk and should receive equal access to audiological and health care services.

Assessment of the relationship between middle ear abnormality and age in this study revealed that the frequency of middle ear abnormality was significantly lower for the age group 3 to 7 years (8%) than the younger (0 to 3 years, 72%) and older (7 to 18 years, 46%) age groups ($p = .038$). This unexpected result cannot be easily explained and may be due to the study's limited sample size. However, as expected, the frequency of middle ear abnormality in the youngest age group (0 to 3 years) was much higher than the oldest age group (7 to 18 years). Martines (2010) in Italy found that with increasing age, the prevalence rate of otitis media with effusion decreased. Caylan (2005) in Turkey is in agreement with the finding of Martines, since he reported that his study groups I (<6 years) and II (7–9 years) had significantly higher otitis media with effusion prevalence than group III (>10 years). Zielhuis et al. (1990) in a review article on prevalence of otitis media with effusion (key article), came to the conclusion that the prevalence rate of this disease has two peaks: one around 2 years of age and the other around the age of 5 years. In the current study, the maximum prevalence rate of middle ear abnormality (72%) was in the youngest age group (0 to 3 years) and is in agreement with the first peak (2 years) reported by Zielhuis. Therefore the present study suggests that although children younger than 3 years of age are more prone to middle ear problems than older children, children of all age groups are in need of appropriate audiological services.

In this study there was no significant relationship between duration of hospitalization and middle ear abnormality ($p = .757$). This result is unexpected, as children who are hospitalized for a longer period of time are more likely to develop middle ear problems since prolonged close contact with other potentially sick children, increases the risk of upper respiratory tract infections with subsequent development of otitis media (Cober & Johnson 2005). This unpredictable outcome may be explained by the fact that participants who were hospitalized longer may have

had oral antibiotics for intercurrent infections that had an additional effect of treating silent middle ear infection. Currently there are no investigations in the literature (using Google Scholar and Pubmed search engines) pertaining to the relationship of duration of hospitalization and middle ear abnormality/OME among children, therefore, it is recommended that this issue should be assessed in future studies.

One of the prime objectives of this study was to determine the relationship between duration of ototoxic drug exposure and the presence of sensorineural hearing loss. Since the information on the date of commencement of ototoxic medication at referral hospitals was not available, this issue could not be fully investigated. Lima et al. (2006) reported that differences in hearing impairment between adult participants who received streptomycin for a period of more than two months and those who were treated for shorter periods of time were not significant (77.8% versus 72.2%, respectively). Similarly, Sturdy et al. (2011) and de Jager and van Altena (2002) concluded that the total duration of aminoglycoside treatment was not significantly associated with the development of sensorineural hearing loss. Conversely, Peloquin et al. (2004) reported that the duration of ototoxic treatment was associated with hearing loss, and in a more recent review article in 2010, Arbex et al. concluded that the risk of sensorineural hearing loss increased with prolonged duration of treatment. These conflicting results warrant further research to ascertain the exact relationship between the duration of drug exposure and the presence of sensorineural hearing loss especially in children.

One of the objective's of the present study was to determine the relationship between the type of ototoxic drugs and the presence of sensorineural hearing loss, however, since 86% of the participants in the present study received amikacin and the remaining 14% were on capreomycin

or streptomycin, statistical analysis of this objective was not feasible. Peloquin et al. (2004) investigated this issue in their study and reported that streptomycin (in adults) was the least ototoxic drug when compared to amikacin in terms of cochleotoxicity. Rybak and Ramkumart (2007) confirmed Peloquin's findings by suggesting that streptomycin produces predominantly vestibular damage, while kanamycin and amikacin mainly affect the cochlea. Sturdy et al. (2011) found that amikacin use was significantly associated with ototoxicity and suggested that capreomycin might be associated with less ototoxicity when compared with amikacin. Kanamycin and amikacin are structurally very similar drugs (Kamal et al., 2008). The above mentioned studies suggest that capreomycin may be a safer alternative to amikacin and other ototoxic drugs in terms of cochleotoxicity. Future large scale studies including a range of ototoxic drugs, in particular, amikacin and capreomycin, will have to determine the least ototoxic drug of choice in children.

In this study the relationship between type of TB and sensorineural hearing loss/ middle ear abnormality could not be investigated, since most of the participants had pulmonary TB with the remaining minority having other forms of TB. An extensive search of the literature, using Google Scholar and Pubmed search, revealed that no study has investigated this issue. Perhaps future large scale studies including children with different forms of TB may be able to determine if there is any significant association between the type of TB and sensorineural hearing loss/middle ear abnormality.

The present study found no significant relationship between middle ear abnormality and comorbid presentation of HIV and TB ($p = .260$). This finding may be explained by the fact that HIV infected children were on Antiretroviral drugs which could limit opportunistic infections,

such as ear infections. Following a search of the literature, using Google Scholar and Pubmed search engines, no other investigations exist on the relationship between middle ear abnormality and comorbid presentation of HIV and TB.

There was no significant relationship between sensorineural hearing loss and comorbid presentation of HIV and TB, in this study ($p = .067$). The use of Google Scholar and Pubmed search engines revealed that no study has ever investigated the relationship between sensorineural hearing loss and comorbid presentation of HIV and TB in the literature. Future studies on duly infected HIV and TB children may help determine if sensorineural hearing loss is more common in this population.

In conclusion, there were high prevalence rates of middle ear abnormality (55%) and sensorineural/mixed hearing loss (48%) among TB participants receiving ototoxic medication at Brooklyn Chest Hospital. The observed prevalence rates reflect that a great percentage of TB children receiving ototoxic medication present with hearing loss. The hearing of these children is often not assessed at TB centers and their parents are most likely unaware of the possibility of ototoxic hearing loss. When hearing impaired children are discharged from medical centers they will be faced with life requirements like formal schooling and daily communications. However, because of their undetected hearing loss, they may face various problems in areas of speech and language learning, educational achievement; social/emotional development with subsequent disablement, costing the state sums of money (Copley & Friderichs, 2010; Northern & Downs, 2002). Thus, implementation of an ototoxicity monitoring program in all TB centers administering ototoxic drugs to children, may be a cost effective modality for early detection of

ototoxicity, which is the prerequisite for prevention of further hearing loss and providing service delivery to possible hearing impaired children.

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Conclusion

Despite the high risk of hearing loss in children with TB exposed to ototoxic drugs, their hearing is not routinely monitored. The current study's attempt was to describe the auditory function of children with TB receiving ototoxic medication at Brooklyn Chest Hospital. An assessment of auditory function of these children revealed that, 55% presented with middle ear abnormality and 48% with hearing loss. The degree of hearing loss in 41% of the hearing impaired participants was mild to profound and in 59%, with their loss restricted to high frequencies, was within the normal range.

The results of the current study indicate that (1) a routine ototoxic monitoring program should be implemented for all children with MDR-TB from the time of ototoxic drug exposure until 6 months post treatment, at district hospital/clinic level. (2) Appropriate services should be provided for hearing impaired children in terms of their need for hearing aids, FM systems and language and educational support at hospital/clinic, school and community levels. (3) The Northern and Downs' degree of hearing loss classification system, based on average thresholds for speech frequencies, is not applicable for ototoxic hearing loss, which initially occurs at high frequencies. It is therefore recommended that in children at risk of ototoxic hearing loss, the average of 4 and 8 kHz (instead of the average at 0.5, 1 and 2 kHz) be used to determine the degree of hearing loss.

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Appendices

Appendix A

Participant Characteristics

No	Age group	Sex	Age (month)	TB drug	Type of TB	HIV infection status	Duration of hospitalization (day)	Type of Drug-resistant-TB
1	III	F	85	Amk	TBM	N	460	MDR?
2	III	F	198	Amk	PTB	N	283	MDR
3	III	M	134	Amk	PTB	N	159	MDR
4	II	F	50	Amk	PTB	N	90	MDR
5	I	M	28	Amk	PTB	N	155	MDR?
6	III	M	171	Amk	TBM	P	88	MDR?
7	I	M	29	Cap	PTB	N	173	MDR?
8	III	F	141	Amk	PTB	P	320	MDR
9	I	F	19	Amk	TBM	N	256	MDR
10	III	F	159	Amk	PTB	N	137	MDR
11	II	F	51	Cap	HJ	N	89	XDR
12	III	M	188	Strep	PTB	N	643	XDR
13	I	F	8	Amk	PTB	N	81	XDR?
14	II	F	62	Amk	PTB	N	214	MDR?
15	III	F	89	Amk	PTB	P	225	MDR
16	I	M	27	Amk	PTB	P	133	M-Rif
17	II	F	64	Amk	PTB	N	142	MDR
18	III	F	123	Amk	PTB	N	97	MDR
19	I	M	28	Amk	PTB	P	108	M-Rif
20	II	M	53	Amk	PTB	P	118	MDR
21	II	F	97	Amk	PTB	N	43	MDR?
22	III	M	112	Cap	PTB	P	103	XDR
23	III	F	103	Amk	PTB	P	224	MDR
24	I	M	17	Amk	PTB	P	149	MDR?
25	III	F	138	Amk	DTB	N	199	MDR?
26	I	M	9	Amk	PTB	N	160	MDR
27	III	M	190	Amk	PTB	P	335	MDR?
28	II	M	51	Amk	PTB	N	96	MDR
29	I	F	7	Amk	PTB	P	45	MDR

Note. No= number of participants. MDR=multi-drug-resistance TB. MDR?= suspected multi-drug-resistance TB. XDR=extensively drug-resistant TB. Amk=Amikacin. Capreomycin. mono-rifampicin resistant. DTB=disseminated TB. TBM=TB meningitis. PTB=pulmonary TB. F=female. M=male. N=negative. P=positive. HJ=Hip joint. M-Rif= mono-rifampicin resistant.

Appendix B

Proof of Registration with HPCSA



CERTIFICATE OF REGISTRATION

THIS IS TO CERTIFY THAT

SURNAME: GHAFARI
FIRST NAMES: NAZANIN
REGISTRATION NUMBER: AU S 0002879
QUALIFICATIONS:
REGISTER: STUDENT AUDIOLOGIST

IS REGISTERED AS A
STUDENT AUDIOLOGIST
in the Category
STUDENT (AUDIOLOGY)

Valid effect from
11 Jun 2009



BE DASTAR
PRETORIA

HPCSA Building
553 Vermeulen St
Arcadia, Pretoria
05057649 2009/10/21

Appendix C

Ethical Approval from UCT's Faculty of Health Sciences Research Ethics Committee



UNIVERSITY OF CAPE TOWN

Health Sciences Faculty
Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6338 • Facsimile [021] 406 6411
e-mail: samayah.arietdien@uct.ac.za

22 February 2010

REC REF: 010/2010

Ms N Ghafari
Communication Sciences & Disorders

Dear Ms Ghafari

PROJECT TITLE: A PROFILE OF THE AUDITORY FUNCTIONING OF CHILDREN WITH TB RECEIVING OTOTOXIC MEDICATION AT BROOKLYN CHEST HOSPITAL.

Thank you for submitting your study to the Research Ethics Committee for review.

It is a pleasure to inform you that the Ethics Committee has **formally approved** the above-mentioned study.

Approval is granted for one year till the 22nd February 2011.

Please submit an annual progress report (FHS016) if the research continues beyond the expiry date. Alternatively please submit a study closure report (FHS 010) if the study is completed within one year so that we can close our file.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

Yours sincerely

PROFESSOR M. BLOCKMAN
CHAIRPERSON, HSE HUMAN ETHICS

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

samayah

Appendix D

Ethical Approval from Provincial Health Research Committee

07.MAY.2010 18:04 0214839335

MDHS

#5407 P.001 /002



Verwysing
Reference
Isalathiso
RP40/2010
Nevrae
Enquiries
Imbuzo
Dr A Dearham
Telefoon
Telephone
Imizumi
021 483 4193

Departement van Gesondheid
Department of Health
iSebe kuzalipilo

Nazarin Ghafari
No 24, Silverboom Ave
Platteklief
Cape Town
8001

FAX: (021) 461 9991

Dear Nazarin Ghafari

RE: A PROFILE OF THE AUDITORY FUNCTIONING OF CHILDREN WITH TB RECEIVING OTOTOXIC MEDICATION AT BROOKLYN CHEST HOSPITAL

Thank you for submitting your proposal to undertake the above-mentioned study. We are pleased to inform you that the department has granted you approval for your research. Please contact the following members of staff to assist you with access to the facilities:

1. Brooklyn Chest Hospital – Natalie Fabrik Tel: 021 508 7403

Kindly ensure that the following are adhered to:

1. Arrangements can be made with managers, providing that normal activities at requested facilities are not interrupted.
2. Researchers, in accessing provincial health facilities, are expressing consent to provide the department with an electronic copy of the final report within six months of completion of research. This can be submitted to the provincial Research Co-ordinator (healthres@pmvc.gov.za).
3. The reference number above should be quoted in all future correspondence.

We look forward to hearing from you.

Yours sincerely

M. J. ...

Page 1 of 2

Departement 4
Postbus 2080
KAAPSTAD
8000

4 Dorp Street
PO Box 2080
CAPE TOWN
8000

Appendix E

An Outline of the Information Shared with the Children who were Old Enough to Participate in the Decision Making

Why we would like to speak with you?

We want to talk with you about being a part of something called a research study. A research study is when doctors collect information to learn more about a disease. Doctors who do research are also called researchers.

If you have any questions during our talk about this study, you can ask them. Don't worry about waiting until the person talking stops speaking to you. You can stop them at any time and ask your question.

We are doing this research study to learn more about the hearing of children with TB, who are taking medication. After we tell you about this research study, we will ask you if you'd like to be in this research study or not. If you decide to be in this research study, you will be asked to sign this paper. If you don't want to be in this research study, no one will be upset with you. If you don't want to be in this research study, just tell us. If you want to be in the research study, tell us that. And, remember, you can say yes now and change your mind later. It's up to you.

This research study is not about getting treatment. You will have treatment for your illness, whether or not you agree to be part of this research study.

Why are we doing this research study?

TB is the disease you have. When you take medication for TB, you may be at risk of hearing loss. In this research study, we will try to find out if you have hearing difficulties. If you have hearing difficulties, you will be asked to do extra tests and receive treatment for your hearing problem. In this research study, there will be about 50 children who have TB.

What will happen to you if you are in the research study?

If you agree to be in the research study, this is what you will be asked to do:

- (1) *Your outer ear will be examined to make sure that there is nothing in your ear and the eardrum is normal.*
- (2) Your middle ear will be tested, to see how well it is functioning. A probe will be placed in your ear and you will be asked to be quite. If you have middle ear problem, you will be referred to a doctor.
- (3) Your inner ear and hearing nerve function will be tested by placing headphones on your ear. You will be asked to indicate, when you hear the tones.
- (4) If you have inner ear problem you will be referred for extra tests.

Will it hurt?

No, it won't. The tests are not painful.

Will I get paid?

You will receive a pen or a sticker for participating in this study.

Your parent/guardian knows about this study and wants you to be in the study if you want to. If you sign below it indicates that you do want to be in the study, but you know that you can stop being in the study any time you want to. You know that your study doctor can talk about the study with your parent/guardian, but will not talk about it with anyone else who is not working on the study unless you and your parent/guardian say it is OK. You can call the study doctor any time you have any questions.

Signature of Child

Date

Signature of Person Obtaining Assent/Consent

Date

University of Cape Town

Appendix F

Informed Consent Forms in English

Informed consent form for parents of participants under 3 years of age

Dear Parent/Legal Guardian

I am Nazanin Ghafari a postgraduate student in Audiology at the University of Cape Town. I am conducting research on hearing of children receiving TB medication. For the purpose of this study I need to access your child's medical records to obtain medical history and other relevant information. This study has been given ethical approval by the Research Ethics Committee (REC) of the Faculty of Health Sciences, University of Cape Town. (REC Reference Number: 010/2010).

Purpose of the study:

Children sometimes may receive TB medication that places them at risk for developing a hearing loss. The purpose is to identify whether children who have TB and who receive TB drugs have hearing difficulties. The earlier a hearing loss is detected the better for the child. If the child is found to have a hearing loss, he/she can be referred for further assessments/management (of their hearing) and can be given early therapy. The child will then have the best chance of continuing to develop his/her language and communication skills. It also alerts the doctors, so that they can consider alternative medicines for your child, medicines that may not be harmful to your child's hearing.

What does taking part in the study mean?

The researcher will first examine the outer ear of your child. It is important to look in the child's ear, in order to make sure that there is nothing in the ear and that the eardrum is normal. Your child's middle ear will be tested to see how well it is functioning. During this test (Tympanometry & Acoustic Reflex) a probe will be placed in your child's ears. If your child has a middle ear problem, he/she will be referred to a doctor at Brooklyn Chest Hospital.

Your child's inner ear will be tested by putting a probe fitted with a soft tip in the ear canal (This procedure is similar to the one nurses/doctors use to measure your child's temperature from the ear). The probe produces a sound and has a microphone which will record the response of your child's inner ear. The other end of the probe is connected to the screening machine which will tell us whether your child's inner ear is normal or whether we need to refer your child to audiology services. Your child may be sleep or awake while this test is being done. The researcher will then test the function of your child's hearing nerve. For this test (Automated Auditory Brainstem Responses), I will use a cotton swab to clean the skin of your child's scalp, forehead and one earlobe. Thereafter I will place some paste on the skin in these areas and attach electrodes. An electrode has a tiny disc at one end which will pick up the signals produced by your child's hearing nerve in response to a click sound. The electrodes are connected to a computer so that the results can be analyzed.

If your child does not pass the inner ear and hearing nerve tests, she/he will be referred to Red Cross Hospital for further diagnostic tests (Auditory Brainstem Responses & Auditory Steady-State Responses) to determine the level at which your child can hear. This procedure will be performed at Red Cross Hospital by the audiologists who are employed there.

For this purpose, four small stickers will be placed on your child's head and these will be connected to the computer. Earphone will then be placed on your child's ears. Sounds will be presented through the earphone to each ear separately while the computer records the results.

Your child should be sleeping for the duration of the test. If your child is under the age of six months, he/she will not be sedated, and the test is performed while he/she is naturally sleeping, following a feeding. If your child is over the age of six months, he/she will be examined by the doctor who will check that your child is well enough to receive medication - to make your child sleep during the test. If your child is well enough, the doctor will give her/him the medication. The reason that your child needs to be asleep for the test is that she/he needs to remain very still and quiet during the test, and this is difficult for small children. The audiologist at the hospital will conduct the hearing test on your child, while she/he is sleeping. The hearing test does not cause any harm or injury and is done routinely at the hospital for all small children who need such tests. A nurse will remain with your child throughout the test and will make sure that your child is fully awake before she/he is discharged. The researcher will access the results once the test has been performed.

For these tests, your child will be seated or rest comfortably, we will only carry out the tests once your child has agreed to the tests. The tests will take approximately 30 to 40 minutes depending on hearing status of the child. For children referred to Red Cross Hospital for further diagnostic tests, the tests will take about 2 hours.

Risk and Discomfort:

- These tests are used routinely in hearing assessments of children.

- All tests are non-invasive and are not painful to your child.
- Children referred to Red Cross Hospital for additional audiometric examinations under sedation; there are some side effects of the medication that may occur, but these are very unusual. Sometimes the medicine may make your child restless before they fall asleep. In children who are obese i.e. very fat, or who have problems with their nervous system, there is a slightly increased risk that the medication could induce a coma and even death. We do wish you to become alarmed by this information. This is a very rare event and has not occurred in the Cape Town area in the last 20 years. A medical professional (doctor or nurse) is routinely responsible for managing the medication and the test is conducted at a hospital, which has all the equipment to help your child should the need arise. You will be informed of the date and time of the appointment and we would like to encourage you, if at all possible, to be with your child. Please do not be alarmed. While this sounds very worrying, it is a routine test done regularly at this hospital and around the world, to test the hearing of very small children.

Benefits:

If your child has a hearing loss we will be able to identify it early and refer her/him for further tests or examination by an ear, nose and throat doctor. If the doctor is alerted to the effect of medication on your child's hearing, he/she may be able to change the medication and in this way your child is protected from further drug related hearing loss. Your child will receive stickers or a pen for participating in the study. The results of the study may also contribute to a range of services being provided to children with TB, who receive medications that may affect their hearing.

Voluntary Participation:

Participation in this study is voluntary. If you decide that you do not want your child to participate in this study, your child will continue to receive standard care without prejudice or penalty. If you agree to let your child participate but later decide to discontinue the hearing tests you are welcome to do so at any time.

I would like to encourage you to have your child's hearing assessed so that he/she can get the necessary care that is required. If you wish, the resident audiologist at Brooklyn Chest Hospital can assess your child's hearing. If you decide not to have your child's hearing tested, we would like to advise you to pay careful attention to whether your child responds to sounds around him/her, especially whether she/he pays attention when you talk to him/her. It is important for your child to hear people talking, so that she/he can continue to learn communication skills. If you become concerned about your child's hearing at any time in the future, please go to Red Cross Children's hospital or Tygerberg Hospital for hearing tests.

Confidentiality:

All information collected during your child's stay at Brooklyn Chest Hospital and after discharge will be handled with confidentiality. Your child's hospital records and the results of the tests will be handled with caution, and will not be shown to anyone other than the healthcare professionals working with your child. You and your child will not be identified in any publications of this study.

For any further information please feel free to contact me and my supervisors. My name is Nazanin Ghafari, my contact number is 0788335350 and my email address is nazanin_gh59@yahoo.com.

My supervisors are:

1. Prof Shajila Singh

Phone: 021-4066041; email: Shajila.Singh@uct.ac.za

2. Lucretia Petersen

Phone: 021-4066993; email: Lucretia.Petersen@uct.ac.za

3. Mrs Christine Rogers

Phone: 021-4066315; email: Christine.Rogers@uct.ac.za

Chairperson of the Research Ethics Committee, Prof Marc Blockman

Phone: 021-4066496

Thank you for your assistance.

Informed consent form for parents of participants older than 3 years of age

Dear Parent/Legal Guardian

I am Nazanin Ghafari a postgraduate student in Audiology at the University of Cape Town. I am conducting research on the hearing of children receiving TB medication. For the purpose of this study I need to access your child's medical records to obtain medical history and other relevant information. This study has been given ethical approval by the Research Ethics Committee (REC) of the Faculty of Health Sciences, University of Cape Town. (REC Reference Number: 010/2010).

Purpose of the study:

Children sometimes may receive TB medication that places them at risk for developing a hearing loss. The purpose is to identify whether children who have TB and who receive TB drugs have hearing difficulties. The earlier a hearing loss is detected the better for the child. If the child is found to have a hearing loss, he/she can be referred for further assessments/management (of their hearing) and can be given early therapy. The child will then have the best chance of continuing to develop his/her language and communication skills. It also alerts the doctors, so that they can consider alternative medicines for your child, medicines that may not be harmful to your child's hearing.

What does taking part in the study mean?

The researcher will first examine the outer ear of your child. It is important to look in the child's ear, in order to make sure that there is nothing in the ear and that the eardrum is normal. Your

child's middle ear will be tested to see how well it is functioning. During this test (Tympanometry & Acoustic Reflex) a probe will be placed in your child's ears. If your child has a middle ear problem, he/she will be referred to a doctor at Brooklyn Chest Hospital.

Your child's inner ear and auditory nerve function will be assessed by placing headphones on your child's ears. She/he will be asked to indicate when she/he hears the tones.

If your child has an inner ear or auditory nerve problem, he/she will be referred to audiology services for further diagnostic assessments.

For these tests, your child will be seated comfortably; we will only carry out the test once your child has agreed to the tests. The tests will take approximately 30 to 45 minutes depending on hearing status of the child.

Risk and Discomfort:

- These tests are used routinely in hearing assessments of children.
- There are no risks for your child, all tests are non-invasive and are not painful to your child.

Benefits:

If your child has a hearing loss we will be able to identify it early and refer her/him for further tests or examination by an ear, nose and throat doctor. If the doctor is alerted to the effect of medication on your child's hearing, he/she may be able to change the medication and in this way your child is protected from further drug related hearing loss. Your child will receive stickers or a pen for participating in the study. The results of the study may also contribute to a range of

services being provided to children with TB, who receive medications that may affect their hearing.

Voluntary Participation:

Participation in this study is voluntary. If you decide that you do not want your child to participate in this study, your child will continue to receive standard care without prejudice or penalty. If you agree to let your child participate but later decide to discontinue the hearing tests you are welcome to do so at any time.

I would like to encourage you to have your child's hearing assessed so that he/she can get the necessary care that is required. If you wish, the resident audiologist at Brooklyn Chest Hospital can assess your child's hearing. If you decide not to have your child's hearing tested, we would like to advise you to pay careful attention to whether your child responds to sounds around him/her, especially whether she/he pays attention when you talk to him/her. It is important for your child to hear people talking, so that she/he can continue to learn communication skills. If you become concerned about your child's hearing at any time in the future, please go to Red Cross Children's hospital or Tygerberg Hospital for hearing tests.

Confidentiality:

All information collected during your child's stay at Brooklyn Chest Hospital and after discharge will be handled with confidentiality. Your child's hospital records and the results of the tests will be handled with caution, and will not be shown to anyone other than the healthcare professionals working with your child. You and your child will not be identified in any publications of this study.

For any further information please feel free to contact me and my supervisors. My name is Nazanin Ghafari, my contact number is 0788335350 and my email address is nazanin_gh59@yahoo.com.

My supervisors are:

1. Prof Shajila Singh

Phone: 021-4066041; email: Shajila.Singh@uct.ac.za

2. Mrs Lucretia Petersen

Phone: 021-4066993; email: Lucretia.Petersen@uct.ac.za

3. Mrs Christine Rogers

Phone: 021-4066315; email: Christine.Rogers@uct.ac.za

Chairperson of the Research Ethics Committee, Prof Marc Blockman

Phone: 021-4066496

Thank you for your assistance.

University of Cape Town

Division of Communication Sciences and Disorders

I _____ have read (or had read to me by _____) the Information Letter. I understand what is required of me (my child/legal ward) and I have had all my questions answered. I do not feel that I or my child is being forced to take part in this study and we are doing so of our own free will. I know that I and my child can withdraw at any time if we so wish and that it will have no bad consequences for me or my child.

Signed:

Participant

Date and place

Researcher

Date and place

Witness (if necessary)

Date and place

Appendix G

Informed consent form in isiXhosa

Ifomu enika ulwazi kumzali onomntwana oneminyaka emithathu ngokuzalwa.

Mzali obekekileyo/mgcini ngokusemthethweni

Igama lam ndinguNazanin Ghafari ongumnfundi kweze Audiology kwiDyunivesithi yase Ntshona Koloni. Ndenza olu phando ngabantwana abathatha okanye abamele ukuba bathatha amachiza kwisifo sephepha. Injongo yesi sifundo ndisenzayo lujongisele entweni yokuba ndifumane iingcukacha nolwazi oluthe vetshe ngomntwana lowo. Esi sifundo sijongisele kwaye sixhaswa leli qela lingezantsi Research Ethics Committee (REC) of the Faculty of Health Sciences, University of Cape Town. (REC Reference Number: 010/2010).

Injongo yesi sifundo

Umntwana ngelinye ixesha uyakuthi afumane amachiza esifo sephepha, machiza lawo anokuthi abakhokhelisele engozini yokungeva. Injongo zethu zikhokhelisele entweni yokuba abantwana abanesifo sephepha sibancede. Abantwana abafumana amachiza wesifo sephepha bayakwazi ukubanengxaki yokuva kade. Kungcono ukuqaphela komntwana kwangoko. Ukuba umntwana ubonwe ngathi akeva, uyakuthunyelwa kwangoko ayokuhlolwa kwaye kwangoko uyakuthi afumane uncedo.

Emva kwelo ncedo umntwana uye abuyele kwisimo bekufaneleke ukuba abekuzo, ngokuthi akwazi kakuhle ukuthetha ulwimi lakhe kunye nabanye abantwana. Kuyakwaziswa oogqirha ukuze bakwazi ukumnika amachiza, machiza lawo ayakuthi amncede.

Ingaba esi sifundo usithathayo sithetha ukuthini kuwe?

Umphandi lowo uyakuthi ajonge umphandle wendlebe yomntwana lowo. Kubalulekile ukujonga indlebe yomntwana ngaphakathi nangaphandle, ukuze uqiniseke ukuba iindlebe zakhe zisebenza kakuhle. Umphakathi wendlebe yomntwana uyakujongwa ukuba usebenza kakuhle na. xa kusenziwa olu vavanyo lwendlebe olubizwa nje nge Tympanometry & Acoustic Reflex sube kusenzwa uvavanyo. Ukuba kuye kwafunyaniswa ukuba umntwana lowo unengxaki nomphakathi wendlebe yakhe uyakuthi athunyelwe kugqirha, kwisibhedlele ekuthiwa yi Brooklyn Chest Hospital.

Ukuba umntwana wakho uthe wavavanywa waze wafunyaniswa ukuba unengxaki kumphakathi wendlebe yakhe (le nqubo iyafana nqwa nale yenziwa ngoogqirha okanye noomongikazi xa befuna ukubona ubushushu bomntwana endlebeni yakhe. Uphando olo luyakuveza isandi kwaye kuyakusetyenziswa imakrofowuni eyakuthi icishilele iziphumo zomphakathi wendlebe yomntwana. Kwelinye icala lo vavanyo kuyakuboniswa kudityaniswe, umtshini apho uyakuthi kusixelele ukuba usebenza kakuhle umphakathi wendlebe yomntwana wakho. Okanye kufanele umntwana athunyelwe kuncedo lwe- audiology. Ngexesha lo vavanyo kunokwenzeka ukuba umntwana alale okanye angalali. Umphandi lowo uyakuthi anze uvavanyo lokujonga ukuba umthambo wokuva ukuba uyasebenza na. Ngolu vavanyo i-Automated Auditory Brainstem Responses kuyakusetyenziswa isipontshi sokucoca ufele lwentloko yomntwana, isibunzi kunye nomphezulu wendlebe. Emva koko kuyakuthi kudyibhelwe amafutha ayakuthi ancede esi ndawo zikhankanyiweyo ngentla, nalapho kuyakufakwa khona incam yamacingo ombane. (electrodes). Incam yocingo lombane lunecwecwe elincinci eliyakuthi liveze iziphumo zomthambo wokuva

komntwana. La macingo ombane athi atsalwe aze adityaniswe kunye nekhomputha, ukuze iziphumo zibenako ukucaciswa.

Ukuba umntwana uye walitshona olu vavanyo lweendlebe kunye nelo mthambo wendlebe, uyakuthi athunyelwe kwisibhedlele i-Red Cross Hospital apho anokuthi afumane khona olunye uvavanyo lokuthomalalisa Auditory Brainstem Responses & Auditory Steady-State Responses. Apho nokuthi kubonwe khona ubume bomntwana wakho ukuba uva kangakanani na. Enye ingqubo ethe vetshe eyi-Auditory Brainstem Responses & Auditory Steady-State Responses, iyakuthi yenziwe e-Red Cross Hospital kubonwe khona ukuba umntwana lowo uyeva na. Ie nqubo iyakuthi yenziwe ngumqeshwa wakhona obizwa ukuba yi- audiologists.

Isizathu soluvavanyo, kuyakuthi kuncamathiselwe izitika/amaphetshana amane entlokweni yomntwana, kwaye iqhakamishelane nekhomputha. Kuyakuthi kufakwe isimameli-ndlebe ezindlebeni zomntwana. Kuyakuthi gqi isandi kwindlebe nganye sisiza ngesimameli ndlebe, ngalumzuzu ikhomputha ishicilela iziphumo.

Umntwana wakho kufuneka elele ngexesha lo vavanyo. Ukuba umntwaba wakho ungaphantsi kwenyanga ezintandathu, akanako ukunyangwa elele. Kwaye le nqubo isenza xa elele, xa egqibile ukutya. Ukuba umntwana ungaphezu kweenyanga ezintandathu, uyakuthi ahlolwe ngugqirha ukuba uphilile kakuhle na ukuba angawafumana na amachiza, ukuze akwazi ukulala ngexesha lo vavanyo. Ukuba umntwana uphilile kakuhle, ugqirha uyakuthi amnike amachiza (amayeza). Isizakuthu sokuba umntwana kufanele alale ngexesha lo vavanyo kwenzelwa ukuba athomalale, akhululeke ngexesha lo vavanyo. Kwaye lonto inzima kwabantwana abancinci. Umqashwa wasesibhedlele uyakuthi achophele olo vavanyo kumntwana lowo, ngexa umntwana eleleyo. Olo vavanyo alunabo ubungozi, kwaye lwenziwa qho, ngakumbi kubantwana abancinci

abanomdla wokulenza olu vavanyo. Umongikazi uyakuthi ahlala eli liso kwelo vavanyo, uyathi aqisekise ukuthi umntwana uvukile ngaphambi kokuba aphume esibhedlele. Abaphandi bayakuthi bafumane imvume xa uvavanyo lugqityiwe. Emva kolu vavanyo lwenziwayo uyakuthi umntwana ahlaliswe phantsi aphumle, siyakuthi silenze olu vavanyo xa ethe umntwana wakho wakuvuma oko. Olu vavanyo liyakuthatha ixesha elingange mizuzu emashumi amathathu ukuya kwimizuzu emashumi amane. Kuyakuxhomekeka kuvavanyo oluyakwenziwa emntwaneni lowo. Abantwana abayakuthi bathunyelwe eRed Cross Hospital bayakuthunyelwa kuphando lo kuthomalalisa, olo vavanyo luyakuthatha iyure ezimbini.

Ubungozi nobunzima

Olu vavanyo lwenziwa qho ukujonga abantwana.

Lonke uvavanyo alunazo iintlungu emntwaneni.

Abantwana abathi bathunyelwe eRed Cross Hospital beyokuxilongwa malunga novavanyo lwe-additional audiometric, ukunyangwa ngeezizolisi (iipilisi/amayeza), Zikwakhona nezizolisi ezinobungozi kodwa ezi aziqhelekanga kwaphela.

Ngamanye amaxesha amachiza enza ukuba umntwana angonwabi, angaphumli phambi kokuba alale.

Umzekelo: Kubantwana abatyebileyo abanengxaki nobuphaku-phaku kuye kubekho ubungozi/ingxaki, kuba lo machiza abangela ukuba umntu alale kwikhoma okanye abhubhe. Sinqwenela ukunazisa ngesi saziso ukuba zikhona iimpawu ezikuthi zibenobungozi.

Ngumba onqabileyo lona apha ekapa, kuba awuzange wenzeka kangangethuba elingamashumi amabini apha ekapa.

Ugqirha okanye umongikazi owufundeleyo lo msebenzi ufanele ukuba ajongane nayo yonke into eqhubekayo, ajonge uvavanyo namachiza ukuba akhutshwa ngendlele esibhedlele. Zonke izixhobo ezisetyenziswayo kunyanzelekile ukuba zifumanke, ukenzela ukunceda umntwana wakho.

Uzakuthi waziswe olunye usuku omawuyokubela ngalo esibhedlele, siyakukhuthaza kangangoko ukuba ubesecaleni komntwana wakho. Siyakucela ukuba ungothuki okanye ubenedyudyu. Nangona olu vavanyo luxhalabisa kodwa kufanele ukuba lwenziwe qho kwesi sibhedlele okanye jikelele, ukuze kuvavanywe abantwana abancinci kakhulu.

Inzuzo:

Ukuba umntwana wakho uthe wanengxaki yokuva siyakwazi ukuthumela kugqirha amaqaphele kwangethuba. Simthumele enziwe olunye uvavanyo lwendlebe, lwempumlo, nomqala. Ukuba ugqiba uthe ngexesha lo vavanyo wanezinto aziqaphelayo ezingahambi ngendlela uyakwazi ukumtshintsha kwezo pilisi/amayeza ebewasebenzisa. Amkhusele kwamanye amachiza anokuthi amnike ingxaki.

Umntwana wakho uyakuthi afumana amaphetshane okanye ipeni kuba ethe wathatha inxaxheba kwesi sifundo. Iziphumo zolu phando zinalo ugalelo ebantwaneni, kubantwana abanesifo sephepha. Abafumana amachiza anokuthi amkhokhelela ekungaviyo kakuhle.

Ukuzinikela okanye uzigqatse:

Kwesi sifundo uyakwazi ukuzinikela ngokuzigqatsa. Ukuba ufuna umntwana wakho angasingeneli kulungile kodwa yena uyakuhlala eqhubeka ngokuphathwa ngesihoyo ngaphandle kwesohlwayo. Uvumelekile umntwana wakho kuba alungene olu hlobo, kwaye nokuba aphinde aluyeke nanini na usavumelekile. Ndikucebisa ukuba umvumele umntwana ukuba angene koluhlolo. Ukuba uyathanda ungamsa umntwana ayokuhlolwa ukuba uva kangakanani na, kwisibhedlele iBrooklyn Chest Hospital. Ukuba ude wagqiba ukuba umntwana wakho makaye kolu hlobo lokuva, sithanda ukucebisa ukuba uqaphele ukuba umntwana lowo uyeve kakuhle, ngakumbi xa ethe wamamelisisa kulento ayenziwayo. Kubalulekile emntwaneni wakho into yokuba eke okanye amamelisise xa abantu bethetha naye, ukuze azokwazi ukufunda ukuthetha nabanye abantu. Ukuba ungumntu okhathalayo malunga nokuva komntwana wakho ndiyakuthanda ukuba uye nokuba kunini nomntwana eRed Cross Children's hospital okanye eTygerberg Hospital, ayokuhlolwa ukuba uva kangakanani na.

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Yonke ingcukacha efunyanwe ngomntwana wakho ngoku ese Brooklyn Chest Hospital nasemva kokuba ekhululwe khona iyakugcinwa ihlale isemfihlweni kuthi. Amacwecwe okanye oko kubhaliweyo ngomntwana wakho ziyakuhlala kwizandla ezithembekileyo kwaye elugcinweni. Asisoze sibonise nowuphi na umntu, ngaphandle kwabantu abaphethe lo mcimbi wohlonyo okanye abezempilo, kwaye abasebenza ngalo mntwana. Wena nomntwana wakho nikhuselekile kakhulu , anisoze nipapashwe nakancinci kwesi sifundo senziwayo.

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Abaphathi bam ngoo:

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Ochophele lo mcimbi we- Research Ethics Committee, ngu Prof Marc Blockman

Umnxeba: 021-4066496

Enkosi ngoncedo lwakho.

Ifomu enika ulwazi kumzali onomntwana oneminyaka emithathu ngokuzalwa

Mzali obekekileyo/mgcini ngokusemthethweni

Igama lam ndinguNazanin Ghafari ongumnfundi kweze Audiology kwiDyunivesithi yase Ntshona Koloni. Ndenza olu phando ngabantwana abathatha okanye abamele ukuba bathatha amachiza kwisifo sephepha. Injongo yesi sifundo ndisenzayo lujongisele entweni yokuba ndifumane iingcukacha nolwazi oluthe vetshe ngomntwana lowo. Esi sifundo sijongisele kwaye sixhaswa leli qela lingezantsi Research Ethics Committee (REC) of the Faculty of Health Sciences, University of Cape Town. (REC Reference Number: 010/2010).

Injongo yesi sifundo

Umntwana ngelinye ixesha uyakuthi afumane amachiza esifo sephepha, machiza lawo anokuthi abakhokhelisele engozini yokungeva. Injongo zethu zikhokhelisele entweni yokuba abantwana abanesifo sephepha sibancede. Abantwana abafumana amachiza wesifo sephepha bayakwazi ukubanengxaki yokuva kade. Kungcono ukuqaphela komntwana kwangoko. Ukuba umntwana ubonwe ngathi akeva, uyakuthunyelwa kwangoko ayokuhlolwa kwaye kwangoko uyakuthi afumane uncedo.

Emva kwelo ncedo umntwana uye abuyele kwisimo bekufaneleke ukuba abekuzo, ngokuthi akwazi kakuhle ukuthetha ulwimi lakhe kunye nabanye abantwana. Kuyakwaziswa oogqirha ukuze bakwazi ukumnika amachiza, machiza lawo ayakuthi amncede.

Ingaba esi sifundo usithathayo sithetha ukuthini kuwe?

Umphandi lowo uyakuthi ajonge umphandle wendlebe yomntwana lowo. Kubalulekile ukujonga indlebe yomntwana ngaphakathi nangaphandle, ukuze uqiniseke ukuba iindlebe zakhe zisebenza kakuhle. Umphakathi wendlebe yomntwana uyakujongwa ukuba usebenza kakuhle na. xa kusenziwa olu vavanyo lwendlebe olubizwa nje nge Tympanometry & Acoustic Reflex sube kusenzwa uvavanyo. Ukuba kuye kwafunyaniswa ukuba umntwana lowo unengxaki nomphakathi wendlebe yakhe uyakuthi athunyelwe kugqirha, kwisibhedlele ekuthiwa yi Brooklyn Chest Hospital.

Umphakathi wendlebe womntwana wakho uxakuxilongwa ukwenzela kuzobonwa ukuba yonke into iyasebenza, umntwana lowo uzakucelwa ukuba atsho xa esiva izandi.

Ukuba umntwana wakho uthe wanengxaki nendlebe uzokuthunyelwa kuchwephetshe wendlebe ukuze ayohlolwa ngokuphangaleleyo.

Ngalemivavanyo umntwana wakho uzokwazi ukuhlala ngokungakhathazeki, sizokwenza amavavanyo ngokufuna komntwana wakho. Lamavavanyo azothatha malunga nemizuzu eyi 30 uyokumba kwi 45 kuxhomekeke ekuveni komntwana lowo.

Ubungozi nobunzima

- Lamavavanyo asetyenziswa maxa onke ukujonga ukungeva komntwana.
- Akukho loyiko ngomntwana wakho, amavavanyo akavakali kwaye akakho buhlungu emntwaneni wakho.

Inzuzo:

Ukuba umntwana wakho uthe wanengxaki yokuva siyakwazi ukuthumela kugqirha amaqaphele kwangethuba. Simthumele enziwe olunye uvavanyo lwendlebe, lwempumlo, nomqala. Ukuba ugqiba uthe ngexesha lo vavanyo wanezinto aziqaphelayo ezingahambi ngendlela uyakwazi ukumtshintsha kwezo pilisi/amayeza ebewasebenzisa. Amkhusele kwamanye amachiza anokuthi amnike ingxaki.

Umntwana wakho uyakuthi afumana amaphetshane okanye ipeni kuba ethe wathatha inxaxheba kwesi sifundo. Iziphumo zolu phando zinalo ugalelo ebantwaneni, kubantwana abanesifo sephepha. Abafumana amachiza anokuthi amkhokhelela ekungaviyo kakuhle.

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Enkosi ngoncedo lwakho.

University of Cape Town

Division of Communication Sciences and Disorders

Mna _____ othe wafunda le ngcazelo ikule leta _____ Ndiyayazi kwaye ndicacelwa okanye indinika ingcazelo ngokuthe vetshe, kwaye nemibuzo yam iphendulekile. Andiziva ngathi umntwana wam uye wanyanzelwa ukuba azingenele ezi zifundo. Ndiyayazi ukuba ezi zifundo zizakuba yinzuzo kum nakuye.

Isandla esityikityileyo:

Umthathi nxaxheba

Umphandi

Ingqina (ukuba kunyanzelekile)

Umhla kunye nendawo

Umhla kunye nedawo

Umhla kunye nendawo

Appendix H

Informed consent form in Afrikaans

ingelig toestemming vorm vir ouers van deelnemers onder die ouderdom van 3 jaar

Liewelouer/voog

Ek is Nazanin Ghafari, nagraadse damestudent in audiologie aan die Universiteit van Kaapstad. Ek doen tans navorsing betreffende die gehoor van kinders wat medikasie vir Tuberkulose (TB) ontvang. Die doel van hierdie studie vereis egter dat ek toegang tot jou kind se mediese rekords verkry, o.a. sy/haar mediese geskiedenis en ander toepaslike informasie. Hierdie studie het reeds etiese goedkeuring ontvang van die Navorsing Etiese Komitee (rec) van die fakulteit Gesondheidswetenskappe, Universiteit van Kaapstad (rec Verwysingsnommer: 010/2010).

Doel van die studie:

Kinders ontvang soms Tb medikasie wat hulle egter blootstel tot die risiko om 'n gehoorverlies te ontwikkel. Die doel van hierdie studie is om kinders wat Tb het en Tb medikasie ontvang, wat wel gehoorprobleme ondervind, te identifiseer. Vroeër identifikasie van sulke gevalle van gehoorverlies sal ook dus beter vir die kind wees. Indien die kind wel 'n gehoorverlies onderlede is, kan hy/sy verwys word vir verdere ondersoek/behandeling (van hul gehoor) en uiteindelik ook vroeër behandeling kry. Die kind sal dus die beste kans hê te ontwikkeling van sy/haar taal en kommunikasie vaardighede. In aanvulling, vroeër identifikasie dien terselfertyd as waarskuwing vir dokters, sodat hulle selfs alternatiewe medikasie kan oorweeg vir jou kind, wat moontlik nie 'n nadelige uitwerking het op jou kind se gehoor nie.

Wat beteken die deelname aan hierdie studie?

Die navorser sal eerstens die buite-oor van jou kind ondersoek. Dit is belangrik om binne die kind se oor te kyk, ten einde seker te maak dat daar niks in die oor is en dat sy/haar oordrom normaal is. Daarna sal jou kind se middel-oor getoets word om te ondersoek hoe goed dit funksioneer. Gedurende hierdie toets (tympanometrie & Akoestiese refleksie) sal 'n probe in jou kind se ore geplaas word. Indien jou kind wel 'n middel-oor probleem het, sal hy/sy verwys word na 'n dokter by Brooklyn Chest Hospitaal.

Die binne-oor van jou kind sal getoets word deurdat 'n peilstif gepas met 'n sagte punt in die oor kanaal geplaas word (hierdie prosedure is soortgelyk aan die ondersoek waartydens dokters/verpleegsters jou kind se temperatuur vanaf die oor neem). Die wyse waarop hierdie ondersoek geskied behels 'n klank geproduseer deur die probe en wat 'n mikrofoon bevat, wat die reaksie van die binne-oor opneem en registreer. Die ander deel van die probe is gekoppel aan die screening machine, wat uiteindelik sal bepaal of jou kind se binne-oor wel normaal is en indien ons sy/haar moet verwys na audiologie dienste. Jou kind mag slaapend of wakker wees gedurende hierdie ondersoek. Die navorser sal daarna die funksionering van jou kind se gehoorsenuwee toets. Vir hierdie toets (Automatiese hoorbaar brainstem antwoorde), sal ek gebruik maak van 'n cotton swab om die vel van jou kind se kop, voorhoof en een oorskulp skoon te maak. Daarna sal paste geplaas word op die vel in die skoon areas soos voorheen genoem, waarvolgens elektrodes aangeheg sal word. 'n Elektrode bevat 'n klein disket aan een end, wat funksioneer deur seinimpulse geproduseer deur jou kind se gehoorsenuwee sal identifiseer op grond van 'n reaksie op 'n spesifieke "klik" klank. Die elektrodes is gekoppel aan 'n rekenaar sodat die uitslae ge-analiseer kan word.

Indien jou kind nie die binne-oor, en gehoor sensuiewe toetse slaag nie, sal hy/sy na Rooi Kruis Hospitaal verwys word vir verder diagnostiese toetse (hoorbaar brainstem antwoorde & hoorbaar gereelde-toestand antwoorde) om te bepaal tot watter vlak jou kind kan hoor. Hierdie prosedure sal uitgevoer word by die Rooi Kruis Hospitaal deur die audioloog wat daar diensagtig. Vir die doel van hierdie toets sal vier klein plakkers geplaas word op jou kind se hoof, wat verder gekoppel is aan die rekenaar. Oorfone sal oor jou kind se ore geplaas. In die proses sal klanke gestuur word deur die oorfone tot elke oor apart, terwyl die rekenaar die uitslae lees en registreer. Jou kind behoort te slaap vir die duur van hierdie toets. Indien jou kind egter onder die ouderdom van ses maande is, sal hy/sy nie sedated, en die toets sal uitgevoer word terwyl hy/sy normaal slaap, nadat sy/hy gevoed is. Indien jou kind egter oor die ouderdom van ses maande is, sal hy/sy behandel word deur 'n physician/verpleegster by die Rooi Kruis Hospitaal. Hierdie is 'n roetine proses wat in gebruik kom in die geval van klein kinders wat sodanige gehoor toetse benodig. Hierdie toets is nie pynlik of ongemaklik in enige hoedanigheid nie, maar daar word egter verwag dat jou kind slaapend wees ten einde skoon en akkurate opnames gedurende die toets te verkry. Die navorser sal daarvolgens toegang verkry tot die uitslae, sodra die toetse uitgevoer is.

Vir hierdie toetse sal jou kind gemaklike sitplek verleen en rus verskaf word, en sal die toetse alleenlik uitgevoer word sodra jou kind ingestem tot die toetse. Die toetse sal ongeveer 30 tot 40 minute duur, afhangend van gehoorstatus van die betrokke kind. Vir kinders verwys na Rooi Kruis Hospitaal vir verder diagnostiese toetse, sal dit ongeveer 2 ure duur.

Risikoen1Ongerief:

- Hierdie toetse word roetinelik gebruik in gehoorondersoeke van kinders.
- Alle toetse is ook nie-invasie en is nie pynlik vir jou kind.

• Kinders verwys na Rooi Kruis Hospitaal vir addisionele audiometriese ondersoeke onder sedation; daar is sommige nuwe-effekte wat die medikasie mag teweegbring, maar hierdie is egter in baie selde gevalle. Die medikasie mag egter jou kind rusteloos maak voor hulle aan die slaap val. Kinders wat aan vetsug lei, o.a. baie vet, of wie probleme hul sensuweestelsel ondervind, sal daar 'n effense verhoogde risiko wees dat die medikasie tot 'n koma of selfs die dood kan lei. Ons wens dat u dus sal kennis dra van hierdie informasie en wat beteken. Hierdie is egter 'n baie seldsame geval en het nie voorgekom in die Kaapstad area gedurende die afgelope 20 jare. 'n Mediese professioneel (dokter of verpleegster) is op roetine basis verantwoordelik om beheer te handhaaf oor die medikasie en die toetse word by 'n hospitaal gedoen, wat oor al die nodige middele en hulpmateriale beskik, om jou kind te help indien dit wel sou benodig word. U sal in kennis gestel word van die datum en tyd van die afspraak en waarby ons u aanmoedig om, indien moontlik, by u kind te wees. Moet dus asseblief nie verskrik wees nie. Alhoewel dit baie kommerwekkend mag klink, kan ons u aansê dat dit 'n roetine toets is wat gereeld gedoen word by hierdie hospitaal en rondom die wêreld, waarby die gehoor van baie klein kinders getoets word.

Voordele:

Indien jou kind wel 'n gehoorverlies het, kan ons dit op 'n vroeë stadium identifiseer en hom/haar verwys vir verdere toetse of ondersoek deur 'n oor-, neus- en keel-dokter. Indien die betrokke dokter onseker of waaksaamagtig is betreffende die effek van medikasie op jou kind se gehoor, mag hy/sy die medikasie verander en dus op hierdie manier jou kind beskerm teen verder medikasie-verwante gehoor verlies. Jou kind sal plakkers of 'n pen ontvang vir sy/haar deelname aan die studie. Die uitslae van die studie mag ook verder bydra tot 'n reeks van dienste wat voorsien mag word aan kinders met Tb, wie medikasie ontvang wat hul gehoor moontlik mag

affekteer.

Vrywillig1Deelname:

Deelname aan hierdie studie is vrywillig. Indien u besluit dat jy jou kind nie wil laat deelneem aan hierdie studie nie, sal jou kind steeds standaard sorg ontvang sonder enige oordeel of boetes. Indien u instem dat jou kind wel mag deelneem, maar later egter besluit om die gehoortoetse te staak, is u welkom om enige tyd so te doen. Ek wil u aanmoedig om u kind se gehoor te laat toets sodat hy/sy die nodige behandeling en sorg kan ontvang. Indien u so verkies kan die routine audioloog by die Brooklyn Chest Hospitaal jou kind se gehoor toets. Indien u daarteen besluit om jou kind se gehoor te laat toets, wil ons u graag aanraai om aandag te verleen op grond van hoe u kins reageer op klanke rondom hom/haar, veral of hy/sy aandag gee wanneer u met hom/haar praat. Dit is belangrik vir u kind om te luister hoe mense gesels, sodat hy/sy kan voortdurend kommunikasie vaardighede sal aanleer. Indien u begin bekommerd raak rakende jou kind se gehoor in die toekoms, gaan asseblief na Rooi Kruis kinders hospitaal of Tygerberg hospitaal vir gehoortoetse.

Vertroulikheid:

Alle informasie ingesamel gedurende jou kind se verblyf by die Brooklyn Chest hospitaal en selfs nadat hul ontslaan is, sal met alle vertroulikheid hanteer word. Jou kind se hospitaalrekords en die uitslae van die toetse sal versigtig hanteer word, en sal nie aan enigeen getoon word behalwe die gesondheids professioneel lede wie met jou kind gewerk het. U en u kind sal nie identifiseerbaar wees in enige publikasies van hierdie studie nie.

Vir enige verdere navrae voel asseblief vry om my te kontak en my promotor, my naam is

Nazanin Ghafari, kontak nommer is 0788335350, en e-pos adres is nazanin_gh59@yahoo.com

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Chairperson van die navorsing etiek kommitee, Prof. Marc Blockman

Foon: 021-4066496

Dankie vir jou ondersteuning.

University of Cape Town

Ingelig toestemming vorm vir ouers van deelnemers bo die ouderdom van 3 jaar

Doel van die studie:

Ek is Nazanin Ghafari, nagraadse damestudent in audiologie aan die Universiteit van Kaapstad. Ek doen tans navorsing betreffende die gehoor van kinders wat medikasie vir Tuberkulose (TB) ontvang. Die doel van hierdie studie vereis egter dat ek toegang tot jou kind se mediese rekords verkry, o.a. sy/haar mediese geskiedenis en ander toepaslike informasie. Hierdie studie het reeds etiese goedkeuring ontvang van die Navorsing Etiese Komitee (rec) van die fakulteit Gesondheidswetenskappe, Universiteit van Kaapstad (rec Verwysingsnommer: 010/2010).

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Jou kind se binneste oor en hoorbaar senuwee funksie sal wees geskat deur te plaas hooffone op jou kind se ore. she/he sal gevra word om te dui aan wanneer she/he hoor die klanke.

Indien jou kind het 'n binneste oor of hoorbaar senuwee probleem, he/she sal verwys word na audiologie dienste vir verder diagnoseerings assessments.

Vir hierdie toetse, jou kind sal wees gesetel gemaklik; ons sal alleen dra uit die toets sodra jou kind het saamgestem tot die toetse. die toetse sal neem ongeveer 30 to 45 minute afhangend op verhoor status van die kind.

Risikoen1Ongerief:

- These toetse is gebruik roetinelik in verhoor assessments van kinders.
- There is geen risikos vir jou kind, almal toetse is nie-invallende en is nie pynlik tot jou kind.

Vrywillig1Deelname:

Deelname aan hierdie studie is vrywillig. Indien u besluit dat jy jou kind nie wil laat deelneem aan hierdie studie nie, sal jou kind steeds standaard sorg ontvang sonder enige oordeel of boetes. Indien u instem dat jou kind wel mag deelneem, maar later egter besluit om die gehoortoetse te staak, is u welkom om enige tyd so te doen.

Ek wil u aanmoedig om u kind se gehoor te laat toets sodat hy/sy die nodige behandeling en sorg kan ontvang. Indien u so verkies kan die routine audioloog by die Brooklyn Chest Hospitaal jou kind se gehoor toets. Indien u daarteen besluit om jou kind se gehoor te laat toets, wil ons u graag aanraai om aandag te verleen op grond van hoe u kins reageer op klanke rondom hom/haar, veral of hy/sy aandag gee wanneer u met hom/haar praat. Dit is belangrik vir u kind om te luister hoe mense gesels, sodat hy/sy kan voortdurend kommunikasie vaardighede sal aanleer. Indien u begin bekommerd raak rakende jou kind se gehoor in die toekoms, gaan asseblief na Rooi Kruis kinders hospitaal of Tygerberg hospitaal vir gehoortoetse.

Vertroulikheid:

Alle informasie ingesamel gedurende jou kind se verblyf by die Brooklyn Chest hospitaal en selfs nadat hul ontslaan is, sal met alle vertroulikheid hanteer word. Jou kind se hospitaalrekords en die uitslae van die toetse sal versigtig hanteer word, en sal nie aan enigeen getoon word behalwe die gesondheids professioneel lede wie met jou kind gewerk het. U en u kind sal nie identifiseerbaar wees in enige publikasies van hierdie studie nie.

Vir enige verdere navrae voel asseblief vry om my te kontak en my promotor, my naam is Nazanin Ghafari, kontak nommer is 0788335350, en e-pos adres is nazanin_gh59@yahoo. com.

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Chairperson van die navorsing etiek kommitee, Prof. Marc Blockman

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Dankie vir jou ondersteuning.

University of Cape Town

Universiteit van Kaapstad

Divisie Kommunikasie wetenskappe en wanordes

Ek _____ het informasie brief gelees (of is deur _____ aan my voortgelees). Ek verstaan wat van my vereis word (my kind/wettige ward) en dat al my vrae beantwoord is. Ek voel nie dat ek of my kind geforseer is om deel te neem aan hierdie studie nie en sodoende doen ons dit uit vrye wil. Ek weet dat ek en my kind enige tyd kan ontrek indien ons sou wou en dat geen sleg gevolge sal dra vir my of my kind nie.

Geteken:

Deelnemer

Navorsers

Getuie (indien nodig)

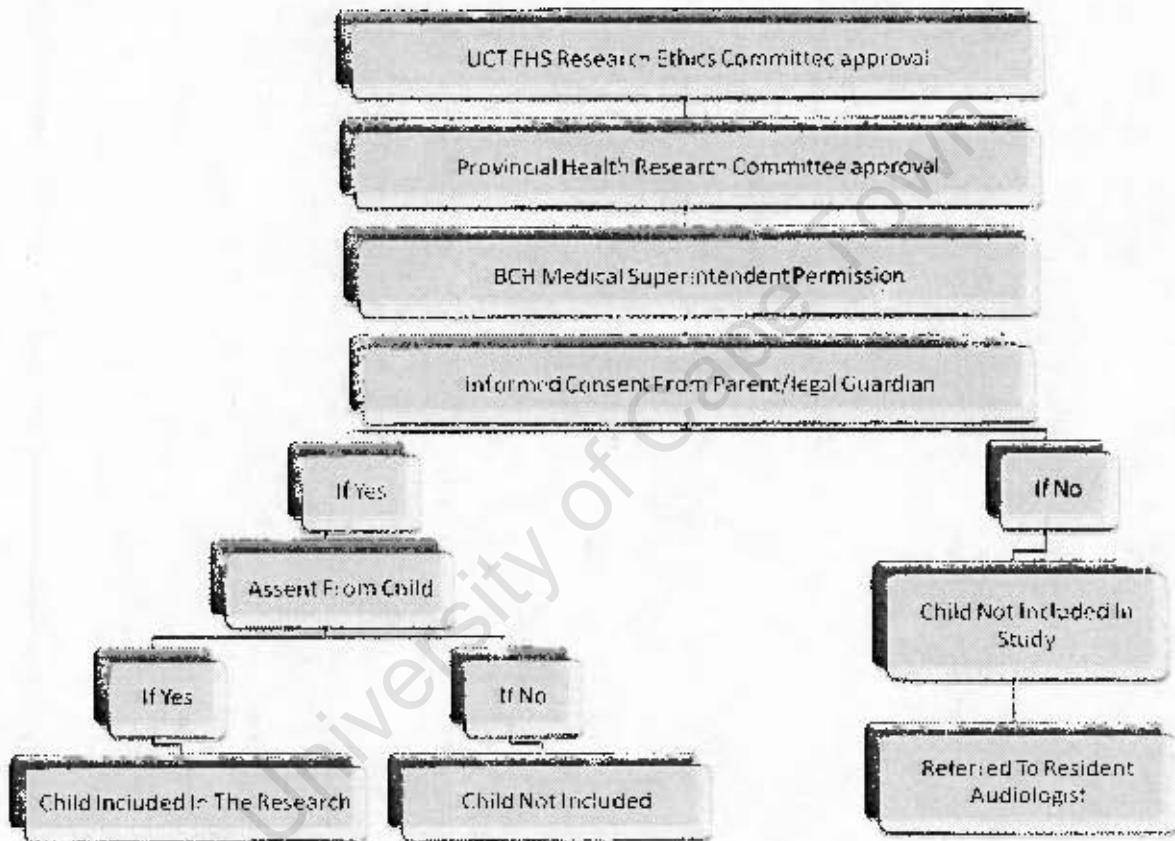
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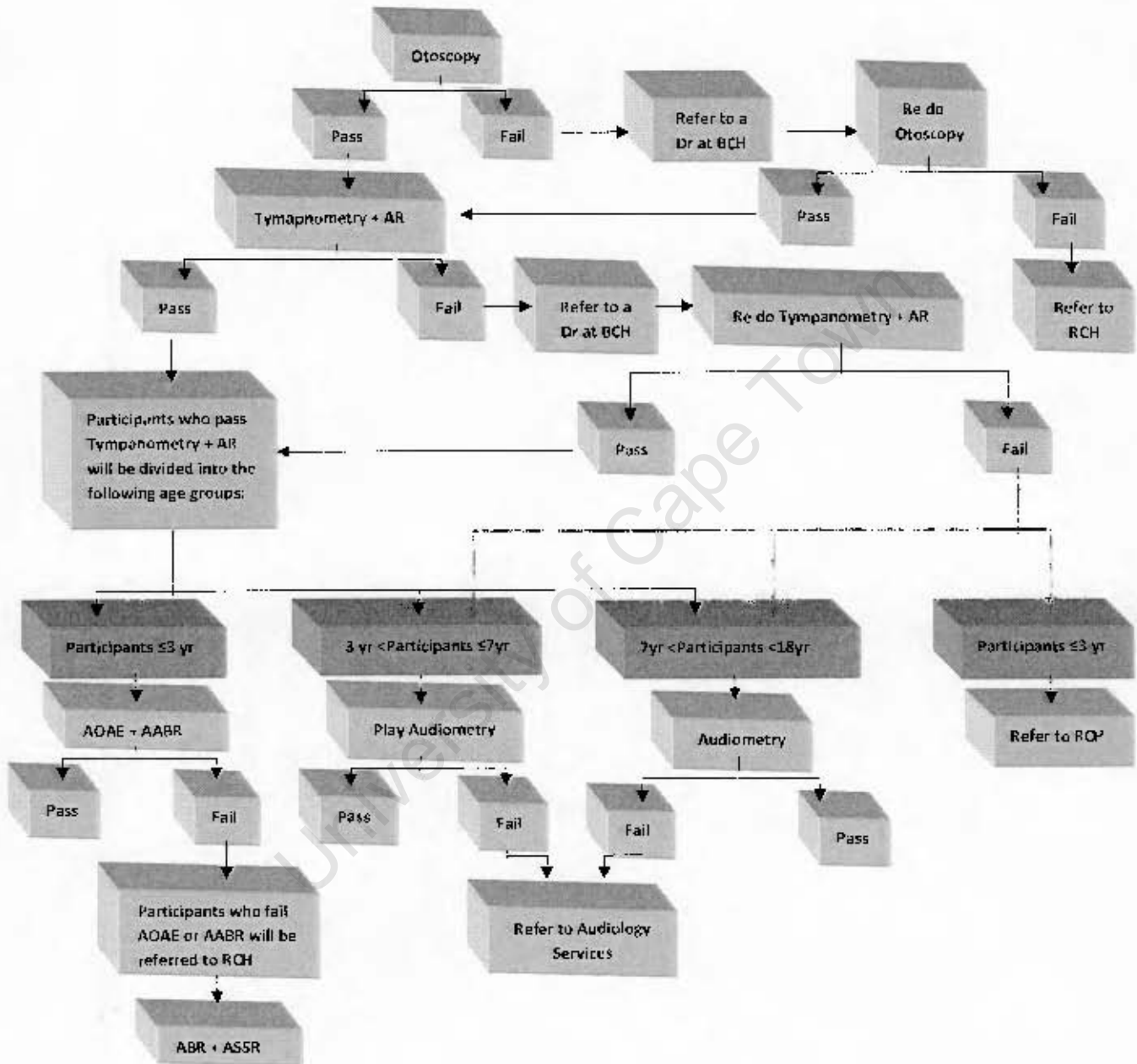
Appendix I

Procedure of Getting Ethical Approval and Consent from Parents and Their Children



Appendix J

Procedure of Audiological Examination



Appendix K

Audiologic Tests Results

No	Age group	Ear	Middle ear status (pre medical intervention)				Hearing status (post medical intervention)			
			Otoscopy		Tymp (Type)	Ipsi AR	Audiometry			OAE + AABR
			Outer Ear	TM			Type	Degree	Shape	
1	III	R	NAD	NAD	A	Present	SNHL	Slight	Flat	-
		L	NAD	NAD	A	Present	SNHL	Slight	Flat	-
2	III	R	NAD	NAD	A	Absent	SNHL	Normal	HFL	-
		L	NAD	NAD	A	Absent	SNHL	Normal	HFL	-
3	III	R	NAD	NAD	A	Absent	-	-	-	Pass
		L	NAD	NAD	A	Present	-	-	-	Pass
4	II	R	NAD	NAD	A	Present	NH	Normal	-	-
		L	NAD	NAD	A	Present	NH	Normal	-	-
5	I	R	NAD	NAD	C	Absent	Discharged	-	-	-
		L	NAD	NAD	B	Absent	Discharged	-	-	-
6	III	R	NAD	NAD	C	Absent	Mixed HL	Slight	HFL	-
		L	NAD	NAD	A	Absent	Mixed HL	Normal	HFL	-
7	I	R	NAD	NAD	C	Absent	-	-	-	Pass
		L	NAD	NAD	B	Absent	-	-	-	Pass
8	III	R	NAD	NAD	A	Present	NH	Normal	-	-
		L	NAD	NAD	A	Present	SNHL	Normal	HFL	-
9	I	R	NAD	Bulging & red	A	Present	-	-	-	Pass
		L	NAD	Bulging & red	A	Present	-	-	-	Pass
10	III	R	NAD	NAD	A	Present	NH	Normal	-	-
		L	NAD	NAD	A	Present	SNHL	Normal	HFL	-
11	II	R	NAD	NAD	A	Present	NH	Normal	-	-
		L	NAD	NAD	B	Absent	NH	Normal	-	-
12	III	R	NAD	NAD	A	Present	NH	Normal	-	-
		L	NAD	NAD	A	Present	NH	Normal	-	-
13	I	R	NAD	NAD	A	Present	-	-	-	Pass
		L	NAD	NAD	A	Present	-	-	-	Pass
14	II	R	NAD	NAD	A	Present	NH	Normal	-	-
		L	NAD	NAD	A	Present	NH	Normal	-	-
15	III	R	NAD	NAD	A	Absent	Mixed HL	Slight	Flat	-
		L	NAD	Perforated	CNT	CNT	Mixed HL	Profound	Flat	-
16	I	R	NAD	NAD	B	Absent	-	-	-	Pass
		L	NAD	NAD	B	Absent	-	-	-	Pass
17	II	R	NAD	NAD	A	Present	SNHL	Normal	HFL	-
		L	NAD	NAD	A	Present	NH	Normal	-	-
18	III	R	NAD	NAD	A	Present	NH	Normal	-	-
		L	NAD	NAD	A	Present	SNHL	Normal	HFL	-
19	I	R	Wax	NAD	A	Present	-	-	-	Pass
		L	Wax	NAD	B	Absent	-	-	-	Pass
20	II	R	NAD	NAD	A	Present	SNHL	Slight	HFL	-
		L	Wax	NAD	A	Present	NH	Normal	-	-
21	III	R	NAD	Grommet	CNT	CNT	NH	Normal	-	-
		L	NAD	NAD	B	Absent	NH	Normal	-	-
22	III	R	NAD	Perforated	CNT	CNT	Discharged	-	-	-
		L	Wax	NAD	B	Absent	Discharged	-	-	-
23	III	R	Wax	NAD	B	Absent	Mixed HL	Profound	Flat	-
		L	NAD	NAD	A	Present	Mixed HL	Severe	Flat	-
24	I	R	NAD	NAD	A	Present	-	-	-	Pass
		L	NAD	NAD	A	Present	-	-	-	Pass
25	III	R	Wax	NAD	A	Present	SNHL	Normal	HFL	-
		L	Wax	NAD	A	Absent	NH	Normal	-	-

26	I	R	NAD	Grommet	CNT	CNT	CNT	-	-	-
		L	NAD	Grommet	CNT	CNT	CNT	-	-	-
27	III	R	NAD	Perforated & D	CNT	CNT	SNHL	Normal	HFL	-
		L	NAD	NAD	A	Present	NH	Normal	-	-
28	II	R	NAD	NAD	A	Present	-	-	-	Pass
		L	NAD	NAD	A	Present	-	-	-	Pass
29	I	R	NAD	NAD	B	Absent	Died	-	-	-
		L	NAD	NAD	B	Absent	Died	-	-	-

Note. Hearing test results could not be ascertained for the empty cells. SNHL= sensorineural hearing loss, NH= normal hearing, CNT= could not test, NAD= no abnormality detected, R= right, L= left, TM= tympanic membrane, AR= acoustic reflexes; D=discharge Participant No 3 was cognitively impaired.

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