ASSESMENT OF HEARING DEFICITS IN CHILDREN WITH DOWN SYNDROME -

A COMPARATIVE CROSS SECTIONAL STUDY

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CERTIFICATE

This is to certify that the dissertation entitled **"Assessment of hearing deficits in children with down syndrome - a comparative cross sectional study" by Dr. Fidha Parvez Khan F,** for M.D Physiology is a bonafide record of the research done by her during the period of the study (2017-2020) in the Institute of Physiology and Experimental Medicine, Madras Medical College, Chennai- 600 003.

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CONTENTS

I.LIST OF TABLES

II. LIST OF GRAPHS

III.LIST OF PHOTOGRAPHS AND FIGURES

IV.ABBREVIATIONS

LIST OF TABLES

LIST OF GRAPHS

LIST OF PHOTOGRAPHS

LIST OF FIGURES

ABBREVIATIONS

1.	NICU	-	Neonatal Intensive Care Unit
2.	IQ	-	Intelligence Quotient
3.	ENT	-	Ear Nose Throat
4.	CNS	-	Central Nervous System
5.	OME	-	Otitis media with effusion
6.	ABR	-	Auditory Brainstem Response
7.	PTA	-	Pure Tone Audiometry
8.	AC	-	Air conduction
9.	BC	-	Bone conduction
10.	PT	-	Pure tone
11.	dBHL	-	Decibel hearing level
12.	BERA	-	Brainstem Evoked Response Audiometry
13.	DS	-	Down syndrome
14.	VSD	-	Ventricular septal defect
15.	ASD	-	Atrial septal defect
16.	PDA	-	Patent ductus arteriosus
17.	NT	-	Nuchal translucency
18.	CRL	-	Crown rump length
19.	AFP	-	Alpha fetoprotein
20.	uE3	-	Unconjugated estriol
21.	INH-A	-	Inhibin-A

22.	PAPP-A	-	Pregnancy associated plasma protein-A)
23.	hCG	-	Human chorionic gonadotropin
24.	EAC	-	External auditory canal
25.	KADS	-	Keratinocyte attachment destroying susbstance
26.	TM	-	Tympanic membrane
27.	IHC	-	Inner hair cells
28.	OHC	-	Outer hair cells
29.	ANF	-	Auditory nerve fibre
30.	ECMO	-	Extracorporeal membrane oxygenation
31.	Hz	-	Hertz
32.	dB	-	Decibel
33.	ABG	-	Air bone gap
34.	EEG	-	Electro encephalogram
35.	AEP	-	Auditory evoked potential
36.	ALR	-	Auditory late response
37.	IPL	-	Interpeak latency
38.	BAEP	-	Brainstem auditory evoked potential
39.	BTE	-	Behind the ear
40.	ITE	-	In the ear
41.	BAHA	-	Bone anchored hearing aids
42.	FM	-	Frequency modulated

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CERTIFICATE - II

This is to certify that this dissertation work titled **"ASSESSMENT OF HEARING DEFICITS IN CHILDREN WITH DOWN SYNDROME - A COMPARATIVE CROSS SECTIONAL STUDY"** of the candidate **DR. FIDHA PARVEZ KHAN F,** with registration Number **201715002** for the award of **M.D** in the branch of **PHYSIOLOGY**. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **12 percentage** of plagiarism in the dissertation.

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Introduction

1. INTRODUCTION

Children with hearing loss, who have special needs make up a large proportion of the paediatric population which are hearing impaired. It is estimated that 2-4% of neonates in the NICU will have a significant bilateral hearing loss (1) The underlying cause for the sensorineural loss could be due to many reasons.Some of the risk factors are low birth weight, low Apgar score, hyperbilirubinemia, ototoxic medication and mechanical ventilation.

Hearing loss may also be conductive or there may be a conductive element to the sensorineural hearing loss. This is often seen in children with Down syndrome or certain other craniofacial abnormalities

1866, an English physician, John Landgdon Haydon Down first described the findings of the clinical symptoms of an unknown syndrome (trisomy 21) and hence it was named Down syndrome or Down's syndrome. From the time of this pioneering work, numerous researches and studies have been carried out on Down syndrome. Its remarkably high occurrence rate, 1 in 770 live births (2), has heralded it, a syndrome for priority research.

Down syndrome, also known as trisomy 21 is a genetic disorder, that occurs due to the presence of all or part an extra chromosome 21. It is associated with a delay in physical growth and mild to moderate intellectual disability. There are certain characteristic facial

features. The average IQ of a person with Down syndrome is around 50, which is equivalent to the mental ability of an 8- or 9-year-old child. But this may vary.

In Down syndrome, no single phenotypic feature is pathognomic. But the combination of facial dysmorphisms is highly specific. But to confirm the diagnosis and to assess the genetic implications for the family, chromosome analysis is necessary.

In 95 % of Down syndrome cases, there is a free extra chromosome 21. This is most often due to a nondisjunction event at the second meiotic division, and the chance of this occuring rises in older mothers (3).

In 4% of Down syndrome cases, the extra chromosome 21 is translocated to or fused with another large or small acrocentric chromosome. This fusion, sometimes described as a whole-arm exchange, is also called a robertsonian translocation in recognition of the American cytogeneticist Robertson’s contribution from his studies of chromosome fusion in insect cytogenetics early last century (3).

In a fetus with Down syndrome, the facies usually appears normal. The probability of survival of a fetus with Down syndrome may be enhanced by absence of severe fetal malformation and by a younger maternal age. In newborns, eight cardinal dysmorphisms or signs in Down syndrome are abundant neck skin, mouth corners turned downward, general

hypotonia, flat face, dysplastic ear, epicanthic eye-fold, gap between first and second toes and protruding tongue (4).

In children, Down syndrome can be identified by brachycephaly, oblique palpebral fissure, flat nasal bridge or root, narrow palate, folded ears, short broad neck, incurved fifth finger, sandal gap between great toe and second toe and hypotonia. As age increases, the facial features change just like in chromosomally normal individuals.

Ear, nose, and throat (ENT) complications cause a lot of morbidity in Down syndrome. They may be inextricably linked with CNS problems, which may cause speech and communication disorders. Deafness is very frequent, and most the of the children have a conductive hearing loss. This is most probably caused by otitis media with effusion (OME). Early and persistent hearing loss in this vulnerable age group may lead to difficulties in listening, communication, behaviour and learning and perception skills. Intervention options for hearing loss associated with OME include ventilation tubes (grommets) and hearing aids

Also common causes of deafness are the effect of anatomical malformations, like eustachian tube abnormalities, persistent mesenchymal tissue in the tympanic cavity, stenotic ear canals, external auditory meatus stenosis and mastoid bone hypoplasia, ossicular chain and cochlear malformation and impacted wax. The Eustachian tube function is additionally compromised due to an anatomically constricted nasopharynx together with adenoid hypertrophy (5).

The difficulties in diagnosing that accompany a hearing examination in small children, especially those with Down syndrome, only add to the problem. All infants with Down

syndrome must be evaluated by pure tone or behavioral audiometry, tympanometry and auditory brainstem response (ABR). The preferred method for screening neonates is ABR when asleep. A hearing examination requires a lot of patience and experience and the use of different examination techniques.

The purpose of PTA is to determine the hearing thresholds for pure tones. Pure tones are sinusoidal signals with a single defined frequency, amplitude and phase. Pure tones are rare in nature. But they can be easily characterized. Therefore they are suitable for quantitative tests for hearing sensitivity.

Audiometers are used to make quantitative measures of air conduction (AC) and bone conduction (BC) pure tone (PT) thresholds. PT thresholds provide information about the type of hearing loss, as well as quantify the frequency specific threshold evaluations that result from damage to the auditory system. AC thresholds asses the entire auditory pathway, and they are measured using earphones. The hearing sensitivity can be can be assessed in each ear separately. BC thresholds are measured by placing a vibrator on the skull. Each ear is assessed separately. A masking noise is applied to the non-test ear. The goal of the BC testing is to stimulate the cochlea directly, thus bypassing the external and middle ears.

A comparison of both the thresholds provides an estimate of the status of the conductive and Sensorineural systems. If the thresholds are elevated equally for sounds presented by AC and BC, it means that the outer and middle ear do not contribute the hearing loss. On the

contrary, if the thresholds are poorer by AC than by BC, then the source of the hearing loss may be the external or middle ear (6)

The acceptable level of ambient noise in the test environment is specified by standard ISO 8253-1:2010 (1).

Pure tone audiometry (PTA) is a subjective test and it's a behavioral measurement of a hearing threshold. It relies on patient responses to the stimuli. Therefore, PTA is largely used on adults and children old enough to cooperate with the test procedure. But testing a child with special needs demands unique skills from the audiologist. Test protocols and tasks must be modified. Many children with Down syndrome have hearing sensitivity within normal limits but they may be unable to respond consistently to auditory stimuli.

Conditioned play audiometry is often used to test hearing in these children as they fail to cooperate. Play audiometry was first described by Lowell et al in 1956 (7). Children can be taught to drop a toy in a bucket or to throw a ring on a stack of rings on a stand, when they hear a sound. The child should be kept entertained and alert until the test is completed. The child has to be conditioned for this play audiometry. It is important that the child actually hears the stimulus before he responds (7).

If a child responds to speech at a normal conversational level, testing can begin by presenting test stimuli at 40 to 50 dB HL. But if a child does not respond to normal speech at a normal conversational level, it is possible that the child has a significant hearing loss and a loud stimulus will be needed.

Auditory brainstem response (ABR) audiometry is a neurologic test of auditory brainstem function. It is used to detect any abnormality in the pathway through which auditory impulses travel from the inner ear to the auditory cortex by the response obtained from auditory (click) stimuli. It can also be referred to as brainstem evoked response audiometry (BERA). It was first described by Jewett and Williston in 1971.

ABR audiometry refers to an evoked potential that is generated by a brief click. It is transmitted from an acoustic transducer in the form of an insert earphone or headphone. Electrodes are kept in the vertex (ground electrode) and over the mastoid of the side that is to be tested (reference electrode). These electrodes elicit the waveform response.

The auditory impulses are carried by the following pathway. Fibres from the cochlear nerve synapse in dorsal and ventral cochlear nuclei. The cochlear nuclei contain second-order neurons. From here the auditory pathway becomes bilateral and complex because of many synapses. Many fibres cross over at the trapezoid body. From here fibres reach the superior olivary nucleus and then the lateral lemniscus in the midbrain. From the lateral lemniscus, the fibres ascend to the midbrain and terminate in the inferior colliculus. From inferior colliculus, the fibres reach the medial geniculate body in the thalamus. In this region the fibres form the acoustic radiation and they end in the auditory cortex in the temporal lobe, Broadman area 41.

In the ABR waveforms,

Wave I represents the peripheral portion of the cochlear nerve,

Wave II represents the cochlear nucleus,

Wave III represents the superior olivary nucleus,

Wave IV represents the lateral lemniscus,

And wave V represents the inferior colliculus (8).

The latencies and interpeak latencies are affected by certain variables like hearing loss, gender, age and rate of stimulus presentation

In this study the absolute peak latency of each of the waves was recorded along with the interpeak latencies between waves I and III, waves III and V and waves I and V. This was done in 30 children with Down syndrome (60 ears), and compared with age and sex matched apparently normal children.

The aim of the present study is to report about the audiological findings in children with Down syndrome and to discuss the diagnostic tools to evaluate them.

Review of Literature

2. REVIEW OF LITERATURE

2.1 DOWN SYNDROME

1. Clinical and genetic aspects:

Down syndrome (DS) (trisomy 21) is the most common genetic disorder. It has a high prevalence rate in the world. Chromosome 21 is the smallest human autosomal chromosome. There are 3 types of chromosomal abnormalities in trisomy 21 – they are free trisomy 21, translocation and mosaicism.

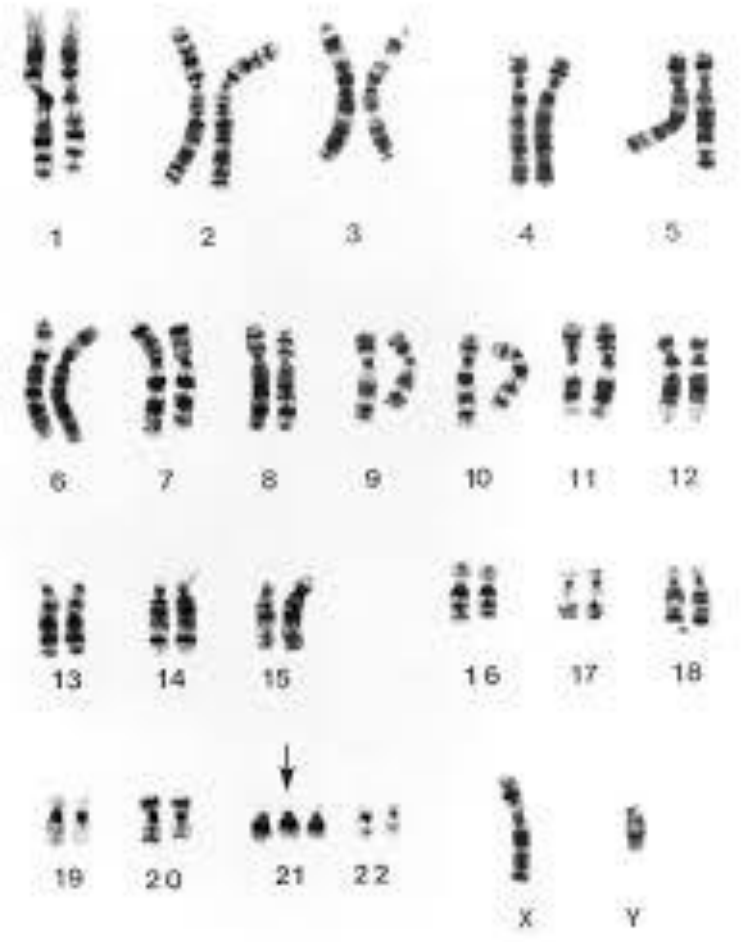


FIGURE-1 TRISOMY 21

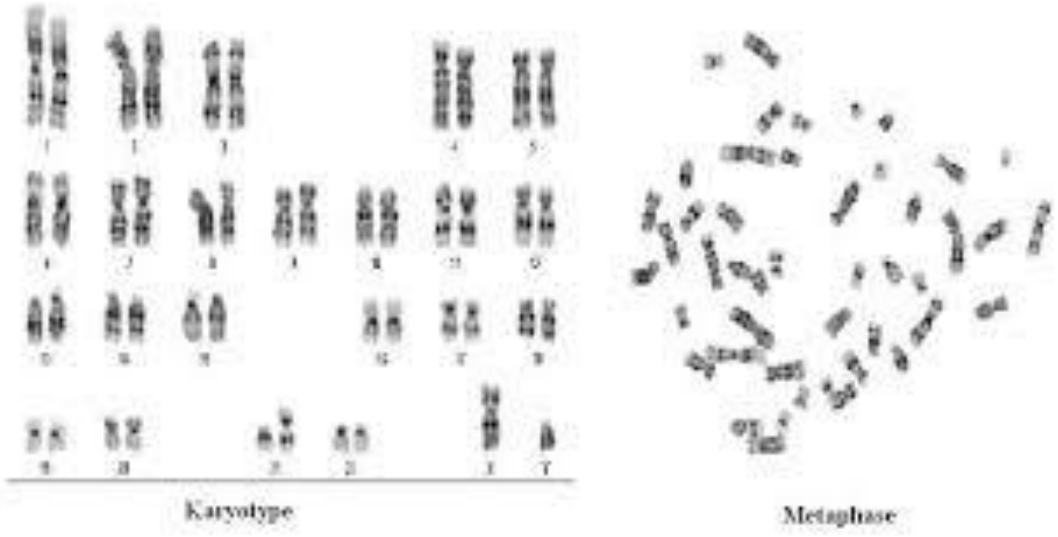


FIGURE-2 ROBERTSONIAN TRANSLOCATION OF TRISOMY 21

In free trisomy 21 there are charateristically three complete copies of the chromosome 21. This type occurs. In about 90 - 95% of DS cases. Most of the cases of chromosomal nondisjunction have a maternal origin. It occurs mostly during the phase of meiosis I. And some of the cases have an additional extra chromosome of paternal origin. And a very small proportion of the cases occurs due to post-zygotic mitotic non-disjunction (9).

Translocations that occur are Robertsonian translocations. They involve chromosomes 14 and 21 and it is being the most common type. And mosaicism is characterized by 46 chromosomes present in some cells and 47 chromosomes in other cells.

The phenotype of Down syndrome is complex. It varies from individual to individual. It may present as a combination of dysmorphic features and developmental delay. Intellectual

disability is a characteristic feature. It is present in all cases of Down syndrome. Some of the other most important clinical features include muscular hypotonias, diastasis rectus abdominis muscle, upslanting palpebral fissures, microcephaly, flat occiput, hyperextensibility of joints, short fingers with broad bands. Short stature, fifth finger clinodactyly, presence of epicanthal fold thickening, low-set ears, a single palmar crease may also be present. Atlantoaxial instability and femoral instability also occur occasionally.

About 50-70% of children with Down syndrome may also have congenital defects of the heart, like ventricular septal defect (VSD), atrial septal defect (ASD), tetralogy of Fallot (TOF), patent ductus arteriosus (PDA) and A-V septal defect (10). These children can also have ocular defects like refractive errors, nystagmus and even retinal abnormalities. Around 80% of the children with Down syndrome have hearing loss, that could be conductive, sensorineural, or mixed hearing loss (11). Patients with Down syndrome also present with hypothyroidism, periodontal diseases, upper airway obstruction and even hypogonadism.

Certain other important conditions are present. They include immunodeficiency states, leukemias and even early onset of Alzheimer's disease. Secondary sexual characteristics develop in these children in a similar way to those of other adolescents. In girl children, the fetal oogenesis seems to be normal. Hence normal reproduction is possible. But on men, the reproductive capacity appears to be diminished. The testicular histology shows oligospermia and hypogonadism often (12).

2. Prenatal screening and diagnosis:

Many methods can diagnose Down syndrome in the prenatal phase. But at the time of detection, it may not be possible to avoid any congenital malformations. The objective of

early detection is to give emotional and psychological support to the family and adequate medical support. Also, in many cases, surgical correction in utero can be done of any anatomical, thereby preventing and attenuating their evolution after birth.

Some of the screening methods for early detection of Down syndrome are the nuchal translucency test, measurement of maternal serum concentrations of certain fetoplacental products and also fetal ultrasound scanning. The nuchal translucency (NT) test measures the fluid filled fold that is present at the back of the neck of the fetus.

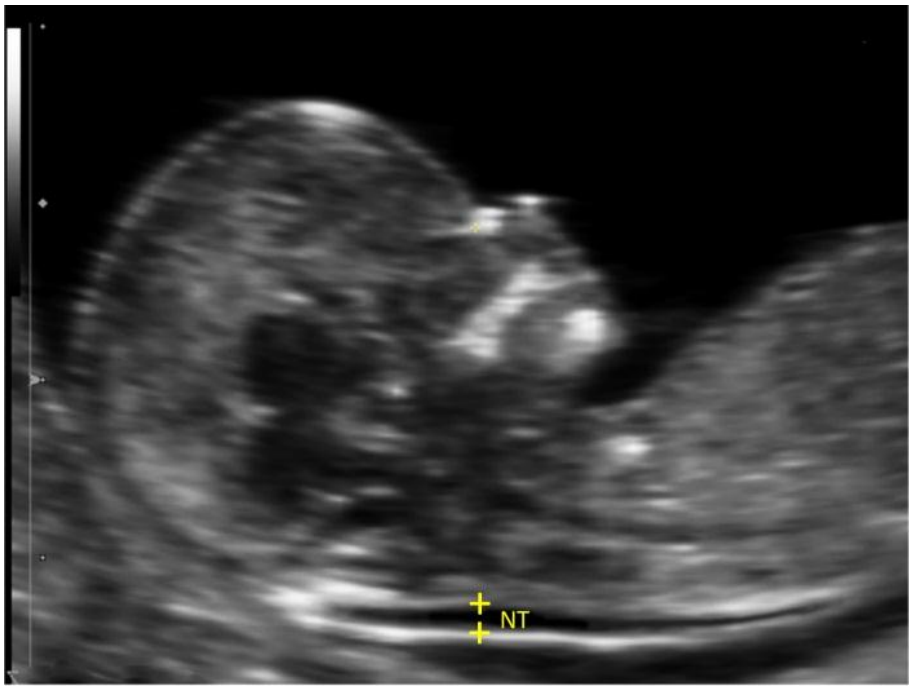


FIGURE-3 INCREASED NUCHAL TRANSLUCENCY

This is done during the first trimester of pregnancy. It is done through a transabdominal ultrasound. Transvaginal sonography can also be done. It is done between the 11th and 13th weeks of gestation. Normally at that time, the crown–rump length (CRL) of the fetus should

be at least 45 mm. It could go up to 84 mm. The nuchal translucency increases with CRL and hence it is important to take into consideration, the gestational age (13). The accumulation of excessive subcutaneous fluid behind the fetal neck could be the reason for the excess skin in the fetus. It is this excess skin that is visualized by ultrasound as increased nuchal translucency. It is a well-established fact these days that the measurement of fetal nuchal translucency thickness is a means of effective and early screening for trisomy 21. It also helps in screening other major aneuploidies like Patau syndrome and Edwards syndrome (trisomy 13 and 18 respectively). If an abnormal NT thickness is found, some additional tests must be done to elucidate the reason for increased nuchal fold (14).

Pregnancies with fetal aneuploidies are associated with altered maternal serum concentrations of certain fetoplacental products like AFP (alpha-fetoprotein), β-hCG (free chorionic gonadotropin), uE3 (unconjugated estriol), INH-A (inhibin A) and also PAPP-A (pregnancy associated plasma protein-A) (15–18). There is also the triple test that measures the concentrations of maternal serum AFP, βhCG and uE3. The yolk sac and fetal liver produce AFP. Placenta produces uE3 and hCG. Presence of Down syndrome in the fetus is suggested by the presence of an elevated β-hCG concentration and decreased levels of AFP and uE3. This is done during the second trimester. There is also a quadruple test in which INH-A is measured in addition to AFP, hCG and uE3 in the second trimester. INH-A is a glycoprotein. It is secreted by the corpus luteum and the placenta mainly. Its serum concentration is raised in Down syndrome pregnancy (18). PAPP-A is also used as a screening tool in the first trimester. If the fetus has Down syndrome, the level of this protein is reduced.

While conducting an ultrasound scan of the fetus, which is also a method for screening, any developmental change in the organs can be visualized easily. Alterations in the CNS of the fetus, changes in the face, neck, heart, gastrointestinal tract, and genitourinary tract can be detected. In the second trimester ultrasound scan, there could also be defects lack of visualization of the nasal bone, reduction in length of femur and humerus, hyperechoic bowel and echogenic intracardiac focus.

2.2 NORMAL ANATOMY OF THE EXTERNAL AND MIDDLE EAR

The ears are a primary warning system, capable of detecting potentially dangerous sounds of the surrounding environment. They are indispensible for survival by accurately detecting head movement, so that the eyes can stay fixed on the prey or the predator. They also play a major part in balance of the body. They give information about sudden changes in the environment, to avoid falls and injury. In addition to this, the ears form a major part of the communication system.

The ear is separated into its three parts – external, middle and internal – for descriptive purposes.

1. THE EXTERNAL EAR

A. The auricle

The auricle, also known as the pinna projects at a variable angle from the side of the head. Its function is to collect sound. The lateral surface of the auricle has prominences and depressions. They are different in each individual, even in twins. This unique pattern can be comparable to fingerprints. It can be used for identification of persons

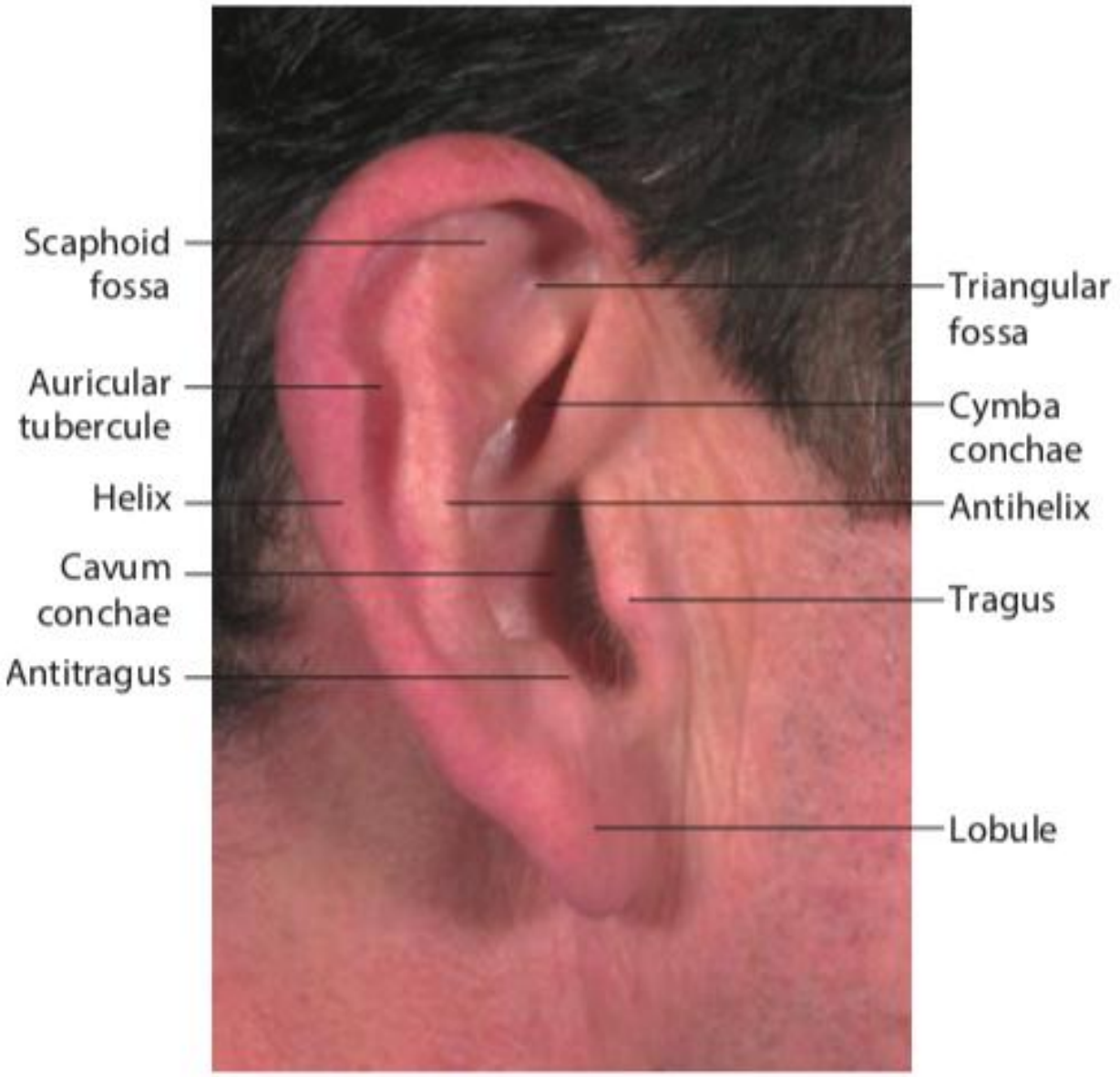


FIGURE-4 RIGHT AURICLE

The curved rim is the helix. In some people, it has a small prominence at its posterosuperior aspect, called Darwin's tubercle. The antihelix is present anterior to and parallel with the helix. Superiorly, the helix divides into two crura. In between them is a triangular fossa called the scaphoid fossa. In front of the antihelix is the concha. It partly encircles the concha. The crus of the helix rests just above the external auditory meatus. The smaller part superiorly above the crus of the helix is the cymba concha. The tragus is present below the

crus of the helix. It then overlaps the external auditory meatus. It is a little, blunt triangular prominence that points posteriorly. Opposite the tragus, there is a structure called the antitragus. It is at the inferior limit of the antihelix. The tragus and the antitragus are separated by a notch, called the intertragic notch. The lobule lies below the antitragus. It is a soft structure. It contains fibrous tissue and fat. The medial surface of the auricle has elevations. They correspond to the depressions on the lateral surface. It possesses corresponding names, for example the eminentia conchae.

Branches of the external carotid artery give blood supply to the auricle. The posterior auricular artery is the dominant one. It gives blood supply to the medial surface, except the lobule. It also gives its supply to the concha, the middle and lower portions of the helix and the lower part of the antihelix. The anterior auricular artery branches that arise from the superficial temporal artery supply the upper portions of the helix, antihelix, triangular fossa, tragus and lobule. The superior auricular artery is the one that connects the superior temporal artery and the network of posterior auricular artery. A branch from the occipital artery also gives its supply to the medial surface of the auricle.

The cranial branchial nerves and somatic cervical nerves supply the auricle. The greater auricular nerve is constantly present on the lateral and medial surfaces.

Lymphatic drainage from the posterior surface of the ear drains into the mastoid tip. Lymph drains into the preauricular nodes from the tragus and upper part of the anterior surface of the ear. From the rest of the auricle drainage occurs into the upper deep cervical nodes.

B. THE EXTERNAL AUDITORY CANAL

The external auditory canal (EAC) runs from the concha to the tympanic membrane. Its length is about 2.4 cm long. The canal wall is made up of only cartilage in the lateral one-third. Bony part makes up the medial two-thirds. Its diameter varies greatly between individuals and races. In adults, the cartilaginous part of the EAC runs downwards, forwards and medially. In neonates, there is no bony external meatus. This is because the tympanic bone is not yet developed. Also, the tympanic membrane is more horizontal.

In adults, the lateral cartilaginous portion of the EAC is about 8mm in length. It is continuous with the auricular cartilage. The medial border is attached to the rim of the bony canal by fibrous bands. There are also two horizontal fissures that lie anteroinferior in the cartilaginous portion. They were described by Santorini. They allow the passage of infection or tumor into the parotid gland.

The bony canal wall is about 1.6mm long. It becomes smaller near the tympanic membrane.

The EAC is lined by keratinizing stratified squamous epithelium. This lacks rete pegs and skin appendages in the thin skin of the bony canal. Normally, body skin grows from the basal layers up to the surface directly. Then it is shed into the surroundings. When there is an excess proliferation in the scalp, it is called dandruff. But if this occurs in the EAC, the canal would only be filled with desquamated skin. To prevent this from occurring, there is an outward and oblique growth of the epidermis of the skin over the EAC and pars flaccida of the TM. Therefore, the surface layers, migrate effectively towards the external opening of the canal. The normal rate of migration is about 0.1mm/day (19)**.** But this range varies greatly. In some people, there is a complete failure of migration of desquamated skin. This leads to a build-up of the keratin in the EAC. Patients who are prone to cerumen impaction

may lack a substance called ‘keratinocyte attachment destroying substance’ (KADS) (1). However, the property of canal skin to migrate can cause a lot of problems. It can cause a cholesteatoma.

The EAC has also some short hairs that project towards the opening of the canal. There are fine vellus hairs and larger terminal hairs. They are called tragi (Greek: ‘goat’). These tend to be more prominent in males. They are also a secondary sexual characteristic in them. The hairs are oriented with their tips laterally. They help prevent the entrance of foreign bodies. The skin of the cartilaginous part of the EAC, clusters of ceruminous and sebaceous glands are present. The ceruminous glands are modified apocrine sweat glands. They open into the root canal of the hair follicles. This produces a watery and white coloured secretion. It slowly darkens and it becomes semi-solid and sticky when it dries.

The sebaceous glands are also present in the canal which produces an oily material (sebum). Usually, it is usually excreted into the root of the hair follicles. The mixture of desquamated cells, cerumen and sebum is known as wax. In humans, the earwax is determined by a Mendelian trait. There are wet and dry forms. Dry wax does not contain cerumen. It is yellowish/ grey and also brittle, but wet wax is brownish and sticky. A single-nucleotide polymorphism in the *ABCC11* gene determines the earwax type. The *AA* genotype corresponds to dry wax and *GA* and *GG* to wet wax (20).

Cerumen also has certain antibacterial activity. The areas of skin that produce cerumen have the components of an active local immune system and they protect the canal by an antibody-mediated local immune response (21)

The blood supply of the external meatus is derived from the branches of the external carotid artery. Branches of the superficial temporal artery supply the roof and anterior part of the canal. The deep auricular branch from the maxillary artery supplies the anterior part of the canal and also the outer surface of the tympanic membrane. Auricular branches from the posterior auricular artery give their supply to the posterior parts of the canal. The veins drain into the external jugular vein, the maxillary veins and the pterygoid plexus. The lymphatic drainage follows that of the auricle.

2. THE MIDDLE EAR

The middle ear consists of the following - the tympanic cavity, the Eustachian tube and the mastoid air cell system. The tympanic cavity is nothing but an air-filled space within the temporal bone. It lies between the tympanic membrane laterally and the inner ear medially. It consists of the three ear ossicles and also the tendons which attach the ossicles to the muscles of middle ear. The tympanic segment of the facial nerve also runs along its walls and passes through the cavity.

A. THE TYMPANIC MEMBRANE

The tympanic membrane is seen at the medial end of the EAC. It is slightly oval. It is broader above than below. It forms a 55° angle with the floor. Its longest diameter is about 9–10mm. Its circumference is thickened to form a fibrocartilaginous ring called the tympanic annulus. From the superior limits of the sulcus, the annulus forms a fibrous band that runs as the anterior and posterior malleolar folds. It goes up to the lateral process of the malleus. The malleus handle is clearly visible. There is a small, triangular region of the TM above the malleolar folds. It is known as the pars flaccida. The pars tensa forms the rest of

the tympanic membrane. It has its concavity towards the ear canal. The centre of the membrane is called the umbo. To this, the tip of the handle of malleus is attached.

The blood supply arises from the EAC and the middle ear. Deep auricular branch and anterior tympanic branches of the maxillary artery are the main supply to the TM.

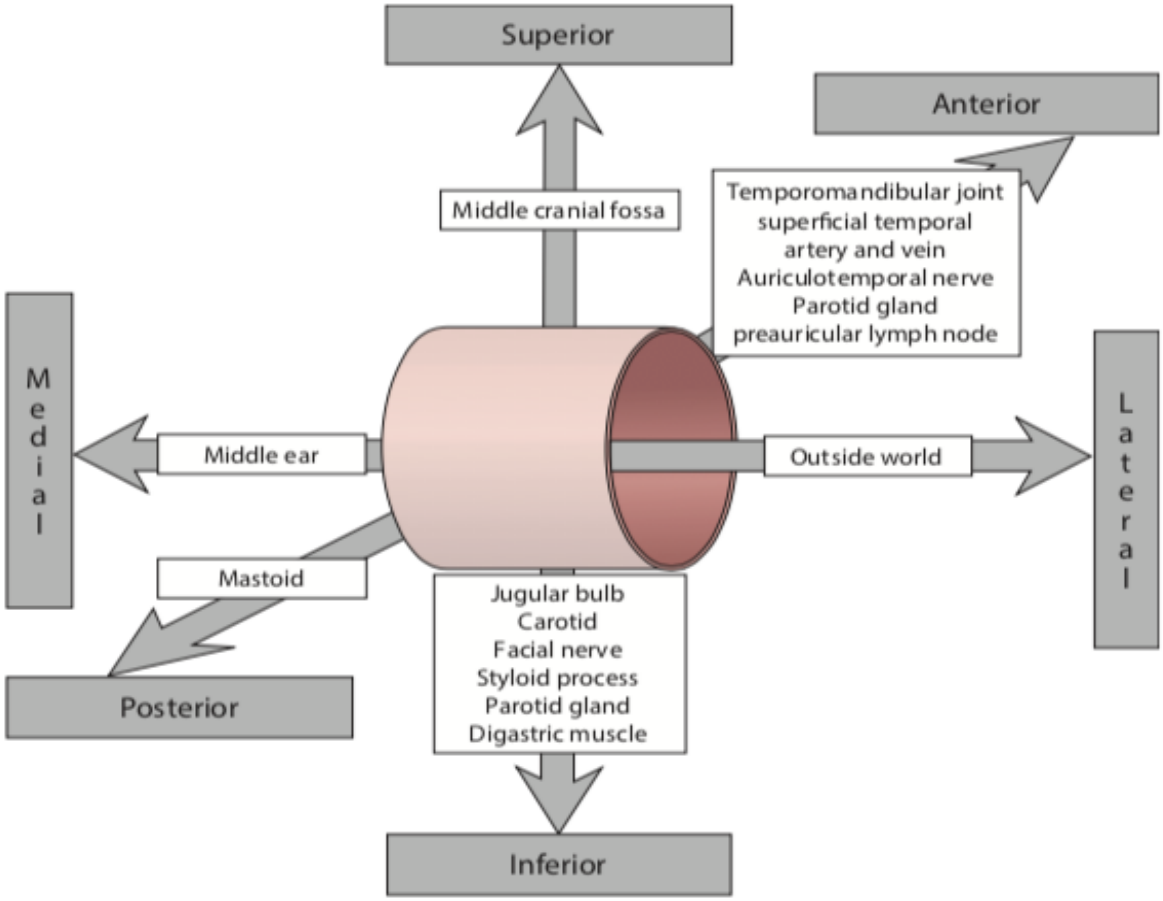


FIGURE-5 RELATIONSHIPS OF THE RIGHT EXTERNAL AUDITORY CANAL

The tympanic membrane is supplied by branches of the auriculotemporal nerve, the auricular branch of the vagus and the tympanic branch of the glossopharyngeal nerve.

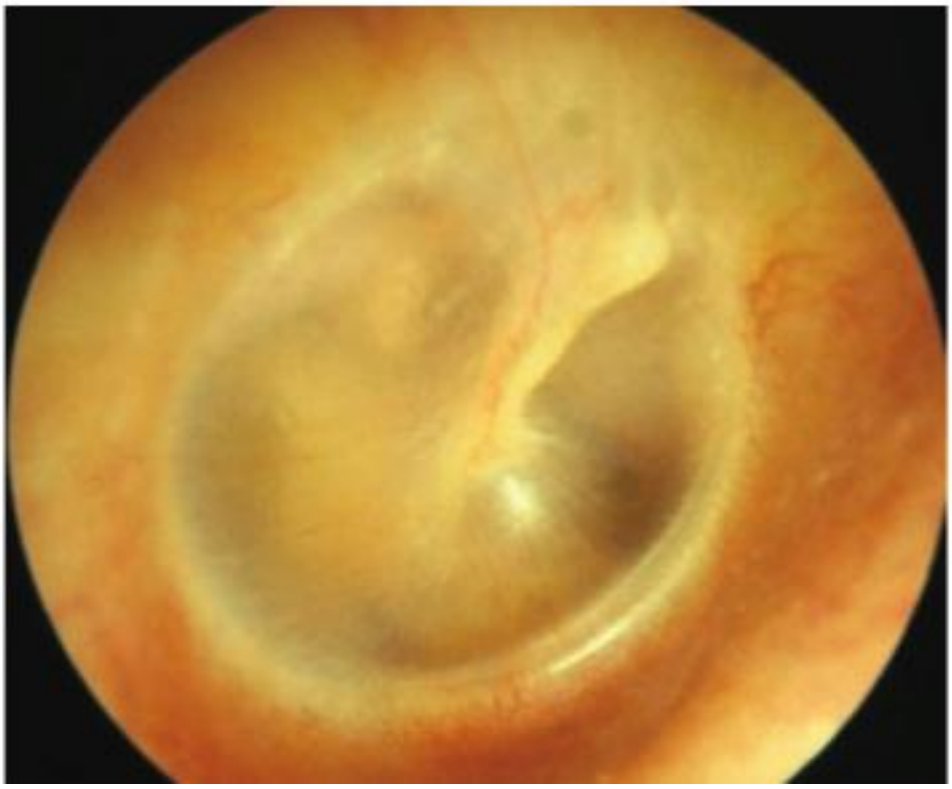


FIGURE-6 ENDOSCOPIC PHOTOGRAPH OF THE RIGHT TYMPANIC MEMBRANE

B. THE TYMPANIC CAVITY

There are three parts in the tympanic cavity- the epitympanum, mesotympanum and hypotympanum. The epitympanum, also called the attic, lies above the level of the malleolar folds. The hypotympanum lies below the level of the tympanic sulcus' lower part. It is continuous with the mesotympanum above. The mesotympanum is that part of the middle ear that is visible through EAC with a microscope.

C. THE LATERAL WALL

The lateral wall of the tympanic cavity is formed by the epitympanum superiorly, the

tympanic membrane centrally and the hypotympanum inferiorly. The chorda tympani nerve carries taste sensation from the anterior two-thirds of the same side of the tongue. It also carries the secretomotor fibres to the submandibular gland. It enters the middle ear through the petrotympanic fissure, through a canaliculus called canal of Huguier. The nerve enters the posterior canaliculus and runs obliquely downwards and medially through the posterior wall of the tympanic cavity where it reaches the facial nerve.

D. THE ROOF

Tegmen tympani forms the roof of the epitympanum. It is a thin bony plate. It separates the middle ear space from the middle cranial fossa. Roof is formed by both the petrous and squamous parts of the temporal bone. The petrosquamous suture line closes during adult life. It provides a route for infection into the extradural space in children.

E. THE FLOOR

The floor is made of compact bone or pneumatized bone with spines and trabeculae. It separates the hypotympanum from the dome of the jugular bulb. At the junction of the floor and the medial wall there is an opening. It is called the inferior tympanic canaliculus. From here the tympanic branch of the glossopharyngeal nerve (Jacobson's nerve) enters the middle ear. It carries preganglionic parasympathetic fibres from the inferior salivary nucleus.

F. THE ANTERIOR WALL

The anterior wall is narrow. This is due to the convergence of the medial and the lateral walls. In the lower one-third, a plate of bone covers the carotid artery while it enters the

skull. This plate is wafer thin. It is perforated by the superior and inferior caroticotympanic nerves that carry sympathetic fibres to the tympanic plexus. It is also perforated by the tympanic branches of the internal carotid artery. In the middle third of the anterior wall, the tympanic orifice of the Eustachian tube is present. Above this, is a canal. It contains the tensor tympani muscle. It eventually runs along the medial wall of the tympanic cavity.

G. THE MEDIAL WALL

The medial wall is present in between the tympanic cavity and the internal ear. The promontory is a rounded elevation in the central portion that occupies much of the medial wall. It also covers a part of the basal turn of the cochlea. The promontory gently inclines in the forward direction and merges with the anterior wall of the tympanic cavity. Behind and above the promontory the oval window is situated. This connects the tympanic cavity with the vestibule, but it is covered by the footplate of the stapes. The round window lies below and behind the oval window.

The facial nerve canal or the Fallopian canal runs above the promontory and oval window. It is marked anteriorly by the processus cochleariformis, which is a curved, bony projection. It houses the tendon of the tensor tympani muscle. Behind the oval window, the facial canal begins descend into the posterior wall of the tympanic cavity.

H. THE POSTERIOR WALL

The posterior wall has a large irregular opening called the aditus ad antrum. It leads back from the posterior epitympanum into the mastoid antrum. Below the aditus there is a small depression called fossa incudis. It houses the short process of the incus and its suspensory ligament. Below the fossa incudis is present a structure called the pyramid. It houses the

stapedius muscle and its tendon. The tendon inserts into the posterior aspect of the head of stapes.

I. THE CONTENTS OF THE TYMPANIC CAVITY

The tympanic cavity consists of three ossicles, two muscles, a chorda tympani nerve and the tympanic plexus. The ossicles are named the malleus, incus and stapes. They form a bony chain for the sound conduction. The malleus is attached to the tympanic membrane, and the stapes, to the oval window.

J. THE MALLEUS

The malleus is the largest ossicle. Its parts are- a head, neck and handle or manubrium. The head has a saddle-shaped facet on its surface to allow articulation with the body of the incus. This joint is a synovial joint. Below the neck of the malleus is a small prominence called lateral process, the anterior process, and the handle. The lateral process is a prominent landmark on the tympanic membrane**.** The chorda tympani crosses the malleus handle above. The neck of the malleus connects the handle with the head. The tensor tympani tendon gets inserted into the handle of the malleus

K. THE INCUS

The incus articulates with the malleus. Its parts are- a body and two processes. The body is present in the epitympanum. It has a cartilage-covered facet and it corresponds to the one on the malleus. The short process of incus projects backward from the body and it lies in the fossa incudis. The long process is present behind and medial to the handle of the malleus. The lenticular process articulates with the head of the stapes.

L. THE STAPES

The stapes is shaped like a stirrup, which is its other name. It has a head, neck, two crura - anterior and posterior, and a footplate. The head articulates with the lenticular process of the incus. The stapedius tendon inserts into posterior crus of the stapes. The two crura join at the footplate of the stapes. The footplate lies on the oval window .

M. THE STAPEDIUS MUSCLE

It arises from within the pyramid. A slender tendon emerges from the apex of the pyramid and inserts into the stapes. The muscle is supplied by the stapedial branch of the facial nerve.

N. THE TENSOR TYMPANI MUSCLE

This is a long and slender muscle. It arises from the walls of the bony canal that is present above the Eustachian tube. Some parts of the muscle arise from the cartilaginous part of the Eustachian tube and the greater wing of the sphenoid. The muscle is supplied by the medial pterygoid branch of the mandibular nerve

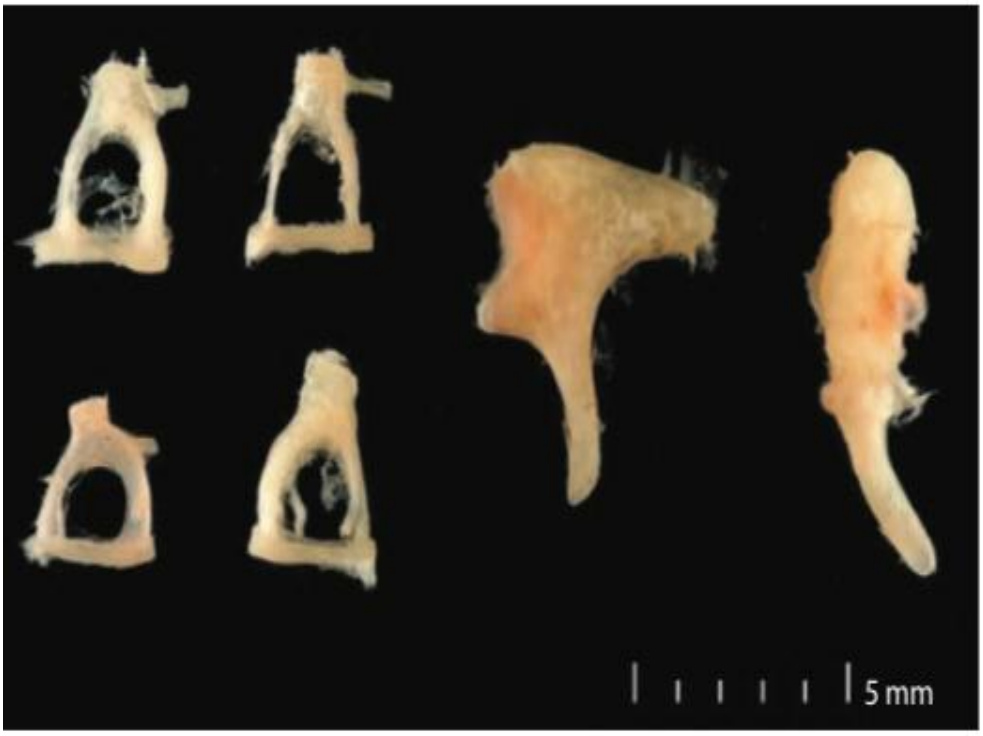


FIGURE-7 STAPES, INCUS AND MALLEUS WITH SCALE

O. THE EUSTACHIAN TUBE

The Eustachian tube is nothing but a channel. Itlinks the middle ear with the nasopharynx. In adults, its length is about 36mm. This size is reached when a child reaches the age of 7 approximately. It runs downwards from the middle ear at an angle of 45°. It then turns forwards and medially. The tube is considered to be made of two unequal cones. They are connected at their apices. The lateral third is the bony part. It arises from the anterior wall of the tympanic cavity. It joins the medial cartilaginous part. This part makes up the majority two-thirds of the total length of the Eustachian tube. The narrowest portion of the tube is called the isthmus. The tube has a lining of respiratory mucosa which contains goblet cells

and mucous glands. Ciliated epithelium is present on its floor. At the nasopharyngeal end, there is completely and truly a respiratory mucosa. Towards the middle ear, the number of goblet cells and glands begin to decrease. The ciliary epithelium also becomes less profuse.

The length of the cartilaginous part of the tube is about 24 mm. The cartilage is fixed to the skull base in between the petrous part of the temporal bone and the greater wing of the sphenoid. The cartilage's apex is attached to the isthmus of the bony portion. The wider medial end protrudes into the nasopharynx. It lies under the mucosa of the nasopharynx to form a mound called the torus tubarius.

Inside the nasopharynx, the Eustachian tube opens about 1–1.25cm behind and below the posterior end of the interior turbinate. The opening is a triangular one. It is surrounded above and behind by the torus. Behind the torus is a recess, known as the fossa of Rosenmüller. There is lymphoid tissue around the orifice of the tube and the lymphoid tissue in the fossa of Rosenmüller may be prominent in childhood.

3. THE INNER EAR

The inner ear is responsible for collecting, packaging and delivering sensory information related to hearing via the cochlea and about balance via the vestibular system. It converts movements initiated by sound waves in the cochlea and by changes in the position of the head in space in the vestibular system, into electrical signals. These are then passed to the brain through the auditory or vestibular pathway.

A. THE COCHLEA

The cochlea is made up of three parallel canals called scalae (meaning ‘ladders’ in Latin). These scalae are coiled in a spiral around a central ‘stalk’ called the modiolus**.** The axons of auditory nerves which project centrally, and innervate the sensory epithelia, and the vessels cochlear artery and cochlear vein, run through the length of the modiolus. There are two and a half turns in the cochlea. The central canal which is called the scala media is lined by epithelia. It is a part of the membranous labyrinth. It is filled with endolymph. In the cross sections of the cochlea, it appears that the scala media is bound by three walls. It appears triangular in shape. The sensory epithelium which is the organ of Corti runs along the basilar membrane**.** It forms the floor of the triangle. The stria vascularis, which is the primary ion-transporting epithelium, runs along the lateral side. The Reissner’s membrane forms the roof of the scala media. Above the Reissner’s membrane is the scala vestibuli, and underneath the basilar membrane is the scala tympani. These are filled with perilymph. The Reissner’s membrane is the barrier between the endolymph and the perilymph in the scala vestibuli. Perilymph from both the scala vestibuli and scala tympani is freely permeable into the intercellular spaces of the spiral ligament that underlies the stria vascularis.

At the basal end, the scala tympani ends at the round window, whereas the apical surface of the outer epithelium is exposed to air in the middle ear. The inner epithelium is bathed in perilymph. The scala vestibuli at its basal end is continuous with the vestibule and the vestibular system. The oval window is covered by a membrane and is covered by the footplate of the stapes. At the apical end, the helicotrema is the connection between the scala vestibuli and scala tympani. The movements of the tympanic membrane due to sound, cause the footplate of the stapes to move like a piston with ‘in–out’ movements. This displaces incompressible perilymph along the scala vestibuli and through the helicotrema**,** down the scala tympani which leads to ‘out–in’ movements of the round window. As the

fluid is displaced, the pressure difference across the scala media between the produces vibrational movement of the basilar membrane. This was described by Von Békésy as the 'travelling wave' theory. This travelling wave stimulates the sensory cells in the organ of Corti which sits on the vibrating basilar membrane.

B. ORGAN OF CORTI

The mature organ of Corti is a ridge of cells present on the basilar membrane. The tectorial membrane overlies it. The thickness of the basilar membrane and the height of the organ of Corti increase progressively from base to apex (22)**.** These changes in the mechanical properties of the basilar membrane, along with changes in the mass on the membrane, lead to various frequencies producing maximum vibrations at various locations along the cochlea. High frequencies are identified at the basal end of the cochlea and low frequencies at the apex. This 'tonotopic' relationship (frequency-place) is preserved along the neural auditory pathways in the brain. The nerves innervating the hair cells at the basal end (high-frequency end) of the cochlea project to a specific place in the cochlear nucleus. The nerves innervating hair cells in the apical region (low-frequency) project to a different, specific place in the cochlear nucleus. This tonotopic map projected onto the cochlear nucleus is carried on through the auditory pathway.

The two types of hair cells in the organ of Corti are the inner and outer hair cells (IHCs and OHCs). They are regularly arranged into a single row of IHCs on the inner side of the spiral and three or four rows of OHCs are present on the lateral outer side. Within the body of the organ of Corti there seem to be large extracellular spaces called the spaces of Nuel around the OHCs. The tunnel of Corti is present between the OHC region. These two spaces are created during the maturation of the organ of Corti. The spaces are filled with perilymph(1).

C. INNER HAIR CELLS

The IHCs are present above a thin bony extension from a bone which surrounds the modiolus. The IHCs are flask-shaped have the shape of a shallow ‘U’. They appear to form t continuous fence along the medial side of the organ of Corti. The IHC hair bundles do not contact the TM directly. They are exclusively innervated by the afferent nerve fibres. More than 90% of all the afferent fibres from the cochlea to the brain arise from IHCs. This makes them the main receptor cells which send auditory information to the brain. Efferent nerve fibres terminate in the IHC region. These nerve fibres arise from the ipsilateral lateral superior olive in the mid-brain.

Each IHC forms synapses with several (up to around 20) different afferent nerve endings that surround its basolateral membrane (23). But a single auditory nerve fibre (ANF) innervates only a single IHC. The synapses between an IHC and its ANF are called ‘ribbon’ synapses. They are specialized synapses. The presynaptic IHCs contain secretory vesicles containing the neurotransmitter glutamate. The glutamate binds to receptors on the post-synaptic membrane and it initiates action potentials in the ANF.

There is now increasing evidence that the subpopulations of afferent fibres that innervate an individual IHC are differentially sensitive to the effects of noise and ageing and the loss of a subpopulation of the afferent terminals under these conditions results in what has become known as ‘hidden hearing loss’ (24,25). Hence, because the IHCs still have some of the neural connections, the auditory thresholds that are measured by standard pure tone audiometry tests may be normal. But there may be deficits in subtle but certain critical aspects of audition, like the ability to discriminate sounds in noise.

D. OUTER HAIR CELLS

OHCs are present across the flexible part of the basilar membrane. They are cylindrical in shape with a nucleus that is pointed basally. Their hair bundles form a ‘W’ shape. They come in contact with the underside of the tectorial membrane. The impressions of the longest OHC stereocilia are seen on it. The tips of the longest stereocilia and their insertion into the tectorial membrane are linked by a fibrous protein, called the stereocilin, Any mutations in the gene encoding for stereocilin may be associated with impairment in hearing. Deflection of the stereocilia generates a change in the membrane potential in the cell, called a receptor potential. OHCs increase in length systematically from the base of the cochlear spiral to the apex. The longest stereocilia on OHCs also increase in height systematically along the base-to-apex length of the cochlea. These systematic (tonotopic) changes suggest that the length of the cell body and height of the stereocilia for a particular OHC are precisely defined for its particular position on the basilar membrane. The OHCs are directly innervated at their basal ends, by several large bouton-like efferent endings About 80% of the efferent cochlear innervation terminates on OHCs.

On stimulation, the activity of OHCs is to generate a radial flow of endolymph across the surface of the organ of Corti which deflects IHC stereocilia which stimulates IHC responses. So, at lower sound pressure levels (below about 60dB) OHC activity drives IHC responses. But at higher sound pressure levels the larger movements of the organ of Corti produce fluid flow that deflects IHC stereocilia, and stimulation of the cell, directly (26).

4. CLINICAL SIGNIFICANCE

Hearing sensitivity is reduced if hair cells are damaged. Hair cells cannot regenerate and produces permanent hearing loss resulting in defective action potential production and delayed transmission to higher centre (27).

5. HEARING LOSS IN CHILDREN WITH DOWN SYNDROME

The ability to hear is an essential part of our lives and it enriches our lives. The many ways of communication used by human beings includes facial expressions, body language, sign and spoken languages. Communication is necessary for early social development in early. It is important to hear the expressive intent of the other person. Children with Down syndrome have difficulty in receptive and expressive communication, even if they do not have a hearing deficit. And hearing loss only exacerbates an already existing barrier of communication. Hearing loss in these children occurs mostly due to some characteristic anatomical defect of the peripheral auditory system.

6. CERTAIN ANATOMICAL FEATURES SPECIFIC TO DOWN SYNDROME:

A. OUTER EAR:

Pinna is the source of entry of sound into the ear. It also transmits spectral cues that are extremely important for localization of sound. The pinna is much smaller in infants and children with Down syndrome. Malformations involving the pinna are also seen very commonly. They are present lower than the normal position and they are also rotated slightly backwards relative to the front of the skull.

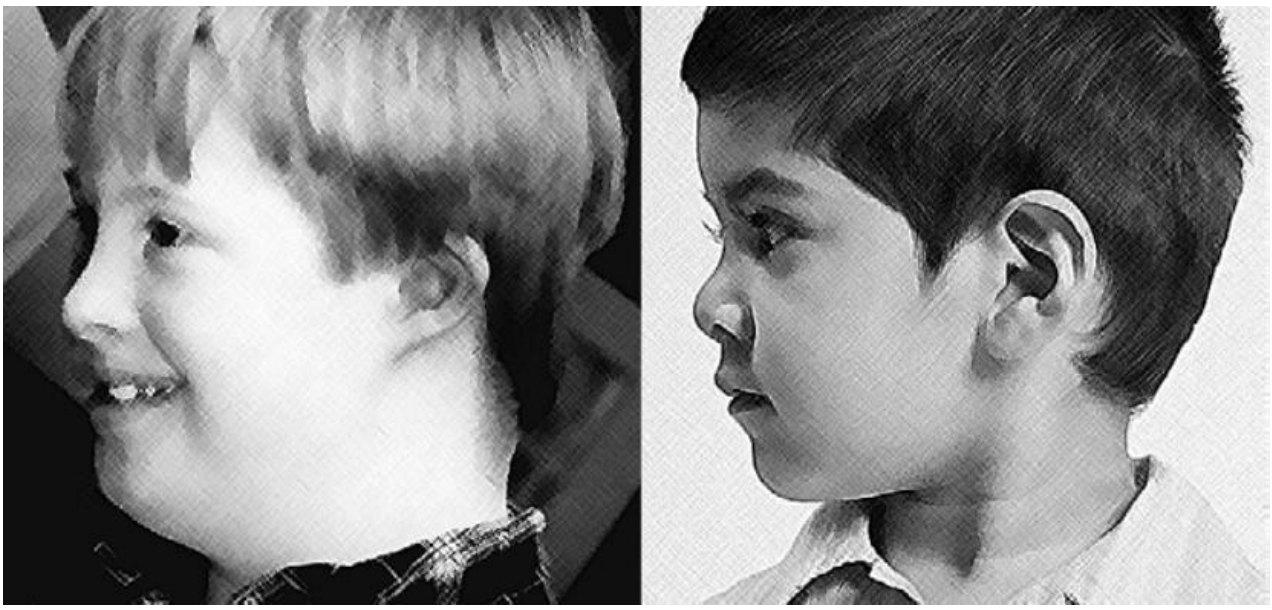


FIGURE-8 DEFORMED PINNA - THE OUTER EAR OF A TYPICALLY DEVELOPING CHILD AND A CHILD WITH DOWN SYNDROME.

As such, newborns with Down syndrome are likely to have ear lengths of 3.4 cm or less (28)**.** They do not localize sounds as well as normally developing children. It may be partly due to the reduced spectral cues because of having smaller pinnae compared to adults. Individuals with Down syndrome also have small pinnae; hence their ability to localize sounds is negatively affected. Poor localization of sound can affect the safety of the individual. Also because of the small pinnae, medical or surgical intervention is difficult. They also may have difficulty in supporting hearing technology like hearing aids.

RISK INDICATORS ASSOCIATED WITH PERMANENT CONGENITAL, DELAYED-ONSET, OR PROGRESSIVE HEARING LOSS IN CHILDREN WITH DOWN SYNDROME

- Neonatal intensive care of more than 5 days or any of the following regardless of length of stay: extracorporeal membrane oxygenation (ECMO), assisted ventilation, exposure to ototoxic medications (gentamycin and tobramycin) or loop diuretics (furosemide/Lasix), and hyperbilirubinemia that requires exchange transfusion.

- Craniofacial anomalies, including those that involve the pinna, ear canal, ear tags, ear pits, and temporal bone anomalies.

- Syndromes associated with hearing loss or late-onset hearing loss, such as neurofibromatosis, osteopetrosis, and Usher syndrome; other frequently identified syndromes include Waardenburg, Alport, Pendred, and Jervell-Lange-Nielson syndrome.

After the pinna, it is the external auditory canal that carries the sound. The EAC is also affected in Down syndrome. It could be stenotic, or narrow. This may cause a frequent blockage of the ear canal due to cerumen and other cell debris. This can cause an intermittent or permanent conductive hearing deficit. Such stenotic ear canals also have an impact on medical or surgical intervention, and in hearing technology choices. Normally for conventional hearing aids to be effective, they input sound into the ear through an ear mold which sits deeply in the ear canal. So if the EAC is stenotic, getting a good ear mold fit is extremely difficult. If the hearing aid is not fitted properly, the amplified sound can leak. This reduces the effectiveness of the hearing aid.

B. MIDDLE EAR:

From the EAC, sound passes through the tympanic membrane and enters the middle ear. The sound is converted from acoustic to mechanical energy as it passes through the

tympanic membrane. It is then conducted through the middle ear space by the three ear ossicles. Ossicular malformations are common in infants, young children, and adults with Down syndrome (29).Such ossicular deformations are mostly congenital. But there are also great chances that these Down syndrome individuals are influenced by chronic ear infections. The most common ossicle to be involved is the incus, in middle ear pathologies. But it does not rule out that the stapes or malleus could be malformed or eroded too. Chronic ear infections afflict approximately 70% of children with Down syndrome (30). The accumulation of secretions in the middle ear, called effusion is the cause for ear infections. The amount of viscosity of the middle ear effusion determines the degree of conductive hearing loss. The Eustachian tube orifice is found in the nasopharyngeal mucosa. Although it is not directly involved in transmission of sound, their role is to maintain air flow into the middle ear cavity and vice versa. This role of the Eustachian tube is vital in keeping the good health of middle ear mucosa and the contents of the middle ear.

The nasopharynx and its bony confines are comparatively smaller in children with Down syndrome. But the amount of soft tissue present in the nasopharynx is the same as in the normally growing children (31)**.** Since there is a relative increase in the soft tissue mass in the nasopharynx, there occurs a diminished airway space in these children. Children with Down syndrome also have generalized hypotonia. It may affect the tensor veli palatine muscle and the stapedius muscle. These muscles are important in assisting the Eustachian tube and the ossicular function of the middle ear. This relatively decreased nasopharyngeal space along with hypotonic muscles causes dysfunction of the Eustachian tube. There are also chronic upper respiratory tract illnesses along with frequent acute exacerbations. These also contribute to the middle ear pathology. Immune deficiencies are also prevalent in these children with Down syndrome (32). Hence medical professionals must anticipate middle ear

pathology in these children, diagnose it quickly, and treat aggressively. This will avoid permanent effects on the auditory system. About half of the children, by school going age have grommet or ventilation tubes placed in their tympanic membranes, in one or both ears. This causes a healthy flow of air into the middle ear space. It also allows for drainage of fluid from the middle ear. This type of intervention causes an immediate improvement in hearing. But it can still cause a high failure rate, and hence it must be monitored by otoscopy and audiological evaluation regularly.

C. INNER EAR:

In the middle ear space, sound travels by way of mechanical energy. This energy is transmitted to the inner ear by the footplate of the stapes. This footplate is present over the oval window of the cochlea. The cochlea is spiral in shape. It is made up of two and a half turns. The movement of the stapes footplate due to sound causes pressure-induced movements of the endolymph and perilymph of the cochlea. This stimulates the hair cells and the impulses travel along the auditory neural pathway.

Multiple congenital malformations of the cochlea and inner ear have been documented for individuals with Down syndrome (29,33)**.** A narrow internal auditory canal can also be present in Down syndrome. Such changes in the structure of the cochlea can alter the transmission of the auditory impulses. This can cause varying degrees of sensorineural hearing loss. But, Sensorineural hearing loss occurs more often and in older people with Down syndrome. It is also more in severity.

There are a few possibilities on why sensorineural hearing loss occurs more often in older individuals and not in children. Bony growth occurs within the cochlea. This may damage

the auditory nerve fibers. It can lead to loss of hair cells within the cochlea which are responsible for relaying information to the auditory nerve. This pathology is more often seen in presbycusis. This type bony growth in the cochlea can occur in children with Down syndrome who are as young as 7 years of age. Early onset presbycusis is a common feature in these children (34).

D. CENTRAL AUDITORY SYSTEM:

Characteristics of neural structures in individuals with Down syndrome was investigated by the 19th century (35)**.** It was found that the brainstem and cerebellum are shrunken in these individuals when compared to others of similar age and morphological growth. There is also decreased amount of myelin in the white matter of the cerebral cortex. Also branches of the dendrites are longer in some regions of the cortex (36)**.** But when the child with Down syndrome grows up, by two years of age, the neurons become smaller and lesser in number compared to normal children. Apart from these anatomical changes, there are also some neurochemical changes that contribute to the variations in these children.(37).

These anomalies cause the neural conduction time that is measured at the brainstem in response to auditory stimuli to be shorter for individuals with Down syndrome. This is the result of the auditory afferent pathways with shorter and fewer dendritic branches when compared to typically developing peers.

At the same time, the conduction times that are measured at the level of the cortex is longer for older children with Down syndrome than their typically developing peers (37). In addition to this, these individuals experience a slower habituation of cortical responses. This results in short term memory defects. Recognition and neuropsychological learning are

affected due to slow processing and defective integration in the temporal lobe. Storage of auditory information is also affected.

2.3 PURE-TONE AUDIOMETRY

Pure tone audiometry is used to determine the hearing thresholds for pure tones. Pure tones are nothing but sinusoidal signals which have a single defined frequency, amplitude and phase. Pure tones are rare in nature. But they can be easily characterized. This makes them suitable for conducting quantitative hearing sensitivity tests. They are the basic components that are generated by the voice box and also by the musical instruments.

1. EQUIPMENT FOR PURE-TONE AUDIOMETRY

The audiometer is the principal equipment that is required for deriving a clinical audiogram. The audiometer generates pure tones at each frequency. There are also narrow and broad bands of noise in addition to this. Pure tones can also be presented as modulated warble tones or pulses. This helps listeners detect signals when they have tinnitus. Warble tones are also important for going around the standing-wave artifacts. Some of the audiometers can also give higher-frequency hearing assessment up to 16000–20000Hz.

Calibration of the instrument must be done once or twice a year. If a change is done to the type of transducer, like a headphone is changed, to insert earphones, then different calibration settings must be stored in the audiometer. The audiometer, the transducers and even the response buttons that are used by the patient when they hear the stimuli, must be clean. They must function consistently.

FIGURE-9 AUDIOMETER

2. AUDIOMETRIC PROCEDURE FOR CLINICAL ASSESSMENT

BEFORE THE TEST:

The procedure is based on recommendations of the British Society of Audiology (38)**.** The audiologist must rely on the response of the patient for the test's accuracy. This must be established to the patient at the beginning of the test. The patient must understand what he is expected to do. He should feel comfortable in the test environment. The communication difficulties of the patient must be recorded before the test because it may affect the outcome of the test. The test must be carried out in a soundproof room for optimum results. It may cause claustrophobia in some which will make it difficult to test. In such a situation, the

environment must be modified. The door may be kept open. This prevents undue anxiety in the patient. This modification must be noted prior to beginning of the test.

3. MEASURING THE HEARING THRESHOLDS

For air conduction audiometry, testing is usually started in the better ear. The threshold for each pure tone is measured one by one. The order in which the pure tones presented are: 1000 Hz, 2000 Hz, 4000 Hz, 8000 Hz, 500 Hz and 250 Hz. Testing of inter-octave frequencies are done if a difference of 20 dB hearing loss or more occurs in between contiguous frequencies. The threshold at 1000 Hz is tested again in the ear that was tested first. If there is a difference of less than 5 dB between the two tests, then the best hearing threshold is taken. If during the retest, the difference of more than 5dB occurs, the examiner has to recheck if the patient understands the procedure, and if the transducers are in the right place. and if the buttons are working properly. Next the second ear is tested. If there was not much difference between the test and retest ear. Testing must always be preceded by a trial of familiarization. Each signal is introduced at a level that can be easily audible. Then its volume is reduced by 10 dB at each step, till the patient cannot hear the sound. So at the point where the patient doesn't respond to sound, the signal is increased in steps of 5 dB, till the time when the sound becomes audible to the patient, and the patient responds. This technique is called the 'bracketing technique'. It is otherwise called the '10 dB down, 5 dB-up technique'.

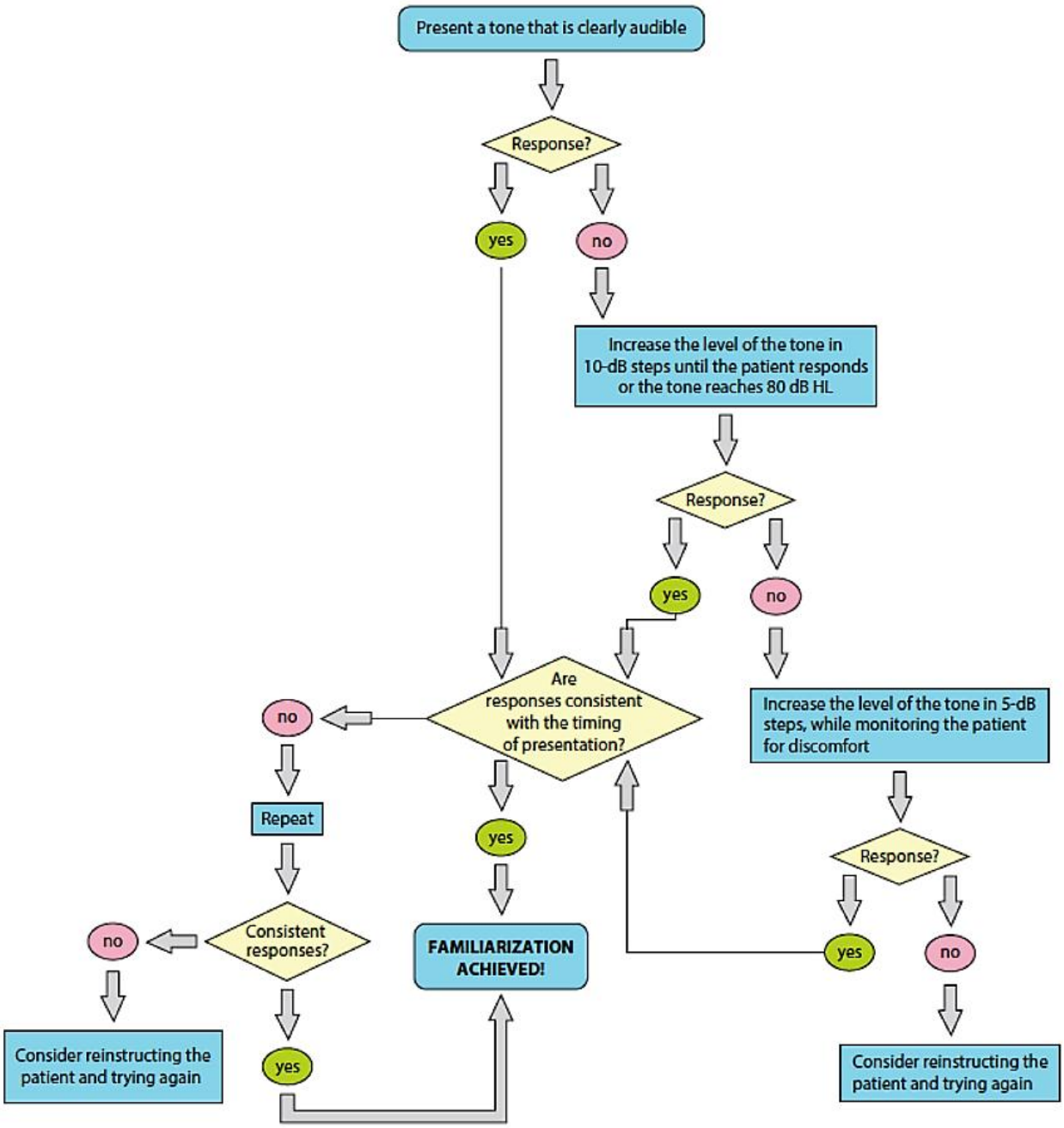


FIGURE-10 PROCEDURE TO ACHIEVE THE FAMILIARIZATION OF THE PATIENT WITH THE TASK

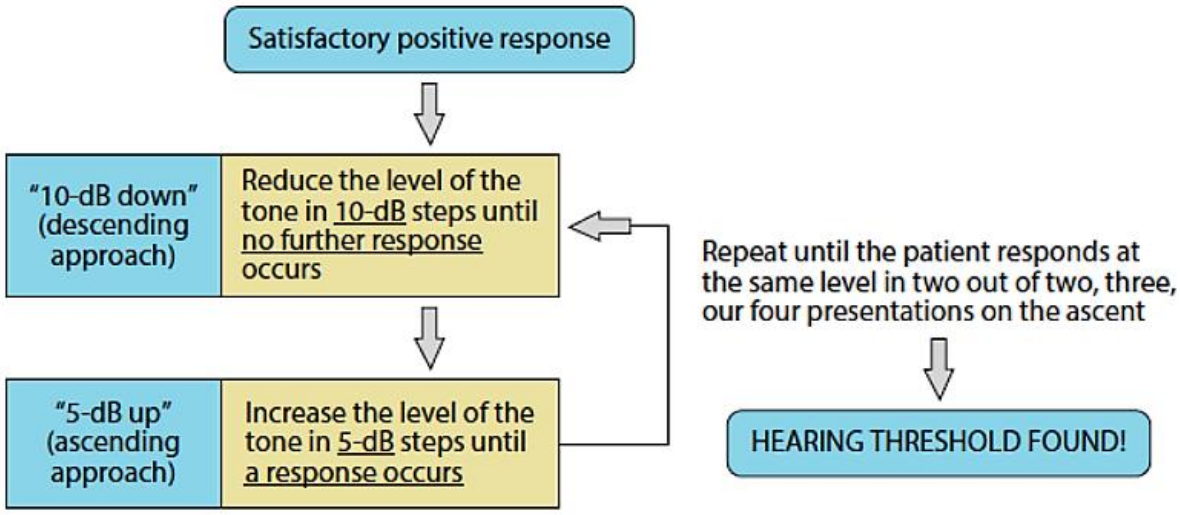


FIGURE-11 10 DOWN – 5 UP METHOD

The signal duration is between 1 and 3 seconds. Signal duration of less than 500 msec is not used during the test. The patient must respond by pressing a button or raising a finger. In case of a child, the response is a little different and play audiometry or behavioral reinforcement audiometry is performed which is explained later. Some unpredictable silent gaps should also be present for effective testing. It can last from 1 to 5 seconds.

After air conduction is tested, bone conduction testing is done. The frequencies for bone conduction testing are in the range of 500–4000 Hz. A retest is not required at 1000 Hz. The mechanism of sound transmission through bone conduction is complex. But, both AC and BC must be compared for finding the type of hearing loss – conductive or sensorineural.

If both AC and BC are affected equally, it indicates a sensorineural hearing loss. If, air conduction is affected more than bone conduction, it indicates a conductive hearing loss. This gap is called an air–bone gap (ABG). Only if the ABG is a minimum of 15 dB, it is considered to be clinically significant, especially at 4000 Hz.

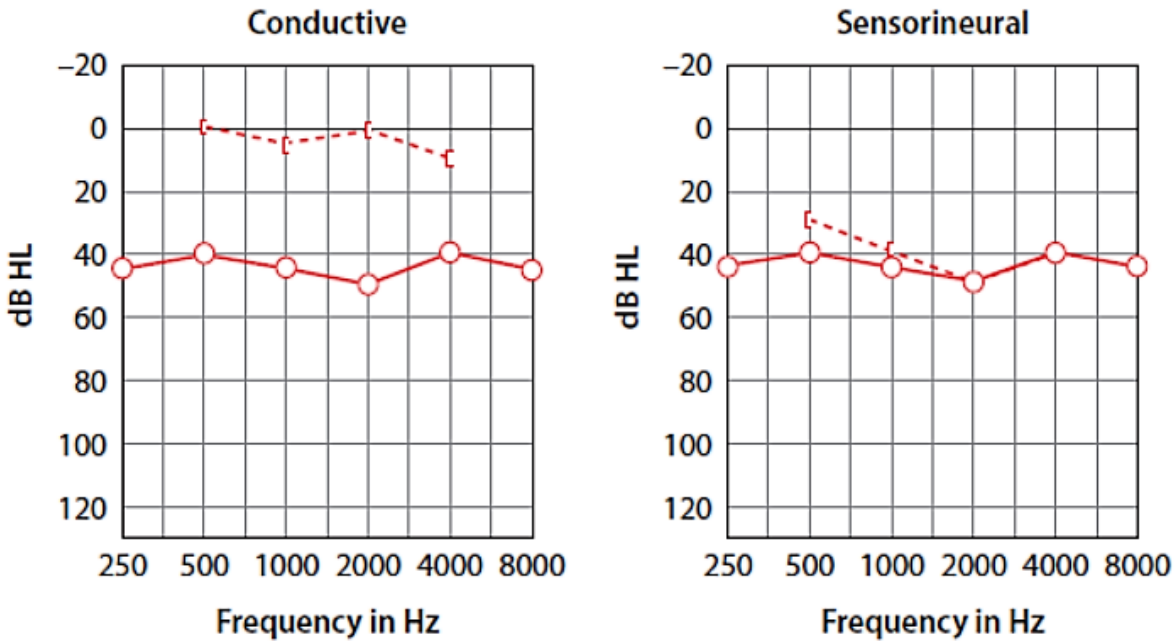


FIGURE-12 PURE TONE AUDIOGRAM IN CONDUCTIVE AND SENSORINEURAL HEARING LOSS

The picture shows a conductive hearing loss and sensorineural hearing loss in a pure tone audiogram. In conductive hearing loss the BC thresholds are normal and the AC thresholds are increased. There is significant ABG. In sensorineural loss, both BC and AC thresholds are increased. There is no significant ABG.

4. PERFORMANCE TESTING (PLAY AUDIOMETRY):

This test was first described by Ewing as a method that is suitable for children from two and a half years of age. It is also done in children with Down syndrome and other children with mental incapabilities, if they do not cooperate for pure tone audiometry. The principle is that the child is conditioned to wait for a sound. Then he responds with a play

activity, like throwing rings on a toy giraffe's neck. The child is conditioned by getting the child's attention first. He holds the response item like a coloured ring kept in front of the child. When a suprathreshold sound stimulus is presented, the examiner responds by throwing the ring on the neck of the giraffe. This sequence is repeated several times. This is also supported by the use of gestures like using a cupped hand over the ear to indicate listening. Then the child is given the response items, i.e. the rings, and he is guided to perform the task. When a correct response is done, the child should be encouraged by praising vocally and clapping. Once the conditioning is over and the child can perform the test without guidance, a flexible descending/ascending technique, similar to that used in pure tone audiometry is used. The interval between the presenting sounds should not be predictable and should be varied.

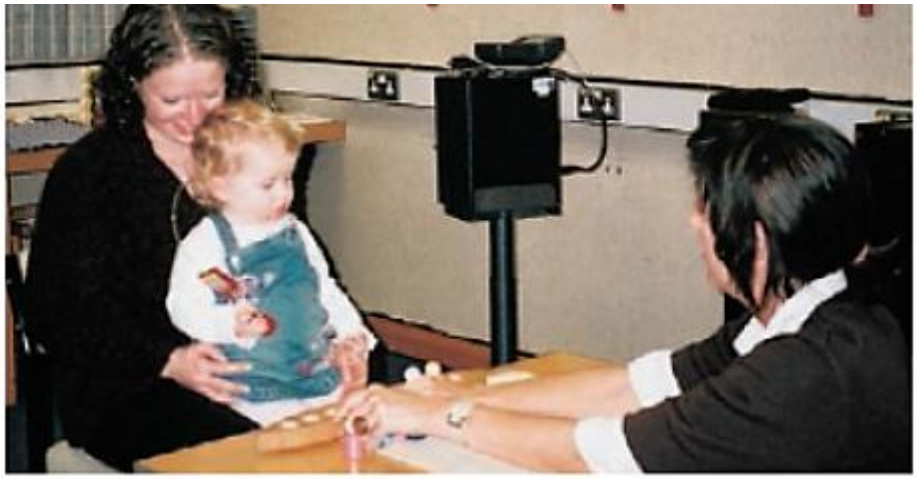


FIGURE-13 PLAY AUDIOMETRY

2.4 AUDITORY BRAINSTEM RESPONSE

1. INTRODUCTION

The excitation of the auditory neurons by auditory stimulus that is presented at the ear, results in electrical activity in the brain. This can be recorded at the scalp using electrodes. Its amplitude is small. This electrical response can be isolated from the background electroencephalogram (EEG). It is an average of the auditory electrical activity of the successive presentations of the auditory stimulus. This averaged auditory electrical response otherwise called auditory evoked potential (AEP) is used to decipher the relative wellbeing of the peripheral and central auditory regions. For example, if there is a reduction in amplitude of the evoked potential or if there is a prolongation of its latency, it may indicate an inability of the auditory neurons to respond efficiently to the stimulus. It may also reflect a decreased ability of the cochlea to respond to the sound and stimulate the auditory neurons. In both cases, the AEP would reflect auditory pathology.

There are various AEPs that are used by audiologists to diagnose hearing disorders. These potentials are the auditory brainstem response (ABR), middle latency response (MLR), and auditory late response (ALR). Most focus is on the ABR. It was initially used as a diagnostic measure in the detection of acoustic neuromas. Now they can be used in assessment of cochlear hearing sensitivity (i.e. threshold ABR). ABR is relatively unaffected by sleep or sedation. Thus, any patient with difficulty to test, or they are too young to assess the threshold by behavioral audiometry can often have their hearing thresholds quantified using the threshold ABR.

2. EVOKED POTENTIAL BASICS

AEPs occur due to synchronous activity in the auditory pathway that results from the presentation of an auditory stimulus. Activity in these auditory neurons or electrical generators creates an electrical field. It has a positive and a negative pole. To measure this activity at the scalp, at least three electrodes must be placed: an inverting electrode, non-inverting electrode and ground electrode (39).

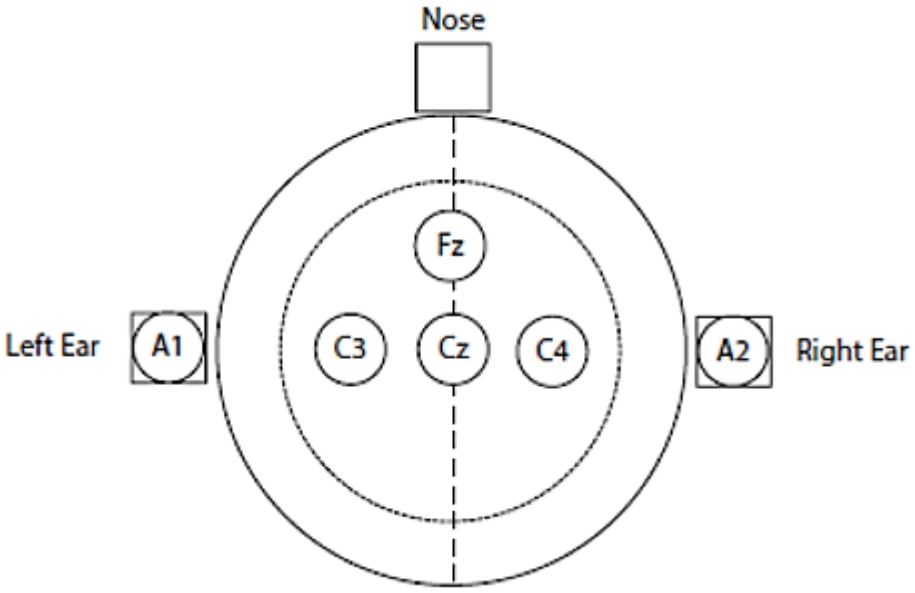


FIGURE-14 PLACEMENT OF ELECTRODES

The noninverting electrode is placed at Fz. The inverting electrode is placed at either A1 (for left-ear stimulation) or A2 (for right-ear stimulation). The ground electrode is placed on the forehead some distance below Fz. There are many sources of noise that can interfere with the acquisition of AEPs.

ABRs are evoked with a click stimulus. It is a 100 microsecond rarefaction or condensation square wave pulse. The rapid acoustic wave front of a click yields an abrupt stimulus onset. The abrupt onset provided by a click will frequently evoke well-formed ABRs. Other stimuli can be used to evoke AEPs. Tone bursts are sinusoidal and, relative to a click. The ABR makes use of shorter duration tone bursts.

Intensity level of stimulus is expressed as dB normal hearing level, or dBnHL. The reference for this dB unit is the average behavioral hearing threshold for normal hearing individuals. For example, if calibrating a click stimulus, an average behavioral threshold would be obtained to the click in a sample of normal hearing individuals. This threshold would correspond to 0dBnHL. And, any given dBnHL presentation level used in the clinic reflects how much higher or lower the presentation level was, relative to the average behavioral hearing threshold for normal-hearing individuals. For example, if an 80dBnHL presentation level was used, this would mean that the level was 80dB above the average normal behavioral threshold to the stimulus.

3. DIAGNOSTIC AUDITORY BRAINSTEM RESPONSE

Overview

The ABR is a response to auditory stimulus. It arises from the auditory nerve and low brainstem. It was first reported by Jewett and Williston (40)**.** They identified a complex that

would occur under 10msec after the onset of an auditory stimulus, comprised primarily of five potentials. These potentials, also called waves, are labelled from I to V. The earliest wave occurs near 1.5msec and the latest wave around 5.5msec in the normal auditory system. The waves were then correlated with various neural generators of the peripheral and the central auditory system (41–43)**.** Wave I reflects a neural response which originates from the distal end of the auditory nerve. Wave II originates from the proximal end of this nerve. Wave III originates from the cochlear nucleus. Wave IV originates from superior olivary complex and lateral lemniscus. And wave V originates from the lateral lemniscus and possibly the inferior colliculus. Frequently, waves IV and V will present as a complex, with wave IV at the peak and wave V as a smaller shoulder to this peak occurring later in latency. A negativity follows wave V.

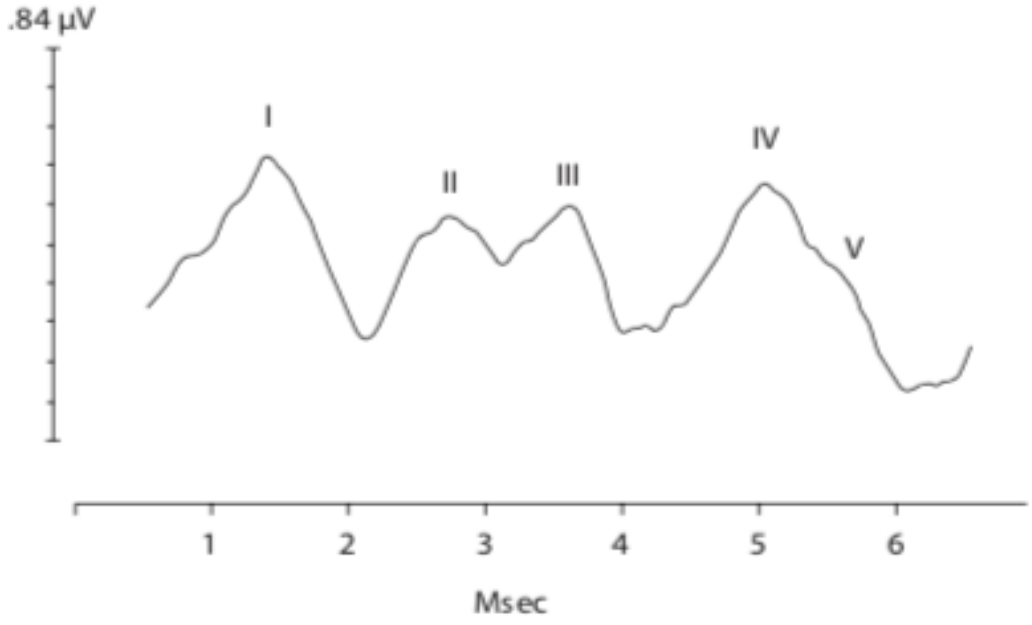


FIGURE-15 WAVES OF ABR

The ABR initially was used as a tool for diagnosis of retro cochlear pathologies, like acoustic neuromas. Presently it is being used as an estimate of hearing sensitivity for patients who are difficult to test by conventional methods.

4. DESCRIPTION OF DIAGNOSTIC PROTOCOL

Many stimulus and recording parameters can be used to acquire ABR. Even small changes in these parameters can affect the quality of the electrophysiological response. Given below is a description of recommended values for each parameter. The ABR is evoked separately from the left and right ears using these settings.

- **Stimulus:** 100msec click stimulus is mostly used to assess retro cochlear function using the ABR. Stimuli are administered through insert earphones for diagnostic ABR testing.

- **Presentation level:** It varies between 80dBnHL and 100dBnHL.

- **Polarity:** A rarefaction click stimulus will yield slightly earlier latencies than a condensation click. It is recommended that this polarity be applied in diagnostic ABR protocols.

- **Time window:** This refers to the duration over which the auditory system's response is recorded following a stimulus. Usually it is about 10–15msec to ensure full view of the ABR response.

- **Filters:** The electrical activity that is recorded from the scalp is filtered out both above and below the frequency range of the ABR response. The ABR electrical energy at the scalp is primarily around 100–3000Hz. Hence the filter is designed to pass energy in this

range only. Additionally, in infants the morphology of the ABR waves may be improved by using a lower high-pass setting.

- **Stimulus rate:** Neurons contributing to the ABR have relatively short refractory periods and, for this reason, the response is acquired at a relatively high stimulus rate of 20–30 clicks per second. A non-integral rate, such as 17.7 clicks per second, should be used to avoid the time locking of periodic noise sources. For fast-rate ABRs, the stimulus rate is increased to 77.7 clicks per second.

- **Number of trials:** At least 2000–3000 trials per recording are recommended. Another option is to acquire a response until a predetermined signal-to-noise ratio has been reached. This method may help to reduce test time.

- **Replications:** The clinical analysis of ABRs requires comments on whether the response was replicable or not. A replicable response appears morphologically similar across two waveforms. After 2000–3000 trials, the ABR is obtained a second time so as to ensure the reliability of the response. If the response in inconsistent a third waveform may sometimes be acquired.

5. DIAGNOSTIC ABR ANALYSIS

The presence of retro cochlear lesions, can affect characteristics of the latency and amplitude of the ABR waves. For example, an acoustic neuroma can prolong the time it takes a click stimulus to reach a particular neural generator. this delays the latency of the wave that arises from that generator and it can reduce the number of neurons being recruited for the response. The amplitude of the wave may also be reduced.

TABLE 52.1 Normal limits for diagnostic ABR indices	
Index	**Normative value (msec)**
Absolute latency of wave V	<6.2
Interwave latency I–III	<2.5
Interwave latency III–V	<2.4
Interwave latency I–V	<4.4
Inter-ear latency difference	<0.5
Fast rate shift	<1.0

FIGURE-16 NORMAL LIMITS FOR DIAGNOSTIC ABR

Latency is defined in two ways. It can be the absolute latency of the wave, which indicates the time it takes for the wave to occur post-stimulus onset, or it can be the interwave latency difference, which is the time it takes for the neural energy to be conducted from one neural generator to the next. Interwave latency differences are calculated as the difference between the absolute latencies of two ABR peaks. Interwave latency differences that are typically obtained are the I–III, III–V and I–V intervals.

Both absolute latency and interwave latency measurements can be delayed abnormally due to lesions that directly involve the ABR neural generators. Absolute latencies can also be delayed due to lesions that occur earlier in the auditory pathway. For example, an acoustic neuroma can delay the latency of wave V even though the lesion occurs in the vicinity of wave II. Also, interwave latencies may be prolonged by lesions that occur in between the two neural generators that contribute to the latency measurement. For example, a lesion between the neural generators of waves III and V will increase the latency of the III–V

interval even if the generators responsible for III and V may not be directly affected by the lesion.

Both absolute and interwave intervals are shown to be sensitive and specific to the diagnosis of retrocochlear abnormality.

Amplitude characteristics of the ABR are also examined to determine the presence of retro cochlear pathology. Amplitude is measured as the ratio of wave V to wave I (V/I). The amplitude is measured from wave peak to the nearest negativity that follows the wave. The ratio is calculated by dividing the wave V amplitude by the amplitude of wave I. The values less than 1.00 mean that wave V amplitude is below that of wave I. The specificity of this measure is relatively high (92%). But the sensitivity is low and this limits the diagnostic utility of this measure (44%) (44). As a result, amplitude is not used as commonly as latency measurements to diagnose any retro cochlear lesions.

6. MIDDLE EAR/COCHLEAR HEARING LOSS AND TEST INTERPRETATION

Middle ear or cochlear hearing loss negatively affect the latency and amplitude of the ABR peaks. They may sometimes complicate interpretation of the diagnostic ABR results. This type of hearing losses prolongs the latency and they reduce the amplitudes of ABR waves. In such circumstances it may not always be clear if these abnormal results are due to the middle ear/cochlear hearing loss or due to a retro cochlear lesion.

7. THRESHOLD AUDITORY BRAINSTEM RESPONSE

OVERVIEW

The ABR is used to obtain hearing threshold by electrophysiological assessment. ABR testing is used to estimate hearing sensitivity in many patients where reliable behavioral

audiometric results cannot be obtained. And it is commonly used in pediatric populations who are too young for a reliable visual reinforcement audiometry. Acquisition of the ABR can estimate the hearing sensitivity that would not be obtainable otherwise.

The morphology of the ABR at the threshold levels is slightly different from the suprathreshold response. When the level of the stimuli decrease, the latency of the waves increase. But the amplitude decrease (45)**.** This is because lesser number of neurons is recruited when less intense stimulus is given. Neuron firing also occurs less synchronously. ABR waves that occur earlier (wave I) are more affected when the changes in intensity occur, than the later waves (wave V). So, ABR may only show a wave V and at threshold when stimulus intensity is less. Therefore ABR threshold estimates are mostly made based on detection of waves I and V.

8. DESCRIPTION OF THRESHOLD PROTOCOL

The parameter settings of the equipment for the threshold ABR are similar to those used for that of the diagnostic ABR. Because the lower stimulus levels that are used in the threshold ABR increase the latency of the ABR peaks, the window time used is longer, between 15msec and 25msec. In addition to this a greater variety of stimuli are used when. The click provides a good estimation of hearing at 2000–4000Hz in many clinical groups (46–48)**.** It is suggested that tone bursts may also be used in the assessment of hearing threshold via ABR. Therefore, low (e.g. 500Hz) and mid-frequency (e.g. 1000Hz) stimuli are added to the protocol. This gives a complete evaluation of the patient's hearing.

The threshold ABR evaluation begins by assessing the click ABR at suprathreshold levels (e.g. 70dBnHL). This provides a good template response for the subsequent click ABR responses. The suprathreshold ABR is done by giving condensation and rarefaction clicks.

This also tests for auditory neuropathy. Getting a suprathreshold response also allows for the evaluation of retro cochlear pathology.

Once the suprathreshold ABR is obtained, the threshold is determined for all the frequencies in the protocol. The threshold level is the lowest level at which wave V is present.

Another way of assessing the threshold is by modified Hughson–Westlake procedure (49)**.** It is used in a similar way to how it is done in pure- tone behavioral audiometry.

ABR must be tested when the patient is totally relaxed or is sleeping so as to minimize an artifact that may be generated by muscle movement. Sometimes, the time taken to complete the test may be limited. It may be interrupted or terminated early if the patient wakes up. Many follow-up appointments may be necessary to obtain complete results in newborns.

Sedation is necessary for patients difficult to test. Sedation provides the uninterrupted time required to perform a thorough examination.

9. CORRELATION BETWEEN ABR AND BEHAVIOURAL THRESHOLD

The aim of doing the threshold ABR is to comment on the patient's sensitivity of hearing. There is a strong correlation between the two. ABR thresholds to clicks show a high degree of correspondence with some behavioral thresholds. There is a strong correlation between the pure- tone average of 2000Hz and 4000Hz and the ABR click threshold. There is an 89% shared variance (47)**.** But the mean difference between the click ABR threshold and this pure-tone average threshold is about 1dB and it can be up to 35dB.

10. CONTRALATERAL MASKING, CONDUCTIVE HEARING LOSS AND ASYMMETRICAL HEARING

Many a time, it is necessary to use a contralateral masking stimulus so that the contribution of the non-test ear is eliminated. When the poorer hearing ear of a unilaterally deaf subject is tested, a response from the contralateral ear can be evoked. This can be successfully eliminated by sufficiently masking that ear (50). The contralateral masking does not influence the ipsilateral waveform (51).

Interpretation of the threshold ABR in cases of conductive hearing loss and asymmetrical hearing should be specially considered. In case a unilateral conductive hearing loss is suspected, the degree of hearing loss that is contributed by the conductive component determined. It is done by obtaining bone-conduction ABR thresholds. Stimuli for bone-conduction can be elicited by an approach similar to that of behavioral thresholds. It is done by placing a bone vibrator on the mastoid process. The contralateral non-test ear of the contralateral side must be masked while assessing the bone conduction threshold of the test ear.

Bone conduction testing has quite a few limitations. 1) The responses that are evoked are more susceptible to stimulus artifact. This decreases the morphology and detectability of ABR waves. So, to minimize this effect, alternating polarity stimuli can be utilized. 2) The artifact may be high even at the mid-intensity levels. Hence the maximum reliably elicited intensity level of bone conduction is often lower than that which is obtained by air conduction. 3) there is a difference in the stimulus spectrum between that conducted through earphones and that conducted through the bone oscillator (52)**.** This implies that there would be a difficulty in equating air and bone conduction thresholds in the hearing impaired. But,

in normal hearing individuals the ABR threshold for air and bone conduction yield a similar result despite the presence of spectral differences. A latency–intensity function can determine if there is contribution from conductive hearing loss (53)**.** The wave V latency is inversely proportional to the intensity of stimulus. When wave V latency is plotted as a function of the intensity of stimulus, a predictable curve is generated in normal hearing subjects. The latency of wave V increases as stimulus intensity decreases. Conductive hearing impairment shifts the latency in the curve. This is relatively equal at all intensities. It causes no change to the slope of the curve. But, in a sensorineural hearing loss there is a greater deviation from normal latency for those stimuli that are closer to the threshold. This causes an increase in the slope of the latency–intensity curve. So, it is from this method the latency–intensity function may be used to differentiate between conductive and sensorineural hearing loss.

When bilateral conductive hearing loss is present, there may be a masking dilemma for the examiner. When assessing cochlear hearing with the help of bone oscillator, contralateral masking is required to prevent the contralateral cochlea from responding. But, when the masking level in the contralateral ear is increased to an intensity more than the level of conductive hearing loss on that side, the masking signal crosses over to the cochlea in the test ear. This increases the bone-conduction threshold in the test ear. This phenomenon therefore creates a condition in which bone conduction thresholds cannot be assessed by standard methods.

11. CENTRAL MATURATION

The ABR morphology changes with age through the first few years of life. When high-intensity stimuli is given, ABR response emerges at 28–32 weeks gestational age (54)**.** A

response with three repeatable peaks is present by 35 weeks gestational age. A relatively well defined full five-peaked response emerges in the first months of life. The ABR morphology similar to adult response emerges by 1–3 years of age.

2.5 ABR IN DOWN SYNDROME CHILDREN

The ABR latencies are shorter for Down syndrome infants, older children, and adults as compared to their age-matched, typically developing peers

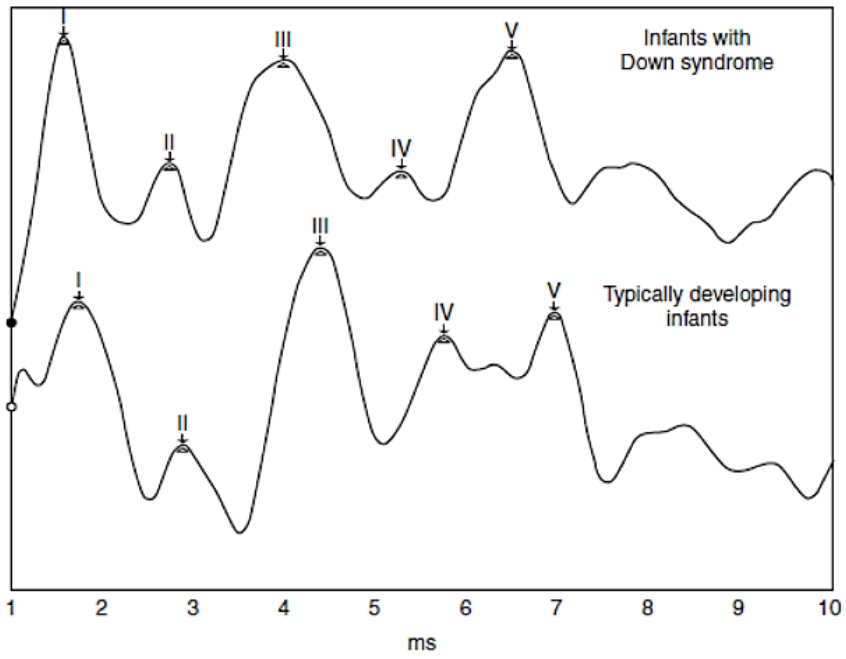


FIGURE-17 ABR WAVEFORMS TO A MODERATELY-HIGH INTENSITY STIMULI FOR HEALTHY INFANTS WITH DOWN SYNDROME AND TYPICALLY DEVELOPING INFANTS

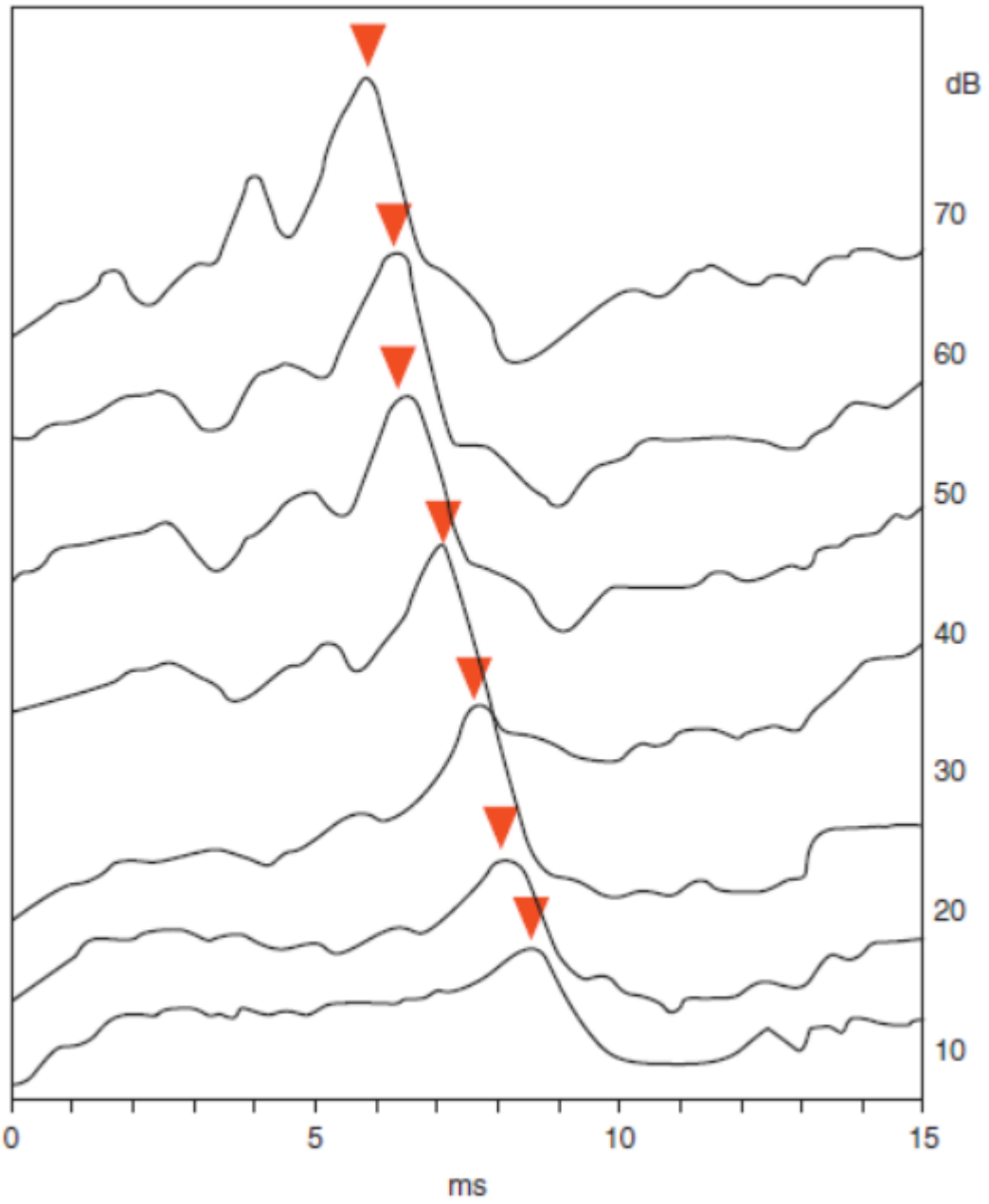


FIGURE-18 AUDITORY BRAINSTEM RESPONSE (ABR) WAVE V AT VARYING INTENSITY LEVELS. WAVEFORMS ARE LARGER AND MORE DISTINCT AT LOUD INTENSITIES (E.G., 70 DB) COMPARED TO SOFT INTENSITIES (E.G., 10 DB)

Aim and Objectives

3. AIM AND OBJECTIVE

Aim:

1. To ascertain the value of Pure Tone Audiometry and Auditory Brainstem Response in children with Down syndrome.

2. To see if these tests can be included in the routine screening of children with Down syndrome.

3. Detection of hearing deficits such as early onset presbycusis can lead to early intervention which may improve their quality of life.

Objective :

1. Using Pure Tone Audiometry to measure the auditory threshold of the child.

2. Using Auditory Brainstem Response (ABR) to assess the retro cochlear region by way of eliciting brainstem potentials in response to audiological click stimuli.

3. Using these tests, in combination with otological examination to diagnose the degree and nature of (conductive, mixed, sensorineural) hearing loss, in comparison with age and sex matched controls of the normal population.

Materials and Methods

4. MATERIALS AND METHODS

The study was conducted in the year between 2018-2019 in the Institute of Physiology and Experimental medicine, Madras Medical College, Chennai. This study was done after getting approval from Institutional Ethics committee, Madras Medical College, Chennai.

4.1 Subject Selection:

60 children were assessed, comprising of 2 groups. Group 1 had 30 children with Down syndrome and group 2 had 30 children from the normal population. The children were age and gender matched, in the age group of 5 to 15 years. The children were selected from the institute of child health and hospital for children, Egmore, Chennai – 8.

4.2 Inclusion Criteria:

1. Children with Down syndrome in the age group of 5 to 12 years

2. Children who are age and gender matched and otologically healthy.

3. Mild to moderate mental retardation.

4.3 Exclusion Criteria:

1. Children having external ear occlusion or obstruction.

2. Children having active middle ear infections.

3. Children with CNS abnormalities.

4. Severe to profound mental retardation.

4.4 STUDY DESIGN: Comparative cross sectional study

4.5 EXAMINATIONS

A. General examination

B. Specific ENT examination

Both the control and study group individuals were subjected for basic ENT examination. It includes external ear examination, tuning fork tests like Rinne's test and Weber's test and otoscopic examination. Children who had ear wax had it removed by syringing. The ear canal was cleaned completely.

1. PURE TONE AUDIOMETRY:

Pure-tone thresholds by air conduction were established for frequencies ranging from 125 to 4000 Hz. The children who were cooperative were tested in an awake and relaxed state. The electrodes were placed over both mastoid processes at the hairline. Air-conducted stimuli were presented via inserted earphones. The frequencies were modulated with respect to amplitude and frequency. A 100% amplitude modulation was used, and 20% frequency modulation was used.

For those children who were uncooperative to insert headphones and those who were afraid of sound in their ears, free field audiometry was done. Whenever the child heard the sound presented to him, he would throw a colourful ring on the neck of a toy giraffe. The child was already conditioned to do this by his mother. The mother was instructed to train him by making him throw an object when she made a clap sound. This conditioning was done by the mother for one week prior to the test.

2. AUDITORY BRAINSTEM RESPONSE:

It was done by Computerized Neurostim, Medicaid system.

Apparatus for BERA

"The apparatus for eliciting ABR were set as per the "Recommended standards for the clinical practice of evoked potentials" which is introduced in Guideline 9A: Guidelines on evoked potential, by the American society of Clinical Neurophysiology."

Pulse generator :

The stimulus was given in the form of clicks or tone pips. It was conducted into the ear through a transducer placed in the headphone.

Recording electrodes

Three recording electrodes were placed as per the International 10-20 electrode placement system.

1. Active electrode- placed on the ipsilateral mastoid process
2. Reference electrode- placed on the vertex.
3. Ground electrode-placed in front of reference electrode

There are two types of electrodes that are used during recording processes.

1. Needle electrodes
2. Surface electrodes

The surface electrodes are commonly used. It does not produce pain

sensation and infection rate also reduced. The subject is asked to wash his/her hair before coming for examination for easy application of electrodes. Disc electrodes of 1cm size and with conducing jelly or paste are used. <5 kilo ohms of electrical impedance are used for good recording.

Filters

A filter is a device that restricts selectively the frequency domain of the signal. Frequency band pass means frequency range of a signal transmitted through the filter.

- Stop band means signal rejected in that particular frequency range.
- Transition lies between the frequency and stop band.

Uses

1. Noise elimination

2. Optimal recording

3. To obtain typical wave forms

Low frequency filter-It removes slowly changing low frequency and allows higher frequencies. It also known as high pass filter.

High frequency filter- It removes rapidly changing high frequency and allows low frequencies. It is also known as low pass filter.

Amplifier

500000 times of amplification is needed before being displayed due to following reasons.

1. Biological signals are small

2. Intrinsic impedance of electrode. It changes with frequency and electrode type used.

3. Impedance of electrode- skin

For the measurement of any electrical activity including action potential which is generated in central nervous system, nerve or muscle should flow through the ground lead.

Electrode impedance produces a drop in the amplitude of the action potential. It amplifies the attenuated action potential. Action potential reaching the amplifiers is attenuated action potential. The impedance of the amplifiers should be greater than electrode impedance to reduce this attenuation. A100:1 ratio of electrode to amplifier impedance is maintained across the range of frequencies in the waveform under study.

1. Due to amplification waveforms distortion are minimized

2. Improves noise rejection.

Signal average

It is difficult to measure electrical activity of brain using sound stimuli given to the ear. Because spontaneous electrical activity is generated within the brain (Back ground potential).So the electrical activity set up in the brain in response to sound stimulus gets masked by spontaneous electrical activity occurring in the brain.

It used to extract small signals. Because it is hidden by large noise like evoked potential buried in EEG. Evoked electrical activity is time specific which occurs at a fixed point of time after the sound stimulation but spontaneous electrical activity occurs randomly and it is

not time specific. By averaging, the time locked signals become prominent and stored in machine.

Electrical safety; All instruments were checked periodically to protect from shock during power fluctuations.

Recordings procedure of BERA

The recording was done in semi darkened and quiet room. The children were asked to wash their hair on the morning of recording. This would make them feel a bit sleepy. The children who did not cooperate were given syrup pedichloryl. The amount was given according to their body weight. The electrodes placing areas are cleaned. Active, reference & ground electrodes were kept in appropriate places. Below 5 kilo ohms levels of resistance was used. Auditory stimulus consisting of clicks of 100 µsec were given in one ear .It was given through electrically shielded ear phones at the rate of 11.1 clicks/sec.

Another ear was masked by pure white noise of 40 dB. This is to prevent false response. To filter out undesirable frequencies in the surroundings we had to use band pass of 150-3000 Hz. Responses to 2000 clicks presentations were averaged.

A graph is plotted to show the result. X-axis contains time (in milliseconds from the onset of stimulus).Y-axis contains amplitude (in µvolts).5-7wave or peaks are seen within 8-10 milliseconds. It is marked with Roman numerals.

Waveforms were analyzed for the following characters.

Latency, Amplitude, Morphology

It gives information about cochlear and retro cochlear function.

Wave I

It gives information about potentials generated in the peripheral part of 8th cranial nerve. It is a prominent initial peak confined to ipsilateral ear and is absent in contralateral ear. It appears 1.5 ms after the application of stimulus .It is decreased in patients with peripheral hearing impairment

Wave II

It is appears as small peak. It appears 2.8ms after application of stimulus. It is absent in lesions of the cochlear nucleus.

Wave III

It is a prominent peak followed by a prominent trough. It appears 3.9 ms after the click stimulus. It is absent in superior olivary nucleus lesion.

Wave IV

It appears as peak in the up going slope of after 5.1ms. Wave IV is absent in lateral lemniscus lesion

Wave V

It is the most prominent peak. It appears 5.5 msec after the stimulus. It is absent inferior colliculi lesions. This wave component is analyzed most often in clinical applications

Wave VI and VII

These waves take origin from subcortical structures like medial geniculate body and auditory radiation. It appears 7.3 and 9.6 ms after initiation of stimulus.

Wave forms interpretation

The parameters taken into consideration for studying the waveforms of ABR are

Absolute latency; It is the time interval and it is measured by milliseconds. It is starting point of stimulus to the peak of the wave.

Absolute amplitude; It is measured in microvolt. It is marked as the height from the peak of the wave to its trough. It is measured by microvolt. Amplitude of the waves is not as constant as latency and not reliable.

Inter peak latency (IPL): The duration between two different waves in the same ear is known as inter peak latency. It is also known as inter wave latency. There are three inter peak latency most commonly used.

1. I-V - latency difference between wave V and I. It denotes the conduction from proximal VIII nerve through pons to midbrain. Normal duration is 4msec. It is shorter in young women and in older men becomes longer. It is prolonged in demyelination, ischemia, tumors, and brain damage due to hypoxia.
2. I-III - it is a latency difference between wave I and III .It denotes conduction from VIII nerve across subarachnoid space. Normal is 2.1msec.It is prolonged in tumor or inflammation affecting the proximal portion of the VIII nerve.
3. III-V - It denotes conduction from lower pons to midbrain .Normal duration is 1.9msc

Amplitude ratio of wave V/I: Wave I is generated outside and wave v is generated inside the central nervous system. This is used to compare the relationship of the expected signal amplitude. Normal ratio is 50 %and 300% if ratio exceeds 300%, it shows peripheral hearing impairment. If ratio is lower than 50%, it denotes central hearing loss.

Inter aural latency difference: It should be less than 0.5msec.It is the time

interval between the two ears for same wave during supra threshold stimulus

Technical factors

Stimulus rate: Number of clicks is given. It is 10-70times/seconds

Intensity of the sound stimulus; High intensity- wave I is decreased with prolonged I-V IPL. With decreasing intensity-I, III, V waves are present. Still lower intensity (10dBSL) V wave is seen.

Stimulus phase or polarity: The pulse can move towards or away from the ear. Movement toward the ear is called condensation phase moves away from the ear it is called as rarefaction phase.

Filter: lower frequency filter -100 or 150 Hz

High frequency filter- 3000 Hz

Nature of sound: Click stimulus was given for 1ms duration. The stimulus applied is usually square wave pulse. The sound stimuli delivered at 50-60 db above the hearing threshold.

Binaural/monaural stimulation: In clinical studies, monaural stimulation is recommended. If both ears are stimulated the amplitude of the waves III, IV, V are increased.

Nontechnical factors

Age: Older adults have longer I-V IPL by 0.1-0.15ms

Temperature: The absolute latency (7% for 1 Celsius) and IPL are prolonged on lowering body temperature.

Hearing status; Ear canal examination and hearing should be tested.

Drugs: "BAEPs are resistant to the effect of drugs, but a slight prolongation of V wave latency with barbiturates or alcohol is attributed to the lowering of temperature"

Terminologies used in evoked potential study

Hearing level - It refers to the number of decibels of intensity compared to the threshold of hearing in a group of normal persons. Zero means threshold at which a normal subject can just perceive 50% of stimuli.

Sensory level (dB SL) - Zero is defined as the point at which the individual can barely appreciate the stimulus.

Decibel (dB=1/10 Bel) - It is defined as '20 log (P1/P2)', where P1 is the intensity of the sound to be measured and P2 is the intensity of the reference sound

4.6 STATISTICAL ANALYSIS

It was done using unpaired student t test. SPSS version 17 was used for data analysis.

Results

5. RESULTS

30 children with Down syndrome were assessed audiologically by pure tone audiometry and brainstem evoked response audiometry in the age group of 5 to 15 years. Age and sex matched controls were also assessed similarly. Therefore 60 ears were examined in both the study group and the control group. All the children underwent otoscopic examination and cleared of any cerumen in the canal.

5.1 PURE TONE AUDIOMETRY FINDINGS

Table 1 - Comparing PTA between study group and control group

Parameters	Study group (n=60)[#]	Control group (n=60)	P value
Pure tone average (dB HL)	16.2166 ± 7.7089	2.9666 ± 3.1513	< 0.0001****

- 3 children (6 ears) were not cooperative.

The pure tone average of the three frequencies - 500 Hz, 1000 Hz and 2000 Hz was calculated. The pure-tone audiometry test required absolute cooperation by the study group and was done only on 54 children. The test was not performed on 3 children (6 ears) due to their inability to cooperate during the examination. The results showed that 25 ears suffered

from conductive hearing loss (>16 dB average). Of these, 18 ears had minimal hearing loss (16 - 25 dB HL), 7 ears had mild hearing loss (26 - 40 dB HL). 29 ears had hearing within normal range (0-15 dB HL). Table 1 shows that a comparison was done between pure tone average between study group and control group and an unpaired student t test was done. It was found to be extremely statistically significant with hearing loss found more in children with Down syndrome.

In table 2, a comparison was made between PTA values of male and female children with Down syndrome. 2 male children and 1 female child did not cooperate for the test. The values were compared using unpaired student t test and it was not found to be significant. This shows that males and females are equally affected and there is no preponderance for hearing loss for a particular sex.

Table 2 - Comparing PTA between male and female study groups

Parameters	**Males with Down syndrome (n=32)**	**Females with Down syndrome (n=28)**	**P value**
Pure tone average (dB HL)	**15.7142 ± 9.6091**	**16.7576 ±5.9940**	**0.6217 [ns]**

ns – not significant

5.2 ABR FINDINGS

The results of latencies and amplitudes for the two groups are described in Tables 3 to 10. 60 ears were tested in each group.

Table 3 - Comparing BERA wave I between study and control group

Parameters	**Study group (n=60)**	**Control group (n=60)**	**P value**
BERA wave I amplitude	**1.66 ± 0.15**	**1.67± 0.14**	**0.9835^{ns}**

ns – not significant

Table 4 - Comparing BERA wave II between study and control group

Parameters	**Study group (n=60)**	**Control group (n=60)**	**P value**
BERA wave II amplitude	**2.75 ± 0.15**	**2.73 ± 0.13**	**0.9722^{ns}**

ns – not significant

Table 5 - Comparing BERA wave III between study and control group

Parameters	Study group (n=60)	Control group (n=60)	P value
BERA wave III amplitude	3.72 ± 3.722	3.69 ± 0.17	0.3456[ns]

ns – not significant

Table 6 - Comparing BERA wave IV between study and control group

Parameters	Study group (n=60)	Control group (n=60)	P value
BERA wave IV amplitude	4.81 ± 0.16	4.78 ± 0.16	0.4489[ns]

ns – not significant

Table 7 - Comparing BERA wave V between study and control group

Parameters	Study group (n=60)	Control group (n=60)	P value
BERA wave V amplitude	5.79 ± 0.29	5.65 ± 0.14	0.2193[ns]

ns – not significant

Table 8 - Comparing BERA IPL I - III between study and control group

Parameters	Study group (n=60)	Control group (n=60)	P value
BERA IPL I - III	2.04 ± 0.21	2.01 ± 0.19	0.5474[ns]

ns – not significant

Table 9 - Comparing BERA IPL III - V between study and control group

Parameters	Study group (n=60)	Control group (n=60)	P value
BERA IPL I - III	**2.07 ± 0.33**	**1.96 ± 0.23**	**0.0426***

* - statistically significant

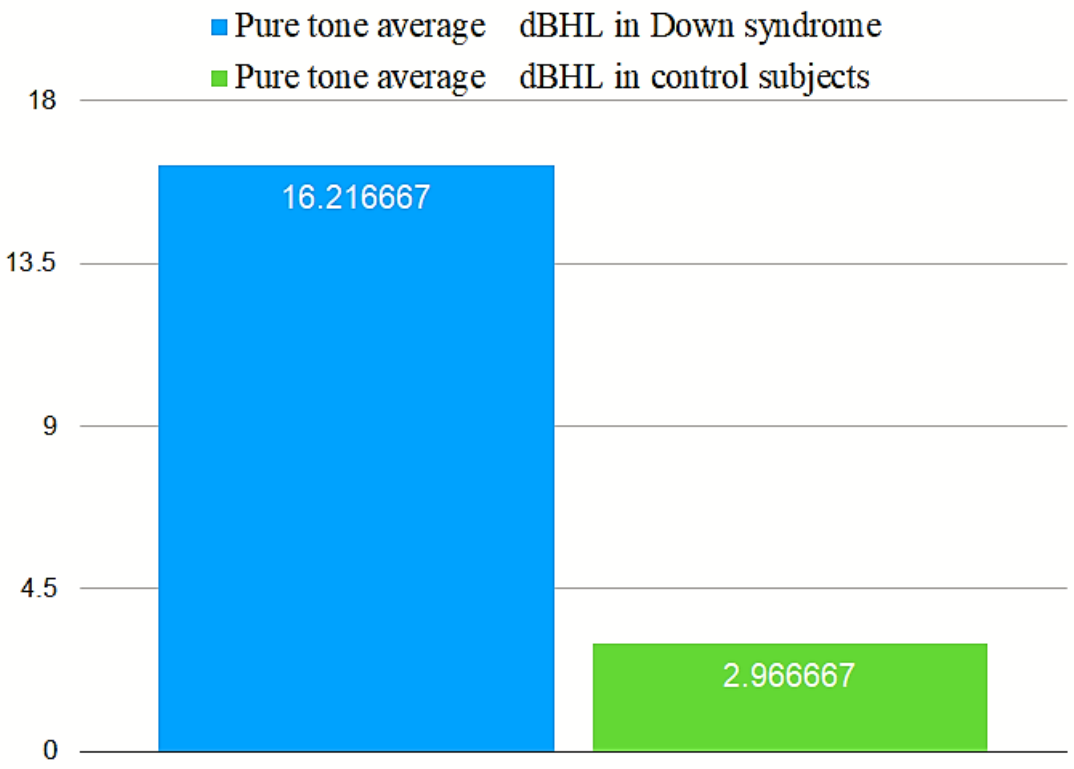
Table 10 - Comparing BERA IPL I - V between study and control group

Parameters	Study group (n=60)	Control group (n=60)	P value
BERA IPL I - III	**4.11 ± 0.31**	**3.97 ± 0.22**	**0.0059****

** - statistically very significant

The values of amplitudes of waves I to V and interpeak latency I - III showed no significance suggesting there is no significant sensorineural component to the hearing loss. But the interpeak latency of waves III - V showed significantly increased values in the study

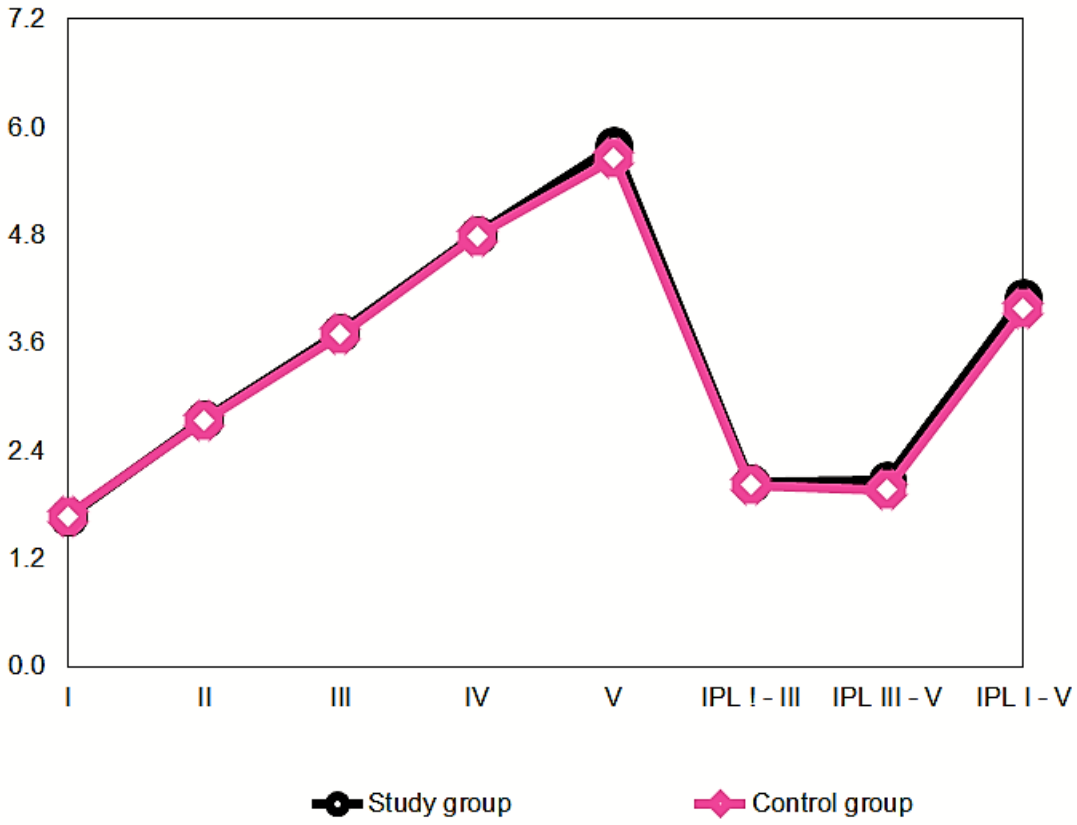
group and the interpeak latency of waves I - V showed a very significant increase in the study group compared to the control group.



GRAPH 1 – COMPARISON OF PURE TONE AVERAGE BETWEEN CHILDREN WITH DOWN SYNDROME AND CONTROL GROUP

Graph 1 shows the comparison between the pure tone averages between the two groups – children with Down syndrome and normal children.

Graph 2 shows the ABR comparison of absolute latency and inter peak latencies between the two groups



GRAPH 2 - WAVE PATTERN IN ABSOLUTE LATENCY AND INTER PEAK LATENCIES IN 30 IN DOWN SYNDROME SUBJECTS (60 EARS) AND 30 CONTROL SUBJECTS (60 EARS)

Discussion

6. DISCUSSION

Bradley McPherson (55) did a study on the hearing loss in children with Down syndrome. A high point prevalence of hearing impairment (78% by ears) was found in Chinese school – aged sample of children with Down syndrome. The degree of hearing loss was mostly mild to moderate. Pure tone audiometry could not be reliably performed on children under 3.5 years of age.

A study done by Saliba et al (56) suggests that ABR testing was done to determine the hearing threshold for all subjects. The average hearing threshold was estimated at 45.88 ± 7.25 dB HL (range was 20–80 dB HL). Wave I, III, and V latencies showed no prolongation at different stimulus intensity levels. ABR hearing thresholds of 50 dB nHL or less were considered having normal hearing levels. Therefore, 17 ears disclosed impaired hearing thresholds. The authors also say that "It is possible to prescribe and fit a hearing aid to a young infant based on data obtained from an ABR assessment. However, it should be noted that the thresholds estimated from the ABR are typically higher when compared to behavioral thresholds. In fact, they can be as much as 20 to 30 dB higher depending on the frequency. This is a significant difference in terms of intervention. Therefore, a correction is applied to the ABR threshold estimates to better predict the behavioral threshold. This corrected ABR is sometimes referred to as the eHL, to distinguish it from a typical ABR referenced in the nHL."

A study was done showing ossicular anomalies in children with Down syndrome by (57)**.** It's these anomalies that cause hearing defects. Temporal bones of infants of Down syndrome who died due to serious congenital anomalies were dissected and histopathological examination was done. They found malleus and incus of some ears to have severe inflammation and the stapes was deformed in some ears. There was also

inflammation of the middle ear mucosa. They also performed surgeries on living children with Down syndrome. A 16-year-old girl with Down's syndrome was found to have bilateral conductive hearing loss, with pure-tone averages of 35 dB and 60 dB. Exploration of the left middle ear showed that the malleus and incus were normal in shape and were mobile. The neck of the stapes superstructure was abnormal with an exaggerated curvature of the posterior crus and an extremely. Short, straight, and narrow anterior crus. The stapes was noted to be fixed on palpation.

Another surgery was done on a 12-year-old girl with Down's syndrome. She had a 60-dB conductive hearing loss on the right and a 30-dB conductive loss on the left had previously had tympanostomy tubes with no change in hearing levels. Exploration of the right ear showed the long process of the incus to be shortened but in contact with the head of the stapes. A small area of anterior fixation of the stapes footplate was noted, but the ossicular chain was intact.

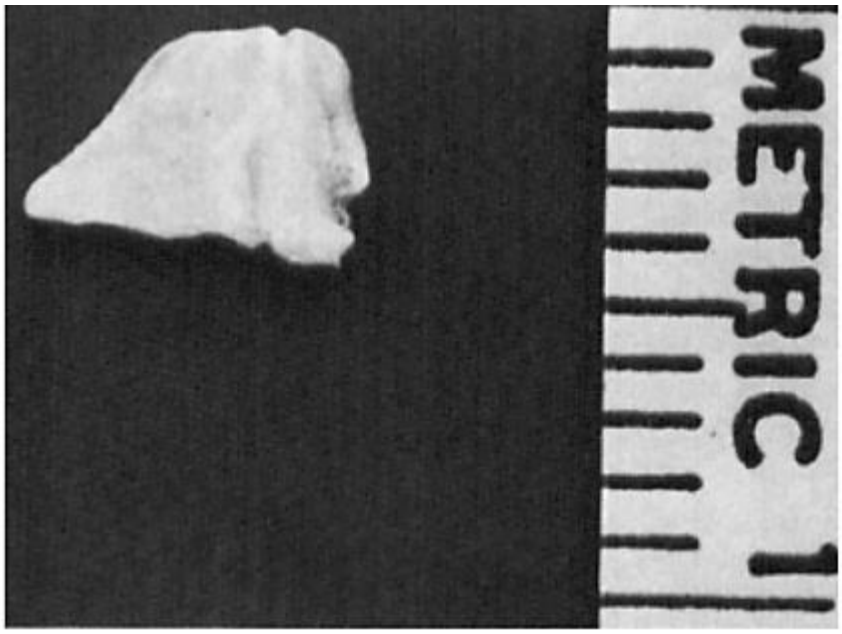


FIGURE-19 FUSED MALLEUS HEAD AND BODY OF INCUS

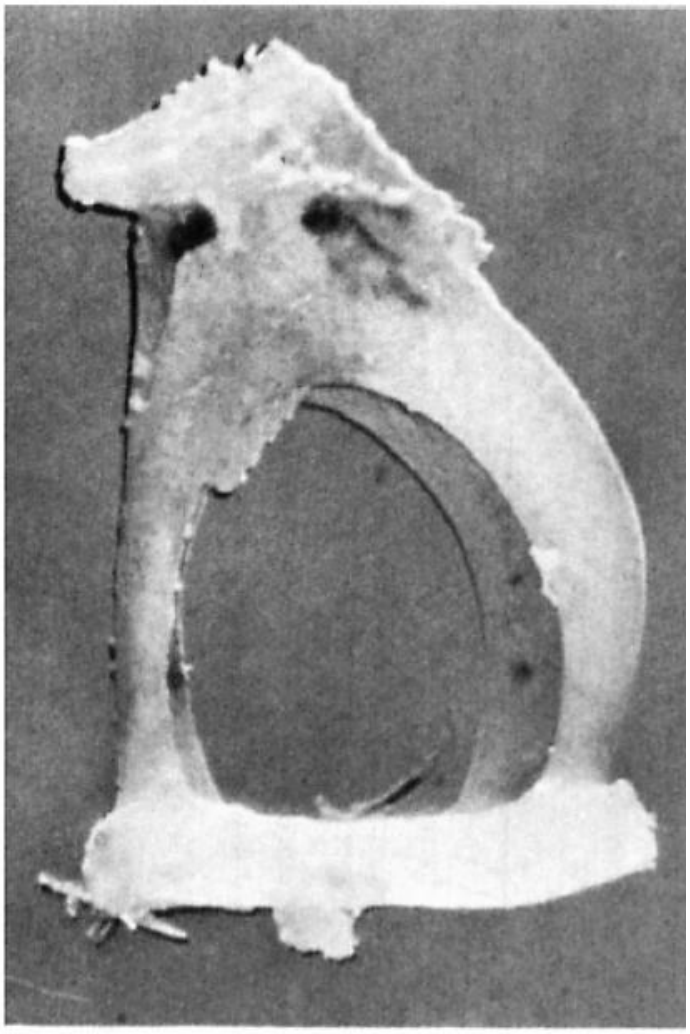


FIGURE-20 DEFORMED STAPES

A study done (58) in Brazil, on auditory evoked potentials in children and adolescents with Down syndrome showed that these children had showed increased latency values of P1, L1 and P2 in both ears compared with the control group

($p < 0.001$). The amplitude analysis did not show a major difference between the groups for the ranges of P1N1 and N1P2 in both ears.

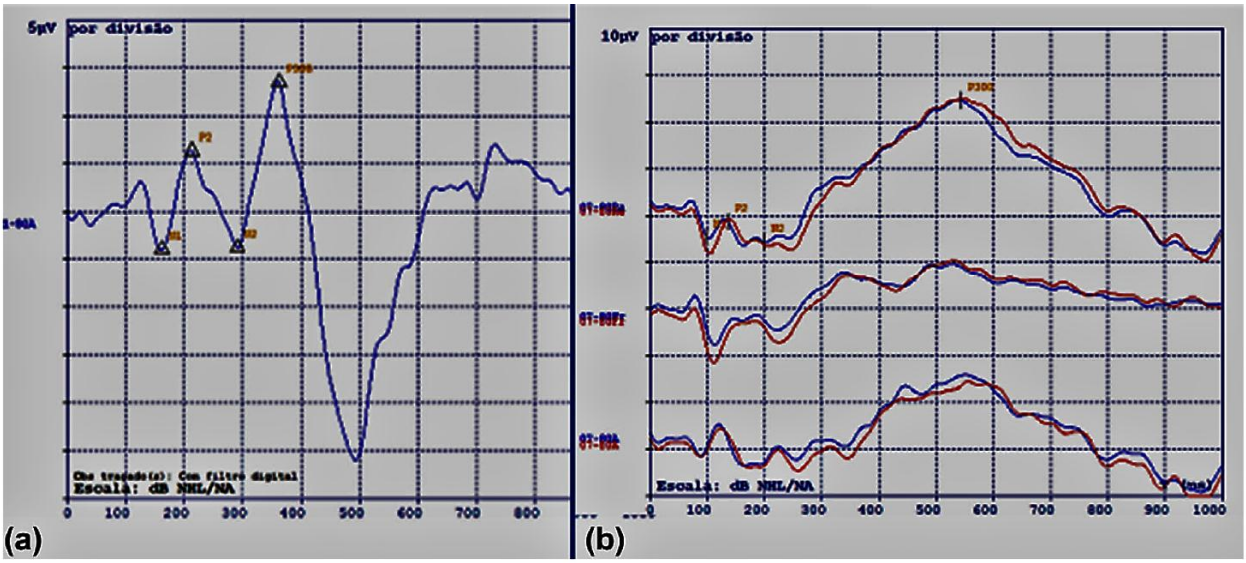


FIGURE-21 AUDITORY EVOKED POTENTIALS OF ONE CONTROL GROUP PATIENT (SHOWING NORMAL RESULTS) (A) AND ONE OF THE RESEARCH GROUP, WITH DOWN SYNDROME, REVEALING LATENCY DELAY (B), RESPECTIVELY (58)

Also another study (34) done on of 152 participants ranging in age from approximately 5 to 60 years of age compared data collected from individuals with Down syndrome to data from individuals with intellectual disabilities but no syndromic association. A decrement in high-frequency hearing sensitivity was seen in a group of individuals with Down syndrome as young as 11–20 years of age.

Conclusion

7. CONCLUSION

Audiological evaluation of children with Down syndrome was done. The main purpose of early identification of hearing loss is to initiate early intervention. Also, hearing technology can be fitted. Behavioral issues like frequent removal of the hearing aid or retention of the hearing aid due to stenotic ear canal can pose a challenge in using hearing aids. Chronic ear infections are also a major drawback. When secretions are present in the external ear canal, the ear molds can obstruct proper aeration of the middle ear. The different types of hearing aids include behind-the-ear (BTE) or in-the-ear (ITE) models, and bone-anchored hearing aids (BAHAs). Frequency-modulated (FM) systems can also be used. It improves the audibility for the children, especially in a classroom environment. Because, here a considerable background noise is present. These FM systems transmit the signals like a teacher's voice through a microphone using FM waves. It is directed to a receiver, which is coupled to a hearing aid (personal FM system). This amplifies the signal and reduces the influence of background noise, thus improving audibility.

If the child suffers from profound hearing loss, conventional techniques of sound amplification will not be enough. They may require a cochlear implant. It is a surgically implanted device with electrodes that are coiled into the cochlea to stimulate the auditory nerve with electrical current.

Limitations of the study: The sample size is small. A larger sample size will be better in getting more accurate results.

Summary

8. SUMMARY

Different types and varying degrees of hearing losses occur individuals with Down syndrome. The majority type of hearing loss is of conductive type. A smaller proportion of individuals with Down syndrome may also have sensorineural hearing loss. Still, the prevalence of both sensorineural and conductive hearing loss is much more than that present in the general population.

The auditory system is affected due to many reasons like (1) stenotic EAC, (2) malformation of the malleus, incus, and stapes, (3) malformation of the cochlea, (4) alteration in the rate of neural transmission at the level of the brainstem as well as at the level of the cortex, and (5) narrowing of the Eustachian tube and surrounding structures.

Diagnosis can be difficult in children with Down syndrome. And when hearing loss is identified, any kind of intervention could be problematic. However, these challenges should not preclude to the use of the hearing technology. Management of hearing loss for individuals with Down syndrome might require device modifications or more diligent monitoring of hearing technology, but these efforts can help individuals with Down syndrome maximize their communicative and cognitive potential.

The findings of this study show that 23% of the children had some degree of conductive hearing loss. There was not a significant sensorineural component to the hearing loss in children with Down syndrome. ABR is an excellent tool in identification of hearing loss especially in children who are unable to cooperate. This study identifies that many children with Down syndrome suffer from audiological development which affects their communication skills. But identification will allow us to intervene early and improve the quality of their lives, so that they are better accepted by their families and the society.

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Annexures

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.Fidha Parvez Khan.F.
Post Graduate in M.D. Physiology
Institute of Physiology and Experimental Medicine
Madras Medical College
Chennai

Dear Dr.Fidha Parvez Khan.F,

The Institutional Ethics Committee has considered your request and approved your study titled **"ASSESSMENT OF HEARING DEFICITS IN CHILDREN WITH DOWN SYNDROME – A COMPARATIVE CROSS SECTIONAL STUDY" - NO.26012018**

The following members of Ethics Committee were present in the meeting hold on **09.01.2018** conducted at Madras Medical College, Chennai 3

1. Prof.P.V.Jayashankar :Chairperson
2. Prof.R.Narayana Babu,MD.,DCH., Dean,MMC,Ch-3 : Deputy Chairperson
3. Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3 : Member Secretary
4. Prof.N.Gopalakrishnan,MD,Director,Inst.of Nephrology,MMC,Ch : Member
5. Prof.S.Mayilvahanan,MD,Director,Inst. of Int.Med,MMC, Ch-3 : Member
6. Prof.A.Pandiya Raj,Director, Inst. of Gen.Surgery,MMC : Member
7. Prof.Shanthy Gunasingh, Director, Inst.of Social Obstetrics,KGH : Member
8. Prof.Rema Chandramohan,Prof.of Paediatrics,ICH,Chennai : Member
9. Prof. Susila, Director, Inst. of Pharmacology,MMC,Ch-3 : Member
10. Prof.K.Ramadevi,MD., Director, Inst. of Bio-Chemistry,MMC,Ch-3 : Member
11. Prof.Bharathi Vidya Jayanthi,Director, Inst. of Pathology,MMC,Ch-3: Member
12. Thiru S.Govindasamy, BA.,BL,High Court,Chennai : Lawyer
13. Tmt.Arnold Saulina, MA.,MSW., :Social Scientist
14. Thiru K.Ranjith, Ch- 91 : Lay Person

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

INFORMED CONSENT FORM

Title of the study"Assesment of hearing deficits in children with Down syndrome - a comparative cross sectional study"

Name of the Participant:

Name of the Principal Investigator: Dr.Fidha Parvez Khan F

Name of the Institution:

Institute of Physiology and Experimental Medicine,
Madras Medical College and Govt. General Hospital,
Chennai - 3 &

Institute of Child Health and Hospital for Children,
Madras Medical College
Egmore
Chennai-8 &

Institute of Audiology, Speech and Language Pathology,
Madras Medical College,
Chennai - 3

Documentation of the informed consent

I _____ have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am the care taker of the minor and I am over 18 years of age and, exercising my free power of choice, hereby give my consent to include my ward as a participant in "**Assesment of hearing deficits in children with Down syndrome - a comparative cross sectional study"**

1. I have read and understood this consent form and the information provided to me.
2. I have had the consent document explained to me.
3. I have been explained about the nature of the study.
4. I have been explained about my rights and responsibilities by the investigator.

5. I have been informed the investigator of all the treatments I am taking or have taken in the past _____ months including any native (alternative) treatment.
6. I have been advised about the risks associated with my participation in this study.
7. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.
8. I have not participated in any research study within the past_____month(s).
9. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.
10. I am also aware that the investigator may terminate my participation in the study at any time, for any reason, without my consent.
12. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the sponsors, regulatory authorities, Govt. agencies, and IEC. I understand that they are publicly presented.
13. I have understood that my identity will be kept confidential if my data is publicly presented.
14. I have had my questions answered to my satisfaction.
15. I have decided to be in the research study.
I am aware that if I have any question during this study, I should contact the investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

Name and signature / thumb impression of the participant (or legal representative if participant is incompetent)

Name _____ Signature_____

Date_____

Name and Signature of impartial witness (required for illiterate patients):

Name _____ Signature_____

Date_____

ஆராய்ச்சிக்கு உட்படும் நபரின் ஒப்புதல் படிவம்

ஆராய்ச்சித் தலைப்பு: "டவுன்ஸ் நோய்க்குறியின் பாதிப்பிற்கு ஆளாகும் குழந்தைகளுடைய காது கேட்கும் செயல்பாட்டில் ஏற்படக்கூடிய குறைபாடுகள் பற்றிய ஒரு ஒப்பீட்டு, குறுக்கு வெட்டு ஆய்வு".

பெயர்: தேதி :
வயது:
பால்: ஆராய்ச்சி சேர்க்கை எண் :

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட விஷயங்களை புரிந்து கொண்டு நான் எனது சம்மதத்தைத் தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில் தான் பங்கு பெறுகிறேன் மற்றும் நான் இந்த ஆராய்ச்சியிலிருந்து எந்நேரமும் பின்வாங்கலாம் என்பதையும், அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் புரிந்து கொண்டேன். நான் "டவுன்ஸ் நோய்க்குறியின் பாதிப்பிற்கு ஆளாகும் குழந்தைகளுடைய காது கேட்கும் செயல்பாட்டில் ஏற்படக்கூடிய குறைபாடுகள் பற்றிய ஒரு ஒப்பீட்டு, குறுக்கு வெட்டு ஆய்வு" என்ற தலைப்பில் மேற்கொள்ளப்படும் இந்த ஆராய்ச்சியின் விபரங்களைக் கொண்ட தகவல் தாளைப் பெற்றுக் கொண்டேன்.

இதன் மூலம் எந்த பின்விளைவும் வராது என மருத்துவர் மூலம் தெரிந்து கொண்டு என்னுடைய சுயநினைவுடன் மற்றும் முழு சுதந்திரத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள சம்மதிக்கிறேன்.

தேதி :

கையொப்பம் :

PROFORMA

Name:

Age/ Sex:

Address:

OP No.:

Informant:

History of consanguinity

Was the child preterm (Yes / No):

Type of delivery (Normal vaginal / Cesaerean section):

History of birth asphyxia:

History of delayed milestones:

History of Down syndrome in the family:

History of hard of hearing:

History of ear discharge

EXAMINATION

General examination:

Temperature:

Pulse rate:

Blood pressure:

ENT examination:

RECORDING OF BERA IN CHILD

PTA IN DOWN SYNDROME

s.no	Age	sex	Pure tone average dBHL	s.no	Age	sex	Pure tone average dBHL
1	10	m	15	**31**	6	m	26.4
2	10	m	16.6	**32**	6	m	26.4
3	9	f	21.6	**33**	8	f	11.2
4	9	f	21.6	**34**	8	f	13
5	5	m	NA	**35**	10	m	15
6	5	m	NA	**36**	10	m	15
7	6	m	25	**37**	7	m	6
8	6	M	25.6	**38**	7	m	6
9	12	f	12	**39**	14	f	22
10	12	f	12	**40**	14	f	21
11	8	f	10	**41**	9	f	25
12	8	f	10	**42**	9	f	23
13	7	m	30	**43**	7	f	10
14	7	m	30	**44**	7	f	10
15	14	f	22	**45**	12	m	5
16	14	f	22.5	**46**	12	m	5
17	13	m	5	**47**	13	m	10
18	13	m	5	**48**	13	m	10
19	9	m	16	**49**	11	f	6.6
20	9	m	18	**50**	11	f	6.6
21	15	m	10	**51**	11	m	35
22	15	m	10	**52**	11	m	35
23	12	m	9.5	**53**	7	m	NA
24	15	m	9.5	**54**	7	m	NA
25	6	f	NA	**55**	6	f	14.6
26	6	f	NA	**56**	6	f	14.6
27	7	m	10	**57**	5	f	24.2
28	7	m	10	**58**	5	f	24.2
29	10	f	21	**59**	13	f	18
30	10	f	21	**60**	13	f	18

PTA IN CONTROL

s.no	Age	sex	Pure tone average dBHL	s.no	Age	sex	Pure tone average dBHL
1	5	m	5	**31**	6	m	0
2	5	m	5	**32**	6	m	0
3	13	f	6	**33**	5	f	0
4	13	f	6	**34**	5	f	0
5	6	m	5	**35**	6	m	5
6	6	m	5	**36**	6	m	5
7	7	m	0	**37**	7	m	5
8	7	M	0	**38**	7	m	5
9	12	f	0	**39**	12	f	0
10	12	f	0	**40**	12	f	0
11	7	f	8	**41**	9	f	0
12	7	f	8	**42**	9	f	0
13	6	m	5	**43**	7	f	0
14	6	m	5	**44**	7	f	0
15	13	f	0	**45**	10	m	5
16	13	f	0	**46**	10	m	5
17	14	m	10	**47**	13	m	6
18	14	m	10	**48**	13	m	6
19	9	m	5	**49**	11	f	6
20	9	m	5	**50**	11	f	6
21	14	m	0	**51**	11	m	5
22	14	m	0	**52**	11	m	5
23	12	m	0	**53**	5	m	0
24	12	m	0	**54**	5	m	0
25	7	f	7	**55**	6	f	6
26	7	f	7	**56**	6	f	6
27	8	m	0	**57**	10	f	0
28	8	m	0	**58**	10	f	0
29	11	f	0	**59**	9	f	0
30	11	f	0	**60**	9	f	0

BERA IN DOWNSYNDROME

s.no (no. of ears)	Age	sex	Wave I	Wave II	Wave III	Wave IV	Wave V	IPL I - III	IPL III - V	IPL I - V
1	10	m	1.74	2.65	3.45	4.89	5.35	1.8	1.9	3.6
2	10	m	1.87	2.99	3.58	4.56	5.9	1.6	2.32	4.02
3	9	f	1.73	2.67	3.84	4.69	5.88	2.11	2.04	4.14
4	9	f	1.87	2.68	3.8	4.89	5.2	1.9	1.4	3.31
5	5	m	1.77	2.69	3.89	4.9	5.89	2.12	2	4.11
6	5	m	1.87	2.45	3.8	4.8	5.9	1.93	2.1	4.03
7	6	m	1.66	2.67	3.72	4.71	5.9	2.06	2.18	4.24
8	6	M	1.6	2.34	3.41	4.4	5.8	1.81	2.39	4.2
9	12	f	1.87	2.7	3.71	4.91	5.91	1.84	2.2	4.04
10	12	f	1.48	2.38	3.4	4.3	5.8	1.92	2.4	4.33
11	8	f	1.78	2.7	3.86	4.93	5.93	2.08	2.07	4.13
12	8	f	1.4	2.5	3.5	4.55	5.9	2.1	2.4	4.5
13	7	m	1.6	2.8	3.7	4.97	5.98	1.99	2.28	4.29
14	7	m	1.33	2.98	3.6	4.98	5.8	2.31	2.2	4.44
15	14	f	1.64	2.77	3.74	4.89	6.2	2.08	2.46	4.51
16	14	f	1.78	2.96	3.99	4.87	5.78	2.21	1.79	3.98
17	13	m	1.65	2.88	3.55	4.8	5.88	1.9	2.33	4.24
18	13	m	1.7	2.9	3.98	4.97	5.86	2.28	1.88	4.15
19	9	m	1.7	2.87	3.65	4.9	5.9	1.95	2.25	4.21
20	9	m	1.9	2.93	3.96	4.99	6.3	2.06	2.34	4.39
21	15	m	1.74	2.78	3.88	4.8	5.91	2.12	2.03	4.16
22	15	m	1.87	2.91	3.96	4.79	5.89	2.07	1.93	4
23	12	m	1.71	2.8	3.5	4.91	5.92	1.8	2.42	4.22
24	12	m	1.86	2.93	3.6	4.69	5.3	1.73	1.7	3.43
25	6	f	1.6	2.82	3.87	4.88	6.2	2.17	2.33	4.5
26	6	f	1.85	2.94	3.89	4.68	5.89	2.05	2	4.04

27	7	m	1.68	2.77	3.76	4.85	5.95	2.07	2.19	4.27
28	7	m	1.89	2.93	4.1	4.98	5.8	2.22	1.7	3.91
29	10	f	1.74	2.77	3.76	4.75	5.2	2.01	1.44	3.46
30	10	f	1.3	2.95	3.97	4.55	5.77	2.68	1.8	4.47
31	6	m	1.64	2.65	3.33	4.79	5.3	1.68	1.97	3.65
32	6	m	1.64	2.88	3.55	4.51	5.2	1.9	1.65	3.55
33	8	f	1.67	2.79	3.85	4.78	5.7	2.17	1.85	4.02
34	8	f	1.87	2.89	3.6	4.49	5.9	1.72	2.3	4.02
35	10	m	1.68	2.78	3.65	4.81	5.7	1.96	2.05	4.01
36	10	m	1.68	2.55	3.88	4.77	6.12	2.12	2.24	4.44
37	7	m	1.66	2.78	3.58	4.91	6.1	1.94	2.52	4.44
38	7	m	1.99	2.58	3.92	4.99	5.88	1.9	1.96	3.89
39	14	f	1.78	2.77	3.99	4.9	5.89	2.2	1.9	4.11
40	14	f	1.55	2.5	3.76	4.98	5.78	2.22	2.02	4.23
41	9	f	1.62	2.71	3.78	4.78	5.4	2.15	1.62	3.77
42	9	f	1.43	2.79	3.55	4.99	6.3	2.11	2.75	4.86
43	7	f	1.54	2.8	3.5	4.76	6.3	1.95	2.8	4.75
44	7	f	1.4	2.75	3.99	4.97	5.9	2.49	1.91	4.4
45	12	m	1.64	2.8	3.75	4.74	5.8	2.1	2.05	4.15
46	12	m	1.44	2.79	3.83	4.98	5.6	2.33	1.77	4.15
47	13	m	1.5	2.87	3.71	4.88	5.86	2.12	2.15	4.26
48	13	m	1.67	2.57	3.4	4.41	5.6	1.7	2.2	3.92
49	11	f	1.55	2.76	3.87	4.9	5.2	2.34	1.33	3.66
50	11	f	1.67	2.75	3.83	4.99	5.9	2.18	2.07	4.23
51	11	m	1.7	2.75	3.79	4.75	5.8	2.09	2.01	4.12
52	11	m	1.4	2.4	3.2	4.98	5.92	1.8	2.72	4.51
53	7	m	1.67	2.76	3.78	4.97	5.91	2.11	2.13	4.25
54	7	m	1.54	2.8	3.75	4.52	5.34	2.21	1.59	3.79
55	6	f	1.77	2.75	3.6	4.79	5.8	1.82	2.2	4.04

56	6	f	1.7	2.87	3.88	4.9	6.2	2.09	2.32	4.42
57	5	f	1.63	2.66	3.3	4.8	6	1.56	2.7	4.21
58	5	f	1.43	2.88	3.8	4.99	5.2	2.49	1.4	3.88
59	13	f	1.5	2.75	3.6	4.84	5.3	2.05	1.7	3.77
60	13	f	1.89	2.59	3.9	4.96	5.95	2.04	2.05	4.09

BERA IN CONTROL

s.no (no. of ears)	Age	sex	Wave I	Wave II	Wave III	Wave IV	Wave V	IPL I - III	IPL III - V	IPL I - V
1	5	m	1.7	2.67	3.65	4.8	5.61	2.02	2.17	3.98
2	5	m	1.6	2.77	3.85	4.87	5.6	2.32	1.61	4.07
3	13	f	1.9	2.82	3.81	4.8	5.72	2.14	1.71	4.05
4	13	f	1.67	2.76	3.68	4.86	5.9	2.13	1.94	4.35
5	6	m	1.53	2.77	3.86	4.88	5.88	2.18	1.97	4.05
6	6	m	1.6	2.81	3.62	4.81	5.81	2.02	1.96	4.2
7	7	m	1.76	2.68	3.94	4.89	5.56	2.18	1.75	3.8
8	7	M	1.51	2.91	3.9	4.88	5.56	2.39	1.91	4.09
9	12	f	1.66	2.79	3.87	4.76	5.66	2.21	2.22	4.13
10	12	f	1.52	2.67	3.55	4.79	5.54	2.03	1.87	4.02
11	7	f	1.65	2.84	3.97	4.9	5.73	2.38	1.76	4.14
12	7	f	1.78	2.83	3.56	4.68	5.6	2.01	2.04	4.05
13	6	m	1.66	2.89	3.64	4.67	5.6	2.02	1.96	3.98
14	6	m	1.54	2.8	3.5	4.97	5.59	1.93	2.09	4.02
15	13	f	1.67	2.78	3.67	4.68	5.55	1.97	2.03	3.85
16	13	f	1.7	2.89	3.44	4.69	5.8	1.74	2.63	4.2
17	14	m	1.94	2.78	3.67	4.9	5.56	1.73	1.86	3.59
18	14	m	1.64	2.68	3.79	4.8	5.6	2.15	1.96	3.93
19	9	m	1.65	2.67	3.4	4.88	5.79	1.75	1.86	4
20	9	m	1.88	2.71	3.9	4.78	5.54	2.02	2.1	3.67
21	14	m	1.59	2.64	3.68	4.79	5.7	2.04	1.88	4.06
22	14	m	1.55	2.56	3.98	4.45	5.6	2.21	2.46	3.83
23	12	m	1.62	2.68	3.65	4.9	5.6	2	1.86	3.95
24	12	m	1.57	2.86	3.98	4.99	5.8	2.44	1.78	4.26
25	7	f	1.7	2.69	3.5	4.9	5.6	1.84	2.25	3.94
26	7	f	1.78	2.55	3.55	4.6	5.67	1.77	1.65	3.92

27	8	m	1.65	2.75	3.4	4.9	5.78	1.75	2.21	3.96
28	8	m	1.55	2.42	3.8	4.97	5.51	2.25	1.9	4.15
29	11	f	1.68	2.77	3.77	4.75	5.32	2.09	2.43	4.52
30	11	f	1.99	2.83	3.69	4.55	5.59	1.7	1.85	3.55
31	7	m	1.63	2.69	3.6	4.8	5.6	2	2	4
32	7	m	1.48	2.69	3.5	4.5	5.6	2.1	2.1	4.2
33	5	f	1.66	2.78	3.73	4.73	5.6	2.03	1.87	3.9
34	5	f	1.79	2.9	3.9	4.8	5.54	2.03	1.64	3.67
35	6	m	2	2.8	3.64	4.86	5.62	2.01	1.98	3.99
36	6	m	1.88	2.73	3.79	4.69	5.7	1.91	1.9	3.79
37	7	m	1.62	2.78	3.6	4.9	5.61	1.98	1.86	4.15
38	7	m	1.57	2.74	3.7	4.99	5.7	2.13	1.58	3.93
39	12	f	1.77	2.9	3.7	4.88	6.2	1.93	2.02	3.53
40	12	f	1.46	2.5	3.34	4.3	5.54	1.88	2.26	4.14
41	9	f	1.6	2.71	3.4	4.76	5.6	1.76	2.2	4.48
42	9	f	1.4	2.91	3.6	4.88	5.68	2.12	2.08	3.96
43	7	f	1.7	2.76	3.5	4.97	5.67	1.85	2.17	3.61
44	7	f	1.87	2.76	3.75	4.75	5.7	1.95	1.95	3.4
45	10	m	1.63	2.67	3.76	4.97	5.7	1.76	1.94	3.84
46	10	m	1.98	2.99	3.7	4.88	5.54	1.72	1.98	3.86
47	13	m	1.68	2.7	3.73	4.74	5.82	2.05	1.88	4.13
48	13	m	1.43	2.99	3.99	4.99	5.56	2.56	2.17	3.65
49	11	f	1.59	2.8	3.55	4.89	5.79	1.96	1.8	4.12
50	11	f	1.42	2.42	3.44	4.44	5.76	2.02	1.6	4.18
51	11	m	1.61	2.85	3.79	4.88	6.1	2.18	2.26	3.96
52	11	m	1.65	2.47	3.3	4.3	5.6	1.65	2.3	4.2
53	5	m	2	2.7	3.65	4.68	5.62	1.65	1.97	4.02
54	5	m	1.8	2.7	3.9	4.77	5.21	2.1	1.31	3.9
55	6	f	1.78	2.7	3.65	4.68	5.63	1.87	1.98	3.7

56	6	f	1.63	2.3	3.88	4.41	5.6	2.18	1.67	3.62
57	10	f	1.53	2.76	3.73	4.94	5.6	2.13	2.07	3.92
58	10	f	1.67	2.65	3.89	4.88	5.58	1.99	1.65	4.15
59	9	f	1.55	2.78	3.55	4.88	5.59	1.88	2.25	4
60	9	f	1.68	2.63	3.88	4.99	5.69	2.35	1.82	4.27