DISSERTATION ON

"EFFECT OF DELIBERATE INGESTION OF ORGANOPHOSPHATE PESTICIDES AND SNAKE BITES ON DISTORTION PRODUCT OTOACOUSTIC EMISSION (DPOAE)"

Dissertation submitted in partial fulfilment

of the regulations for the award of the degree of

M.S.DEGREE BRANCH-IV

OTORHINOLARYNGOLOGY

of

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MADRAS MEDICAL COLLEGE, CHENNAI.

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CERTIFICATE

This is to certify that this dissertation **"EFFECT OF DELIBERATE INGESTION OF ORGANOPHOSPHATE PESTICIDES AND SNAKE BITES ON DISTORTION PRODUCT OTOACOUSTIC EMISSION (DPOAE"** submitted by **Dr.VELAVAN. R.V.S.,** appearing for M.S ENT Branch IV Degree examination in April 2015 is a *bona fide* record of work done by him under my direct guidance and supervision in partial fulfilment of the regulations of the Tamil Nadu Dr .M.G.R Medical University, Chennai. I forward this to the Tamil Nadu Dr .M.G.R Medical University, Chennai, Tamil Nadu, India.

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ABBREVIATIONS

TM	Tympanic membrane
EAC	External auditory canal
dB	Decibel
PTA	Pure tone audiogram
kHz	Kilo hertz
SCC	Semi-circular canal
HOH	Hard of hearing
AC	Air conduction
BC	Bone conduction
OAE	Otoacoustic emission
OHA	Outer hair cell
TOAE	Transient Otoacoustic emission
DPOAE	Distortion product Otoacoustic emission
SOAE	Spontaneous Otoacoustic emission
SPL	Sound pressure level
Ach	Acetyl choline

CONTENTS

INTRODUCTION

Otoacoustic emission testing is a simple non-invasive and quick test that can be performed to analyse preclinical changes in the outer hair cells of patients. Studies suggest that minute sub clinical changes occurring in the outer hair cells' function can be precisely predicted with Otoacoustic emissions.

Ototoxic compounds cause damage by the generation of reactive oxygen species. Snake bites and deliberate ingestion of organophosphate poisons represent an accidental exposure of outer hair cells to ototoxic compounds. The ototoxic potentials of the snake venom and organophosphate compounds has been well documented in studies. By testing the Otoacoustic emission we can estimate the outer hair cell function of normal persons after an accidental exposure to these ototoxic compounds. It is also stipulated to be the main mechanism for outer hair cell damage of the cochlea by organophosphate poisoning as well. Some of the snake venoms are neurotoxic which act by depletion of NADPH similar to the neurotoxic mechanism of organophosphates.

Repeated follow up with similar testing may also help us to pick up further detoriation of the outer hair cell function. Such testing can be used to study and approximately estimate the resilience of outer hair cells to the toxic exposure of these compounds and can be thus extrapolated to other compounds which may

have potential to cause outer hair cell damage. The implications of such studies could be far reaching.

More over since distortion product Otoacoustic emission starts decreasing even before the increase in threshold of hearing becomes clinically apparent, it can also help us to predict the future hearing loss and initiate the preventive lifestyle changes that may be adopted to limit the outer hair cell damage.

AIM

Organophosphate poisoning and snake bite are among the two leading causes of poisoning in India and are known for causing damage to multiple organ systems in the body because of their toxic effects. The ototoxic potentials of these compounds is as yet unexplored in vivo. This study aims to identify the cochlear changes by measuring Distortion Product Otoacoustic Emission in patients with deliberate ingestion of organophosphate poisoning and accidental neurotoxic snake bite. This study would also help to predict the hearing loss in future in such patients and institute early rehabilitative measures.

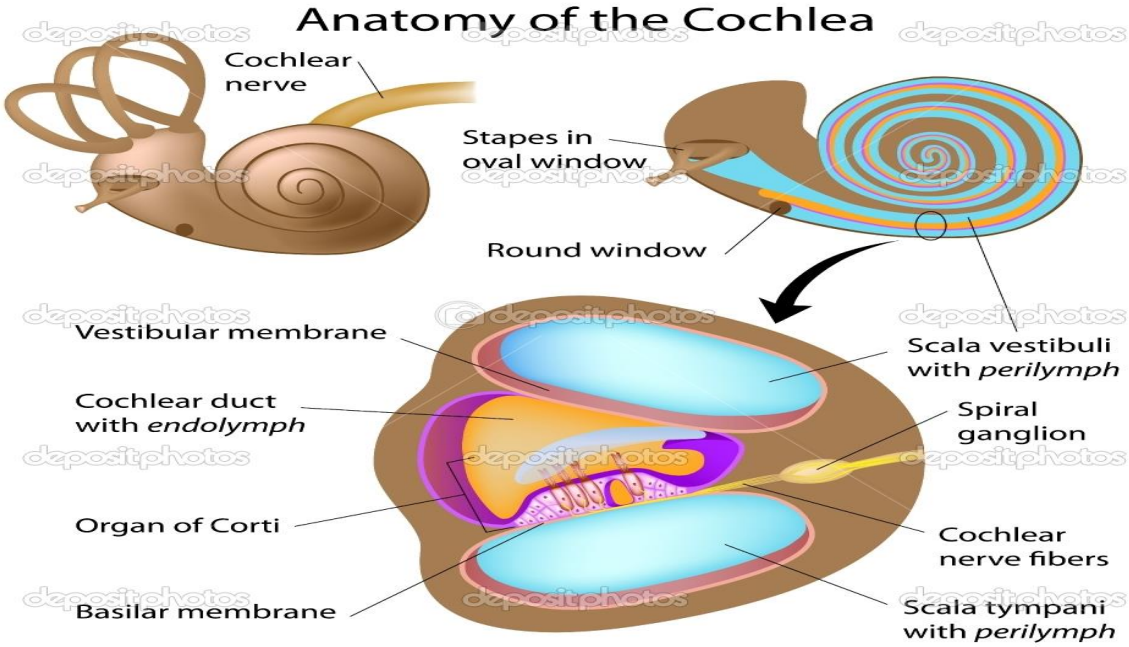
ANATOMY OF INNER EAR

The inner ear or labyrinth lies in the temporal bone in the petrous part. It consists of two portions, a strong bony labyrinth inside of it is the membranous labyrinth these both were usually separated from the bony part by means of fluid perilymph. The membranous labyrinth is filled with endolymph.

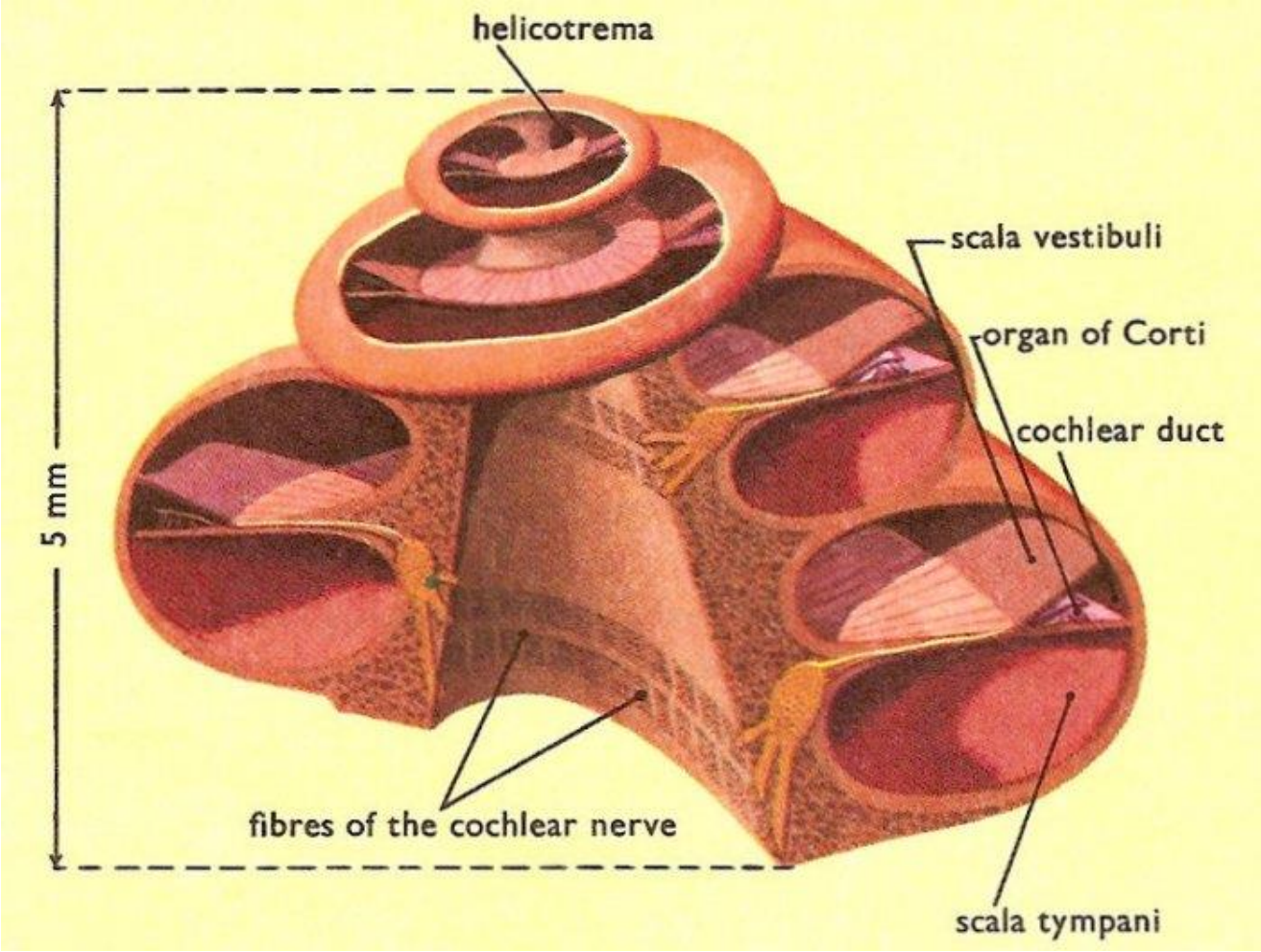
BONY LABYRINTH :-

It consists of three parts –

1. anteriorly – cochlea,
2. vestibule in the middle
3. posteriorly semi-circular canals



COCHLEA

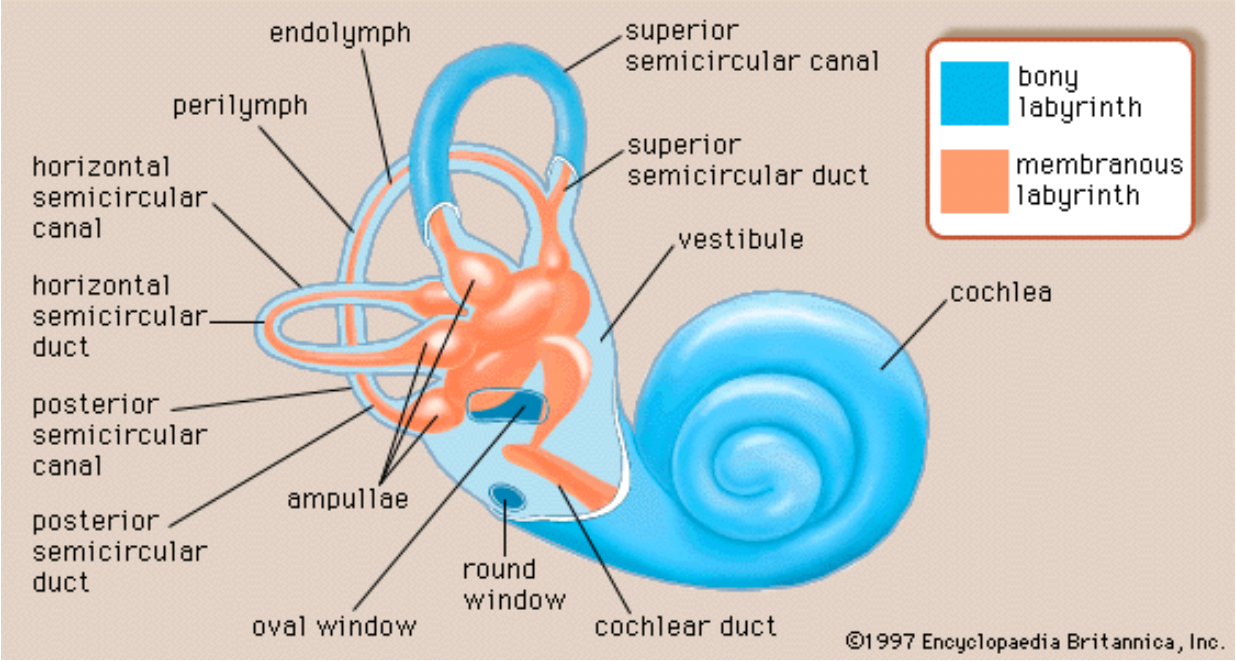


The bony cochlea resembles like a common snail's shell and it forms the anterior part of labyrinth. It has a conical central axis known as modiolus and the cochlear canal makes 2 ¾ turns around it. The modulus is directed forwards and laterally with its apex pointing towards the medial wall of the middle ear in the antero-superior direction and the base points towards the fundus of the internal auditory meatus.

The cochlear canal is partially divided into *scala vestibuli* above and *scala tympani* below by a spiral ridge of bone termed spiral lamina that projects from the *modiolus*. These relationships apply to the cochlear basal turn. The partition between these two passages is usually completed by the basilar membrane. *Helicotrema* is a small opening by which scala vestibuli communicates with scala tympani at the apex of cochlea.

VESTIBULE

The vestibule lies in the central part of the bony labyrinth. The middle ear lies lateral to it and it has an opening in the middle ear at the fenestra vestibuli which is closed by the foot plate of stapes.it has three semi-circular canals that open into its posterior wall. The medial wall is related to the internal auditory meatus and it has elliptical recess behind and spherical recess in front. These two recesses are separated by the vestibular crest which splits inferiorly to enclose the cochlear recess. Just below the elliptical recess there is the opening of the diverticulum, the aqueduct of the vestibule, which opens into a narrow fissure on the posterior aspect of the petrous temporal bone postero-lateral to the internal auditory meatus. It encloses the ductus endolymphaticus and a vein ensuring no perilymph escapes through it.



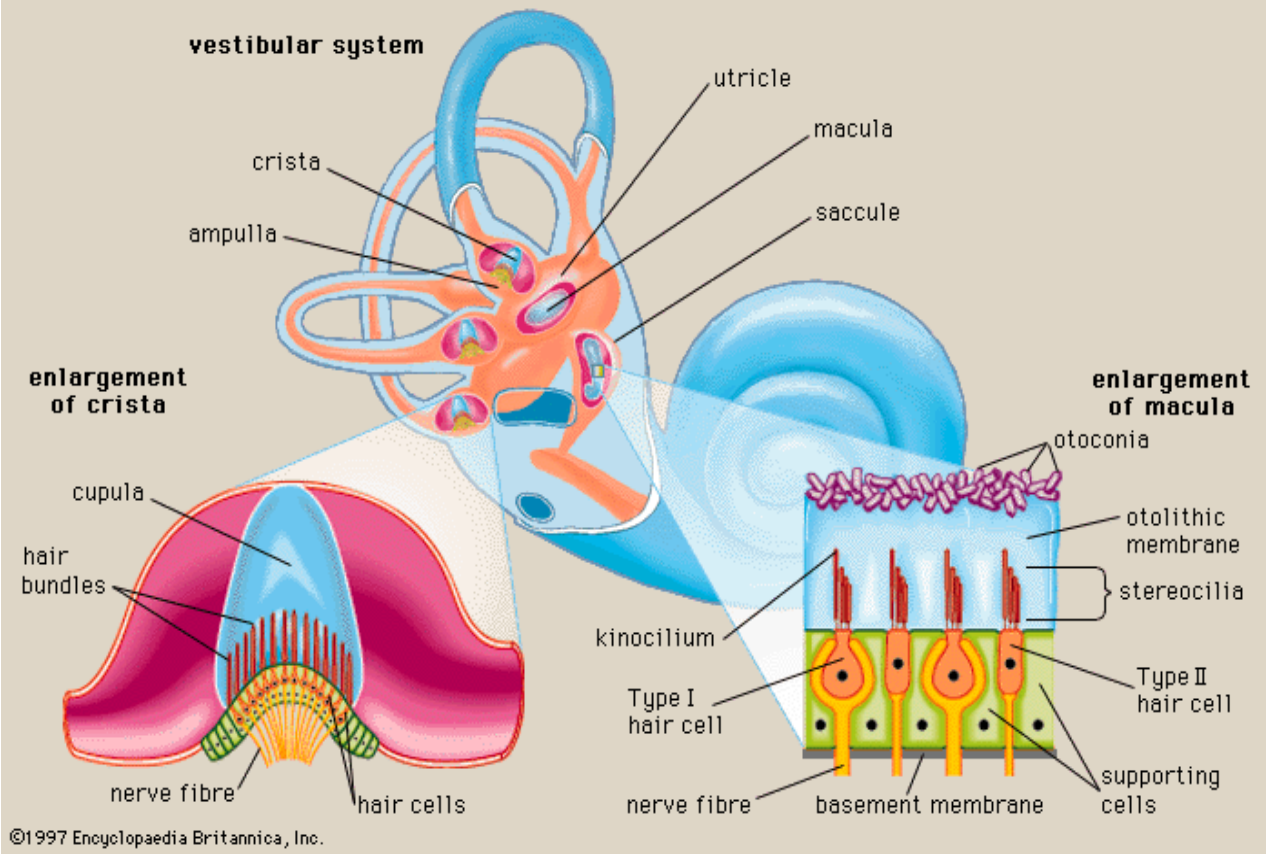
SEMI-CIRCULAR CANAL [SCC]

There are three bony semi-circular canals:

1. Anterior or superior semi-circular canal
2. Posterior semi-circular canal
3. Horizontal or lateral semi-circular canal.

Each SCC has two ends. They lie at right angles to each other postero-superior to vestibule. Each canal is about 2/3rd of a circle and has dilated portion at one end forming the ampulla. These three SCC open into vestibule by means of 5 openings. The anterior canal lies in a vertical plane usually along the long axis of temporal bone petrous part. It is convex upwards and its position is indicated by the arcuate eminence present over the surface of temporal bone petrous part. The ampulla is usually situated antero-laterally. The superior canal and posterior canal

unite at upper end to form crus commune and open into the medial wall of vestibule at lower end. The posterior semi-circular canal lies in a vertical plane parallel to the temporal bone petrous part. Its convexity is directed backwards and its ampulla lies at its lower end. The lateral SCC lies in a horizontal plane with its convexity directed posterolaterally and its ampulla lies close to the ampulla of the anterior canal anteriorly. LSCC of the both sides of the body lie in the same plane whereas the anterior SCC of one side lies in the plane of posterior SCC of the other side.

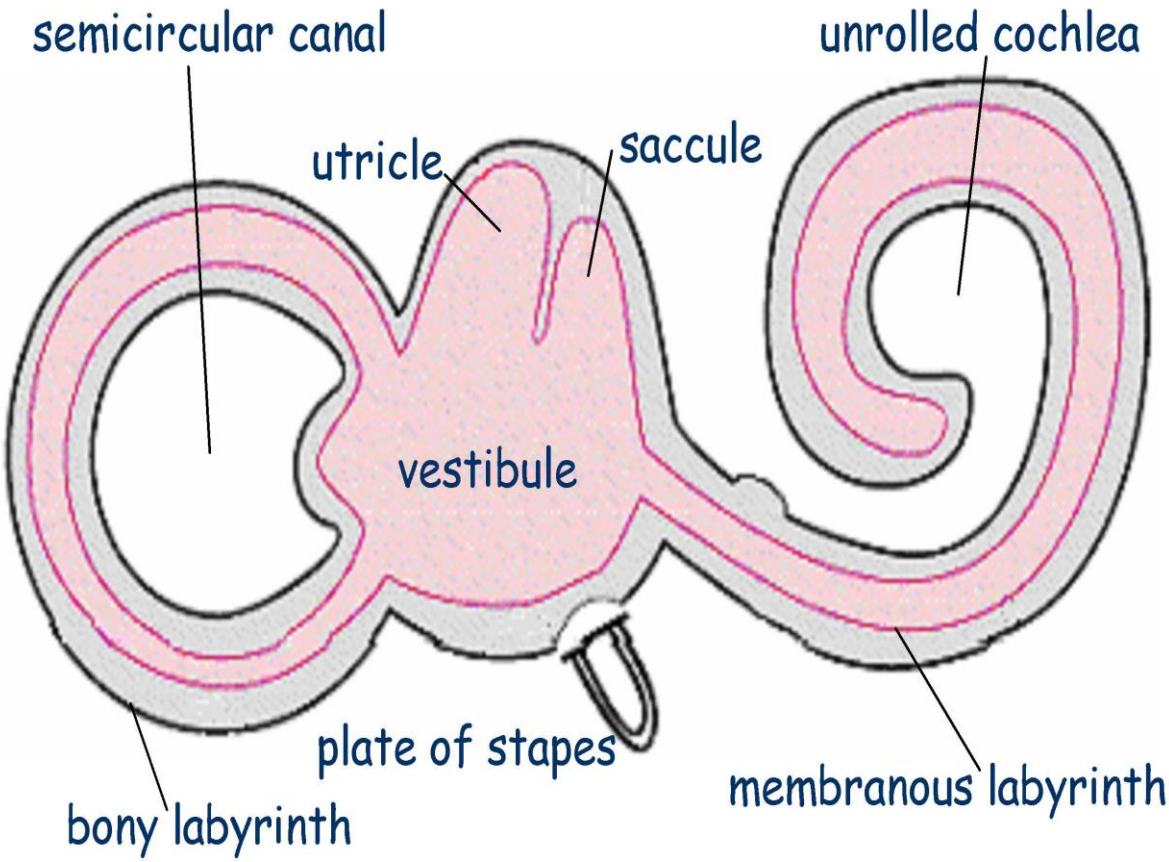


MEMBRANOUS LABYRINTH

It lies within the bony labyrinth as a continuous closed cavity filled with endolymph. Its epithelium is specialized to form receptors for hearing (*organ of Corti*). Static balance is mediated by maculae and kinetic balance is mediated by *cristae*.

Membranous labyrinth consists of two parts

1. Spiral duct of cochlea
2. Utricle and Saccule with maculae

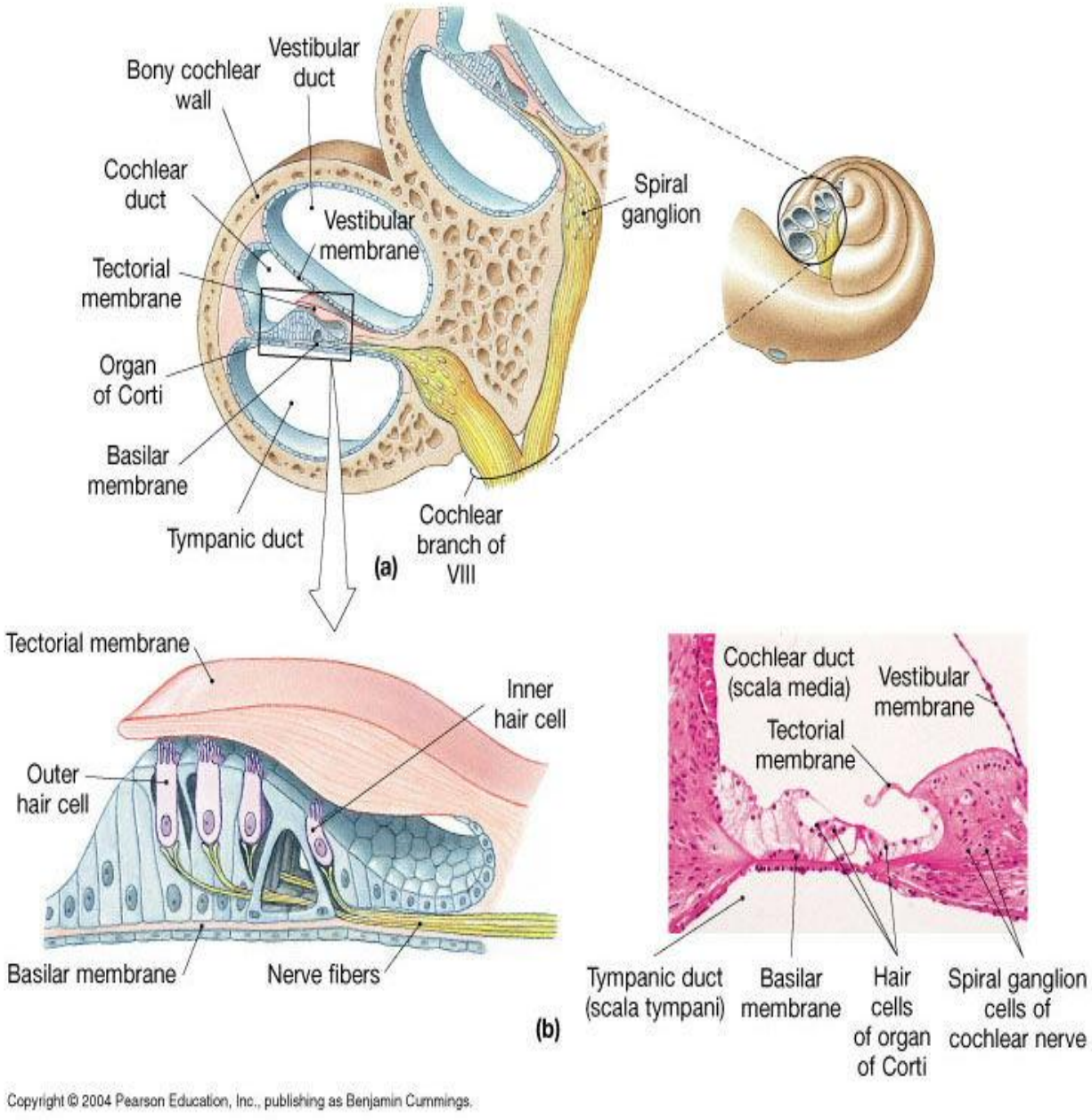


DUCT OF COCHLEA OR THE SCALA MEDIA

It lies in the middle part of the cochlear canal found between the scala tympani and scala vestibuli otherwise named as spiral duct. Its floor is formed by basilar membrane; roof is formed by Reissner's membrane, outer wall by the bony wall of cochlea. The spiral organ of Corti is supported by the basilar membrane. The organ of corti is innervated by the peripheral process of the bipolar cells located in the spiral ganglion. The ganglion is located in the spiral canal present within the modiolus found at the basal lamina. The saccule is connected to the cochlea posteriorly by a narrow duct called the ductus reuniens. The sound waves reaching the endolymph through the vestibular membrane make appropriate parts of the basilar membrane vibrate and so different parts of organ of corti are stimulated by different frequencies of sound. The loudness of the sound is determined by the amplitude of vibration.

OUTER HAIR CELLS

In the human outer hair cells active vibrations within the cell body are triggered by the action potentials. Somatic electro-motility is nothing but a mechanical response to electrical signals which mainly drives oscillations within the length of cell occurring at the frequency of incoming sound and provides amplification of



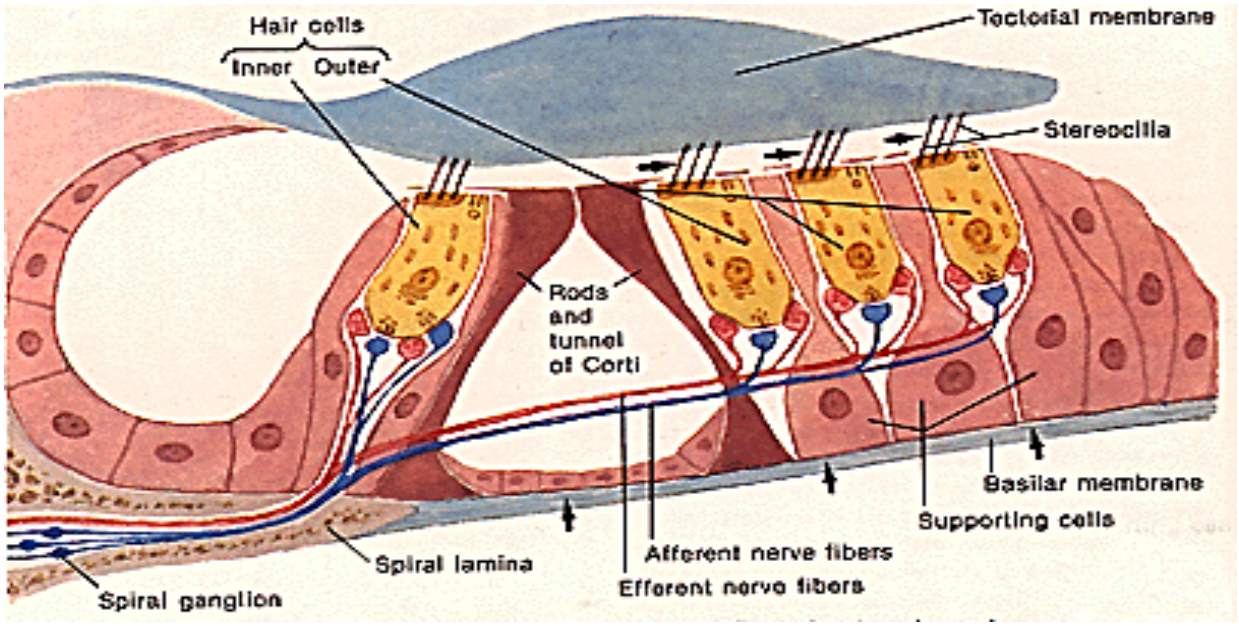
mechanical feedback. Mammals only have outer hair cells. OHC has highly improved frequency selectivity for hearing speech and music.

Non-linear amplification of quiet sound higher than the large ones is the main effect of this system. For this property they are also termed as cochlear amplifier.

In recent years there is a considerable progression in the molecular biology of outer hair cells. Prestin, a protein found in the outer hair cells was found to be compromised by marine pesticides.

Stereo-ciliary bundle found at the apex of outer hair cells is the sensory end whereas the synaptic pole is found at the base where the afferent and efferent nerve fibres usually connect. If they are viewed from above below the apical surface is found to be flattened mainly triangular or heart shaped whereas the cell bodies are found to be cylindrical. The arrangements of stereocilia are in the form of either "W" or "V" shape, in humans there are about 5 rows. As we go about the rows there is an increase in height across the bundle similar to a staircase. The basilar membrane stretches from the spiral prominence to the osseous spiral lamina. Nerve fibres usually seek its entry through the osseous spiral lamina. All the above said structures mainly contribute to the changes that systematically occur in the organ of Corti- basilar membrane complex.

Innervation of organ of corti



The auditory portion of the vestibulocochlear nerve is mainly responsible for transferring the acoustic information to the ipsilateral cochlear nucleus complex in the brainstem from the hair cells where it originated. The cell bodies of spiral ganglion along the organ of Corti reside within the modiolus; the auditory nerve is composed of afferent fibres which are nothing but the projections from neurons of spiral ganglion.

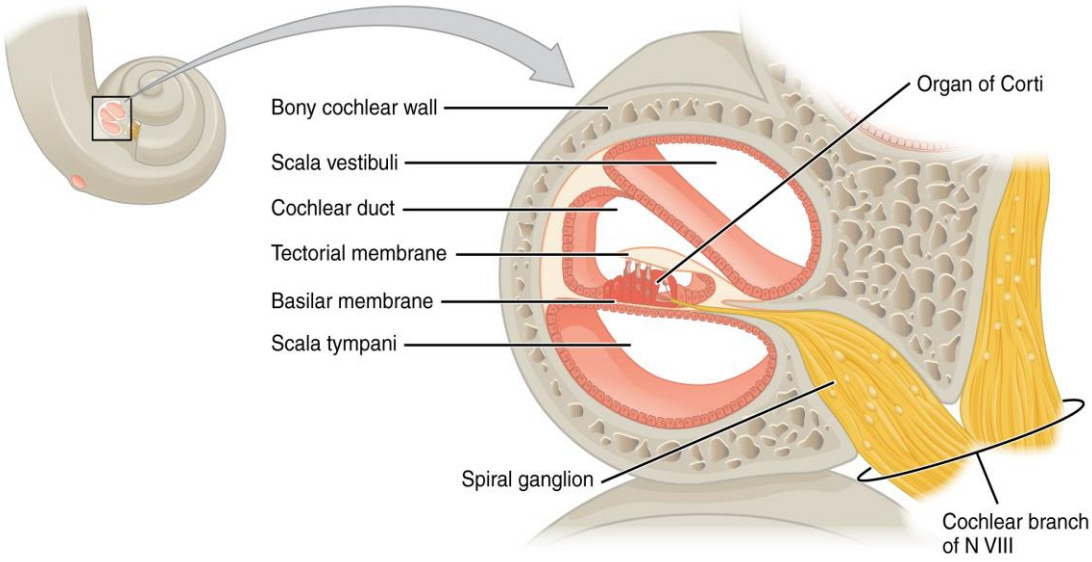
These spiral ganglion neurons are usually of two types. The inner hair cells are innervated by type 1 cells whereas the outer hair cells are innervated by the type 2 cells. The above said outer hair cells and inner hair cells innervated by these two type of nerve fibres have a considerable amount of variation in their innervation corresponding to their number and its distribution of fibres.

PHYSIOLOGY OF INNER EAR

COCHLEA

It is a coiled structure like the shell of a snail. It has two parts

1. Central conical axis formed by spongy bone called modiolus
2. Bony canal which winds around the modiolus.



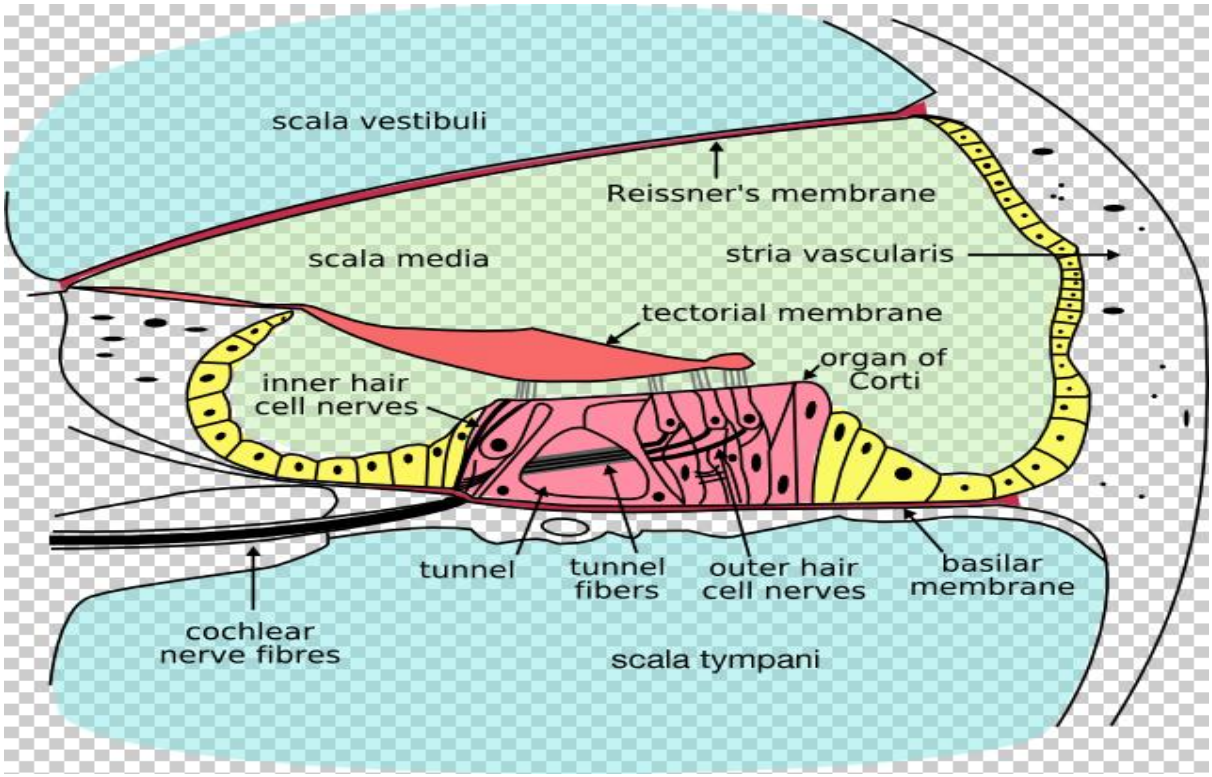
"The cochlea is a system of coiled tubes consisting of three tubes coiled side by side, scala vestibuli, scala media, and scala tympani. The scala vestibuli and acala media are separated from each other by the Reissner's membrane. The scala vestibuli and scala tympani are separated by basilar membrane. The organ of corti is situated in the basilar membrane and it comprises of cells which are usually sensitive both electrically and mechanically, arranged in series. They usually produces response to sound vibrations as they are end organs of reception. Sound vibrations entering though the scala vestibuli through the oval window

from the foot plate of stapes. The oval window is usually closed by the stapes foot plate and by means of a ring like ligament that is loosely attached to the edge. By this it responds to sound vibrations to and fro. Inward motion of stapes causes the perilymph to move along the scala media and vestibuli forward and vice versa".

Basilar membrane

"It is a usually a membrane that is fibrous in nature which separate the scala tympani and scala media. The membrane comprises of about thirty thousand basilar fibres that are projecting from cochlear bony surface. . These fibres are usually stiff elastic in nature and they are attached to bony cochlea at their base but their other ends are mobile and are buried in the basilar membrane."

"The lengths of the basilar fibres progressively increase at the level of the oval window from the basal turn of the cochlea to the apical region. Their size varies starting at a size of 0.04 mm near the oval window and round window to 0.5 mm at the tip of the cochlea, which is about 12 fold increase in length".

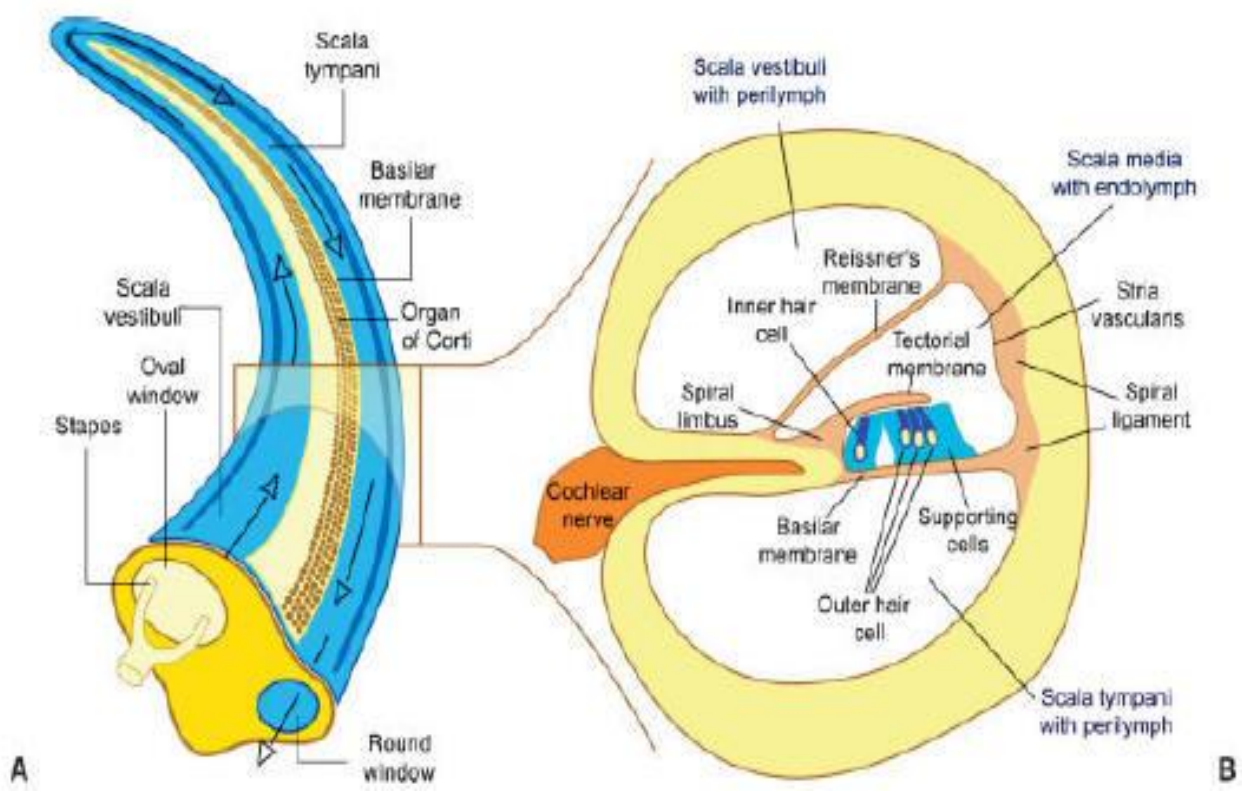


"The fibre's thickness normally shows a decreasing pattern from the oval window to the Helicotrema. So their thickness shows a reduction larger than hundred fold. So by this the short fibres that are usually stiff and found near the oval window found to vibrate best with high frequencies whereas the fibres at the cochlear tip which are comparatively longer vibrate well at low frequencies.

In the basilar membrane the resonance for high frequency is found to occur at the base where the oval window of the cochlea allows the sound waves. In Helicotrema the resonance for the low frequency sound seems to occur due to its reduced fibres and also due to high loading with fluid which vibrates along the tubules of cochlea".

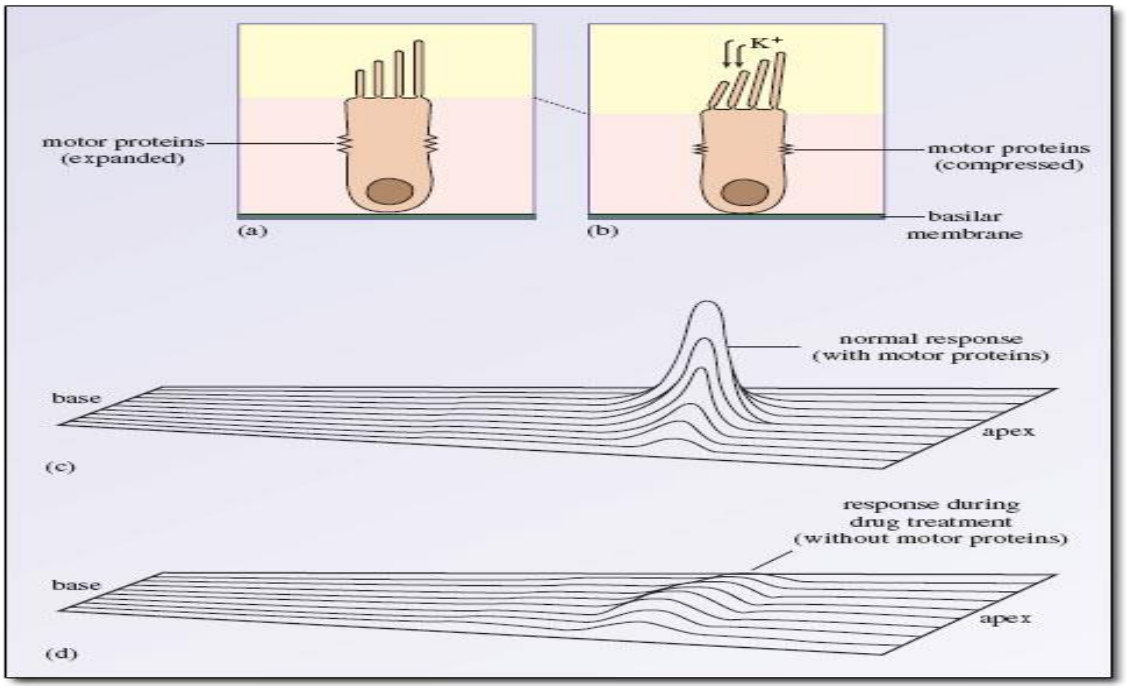
“TRANSMISSION OF SOUND WAVES IN THE COCHLEA -Travelling wave”

“The cochlea is usually surrounded on all its sides by bony walls. The round window usually projects forwards, when the stapes foot plate moves into the oval window. Due to entry of sound wave, it initially causes the basilar membrane found at the cochlear base to move towards the round window. Due to the above movement, an elastic tension is found to develop in basilar membrane as they move along the round window which makes a fluid wave that travels to Helicotrema. By this effect a wave movement is found to occur along the basilar membrane that is compared to the wave travelling along a pond surface.



Physiology

The sound waves which have been collected in the outer ear produces vibrations in the tympanic membrane. So the pressure in the tympanic membrane is increased which is frequency sensitive. This in turn vibrates the middle ear ossicles. A highly efficient impedance transformer will change the high displacement low pressure vibration into low displacement high pressure vibration which is suitable for movement of cochlear fluids. The vibrations perceived in the stapes foot plate transmit the mechanical energy derived from the ossicular chain through the oval window of the cochlea, thereby delivering effectively the sound pressure wave to the scala vestibuli and propagating the mechanical motion into pressure waves that will be transmitted through the cochlear fluids in a compressible chamber at a velocity of approximately 1.5 kilometres per second. The scala vestibuli has a high pressure compared to scala tympani, producing a difference in pressure across the partition of cochlea, thereby creating intra-cochlear forces that are set in motion. The thickness of the basilar membrane increases from apex to base where as the thickness and composition of filaments decreases from base to apex. The high frequency acoustics are selectively transduced at the base of the cochlea because it is stiff. The low frequency acoustics are transduced at the apex.

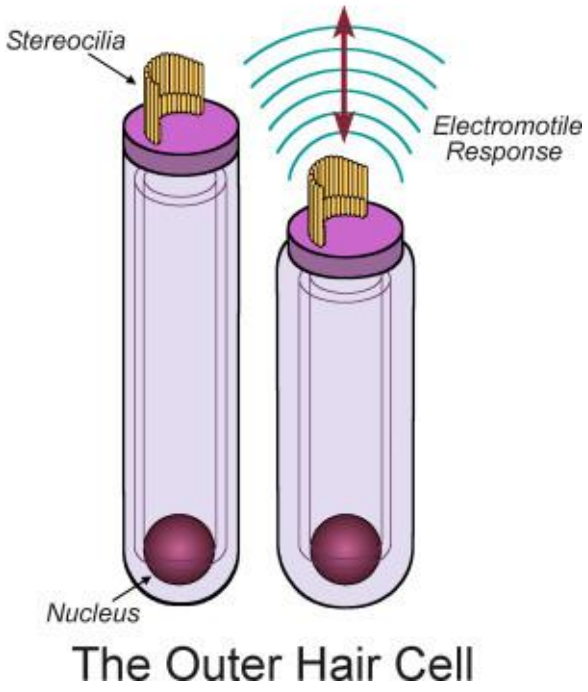


The outer hair cells of the cochlea play an important role in the mechanics of cochlea actively which mainly uses the biological energy to amplify the basilar membrane mechanical vibration which has been sharply tuned for the frequency selectivity. The basilar membrane displacement results in a shearing motion between the tectorial membrane and the reticular lamina which serves as a triggering agent for transudation currents. This shearing motion causes the stereocilia to bend in the modiolus direction or in the direction of spiral limbus depending on the displacement of basilar membrane. The mechanical stimulus to inner hair cells of cochlea causes the stereocilia to move along the flow of endolymph in the subcortical space. During the contraction of outer hair cells the reticular lamina and the tectorial membrane are pulled together there by enhancing the displacement of the basilar membrane during active mechanics.

The displacement of basilar membrane varies in radial dimension both in magnitude and in phase. The tectorial membrane required for outer hair cells to amplify the displacement of the basilar membrane at low frequency levels.

Transduction by hair cells

The apical surface of outer hair cells contains stereocilia which are rigid mechanically mainly due to the presence of actin filaments in it.



The Outer Hair Cell

"Their upper surface usually is covered with inter –links and so they move as one entity. Stereocilia are usually turned in the direction of stereo cilia which are usually taller, which causes stretching at their tip links that leads to opening of ion channels in the membrane, whereas if it occurs vice versa the opposite effect occurs. Thereby the stimulus is coupled to the transducer channels by means of

tip links. The endolymph covering the apex of hair cell has a positive potential of eighty five mV. But a negative potential of seventy mV is present inside the cell. So when a drop in potential occurs, it increases the positivity in the cell. Potassium ions play the major role in the process. Energy for the whole of above process is derived from stria vascularis".

Organ of corti

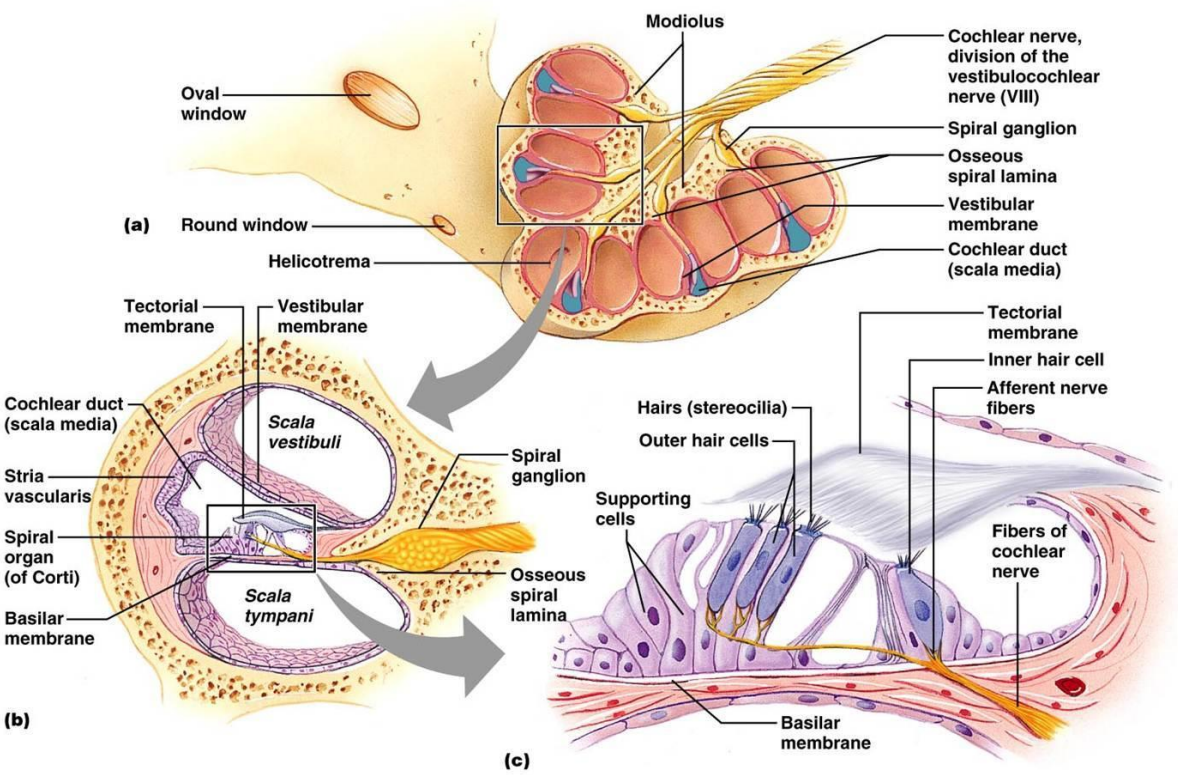
It is a neuro-epithelial structure in cochlea and is the receptor organ for hearing.

Situation and extent

It rests upon the lip of the osseous spiral lamina and basilar membrane and extends throughout the cochlear duct except for a short distance on either end. The roof of the organ of corti is formed by gelatinous tectorial membrane.

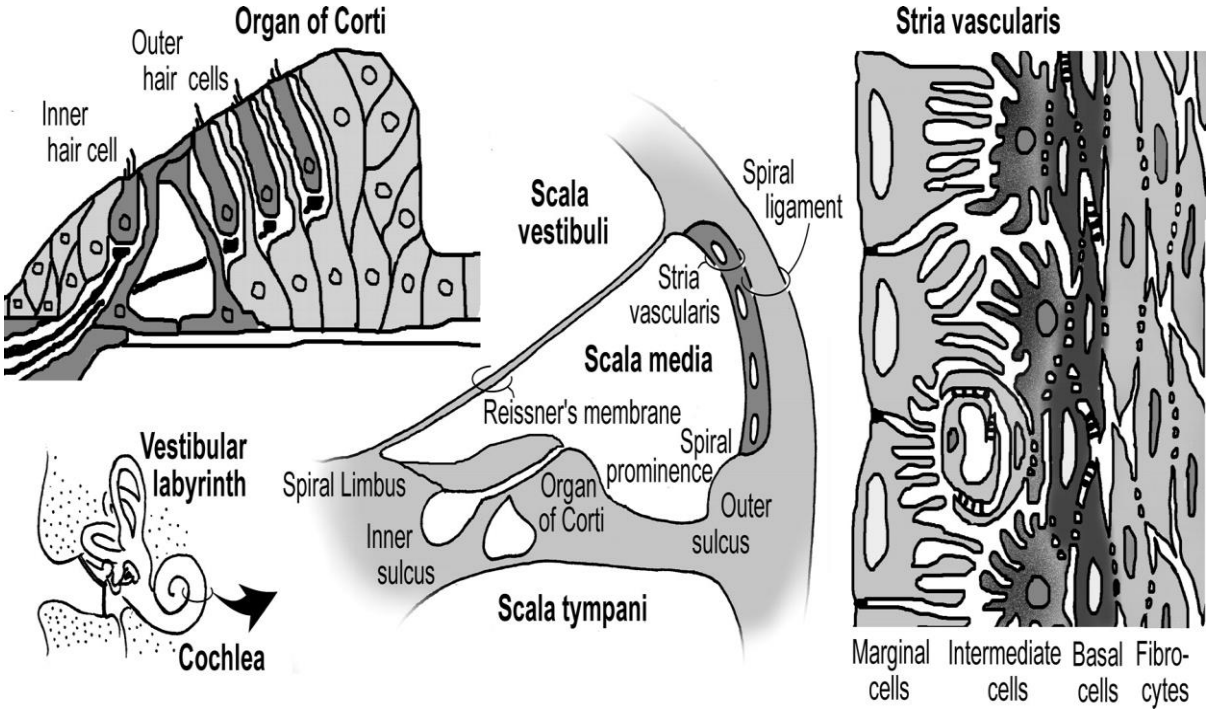
Structure

Organ of corti is made of sensory elements called hair cells and various supporting cells. All cells of organ of corti are arranged in order from centre towards the periphery of cochlea.



Cells of the organ of corti

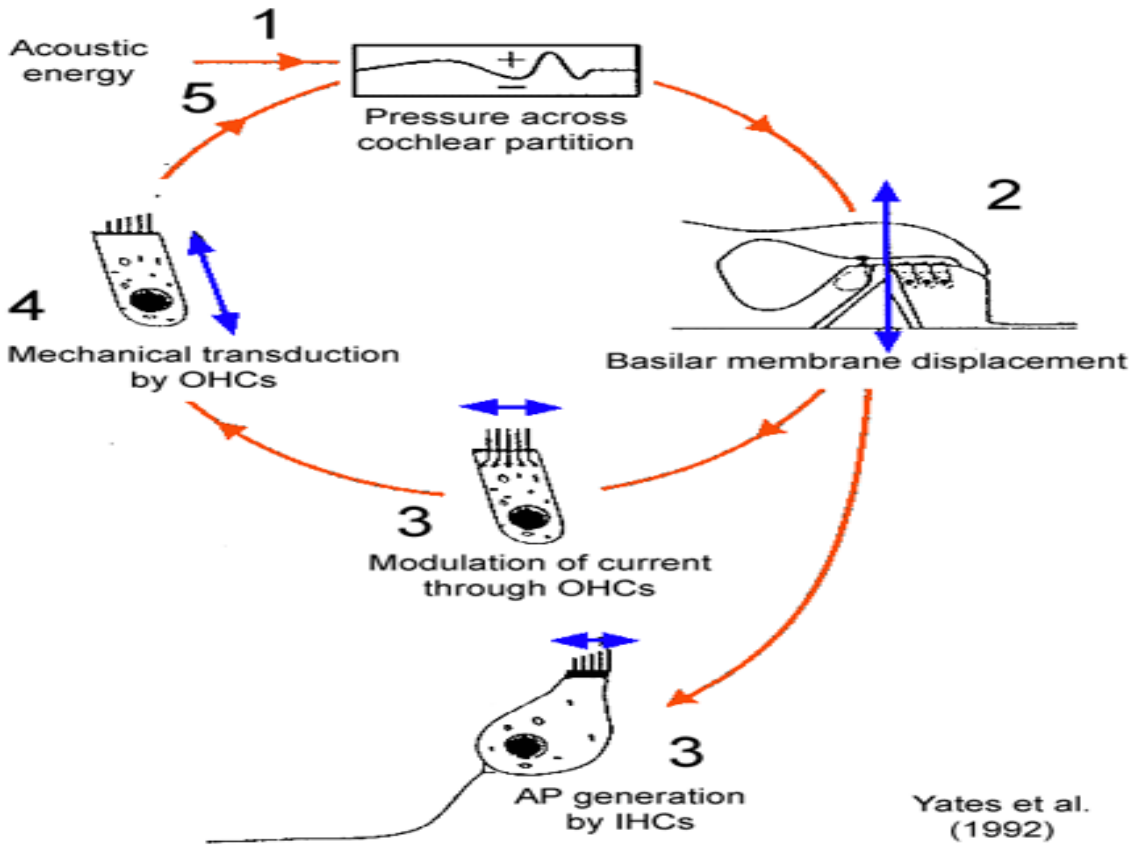
1. Border cells
2. Inner hair cells
3. Inner phalangeal cells
4. Inner pillar cells
5. Outer pillar cells
6. Outer phalangeal cells
7. Outer hair cells
8. Cells of Hensen
9. Cells of Claudius and Lamina reticularis.



Excitation of hair cells

Steriocilia of hair cells of organ of corti are embedded in tectorial membrane. Hair cells are tightly fixed by cuticular lamina reticularis and pillar cells and rods of corti.

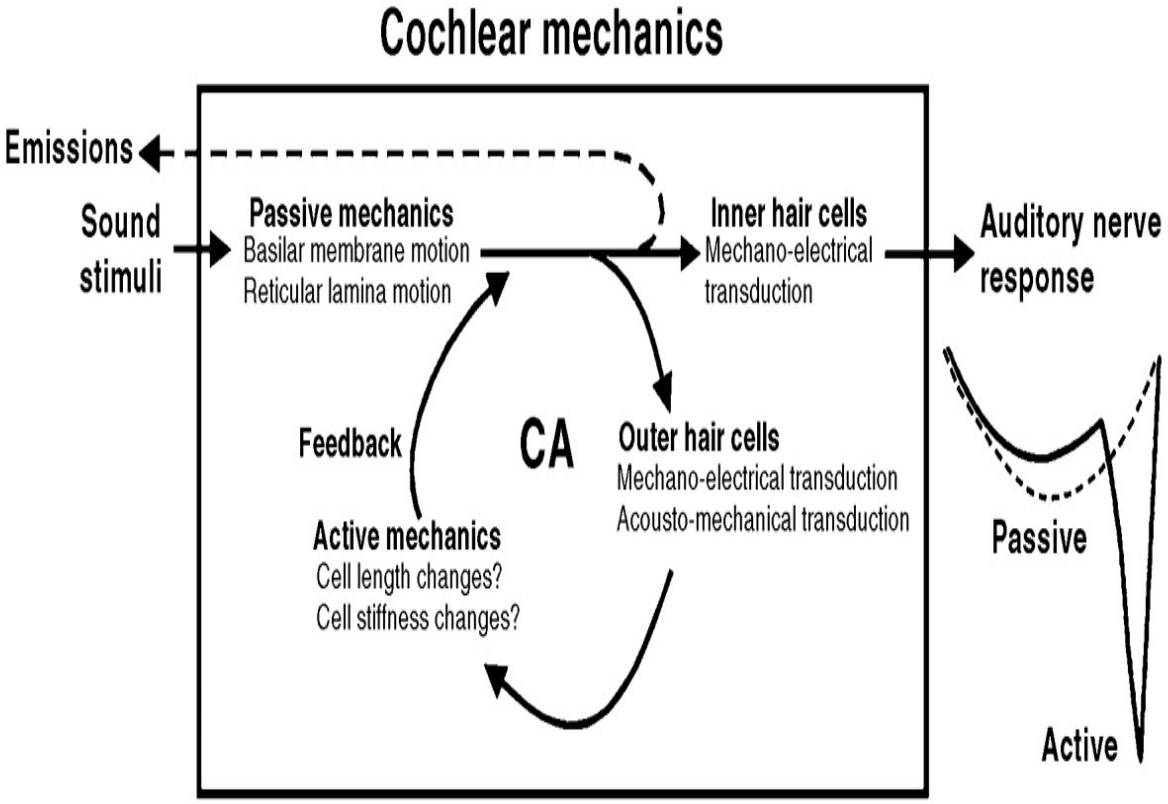
When travelling waves causes vibration of basilar membrane at the resonance point, the basilar fibres, the rods of corti, the hair cells and the lamina reticularis move as a single unit. It causes movement of steriocilia leading to excitement of hair cells and generation of receptor potentials.



Electrical events during the process of hearing

It is a type of sensory transduction in the hair cells by which sound energy is converted into action potential in the auditory nerve fibre. Three types of action potential occur during sound transduction:

1. Receptor potential or the Cochlear micro phonic potential
2. Endo-cochlear potential or Endo-lymphatic potential
3. Action potential in the auditory nerve fibre



Cochlear micro phonic potential

It is a mild depolarization that is developed when sound waves are transmitted to inner ear. Resting membrane potential in hair cells is -60 millivolt. Probable neurotransmitter may be glutamate. Movement of steriocilia causes depolarization whereas its movement in opposite direction causes hyperpolarization.

Hair cells

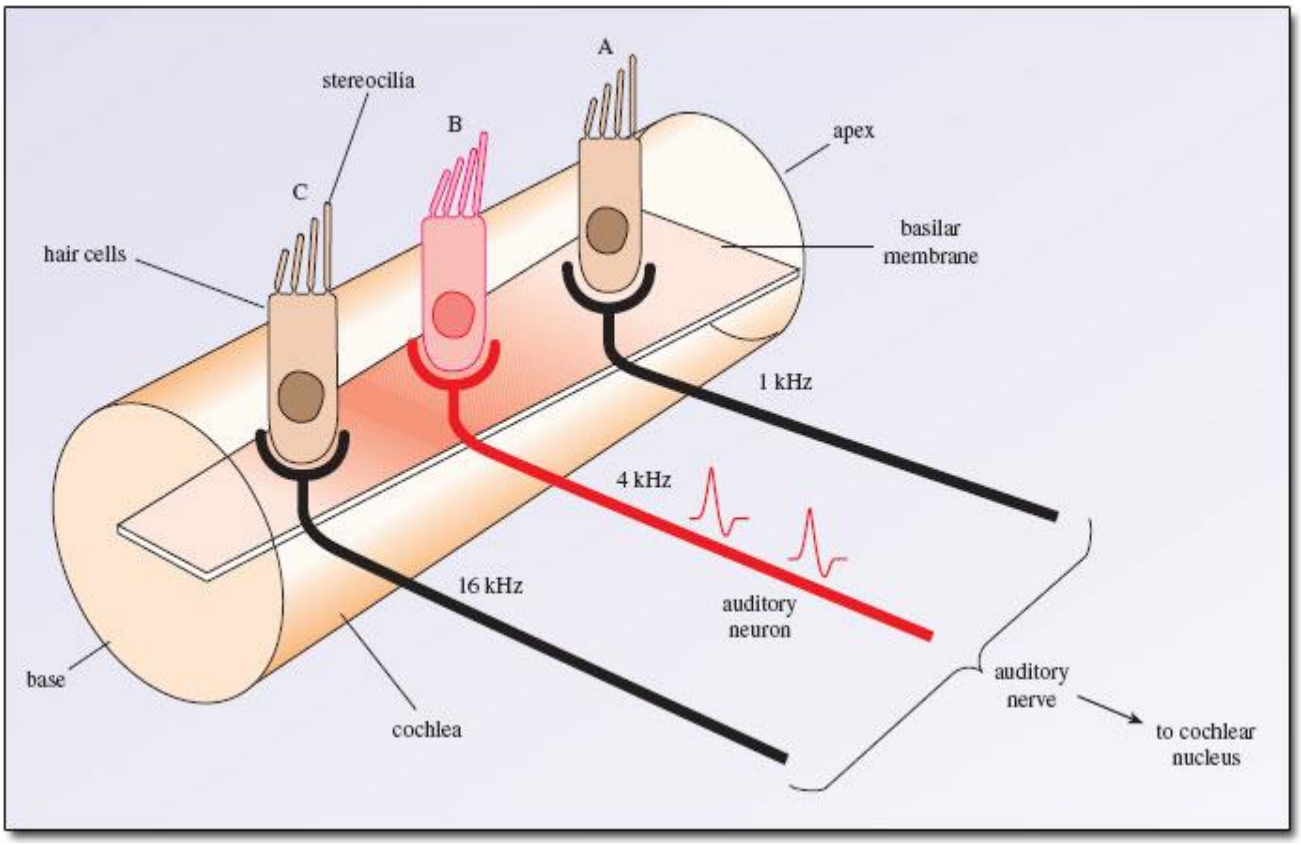
There are mainly two types of hair cells

1. Outer hair cells
2. Inner hair cells

Outer hair cells

“The outer hair cells are shortened during depolarization and elongated during hyperpolarization. This process is called as electro-motility or mechano-electrical transduction. This action facilitates the movement of basilar membrane and increases the amplitude and sharpness of sound. Hence the outer hair cells are also called collectively as the cochlear amplifier. the electro-motility of hair cells is due to the presence of a contractile protein in it, *prestin”*.

“The Outer hair cells are usually situated in the basilar membrane of the organ of corti. They are usually motile and a motor response is elicited by electrochemical response. The outer hair cells have stereo cilia arranged in three rows in a pattern of W. These stereocilia move as a single unit as they are linked together. Otoacoustic emissions are thought to originate from the outer hair cells”.

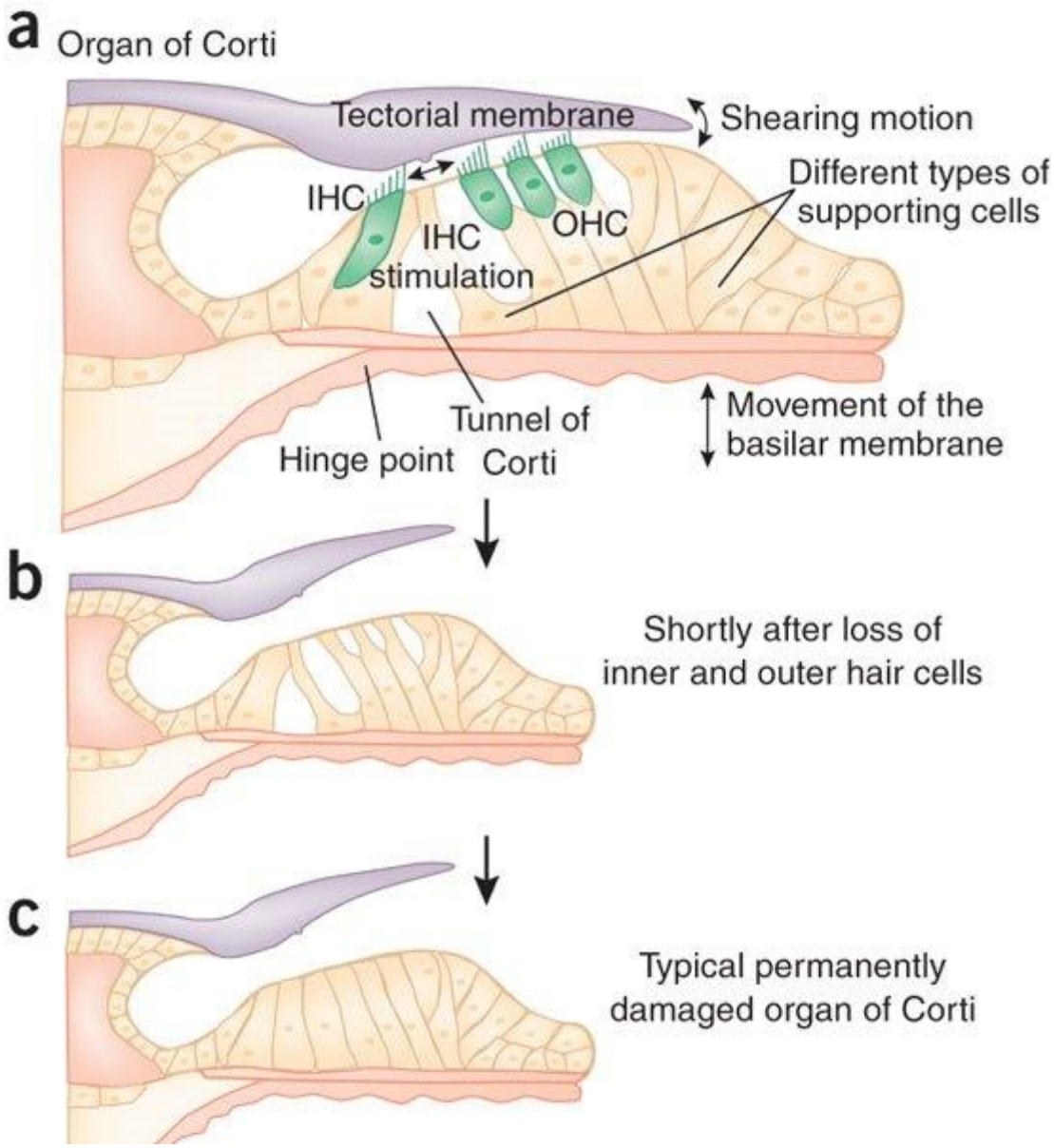


Inner hair cells

They are responsible for sound transduction. These are primary sensory cells that generate action potential in the nerve fibre.

Otoacoustic emissions (OAE)

"Otoacoustic emissions are sounds generated within the normal cochlea either spontaneously or in response to acoustic stimulations. OAEs are now thought to reflect the activity of active biologic mechanisms within the cochlea responsible for its sensitivity, sharp frequency selectivity and wide dynamic range of normal auditory system. There is significant indirect evidence that this mechanism is due



to the function of outer hair cells in the mammalian cochlea. Also absence of Outer hair cells is associated with lack of OAEs supporting the hypothesis that the outer hair cells are responsible for generation of OAEs".

Properties

- OAEs are independent of synaptic transmission and are pre-neural.
- OAEs are unaffected by stimulus rate.

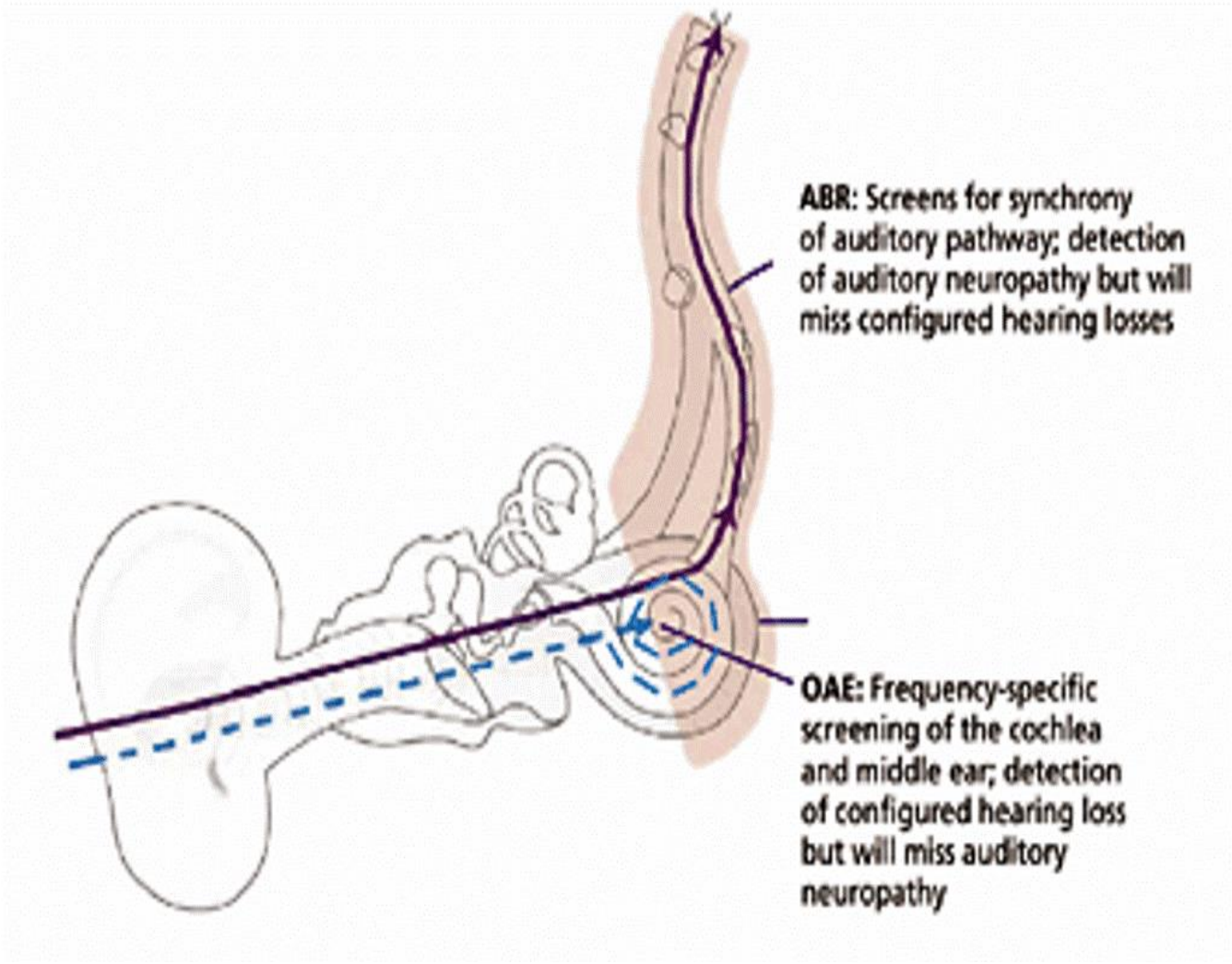
- Evoked OAEs are frequency dispersive
- OAE tuning or suppression curves are very similar to VIII nerve tuning curves.
- OAEs are vulnerable to noxious agents such as ototoxic drugs, neurotoxins like snake venom, organophosphates, and hypoxia.
- It is an objective non-invasive measure of cochlear status in clinical population

"The main objective of Otoacoustic emissions test is to evaluate the condition of cochlea, mainly the function of hair cells. OAE testing can be done even in patients who are unconscious or those who are in sleep because it does not need any behavioural response from the subject".

"Cochlea usually produces sounds of low intensity termed Otoacoustic emissions. These sounds are found to originate due to the contraction and expansion of outer hair cells".

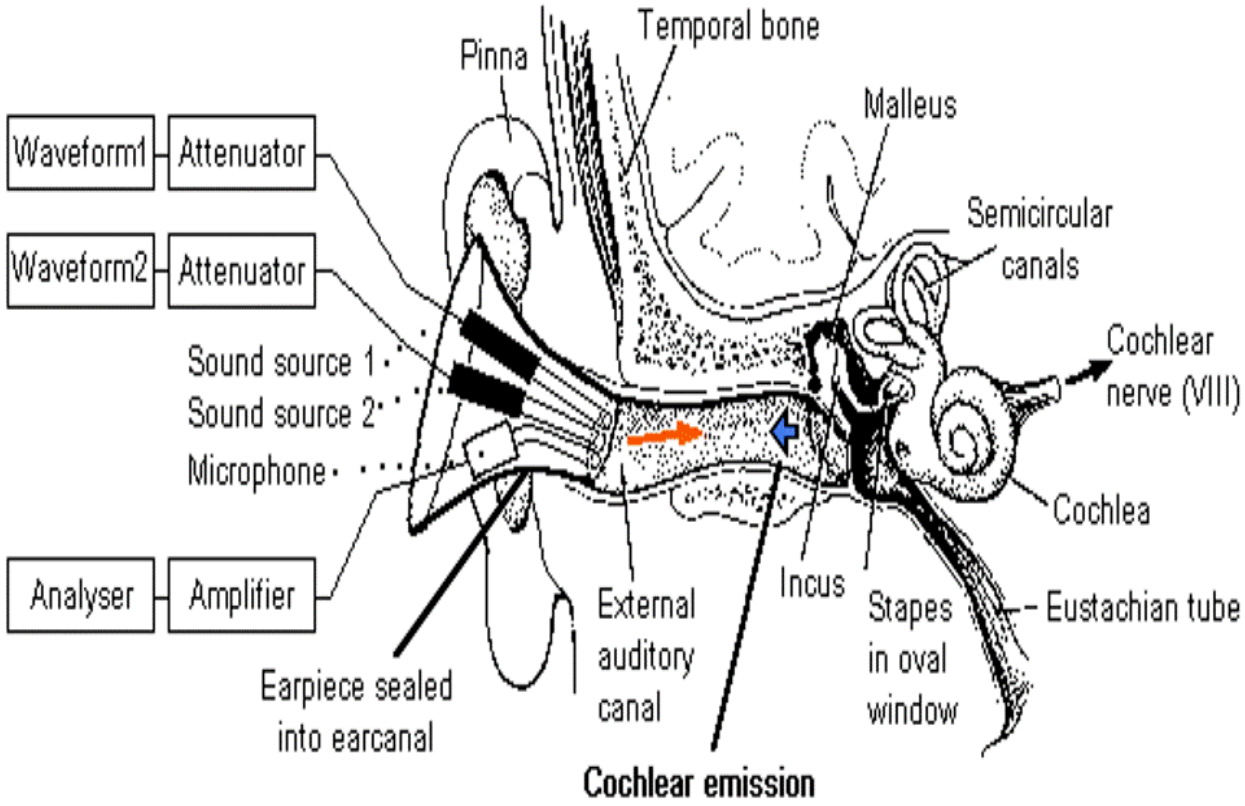
There are four types of OAEs which are as follows:

1. Spontaneous Otoacoustic emissions
2. Transient evoked Otoacoustic emissions
3. Distortion product Otoacoustic emissions
4. Sustained frequency Otoacoustic emissions



"PTA usually evaluates external ear, middle ear, inner ear, vestibulocochlear nerve and auditory system. However the emissions arise from cochlea, the outer and the middle ear need to be in good function for conduction of emitted sounds back to the microphone. So the status of the cochlear function is measured by the OAE testing and it is also used as a screening tool. However the auditory status of a person cannot be fully ascribed by Otoacoustic emissions. But they can help by providing information regarding the region of lesion".

RECORDING



"The probe of the machine is placed in the EAC for the purpose of seal. Various sized probes are available for children and adults due to their external auditory canal volume difference. Sound pressure level will be more effective when it is placed in smaller ear canal.

Many responses are noted and calibrated. The results need to be interpreted in comparison to noise floor. Hence for a good recording, minimal ambient noise and physiological noise is very important. All OAEs are analyzed relative to noise floor. Therefore reduction of physiologic and acoustic ambient noise is

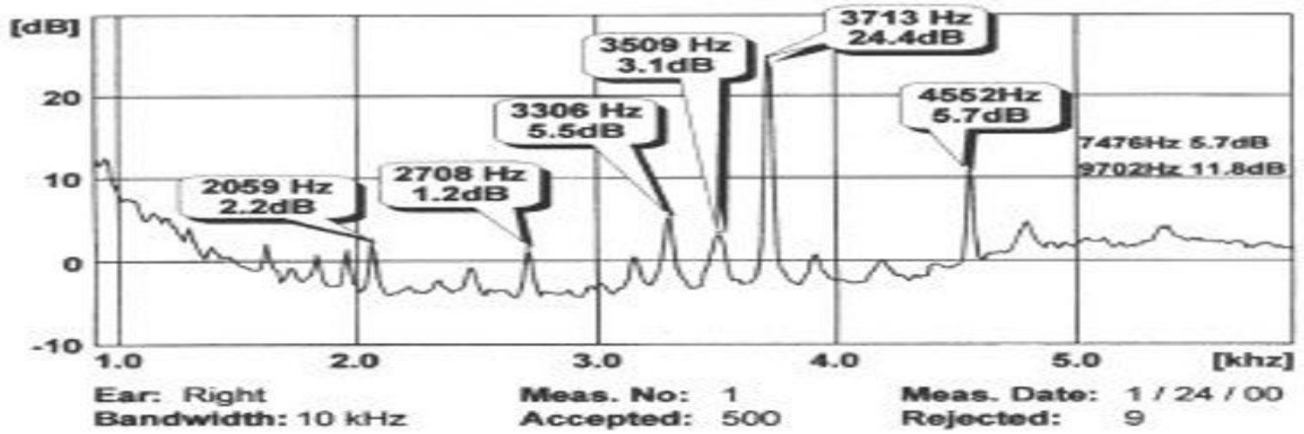
critical for good recording. Since no response from the subject is needed, Otoacoustic emissions can be measured in unconscious patients".

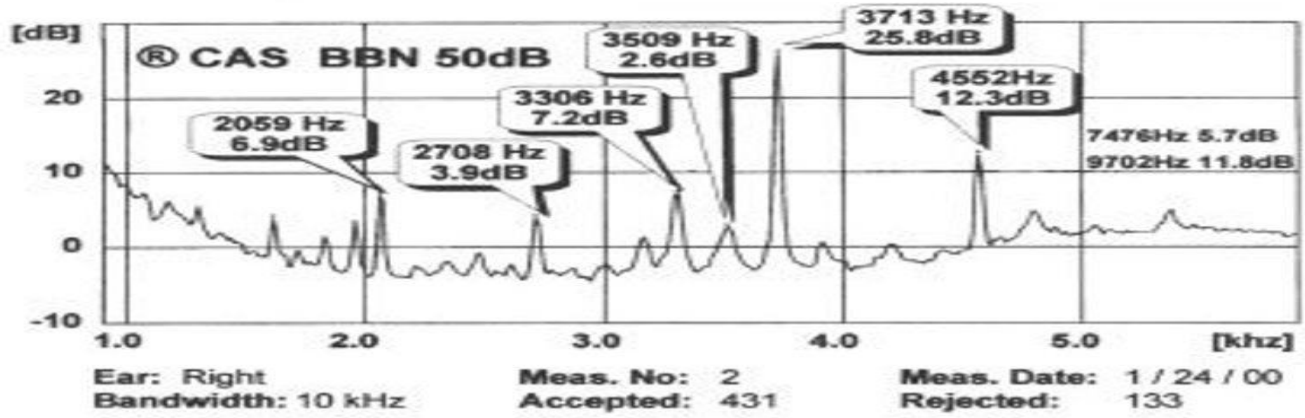
Spontaneous Otoacoustic Emissions

"They are usually spontaneous ones and not in response to any stimulus. They are measured in outer ear. Since stimulus is not needed, many recordings can be obtained from a single patient to confirm its replicability and also to differentiate them from noise floor. These values usually range from five hundred to seven thousand hertz".

"These are usually narrow band signals emitted by the ears of humans, even in the absecne of acoustic stimulus. These were first identified by Gold in 1948. Measurement of SOAEs is relatively simple. In patients with sensory neural hearing loss of grade. Most of the persons are usually un aware of its presence".

"They are measured by using a probe placed in the ear canal attached to a low noise microphone. All the instruments are caliberated for low noise. Filtration of the external noise is of particular importance. They are usually concentrated in the range of one to three kilo hertz. Some studeis say the stability of this spontaneous acoustic emission will vary and the variability was found in their amplitude and frequency within them and sometimes across the session of recording".

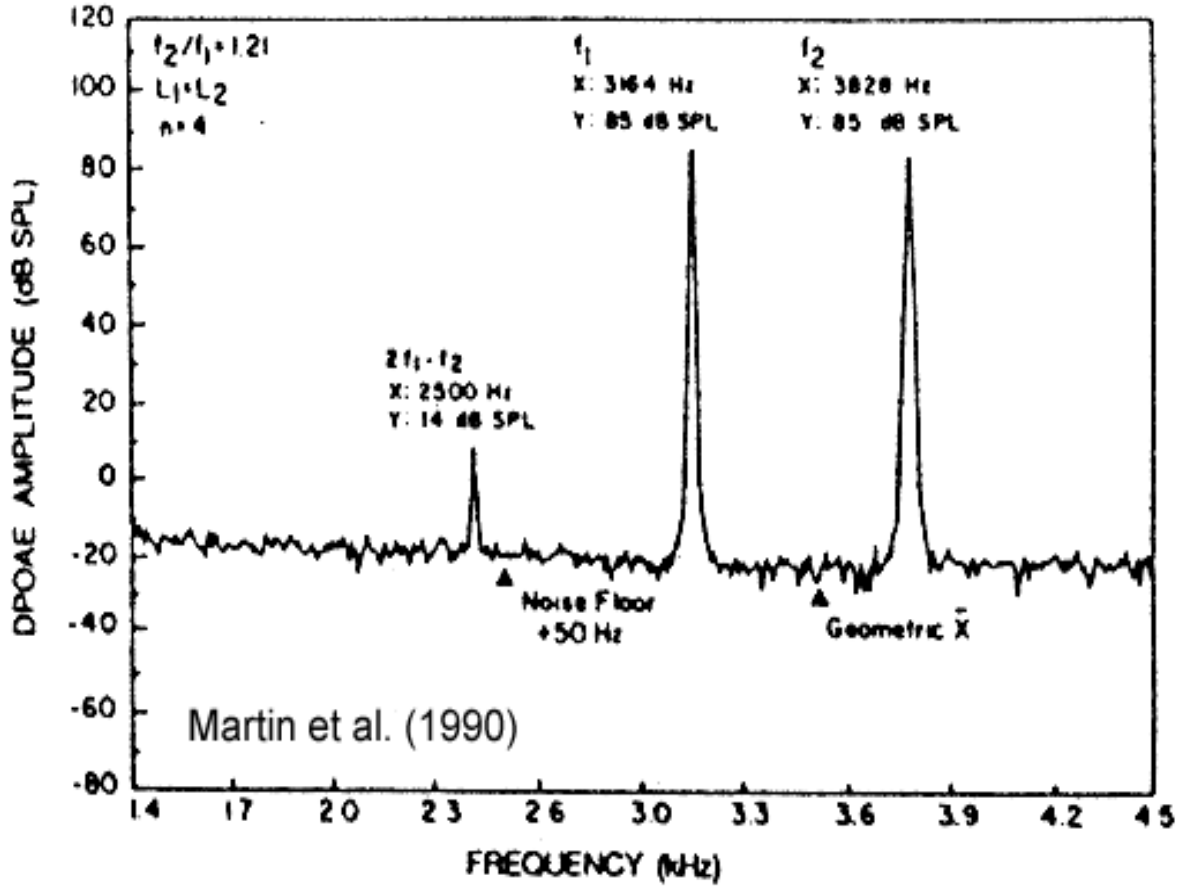




Transient Otoacoustic Emissions

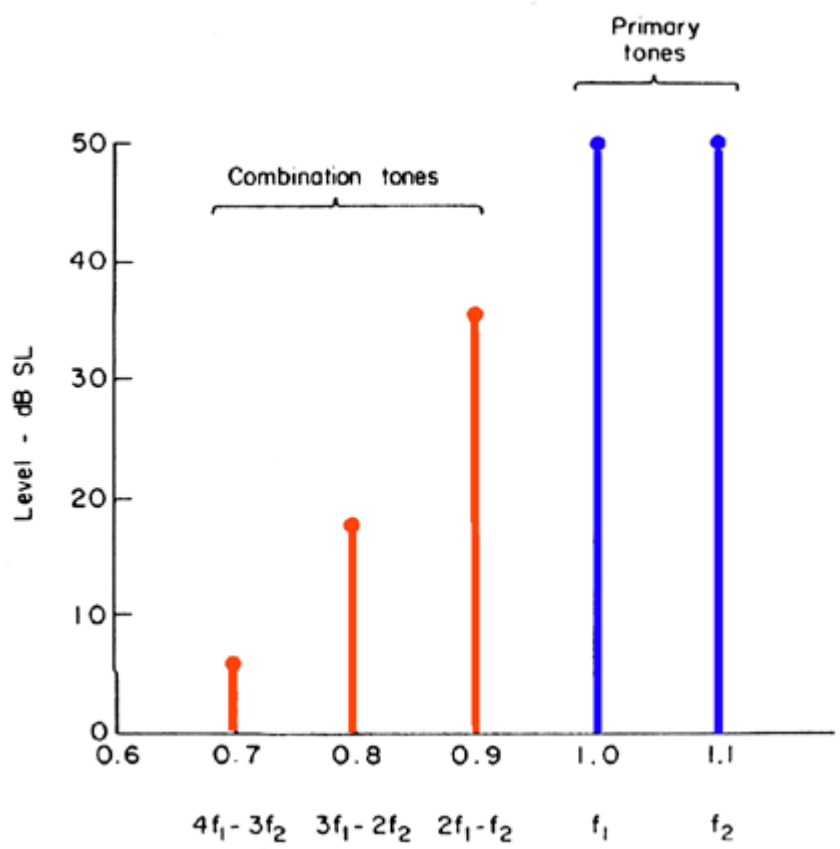
"For measuring TOAEs stimuli mainly used are the clicks, sometimes tone bursts. The SPL stimuli ranges from eighty to eighty five decibels. The rate of stimulation is less than sixty stimuli per second. Recording the TOAES occurs in a time span of nearly twenty milliseconds. The responses are measured in two separate banks A & B. A Response is one which correlates between the memory bank of computers. Noise is one that does not correlate with the same. TAOEs usually span the frequency range of five hundred to four thousand hertz".

Distortion product Otoacoustic Emissions



"For measuring DPOAEs , stimuli commonly used are two pure tones that are at two different frequencies and intensities namely F1, F2 in which F2 value is more than F1. The response is mainly elicited by the relationship between the frequency and intensity levels. The highest DPOAE usually obtained at F1/ F2 ratio and it measures about 1.2 for high and low frequency range and for medium frequency range it measures about 1.3". an optimal response is usually obtained if l1 equals or is greater than l2. DPOAE will be rendered more prone to errors by

lowering of intensities. The commonly used setting is 65/ 55 SPL, l1/l2. Responses are recorded in the frequency emission of 2F1-F2. However they are more commonly calculated according to F2. this is because F2 corresponds to cochlear frequency region in which response is produced."



Prerequisites for obtaining Otoacoustic Emissions

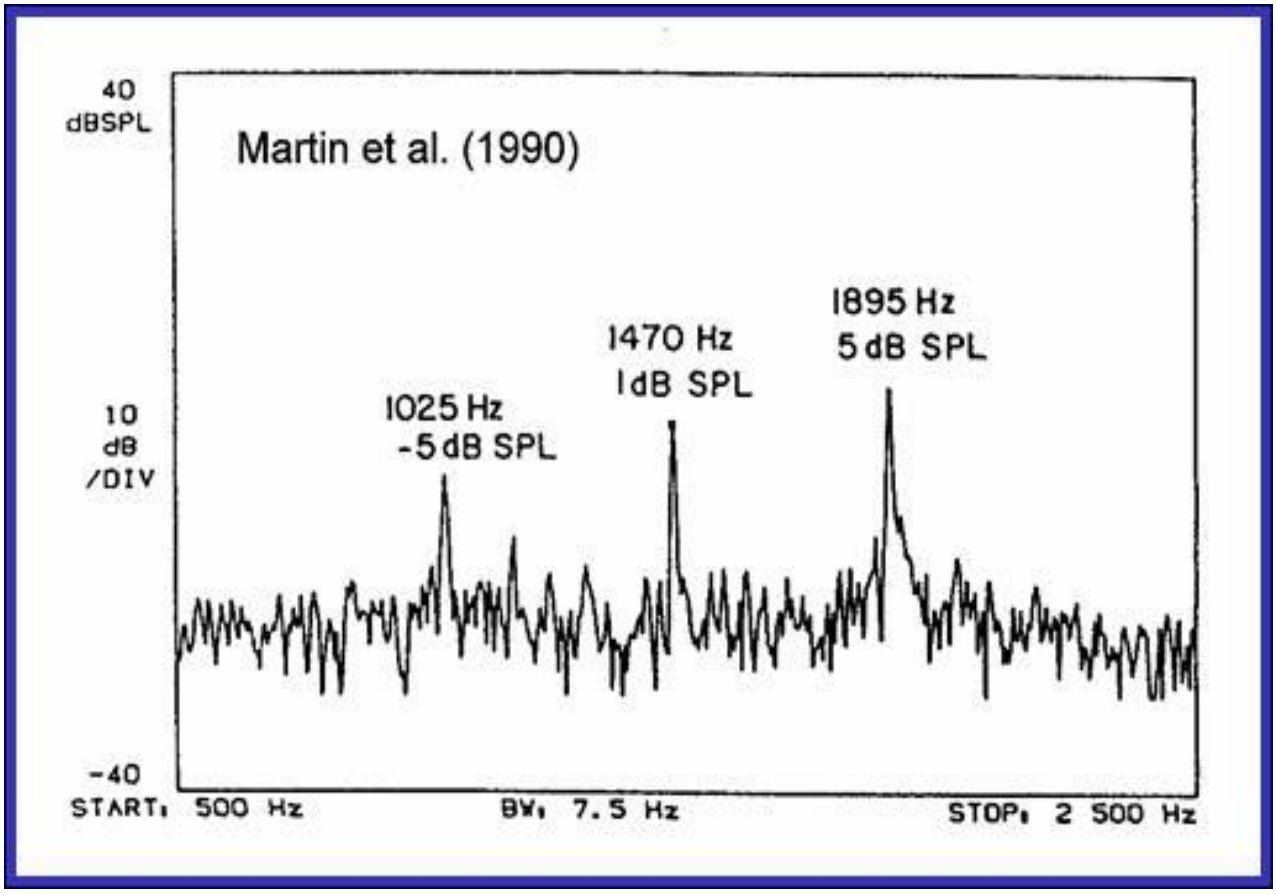
- Unobstructed outer ear canal
- Seal of ear canal with the probe
- Optimal positioning of the probe

- Absence of middle ear pathology
- Functioning cochlear Outer hair cells
- Relatively quiet recording environment

Spontaneous Otoacoustic Emissions

“The usual occurrence of spontaneous Otoacoustic emissions in persons range from thirty five to forty five per cent in whom hearing is normal. Of these, adult population specific range is twenty five to sixty five per cent. But in neonates, around twenty to eighty per cent would have these emissions. SOAEs are usually absent in persons if their hearing threshold is less than thirty decibel. Hence their presence is an index of normal functional cochlea. However, their absence does not mean there is a pathology. Spontaneous Otoacoustic emission occur in a range of thousand to two thousand hertz, whereas the amplitudes range from -5 to 15 decibel sound pressure level. Some persons have broader frequency pattern of SOAEs. These emissions are usually presence in both ears and rarely lateralized. If they lateralize to one ear, right side is more common than the left. In general, they are found to be more in females than in males. Association of these emissions is rare with tinnitus. Since tinnitus usually occurs in cochlear pathology, these emissions are usually absent in this condition. Clinically these emissions are used for the purpose of screening of hearing.

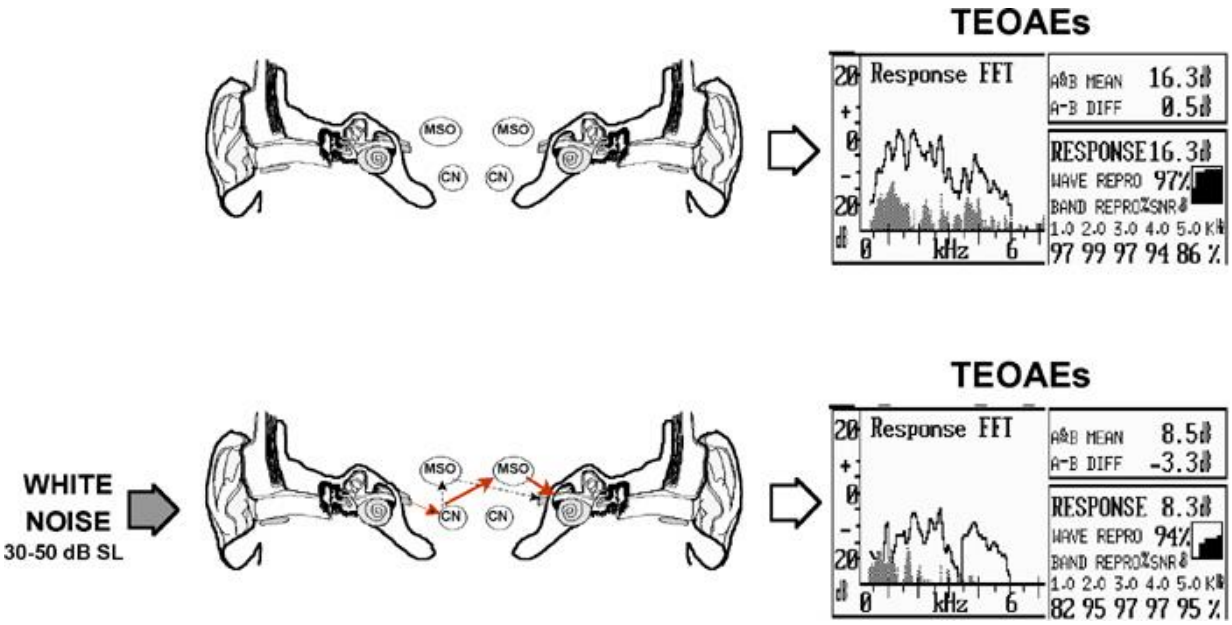
High level of these emissions sometimes may occur in some individuals, which may be heard by others, but these kind of emissions are usually very rare and they are more commonly found in children in comparison to adults".



Transient Otoacoustic Emissions

"The clinical use of measuring transient Otoacoustic emission is mainly for screening of children's hearing in particular that of infants. It helps to interpret the auditory thresholds by validating it electrically and physiologically. Hence it helps to assess the location of lesion. These emissions are usually emitted and recorded for a transient stimulus. Hence the stimulus has narrow specific

frequency range. These emissions usually arise from the broad surface of cochlea".



"Presence of these emissions from a specific frequency range infers the sensitivity of the cochlea corresponding to that region is more or less twenty to forty decibel. In clinical practice, the presence of these emissions in a specific region of the octave band infers that hearing should be thirty decibel hearing loss or better".

Distortion product Otoacoustic Emissions.

"The main differentiating feature of TOAEs and DPOAEs is that their higher specificity in frequency range which are mainly used for recording high frequency range that cannot be done by TOAEs. For these properties, these emissions are highly useful in detecting the cochlear pathology as early as

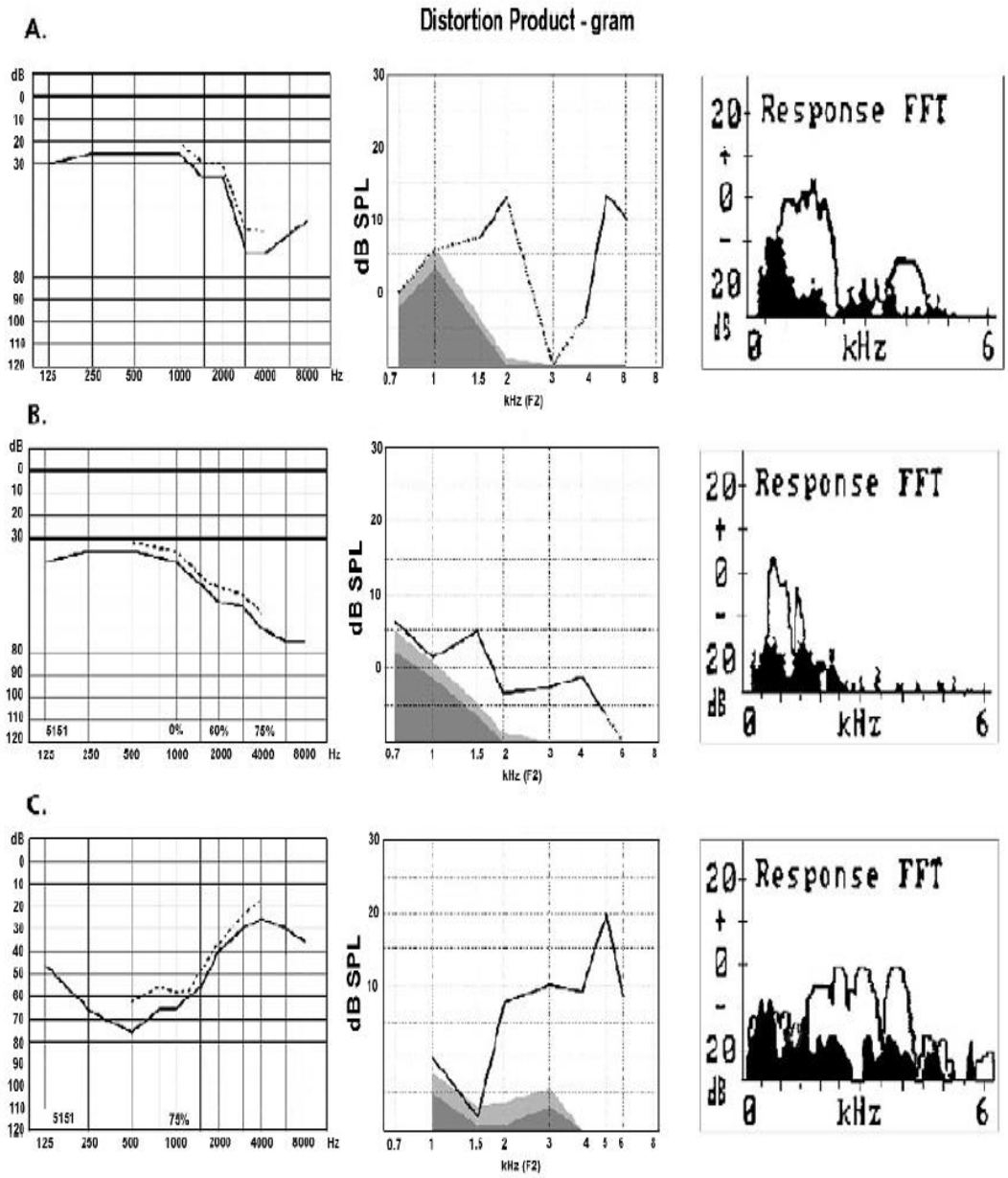
possible particularly in oto toxicity and in noise induced hearing loss. The reliability of these emissions is very high above 1000 hertz".

"For the purpose of screening the hearing of children, especially of infants, both distortion product Otoacoustic emissions or transient Otoacoustic emissions are used. However transient Otoacoustic emissions have been used for a long time for this purpose and are well established.

Based on the technique used, these emissions are usually recorded in persons having hearing loss of mild to moderate degree in whom the transient Otoacoustic emissions are found to be absent. These emissions usually correspond to the configuration of hearing loss audiometrically".

Sustained frequency Otoacoustic Emissions

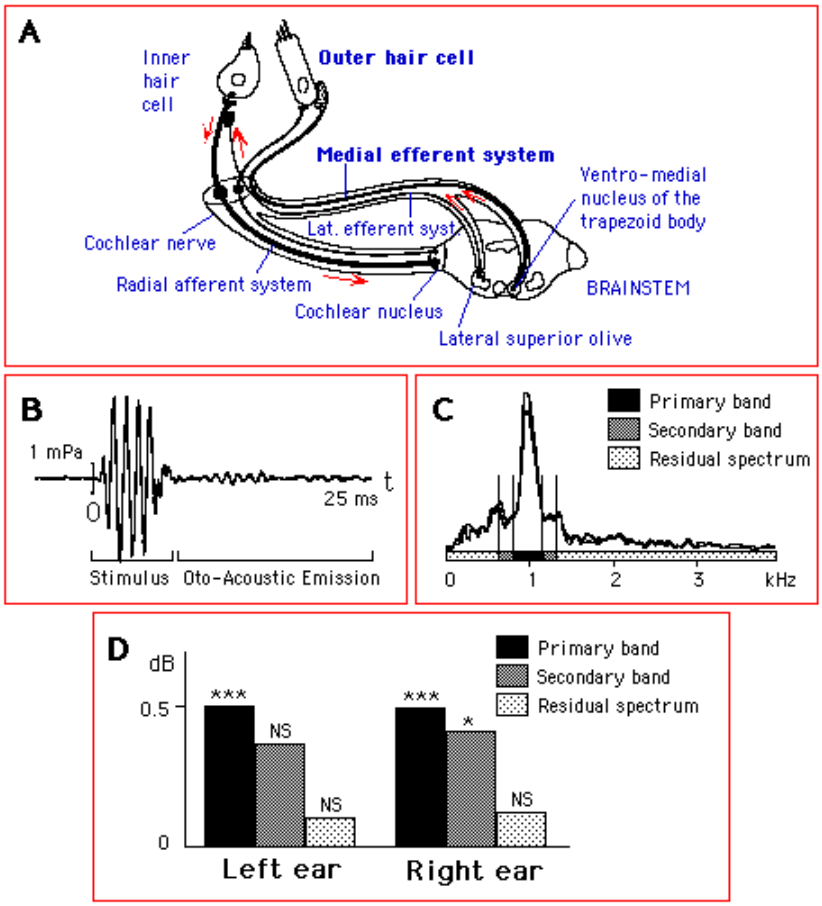
"These emissions are usually the responses which are produced for a continuous tone. Since the emission and the stimulus and its emission superimpose over each other in the external ear, the microphone records both the stimulus and its emissions. Currently sustained frequency emissions are not practically applicable".



Stimulus Frequency Emissions

Stimulus frequency emissions are the most frequency specific and probably the least clinically applicable of emission types. They reflect the response of the cochlea to pure tone input occurring simultaneously with and at the same frequency of the eliciting stimulus.

When a tone is presented to the ear the sound pressure measured in the ear canal is the sum of both the tone presented and the retrograde output of the cochlear amplifier, all other types of evoked Otoacoustic emissions have been separated from the evoking stimulus either temporally or spectrally.



The lack of temporal / spectral separation requires more sophisticated equipment and processing to measure SFEs. They are not currently practical for clinical use. To measure SFEs, a tone frequency is presented to the ear through a probe microphone assembly system, as in measuring other types of emission. Often the tone is swept across a certain frequency range. The SFE is extracted from the

recorded ear canal sound pressure by using vector subtraction. This requires a lock in amplifier to specify the ear canal sound pressure both in terms of amplitude and phase. It also requires that the system of stimulus generation, delivery and measurement is liner in both amplitude and phase.

The SFE is characterized by “dips” and “peaks” indicating the relative strength of SFE. The SFE pattern across frequencies is idiosyncratic, that it is unique for each ear tested. Certain similarities however can be seen across subjects. In general, the frequency separation between adjacent peaks increases with increasing frequency. The SFE pattern fattens or loses definition as the evoking stimulus increases. SFEs seem to relate closely with auditory sensitivity. Specifically comparing auditory threshold microstructure with the SFE pattern reveals that threshold minima are found at frequencies where an SFE maxima occurs. As with other types of Otoacoustic emissions, SFEs are absent in ears with cochlear hearing loss exceeding 40 decibels.

If the amplitude of tone sweeps is measured by using a spectrum analyser, perturbations can be seen at lower levels that are closely related to SFEs. A number of reports in the literature have reported such amplitude data as SFEs. The phase must also be known. However to perform the vector subtraction, as amplitude alone is not sufficient to define the non-linearity or the emission

Non pathologic problems that can cause absence of OAEs

- Poor probe tip placement or poor seal
- Improper waves
- Wax in the ear canal.
- Foreign bodies in the outer ear.
- Uncooperative patients

Pathologic problems that can cause absence of OAEs

- External auditory canal atresia.
- Inflammatory conditions of external ear.
- Negative pressure in middle ear.
- Perforation of ear drum
- Ossicular discontinuity
- Ossicular sclerosis.
- Otosclerosis
- Glue ear.
- Exposure to ototoxic medications
- Noise exposure
- Any other cochlear pathology

Conditions that do not affect OAEs

- Eight cranial nerve pathology
- Lesions in the higher centers for hearing.
- Vestibular pathology

Situations in which there is normal OAEs and unusual behavioural patterns

- Functional hearing loss
- Attention deficits
- Autism
- Auditory neuropathy
- Hyperbilirubinemia
- Neurodegenerative diseases
- Neurometabolic diseases
- Demyelinating diseases.
- Hereditary motor sensory neuropathology
- Inflammatory neuropathy
- Ischemic / hypoxic neuropathy
- Encephalopathy
- Meningitis
- Cerebral palsy

Issues in the clinical implementation of Otoacoustic Emissions

Since OAEs can be measured non-invasively and are sensitive to cochlear status, they are potentially a valuable addition to clinical audiology. To optimize the clinical utility of OAEs, one needs to decide whether a particular application requires knowledge of sensitivity as well as the integrity of the OAE generators.

Finally evoked Otoacoustic Emission should be viewed as an additional objective audiological technique and may be most powerful when used in conjunction with neural sound evoked potentials and its measurements. Ideally sophisticated engineering will allow us to measure external and middle ear impedance simultaneously; all types of OAEs, and sound evoked neural potentials.

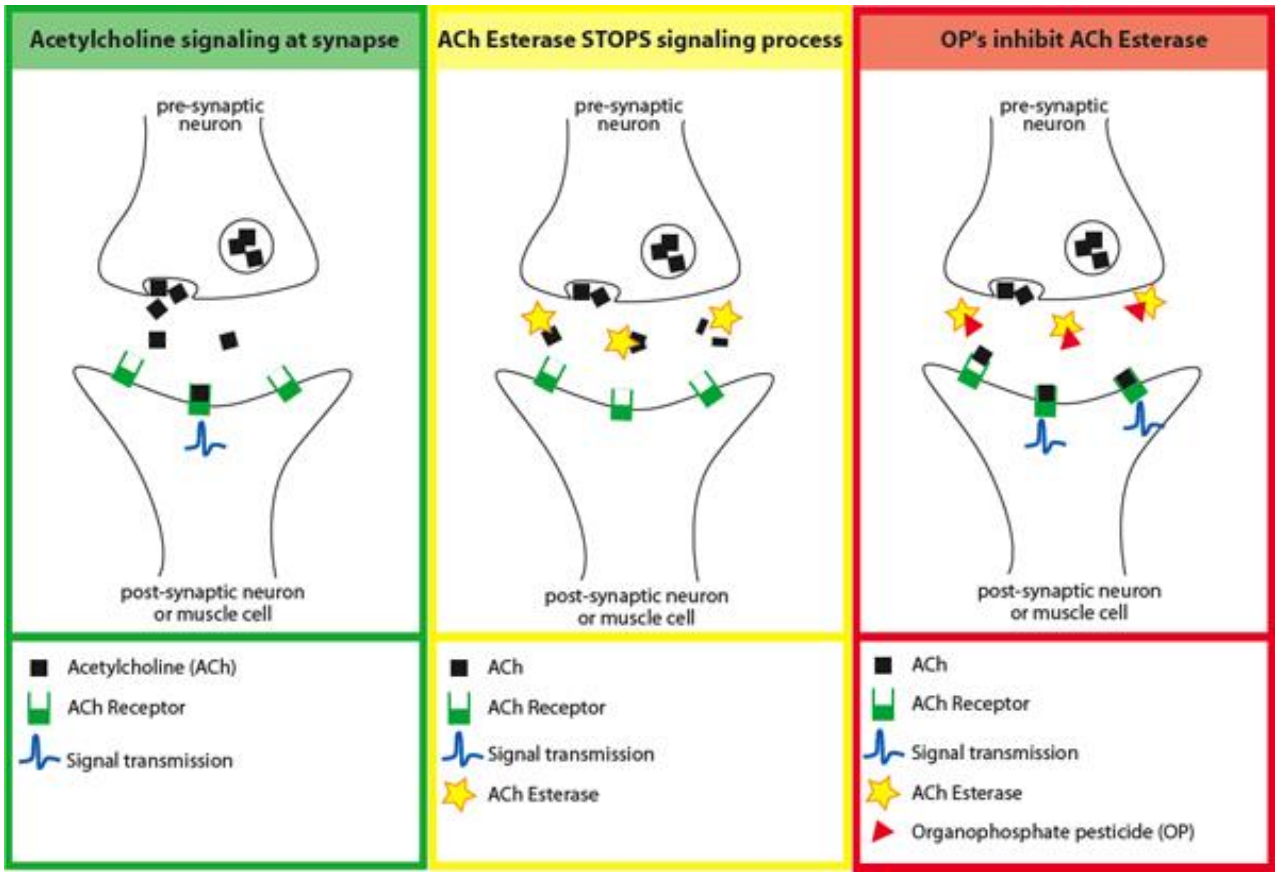
ORGANOPHOSPHATE POISONING

Every year, nearly one million deaths are due to suicide. Deliberate self - poisoning has become an increasingly common response in adults due to emotional distress. Agricultural pesticides are the substances most commonly used for self-poisoning. Among agricultural pesticides the most commonly used substances are organophosphate compounds especially in the developing countries like India and could potentially affect the hearing due to their neurotoxic nature. The principal pharmacological action of all organophospates compounds is acetyl cholinesterase inhibition resulting in overstimulation of acetyl choline receptors. Most of the studies in animals have been documented that these agents have an ototoxic effect and in humans, both peripheral hearing loss and central site have been documented to get affected by these compounds.

Commonly used organophosphorous compounds

- Ethyl parathion
- Methyl parathion
- Monocrotophos
- Dimethioate
- Chlorpyriphos
- Diazinon
- Methamidaphos
- Fenthion

Mode of action



Organophosphates are powerful inhibitors of acetyl cholinesterase which is responsible for hydrolysing acetyl choline to choline and acetic acid after its release and completion of function (i.e., propagation of action potential). As a result there is accumulation of with continued stimulation of local receptors and eventual paralysis of nerve / muscle.

Although organophospates differ structurally from acetyl choline they can bind to acetyl cholinesterase molecule at its active site and phosphorylate the serine moiety. When this occurs the resultant conjugate is infinitely more stable than the acetylcholine-acetylcholinesterase conjugate, although the endogenous hydrolysis

does occur. Depending upon the amount of stability and charge distribution the amount to hydrolysis is increased. Phosphorylated enzymes degrade very slowly over days to weeks making the acetyl cholinesterase essentially inactive.

Once the acetyl cholinesterase is phosphorylated, over the next 24-48 hours an alkyl group is eventually lost from the conjugate, further exacerbating the situation. As this occurs the enzyme can no longer spontaneously hydrolyse and becomes permanently inactivated.

Apart from acetyl cholinesterase, organophosphates exert powerful inhibitory action over other carboxylic ester hydrolases such as chymotrypsin, pseudo - cholinesterase, plasma and hepatic carboxyl esterases, butryl cholinesterase and other non-specific proteases. It has been proposed that delayed peripheral neuropathy caused by organophosphates is due to phosphorylation of some esterases other than acetyl cholinesterase such as neurotoxic esterase also known as neuropathy target esterase (NTE). Neuropathy caused by inhibition of NTE may develop 2-5 weeks after acute poisoning.

Pathophyisology

Paroxonase (PON1) is an important enzyme in the organophosphate metabolism. It can inactivate the organophosphate through hydrolysis. It hydrolyses the active metabolites of compounds and not the parent compound the presence of

paroxonase polymorphisms implies that to be different enzyme levels and efficiency of catalysis of this esterase which in turn implies that different level of susceptibility to the toxic effects of organophosphates.

The level of paroxonase plasma hydrolytic activity actually provides protection against organophosphates. It plays as significant role in regulating the degree of toxicity of organophosphates depending on the type of compounds. The degree of protection of paroxonase depends on its catalytic efficiency. So higher its concentration, more will be the protection. The level of paroxonase is more in the adults compared to neonates. Thus the wide range in the enzyme level variability determines human sensitivity to organophosphates.

Clinical features

Organo phosphate compounds cause both cholinergic and nicotinic symptoms.

1. **Cholinergic excess**
    a. ***Muscarinic effects*** (hollow organ parasympathetic manifestation)
        - Bronchoconstriction
        - Wheezing
        - Dyspnoea
        - Cough
        - Pulmonary oedema

- Vomiting
- Diarrhoea
- Abdominal cramps
- Increased salivation
- Lacrimation
- Sweating
- Bradycardia
- Hypotension

  Among the above, Bradycardia and hypotension occur following moderate to severe poisoning.

b. ***Nicotinic effects*** (autonomic ganglionic and somatic motor effects)

- Fasciculation
- Muscle Weakness
- Hypertension
- Tachycardia
- Fatigability

Hypertension can occur in up to 20 % of patients. Cardiac arrhythmias and conduction defects have been reported in severely poisoned patients. ECG abnormalities may include sinus Bradycardia / tachycardia, atrio-ventricular conduction delay, idio-ventricular rhythm, premature

ventricular extra-systole, ventricular tachycardia, ventricular fibrillation, QT prolongation and atrial fibrillation

c. CNS effects

- Restlessness
- Headache
- Tremor
- Drowsiness
- Delirium
- Slurred speech
- Ataxia
- Convulsions

Coma is seen in later stages. Death usually results from respiratory failure due to weakness of respiratory muscles as well as depression of central respiratory drive. Non cardiogenic pulmonary oedema is a common manifestation of severe poisoning. Acute respiratory insufficiency is the main cause of death in acute OP poisoning. Metabolic acidosis has occurred in severe poisoning. Characteristic kerosene like odour is often perceptible in the patients since the solvents used in many OP insecticides is a derivative of petroleum.

Miosis as a characteristic feature may not be apparent in the initial stages. Blurred vision may persist for several months.

Organophosphates rapidly produce symptoms of mucous membrane and upper airway irritation leading to bronchospasm following systemic absorption. Other cause of death in Organophosphate poisoning include hypoxia, hyperthermia, renal failure, hepatic failure. Patient with QT prolongation are more prone for respiratory failure. Aspiration of preparations leads to chemical pneumonitis.

Intermediate syndrome

It sometimes occurs 1-4 days after poisoning due the long lasting cholinesterase inhibition and muscle necrosis. Main feature include muscle weakness and paralysis characterized by motor cranial nerve palsy, weakness of neck flexors, proximal limb muscles and acute respiratory paresis.

Paralytic signs include inability to lift the neck or sit up ophthalmoparesis, slow eye movements, facial weakness, difficulty in swallowing, limb weakness, areflexia, respiratory paralysis and death. It may be due to inadequate treatment of the acute episode especially involving sub therapeutic administration of oximes or inadequate assisted ventilation. Several investigators have proposed

that intermediate syndrome may develop as a result of several factors, inadequate oxime therapy, the dose and route of exposure, chemical structure of organophosphate, time taken to initiate therapy, and possibly efforts to decrease absorption or enhance elimination of organophosphates.

Once it sets in the intermediate syndrome will have to be managed by supportive measures since it does not respond to oximes or atropines.

Delayed syndrome

It sometimes occurs 1-4 weeks after poisoning due to nerve demyelination and is characterized by flaccid weakness and atrophy of distal limb muscles or spasticity, ataxia. A missed motor sensory neuropathy usually begins in the legs causing burning or tingling and then weakness. This syndrome also does not respond to oximes or atropine. Severe cases progress to complete paralysis impaired respiration and death. The nerve damage of organophosphate induced delayed neuropathy is frequently permanent. The mechanism appears to involve phosphorylations of esterases in peripheral nervous tissues and results in a “dying back” pattern of axonal degeneration.

Patients poisoned with highly lipid soluble organophosphates develop extra pyramidal effects including dystonia, resting tremor, Cog wheel rigidity, choreoathetosis. These effects begin 4-40 days after poisoning and spontaneously

resolve over 4 weeks. It is important to note that children may have different predominant signs of OP poisoning compared to adults, mainly CNS depression, stupor, flaccidity, dyspnoea and coma rather than the classical signs of OP poisoning.

Neurotoxic effects

Organophospates poisoning usually causes 4 neurotoxic effects in humans

- Cholinergic syndrome
- Intermediate syndrome
- Organophosphate induced delayed neuropathy
- Chronic organophosphate induced neuropsychiatric disorder.

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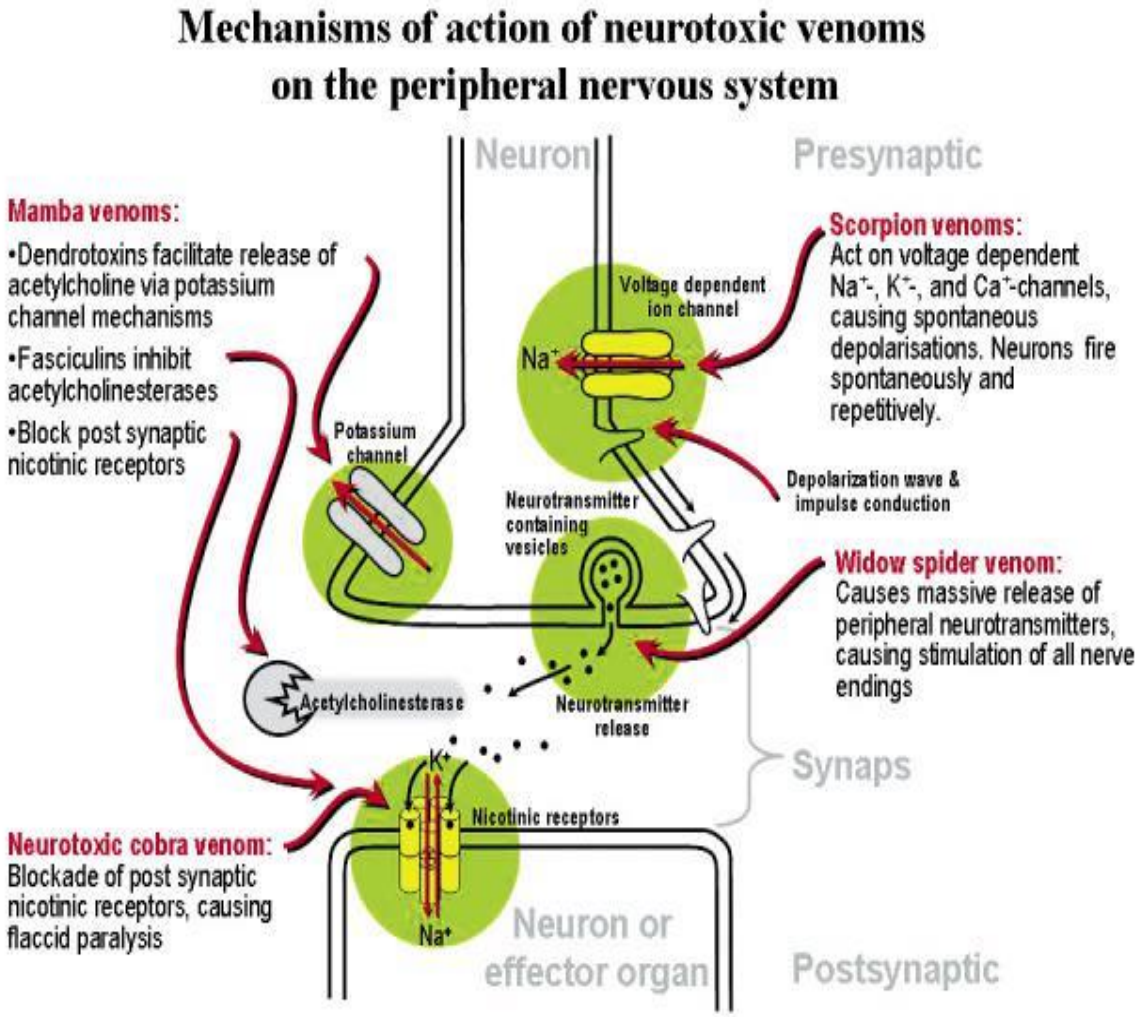
SNAKE BITE

Snake bites contribute to major health problems in India and continue to be a major medical concern. In India approximately one person is bitten by a snake and every two hours one case of snake bite proves fatal. Reports say that about 10 % of deaths are of the victims who come to the hospital and about 90% die outside having gone for other regional remedies.



Epidemiology

In India nearly four lac persons are bitten by snakes every year. Envenomation happens in approximately 82,000 and death occurs in 11,000 victims. Many deaths happen before victim reaches the hospital. Snake bite is observed all over the country with a rural urban ratio of 9:1 and more during monsoon and post monsoon season. Snake bites are often seen among agricultural workers than those going to the forest. Many of the susceptible populations are poor and those living below poverty line. They live in rural areas with less access to healthcare. The ratio between male to female among the victims is approximately 3:2. Majority are young and their age is around 25-44 years. Majority of the bites are noted in the extremities. The hospital stay varies from two to thirty days with median being four days. The in hospital mortality varies from 5-10 % and the causes are:

- Acute renal failure,
- Respiratory failure,
- Bleeding,
- Sepsis,
- Multi organ failure,
- Death.

Classification of snakes

There are more than 3,000 species of snakes in the world. For the purpose of clinical practice, the snakes are classified into poisonous and non- poisonous snakes. Poisonous snakes are classified under three families and they are :

- Cobra group (*Elapidae*)
- Viper group (*Viperidae*)
- Sea snake group (*Hydrophidae*)

Study of snakes of medical importance has reflected the view that four main species are responsible for mortality in snake bites in India. They are:

- Indian cobra *(Naja naja*)
- Common krait *(Bungarus caeruleus)*
- Russell's viper (*Daboia russelii*)
- Saw scaled viper (*Echis carinatus*)

And recently Hump nosed pit viper (Hypnale hypnale) has been identified as being capable of causing lethal envenomation and that this problem was being concealed by systematic misidentification of the above four said species.

Statistics On Clinical Aspects Of Snake Bites And Outcomes

Type of snake	Number treated	Local signs	Neuro-toxicity	Hemo-toxicity	Mech. Vent.	Hemo-dialysis	Fasci-otomy	No. of dead.
Cobra	118	80	118	-	90	-	-	2
Krait	82	-	51	82	60	3	-	2
Russell's viper	42	42	-	42	6	23	1	1
Hump nosed viper	4	4	-	4	-	4	-	1
Saw scaled viper	16	16	-	16	-	3	-	1
Sea snake	3	3	-	-	-	-	-	-
Non poisonous	16	6	-	-	-	-	-	-

Snake bite is an injury that is often a punctured wound inflicted by the fangs (modified teeth) of the animal sometimes leading to envenomation.

Most of the snake species are non-venomous which kill their prey by means of constriction and asphyxiation rather than envenomation. Snake bite's outcome usually depends on the following factors

- Species of the snake
- Quantity of venom injected
- General health condition of the person

Bites from non-venomous snake may cause injury which is often due to the laceration produced by its teeth or due to subsequent infection of the bite. Sometimes it may even trigger an anaphylactic reaction.

Snake venom

Snake venom is nothing but the toxic saliva secreted by the modified parotid glands. It is a clear amber coloured fluid when fresh. It is the most complex of all poisons containing more than 20 components. The components of venom show diurnal and seasonal variation. Bites inflicted at night and immediately after hibernation are most severe. Most of the dry weight of the venom is made up of proteins comprising a variety of enzymes, non-enzymatic polypeptide toxins and non-toxic proteins. Non- protein ingredients of venom includes carbohydrates and metals, lipids, free amino acids, nucleotides and biogenic amines. The lethal and the most deleterious fractions of snake venom are certain peptides and proteins of relatively low molecular weight. The peptides appear to have very specific

receptor sites both chemically and physiologically. The role of the peptides in snake bites is usually overlooked by the physicians.

The polypeptide toxins often called neurotoxins are found most abundantly in elapid and hydophid venoms. post synaptic alpha neurotoxins such as *alpha – bungarotoxin* and *cobrotoxin* contain about 60-70 amino acid residues and bind to acetyl choline receptors on receptor end plate. Post synaptic beta neurotoxins such as *beta- bungarotoxin, cobrotoxin* contain about 120-140 amino acid residues and a phospholipase A sub unit and prevent release of acetyl choline at the neuromuscular junction. Krait *beta bungarotoxin* causes an initial release of acetylcholine but subsequently damages the nerve terminal and prevents any further release. It is for this reason that krait victims often take longer time to recover than cobra victims.

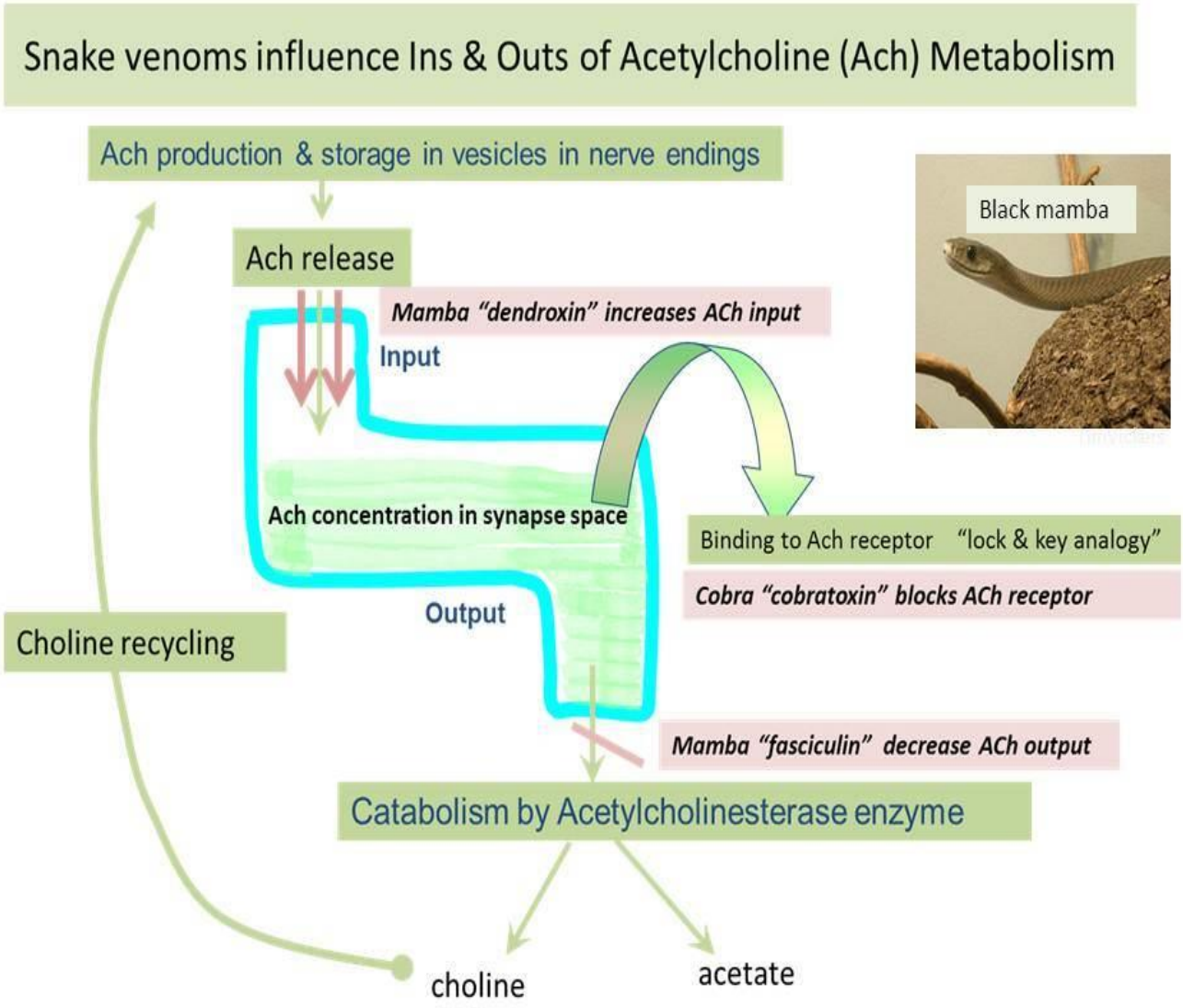
Enzyme function and pathological manifestations are most clearly evident in case of viper venom constituents. Russell's viper venom contains 2 proteases that stimulate the blood clotting cascade. RVV-X, a glycoprotein activates factor X by a calcium dependent reaction and it also acts on factor IX and protein C. RVV-V, an arginine ester hydrolase activates factor V. saw scaled viper venom contains a Zinc metallo-protein which activates prothrombin. It is important to know that Russell's viper can cause neurotoxic symptoms in addition to hemotoxic symptoms.

Hyaluronidase may serve to promote the spread of venom through tissue. Proteolytic enzymes may be responsible for local changes in vascular permeability leading to oedema, blistering and bruising and finally necrosis. Biological amines such as histamine and 5 hydroxy tryptamine may contribute to local pain and permeability changes at the site of snake bite. Since snake venom is mostly comprised of protein, it is not surprizing that anaphylactic shock can be induced if a person is bitten by the same species of snake the second time after a variable interval following the first bite.

The variation of venom composition from species to species explains the clinical diversity of snake bites. There is also considerable variation in the concentration of different venom constituents within the same species in different geographical locations and seasons. Sea snake venom contains

- Hylauronidase
- Acetyl cholinesterase
- Leucine amino-peptidase
- Phospholipase
- Phospho-monoesterase.
- Phospho-diesterase
- 5’ nucleotidase

SYMPTOMATOLOGY OF ELAPID BITE



Local effects

Mild pain and swelling with blistering and tenderness, sometimes causing early onset of gangrene. Contact of the venom with the eye results in venom ophthalmia characterized by intense irritation, conjunctivitis, corneal erosion, anterior uveitis and secondary infection

Systemic effects

Neurotoxicity is the dominant clinical feature of elapid bites. It consists of mainly two stages

a. *Pre- Paralytic stage*

- Vomiting
- Ptosis
- Blurred vision
- External ophthalmoplegia
- Paraesthesia around the mouth
- Hyperacusis
- Headache
- Myalgia
- Vertigo
- Hyper-salivation

b. *Paralytic stage*

Facial muscles, muscle of articulation and deglutition all become progressively flaccidly paralysed. Respiratory arrest may occur due to obstruction of paralysed tongue or due to paralysis of intercostal muscles and diaphragm. Loss of consciousness and convulsions are terminal phenomena resulting from hypoxemia.

Neurotoxicity, if it develops, generally begins 1-5 hours after envenomation but may be delayed as long as 19 hours. Cranial nerve palsy is found in some patients.

General features of envenomation of viperidae

- Swelling and local pain
- Enlargement of regional nodes
- Bleeding from gingiva and epistaxis
- Abdominal tenderness due to gastrointestinal bleeding
- Petechiae, purpura, ecchymosis
- Low back pain- indicator of early renal failure
- Hemoglobinuria
- Lateralizing neurological signs indicative of intracranial bleeding
- External ophthalmoplegia, ptosis, dysphagia
- Deep vein thrombosis and compartment syndrome

The actual strength of the snake venom differs considerably between different family and species and its strength is measured as Median Lethal Dose (LD50) in mice. Amount of venom produced also greatly differs between the snake species and families. Earlier particular snake venom was considered either neurotoxic or

hemotoxic but the updated literature clearly explains the complex nature and composition of snake venom.

Feature	**Cobra**	**Krait**	**Russell's viper**	**Saw scaled viper**	**Hump nosed viper**
Local pain / tissue damage	Yes	No	Yes	Yes	Yes
Ptosis / neurological signs	Yes	Yes	Yes	No	No
Hemostatic abnormalities	No	No	Yes	Yes	Yes
Renal complications	No	No	Yes	No	Yes
Response to neostigmine	Yes	No	No	No	No

MATERIALS AND METHODS

Study place

Rajiv Gandhi Govt. General Hospital,

Chennai - 600 003.

Collaborating department

Upgraded Institute of Otorhinolaryngology,

Department of audiology

Institute of internal medicine

Study design

Retrospective study

Study period

July 2013 to October 2014.

Inclusion criteria

1. Age of the individual – 20-35 years
2. No previous history of
    i. Ear discharge
    ii. Hard of hearing
    iii. Tinnitus
    iv. Vertigo

v. Noise exposure

vi. Intake of ototoxic drugs

3. Normal and intact tympanic membrane on otoscopic examination
4. Pure tone audiometric thresholds within normal limits.

Exclusion Criteria

1. Age less than 15 years
2. Age above 35 years
3. Previous history of
    i. Ear discharge
    ii. Hard of hearing
    iii. Tinnitus
    iv. Vertigo
    v. Noise exposure
    vi. Intake of ototoxic drugs
4. Abnormal tympanic membrane findings
    i. Perforation
    ii. Retraction
    iii. Cholesteatoma
    iv. Atlectatic tympanic membrane

Pre-workup procedure

Detailed history of the condition of the patient prior to admission in the hospital for treatment of organophosphate poisoning / neurotoxic snake bite.

Detailed Initial Assessment Of The Patient.

Proforma

1. Name :
2. Age :
3. Sex :
4. Cause of admission : OP poisoning / neurotoxic snake bite
5. Hospital No.:
6. Occupation :
7. Address :
8. Contact No.:
9. Date of admission :
10. **Questionnaire**

Previous history of..	**Yes**	**No**
Ear discharge		
Hard of hearing		
Tinnitus		

Vertigo		
Exposure to noise		
Intake of ototoxic drugs		
Trauma		

11.Examination

a. General examination

i. Level of consciousness

ii. Ventilator support – present / absent

iii. Vital signs

1. Pulse
2. Blood pressure
3. Respiratory rate
4. Temperature

b. Systemic examination

i. Respiratory system

ii. cardiovascular system

iii. central nervous system

iv. per abdomen

c. ENT examination

i. EAR

Part	Right	Left
Pinna		
Pre-auricular region		
Post auricular region		
External auditory canal		
Tympanic membrane • Perforation • Retraction • Cholesteatoma • Atelectasis	**Yes / no**	**Yes / no**

DPOAE

	Right ear	Left ear
Present		
Absent		

Pure tone audiometry

Special audiological tests

AUDX pro measurement system

"It uses both hardware and software to carry out the testing. AUDX pro usually produces some controlled type of acoustic signal in external auditory canal and helps to measure the evoked emission that are usually generated in cochlear outer hair cells. This system usually averages the collected data samples until measurement parameters are achieved in a specified one.

For DPOAEs, noise of the floor is usually seen on the LCD screen. A "PASS" or "REFER" criterion is usually assigned mainly based on comparison of Otoacoustic emissions of patients at the end of the test in response to a data that has been normalized. Clinician needs to see and interpret the results.

The AUDXpro contains a large colour display that supports graphical icons and means to facilitate programme operation and can display test data graphically. It comprises of a total of seven membranes which switch to manoeuvre through the program menu and operations".

AUDXpro is a medical device that produces information about the auditory system of the patient. This information is then available for medical diagnosis or screening.

Ear probe instructions

Removal and cleaning of probe nozzle

"The ear piece is usually a easily disposable one. If nozzle probe is found to contain any debris or dirt, we need to clean it carefully with tissue paper or cotton pads mainly along the grooves. We need to ensure that we clean from the base to apex. This will help in preventing the debris to go back to the groove space mainly through the channels. the nozzle is cleaned with

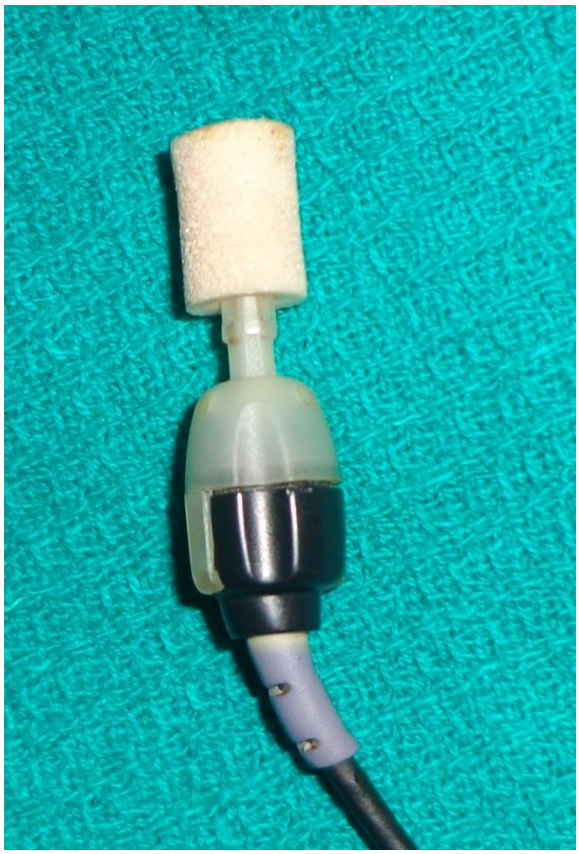
spirit. There should be no over-usage of spirit. There are usually clips which are found in the nozzle to attach it securely to the body of the probe. The clip at the base is very smooth to touch. The apex of the clip has one more plastic ridge found on its surface".

Installation of Replacement probe nozzle

To install a nozzle on to the probe body, align the clips in the probe nozzle with the corresponding slots on the probe body. Be sure that the probe nozzle component is oriented in such a way that the shape of the cavity matches the shape of the probe body, once the two pieces are aligned to match, slide the nozzle clips and fix until they lock with each other well. Make sure that the nozzle component is securely attached to the probe body.

Foam ear tips

- The tube is properly inserted into the nozzle of the probe.
- Make sure that the tube fully covers the nozzle.
- There should be no gap found at the bottom between the nozzle and the tip
- Handle with care while removing the foam from the tube.



Indications for use

"The AUDXpro Otoacoustic emission measurement system when placed in the external ear canal usually produces an acoustic signal and the Otoacoustic emission evoked in response to the signal which are produced from the cochlear outer hair cells are measured. It performs measurements of both TOAES and DPOAEs which can be used for screening and diagnostic purposes.

Environment and patient preparation

"There is not much need for specific preparation for OAE testing. Since the test usually records a normal physiological occurrence, there is not much response needed from the subject. Hence these emission testing can be done in patients who are unconsciousness and who are in a stage of coma.

The only thing needed is the cooperation of the person to not remove the ear probes from his / her ear canal till the testing is finished. Duration of the test depends on the subject's emission, noise from the background, and the parameters of the test.

Since in this test, the probe in the outer ear usually measures soft sounds, the back ground noise should be kept in control and the test will be relatively quicker if we proceed according to this, keeping the background noises are very low. If possible, perform testing in a quiet environment".

Patient preparation

- "The otoscopic examination of the external ear is mandatory before placing the probe in the ear. Make sure the outer ear is free from wax since it can interfere with testing of the person. The testing is usually not advised for persons with active ear discharge.

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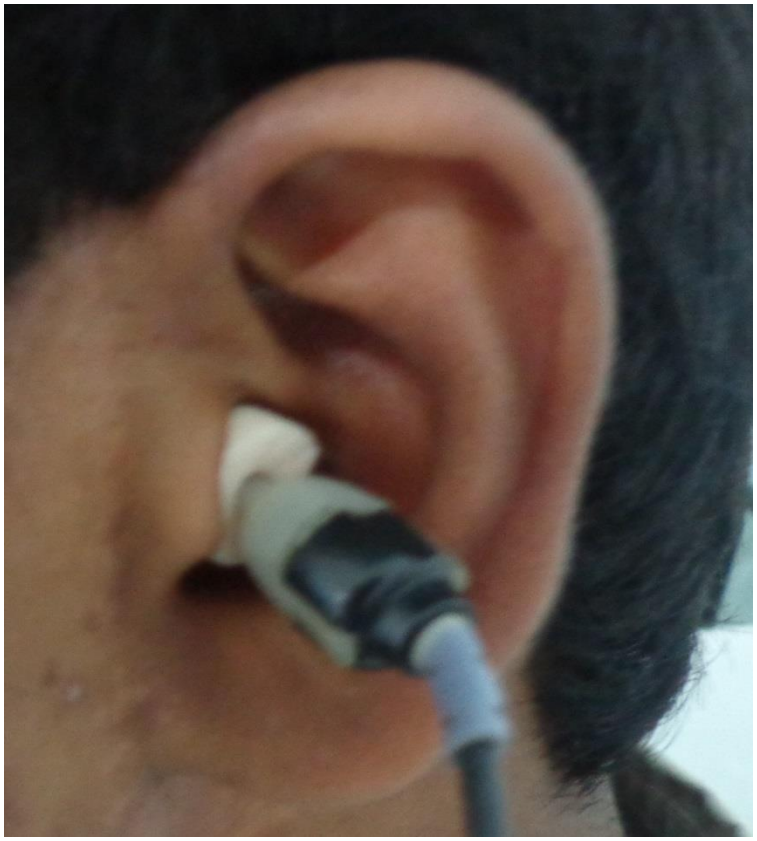
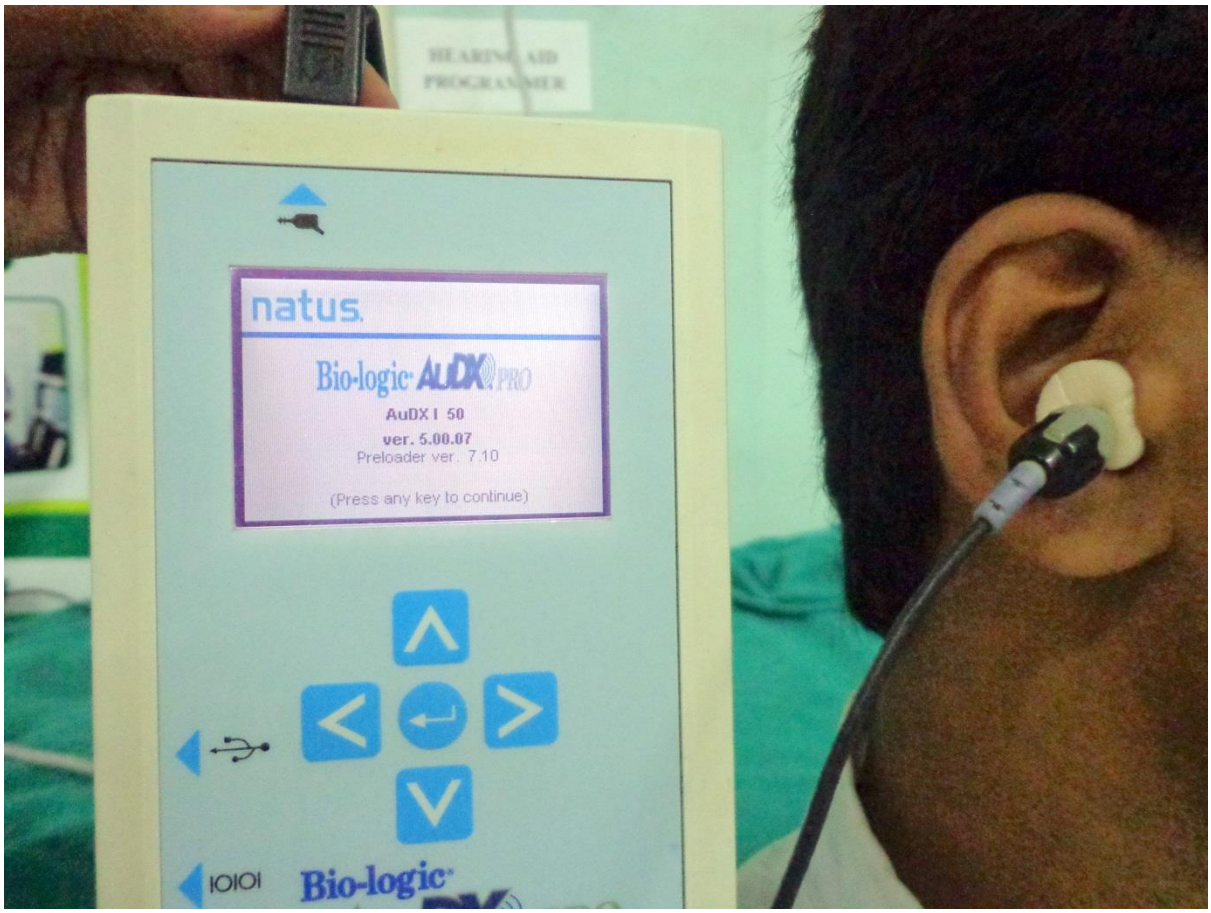


- Since there are variety of probes depending on the size, we need to use correct size of the probe depending on the size of ear canal, preferably use a larger ear tip since smaller ones may lead to improper results.
- After insertion of the tip in the patient's outer ear give few seconds for its expansion inside the ear canal.
- For uncooperative children clipping of the probe to the shirt may be done.

Patient instructions

For well cooperative and oriented persons, the information need to be conveyed are

- the ear tip need to be inserted in the outer ear
- a series of sounds of short span will be heard by him / her.
- The testing will be more precise and quick if he remains silent throughout the testing.



T-TEST

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Age	Case	50	28.36	8.727	1.234
	Control	50	25.74	2.431	.344

The mean age of subjects in "Cases" (organophosphate ingested and neurotoxic snake bites victims) group was 28.36 years and the mean age of persons in control group was 25.74 years.

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Age	Equal variances assumed	30.861	.000	2.045	98	.044	2.620	1.281	.078	5.162
	Equal variances not assumed			2.045	56.561	.046	2.620	1.281	.054	5.186

The independent samples and their variances using Levine's test have been computed and the t test for equality of means has been arrived along with the confidence interval of the difference.

Crosstabs

Sex Group

Among 50 cases and 50 controls, there were 62 % males and 38 % females.

Crosstab

			Group		
			Case	Control	Total
Sex	Male	Count	37	25	62
		% within Group	74.0%	50.0%	62.0%
	Female	Count	13	25	38
		% within Group	26.0%	50.0%	38.0%
Total		Count	50	50	100
		% within Group	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	6.112[b]	1	.013		
Continuity Correction[a]	5.136	1	.023		
Likelihood Ratio	6.192	1	.013		
Fisher's Exact Test				.023	.011
Linear-by-Linear Association	6.051	1	.014		
N of Valid Cases	100				

a. Computed only for a 2x2 table

b. 0 cells (.0%) have expected count less than 5. The minimum expected count is 19.00.

Organophosphates poisoning / neurotoxic Snakebite * Group

Among the cases, 50 % were Organophosphate poisoned and other 50% were neurotoxic snake bite victims.

Crosstab

			Group	
			Case	Total
organophos-phorous poisoning / Snakebite	OP. Poisoning	Count	25	25
		% within Group	50.0%	50.0%
	Snake Bite	Count	25	25
		% within Group	50.0%	50.0%
Total		Count	50	50
		% within Group	100.0%	100.0%

Chi-Square Tests

	Value
Pearson Chi-Square	.[a]
N of Valid Cases	50

a. No statistics are computed because Group is a constant.

Previous H/O HOH, Ear discharge Tinnitus, Vertigo * Group

All cases and controls did not have previous history of hard of hearing, tinnitus, ear discharge, vertigo.

Crosstab

			Group		
			Case	Control	Total
Previous H/O HOH, Ear discharge Tinnitus, Vertigo	No	Count	50	50	100
		% within Group	100.0%	100.0%	100.0%
Total		Count	50	50	100
		% within Group	100.0%	100.0%	100.0%

Chi-Square Tests

	Value
Pearson Chi-Square	.[a]
N of Valid Cases	100

a. No statistics are computed because Previous H/O HOH, Ear discharge Tinnitus, Vertigo is a constant.

Tympanic Membrane Group

The tympanic membrane was found to be intact in all cases and controls.

Crosstab

			Group		
			Case	Control	Total
Tympanic Membrane	BETM intact	Count	50	50	100
		% within Group	100.0%	100.0%	100.0%
Total		Count	50	50	100
		% within Group	100.0%	100.0%	100.0%

Chi-Square Tests

	Value
Pearson Chi-Square	.[a]
N of Valid Cases	100

a. No statistics are computed because Tympanic Membrane is a constant.

Pure Tone Audiometry group

The pure tone audiometry was found to be normal in both cases and controls.

Crosstab

			Group		
			Case	Control	Total
PTA	No	Count	50	50	100
		% within Group	100.0%	100.0%	100.0%
Total		Count	50	50	100
		% within Group	100.0%	100.0%	100.0%

Chi-Square Tests

	Value
Pearson Chi-Square	.[a]
N of Valid Cases	100

a. No statistics are computed because PTA is a constant.

Crosstabs

DPOAE - Right Group

Among the 50 cases DPOAE was present in 10% and absent in 90% whereas in controls DPOAE was found to be present in 86% and absent in 14% on the right side.

Crosstab

			Group		
			Case	Control	Total
DPOAE - RT	Present	Count	5	43	48
		% within Group	10.0%	86.0%	48.0%
	Absent	Count	45	7	52
		% within Group	90.0%	14.0%	52.0%
Total		Count	50	50	100
		% within Group	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	57.853[b]	1	.000		
Continuity Correction[a]	54.848	1	.000		
Likelihood Ratio	65.465	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	57.274	1	.000		
N of Valid Cases	100				

a. Computed only for a 2x2 table

b. 0 cells (.0%) have expected count less than 5. The minimum expected count is 24.00.

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for DPOAE - RT (Present / Absent)	.018	.005	.061
For cohort Group = Case	.120	.052	.278
For cohort Group = Control	6.655	3.318	13.346
N of Valid Cases	100		

DPOAE - LT * Group

Among the 50 cases DPOAE was present in 10% and absent in 90% whereas in controls DPOAE was found to be present in 86% and absent in 14% on the left side.

Crosstab

			Group		
			Case	Control	Total
DPOAE - LT	Present	Count	5	43	48
		% within Group	10.0%	86.0%	48.0%
	Absent	Count	45	7	52
		% within Group	90.0%	14.0%	52.0%
Total		Count	50	50	100
		% within Group	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	57.853[b]	1	.000		
Continuity Correction[a]	54.848	1	.000		
Likelihood Ratio	65.465	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	57.274	1	.000		
N of Valid Cases	100				

a. Computed only for a 2x2 table

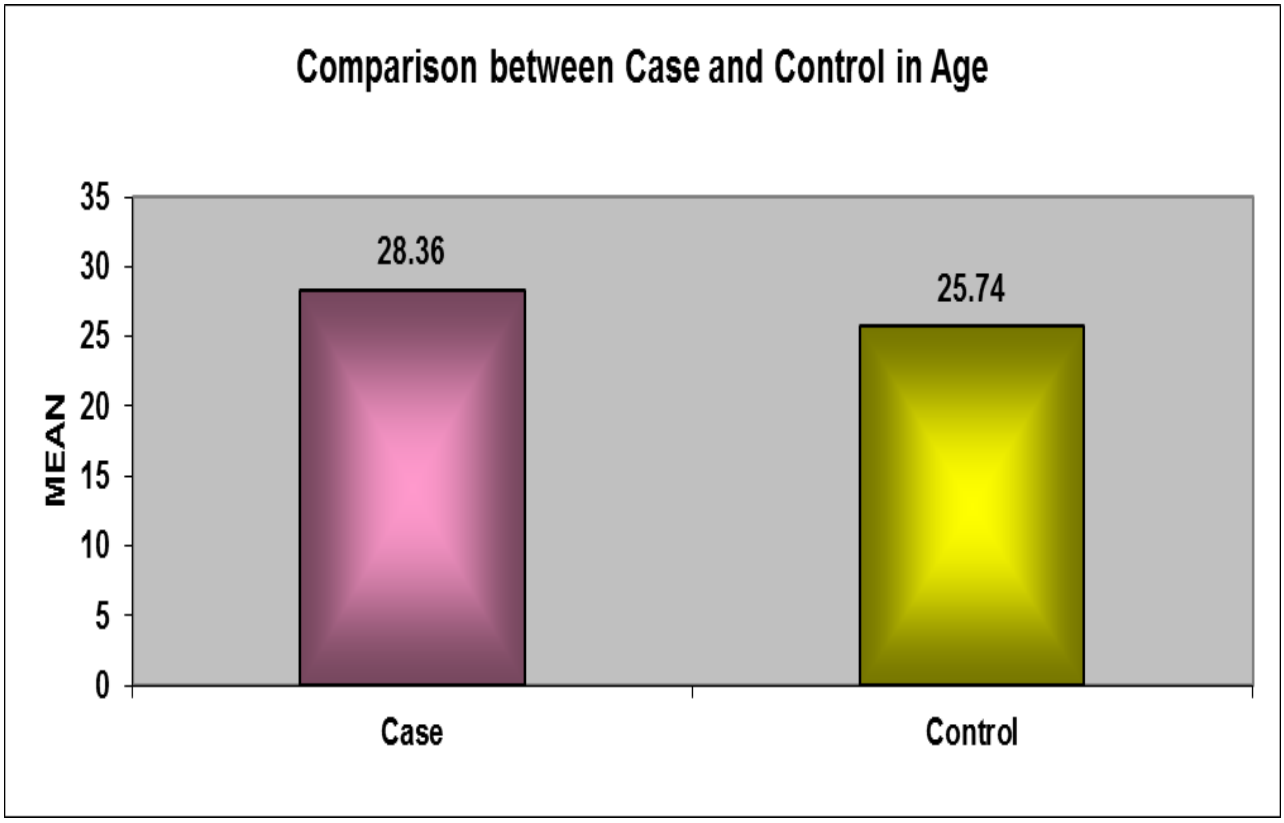
b. 0 cells (.0%) have expected count less than 5. The minimum expected count is 24.00.

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for DPOAE - LT (Present / Absent)	.018	.005	.061
For cohort Group = Case	.120	.052	.278
For cohort Group = Control	6.655	3.318	13.346
N of Valid Cases	100		

Comparison between cases and control in age

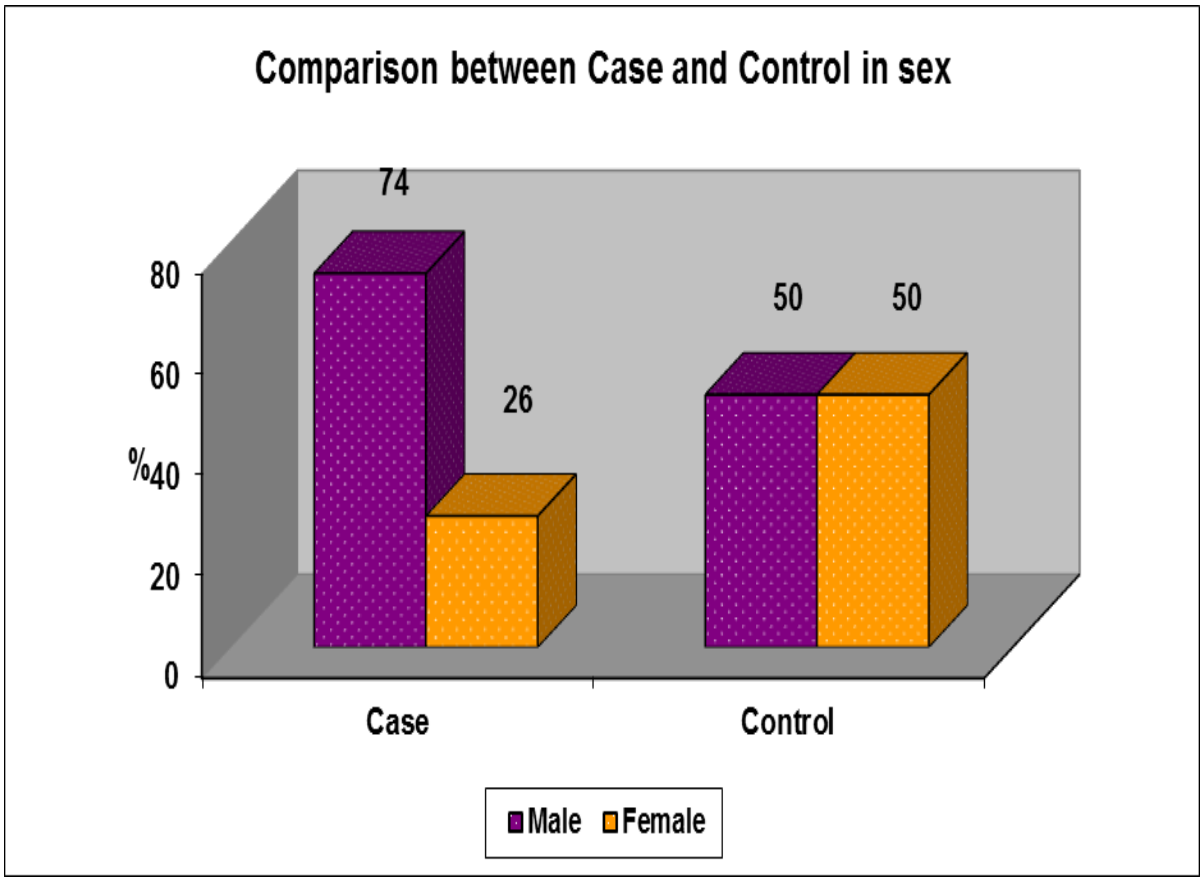
	Age in years
Cases	**28.36**
Control	**25.74**



Among the cases (neurotoxic snake bite victims and organophosphate poison ingested persons), mean age was found to be 28.36 and among the controls (normal population) mean age was 25.74 years

Comparison between cases and control in sex

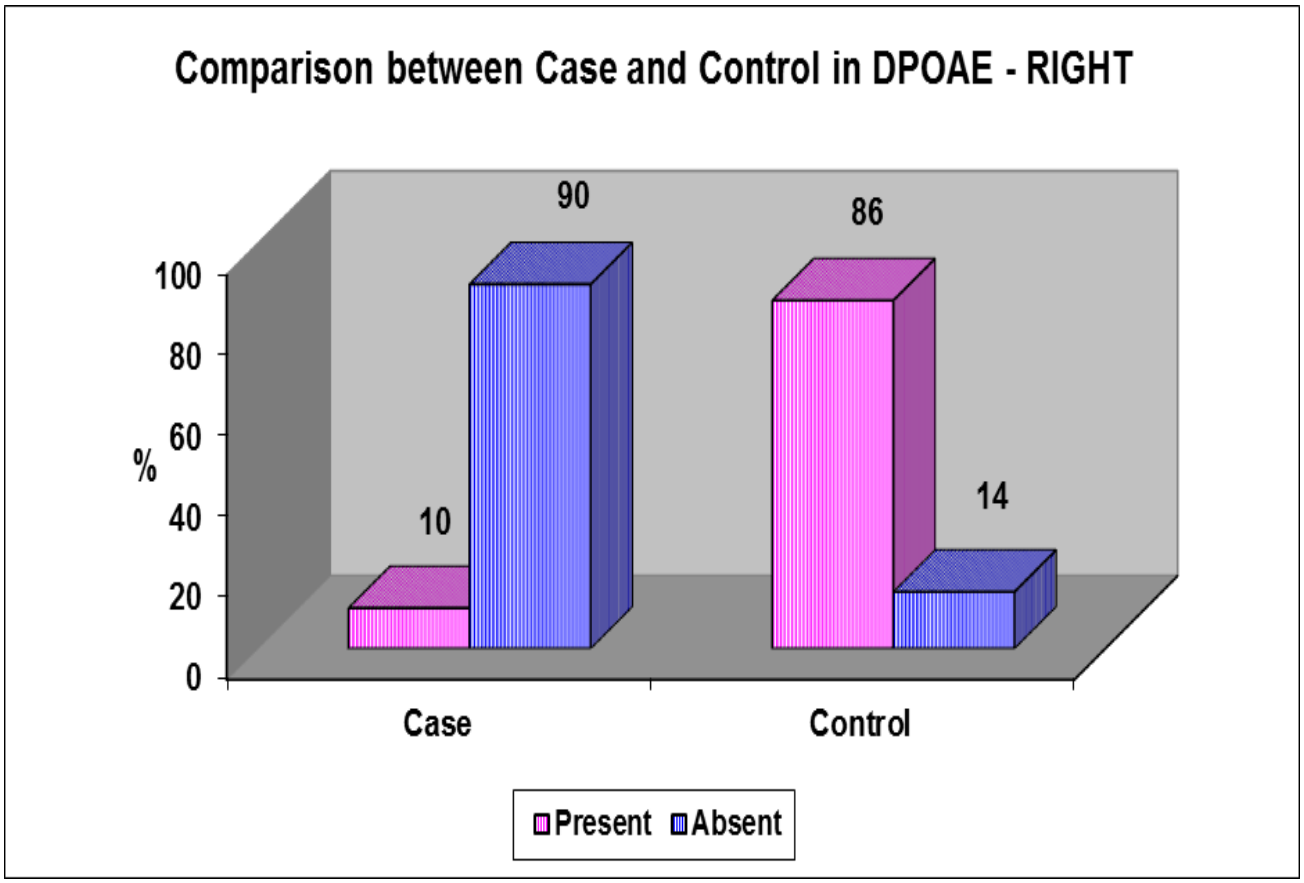
	Cases	Controls
Males	74	50
Females	26	50



Among the cases (neurotoxic snake bite victims and organophosphate poison ingested persons), 74 % were males and 26 % were females. Among the controls the males and females were in equal proportion.

Comparison between cases and control in DPOAE right

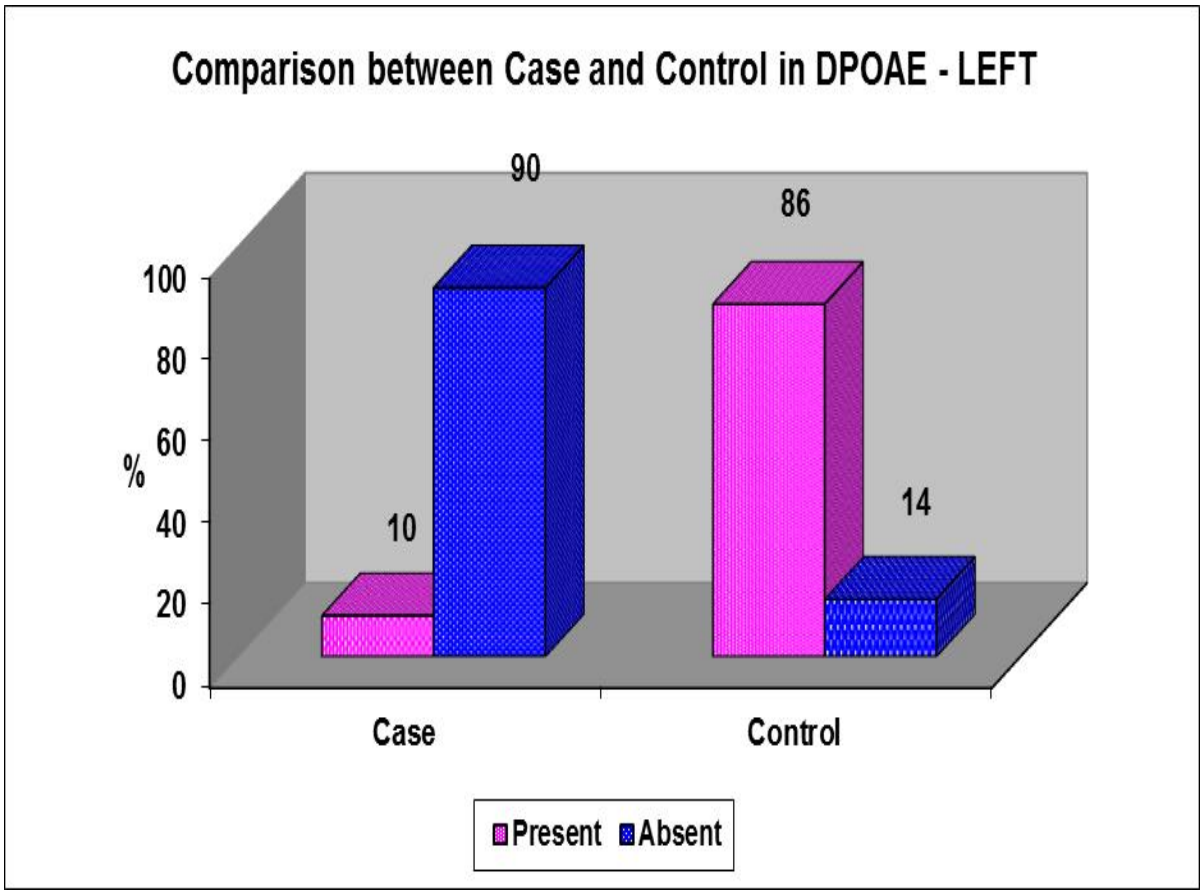
	Cases	Control
Present	10	86
Absent	90	14



Among the 50 cases DPOAE was present in 10% and absent in 90% whereas in controls DPOAE was found to be present in 86% and absent in 14% on the right side.

Comparison between cases and control in DPOAE left

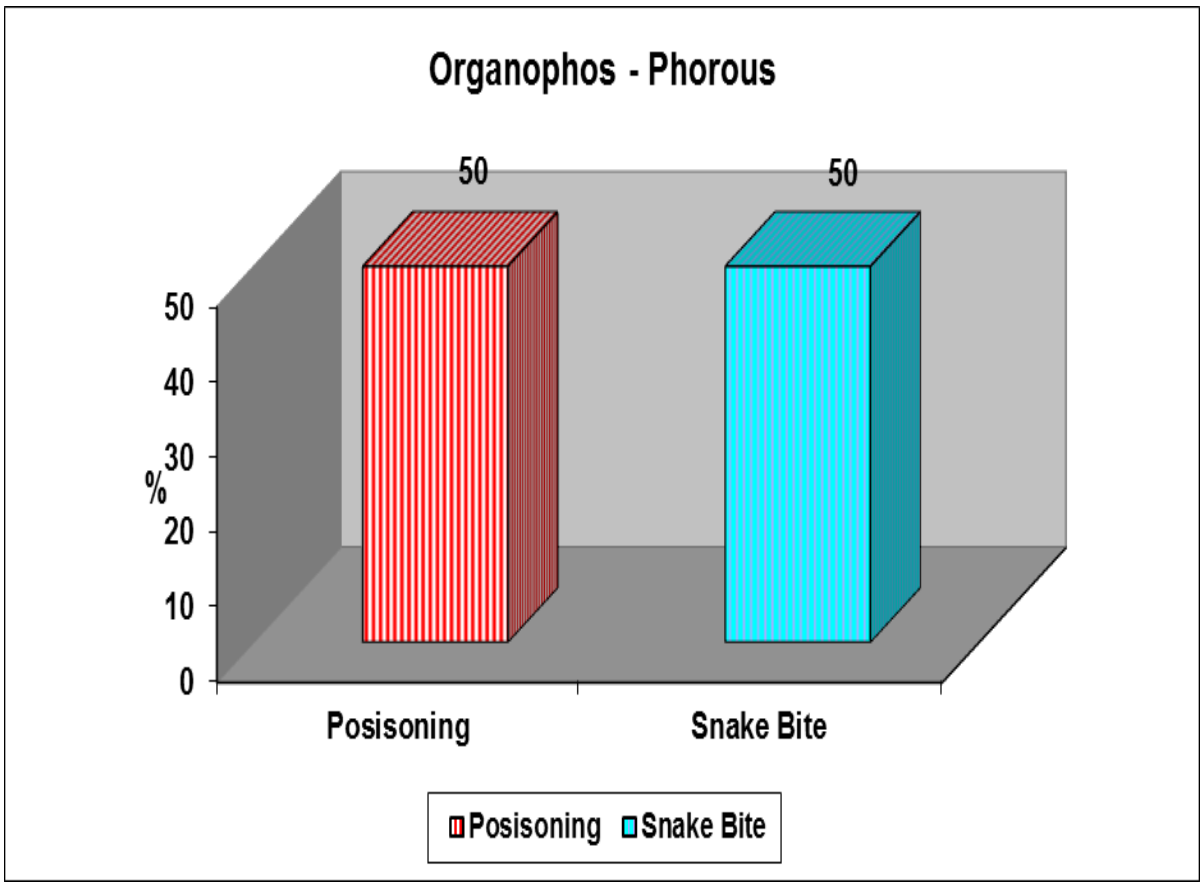
	Cases	Control
Present	10	86
Absent	90	14



Among the 50 cases DPOAE was present in 10% and absent in 90% whereas in controls DPOAE was found to be present in 86% and absent in 14% on the left side.

Comparison between OPC and snake bite

Organophospates	**50**
Snake bite	**50**



Among the cases 50% were those persons who had deliberately ingested organophosphate poison and the remaining 50 % were victims of neurotoxic snake bites.

DISCUSSION

Otoacoustic emissions are produced by the cochlea. These are low intensity sounds produced in response to acoustic stimulus. Deliberate self -poisoning by organophosphates has become an increasingly common response to emotional stress and depression in the young adult population of India. They comprise about seventy six per cent of pesticide poisoning in total. Several organophosphate pesticides have neurotoxins which have a great potential to affect hearing and animal studies show change in the threshold of hearing and outer and inner hair cell damage following organophosphate ingestion. But such studies in humans are very few.

Another major cause of poisoning apart from organophosphates are accidental snake bites many of which are neurotoxic. Neurotoxic snakes have a great potential to cause functional alterations of hair cells and hearing by the effects of their neurotoxins. Snake bite is an injury caused by bite from a snake, often resulting in puncture or wounds inflicted by the animal's fangs and sometimes resulting in envenomation. Usually snake bite presents with symptoms of drowsiness, abdominal pain, neurologic or neuromuscular manifestations such as ptosis, dysphagia, blurring of vision, ataxia, and headache. Hearing loss is a rare symptom followed by snake bite. Only few case studies on hearing loss following

snake bite are reported in the literature [5]. The venom of Bungarus caeruleus (krait) contains a mixture of alpha,beta-bungarotoxin and caerulotoxin [2].

Alpha-bungarotoxins cause failure of neuromuscular transmission by binding to post synaptic AchR at neuromuscular junction, Beta-bungarotoxins contains 20% protein content of the venom and are most toxic components of the venom. They are pre-synaptically active neurotoxic phospholipases [2].Exposure to these toxins in vivo and in vitro causes the failure of neuromuscular transmission for two to three hours and depletion of synaptic vesicles from the nerve terminal endings. Caerulotoxin. a minor component of the venom , found exclusively in kraits and are structurally similar to alpha-bungarutoxins. Alpha bungarutoxin and caerulotoxin act on post synaptic membrane.

Need of the study

The advantages of the Otoacoustic Emission testing include

- Non-invasive nature
- Objectivity,
- Sensitivity,
- Specificity,
- Accuracy and
- Reliability

These advantages help in easily assessing the minor / sub clinical changes in the outer hair function even before they are clinically apparent.

Literature suggests damage to the auditory system due to the solvent exposure of organophosphates in occupational settings. So it is clearly inferred that damage to auditory system will be more serious due to direct ingestion of organophosphates orally. Hence the purpose of the present study is to ascertain the functional alterations in cochlear outer hair cells in the persons who deliberately ingested the organophosphate compounds and the victims of neurotoxic snake bites.

As it has been clearly explained previously, the mechanism of action of neurotoxic snake venom is very much similar to that of organophosphates. Hence it is very much possible that the neurotoxic snake venom could also possible result in functional alterations in the cochlea and in outer hair cells like the organophosphate compounds.

In numerous literatures researchers have concluded changes in Otoacoustic emissions precedes the changes in the hearing in those patients receiving drugs having ototoxic potential wherein the pure tone audiometric thresholds were found to be normal within the conventional frequency range.

The above said great range of susceptibility of Otoacoustic emission to the ototoxic damage has been compared to behavioural testing reflect distortion

product Otoacoustic emissions' sensitivity to the sub clinical changes in the cochlear outer hair cell function.

The above mentioned evidence supports the potential use of Otoacoustic emission testing clinically for very early detection of organophosphate solvent induced functional alterations in outer hair cells of cochlea and hearing loss. It implies decrease in the distortion product Otoacoustic emission is found to occur very early, even before the onset of changes in the hearing threshold becomes clinically apparent. So it is possible for us to predict the further changes in the hair cells and also to predict future hearing loss.

Hence there is a need for identification of the changes occurring in the distortion product Otoacoustic emission following deliberate ingestion of organophosphate poisoning and in snake bites and helps us to explore the cochlear changes among the individuals in whom the audiometric thresholds are found to be within the normal limits.

Procedure

The subjects who underwent the study have been divided into two groups.

- Group 1
- Group 2

Group 1 included those persons who had deliberately ingested organophosphate compounds orally and those persons who had been victims of neurotoxic snake bites.

Group 2 included normal persons.

Both **Group 1** & **Group 2** were matched for the following criteria

Inclusion criteria

1. Age of the individual – 20-35 years
2. No previous history of
    i. Ear discharge
    ii. Hard of hearing
    iii. Tinnitus
    iv. Vertigo
    v. Noise exposure
    vi. Intake of ototoxic drugs
3. Normal and intact tympanic membrane on otoscopic examination
4. Pure tone audiometric thresholds within normal limits.

Exclusion Criteria

1. Age less than 15 years

2. Age above 35 years
3. Previous history of
    i. Ear discharge
    ii. Hard of hearing
    iii. Tinnitus
    iv. Vertigo
    v. Noise exposure
    vi. Intake of ototoxic drugs
4. Abnormal tympanic membrane findings
    i. Perforation
    ii. Retraction
    iii. Cholesteatoma
    iv. Atlectatic tympanic membrane

Once the appropriate patients were selected according to the above criteria, they were evaluated by testing of Distortion product Otoacoustic Emission testing. The results were mainly grouped under two categories, “pass” or “fail” criteria. The responses were considered as “pass” only if seven out of nine frequencies were found to be above six decibel noise level. The responses were considered “fail” if less than seven frequencies were above the six dB noise level.

Results

Distortion product Otoacoustic emissions findings of the above said two groups revealed the “pass” or “fail” criteria.

In **Group 1**, i.e., who had the deliberate ingestion of Organophosphate poison and victims of neurotoxic snake bites, were found to have

- “Passed” criteria - 10 %
- “Failed” criteria - 90 %

In **Group 2**, i.e., healthy subjects

- “Passed” criteria -86 %
- “Failed” criteria – 14 %

The “failed” criteria result of distortion product Otoacoustic emission in **Group 1,** were found to be noticed bilaterally, which clearly infers the absence of DPOAEs in both the ears.

The “failed” criteria results of DPOAEs of both the groups were compared and Chi square analysis has been done and it has been found to be statistically significant one.

The current study shows significant failure statistically while measuring DPOAEs in Group 1 subjects, clearly explains the changes in the cochlea following Organophosphate poisoning and neurotoxic snake bite.

The important underlying pathology in organophosphate poisoning and in neurotoxic snake bite is

- Generation of reactive oxygen species
- Depletion of NADPH, which is essential for the normal functioning of the cell

Studies and literature suggest that the root of intoxication of these neurotoxic compounds to the inner ear need to be blood borne from the stria vascularis. Also these compounds readily diffuse through the lipid rich contents of the membranes and through the cells of Hensen which are in close relation to the Deiter cells and they are found to be located under the outer hair cells and thus the target site has been reached. Hence the current study explains the functional alterations in the cochlea which has been represented by the significant absence of Distortion product Otoacoustic Emission in the study group. And this study infers that exposure to organophosphates and neurotoxic snake venom may contribute to hearing loss. The future research should be focussed on determining the frequency specific responses of the distortion product Otoacoustic emissions which will be of great use.

Conclusion

Our current study clearly concludes the significant functional changes in the outer hair cells of the cochlea following deliberate ingestion of organophosphate compounds and neurotoxic snake bite which has been clearly reflected by the presence of "Failed" criteria found in the distortion product Otoacoustic emissions of the above said groups. So these agents may induce auditory damage not only in the animals (which has been clearly proved in the literature and animal studies) but also in humans. The clinician should be alert to the ototoxic potentials of organophosphate compounds and neurotoxic snake bites and needs to conduct a comprehensive assessment of the auditory system periodically on these patients in order to predict the hearing loss in future and institute early and appropriate rehabilitative measures.

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Effect of Deliberate Ingestion of Organophosphate Pesticide on Distortion Product Oto-Acoustic Emissions (Dpoae)

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512

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MASTER CHART (CASES)

S. No.	Name	Age	Sex	IP No.	organophosphate poisoning / Snakebite	Previous H/O HOH, Ear discharge Tinnitus, Vertigo	Tympanic Membrane	PTA	DPOAE	
									RT	LT
1	Shankar	25	M	77327	OP. Poisoning	No	BETM intact	N	Absent	Absent
2	Karthikeyan	35	M	79086	OP. Poisoning	No	BETM intact	N	Absent	Absent
3	Govindraj	24	M	81427	OP. Poisoning	No	BETM intact	N	Absent	Absent
4	Vignesh	21	M	84331	OP. Poisoning	No	BETM intact	N	Absent	Absent
5	Iyyapan	24	M	85363	OP. Poisoning	No	BETM intact	N	Absent	Absent

6	Boopathy	20	M	86175	OP. Poisoning	No	BETM intact	N	Absent	Absent
7	Kabilan	29	M	88421	OP. Poisoning	No	BETM intact	N	Absent	Absent
8	chella Durai	32	M	88422	OP. Poisoning	No	BETM intact	N	Absent	Absent
9	Ramadurai	21	M	88454	OP. Poisoning	No	BETM intact	N	Absent	Absent
10	Santhosh	29	M	88418	OP. Poisoning	No	BETM intact	N	present	present
11	Karthick	29	M	88423	OP. Poisoning	No	BETM intact	N	Absent	Absent
12	Kullammal	30	F	20267	OP. Poisoning	No	BETM intact	N	Absent	Absent
13	Ilayaraja	35	M	20188	OP. Poisoning	No	BETM intact	N	Absent	Absent

14	Vijay Kumar	25	M	18913	OP. Poisoning	No	BETM intact	N	Absent	Absent
15	Parthiban	27	M	17358	OP. Poisoning	No	BETM intact	N	Absent	Absent
16	Edwin	34	M	16953	OP. Poisoning	No	BETM intact	N	Absent	Absent
17	Muthu	28	M	12540	OP. Poisoning	No	BETM intact	N	Absent	Absent
18	Aruna	18	F	12343	OP. Poisoning	No	BETM intact	N	Absent	Absent
19	Usha	23	F	11331	OP. Poisoning	No	BETM intact	N	Absent	Absent
20	Gomathy	18	F	11315	OP. Poisoning	No	BETM intact	N	present	present
21	Narayana Moorthy	23	M	10900	OP. Poisoning	No	BETM intact	N	Absent	Absent

22	Gopinath	34	M	8376	OP. Poisoning	No	BETM intact	N	Absent	Absent
23	Selva Kumar	21	M	122905	OP. Poisoning	No	BETM intact	N	Absent	Absent
24	Ramakrishnan	24	M	5970	OP. Poisoning	No	BETM intact	N	Absent	Absent
25	Sabarirajan	21	M	15694	OP. Poisoning	No	BETM intact	N	Absent	Absent
26	Sundari	30	F	45214	Snake Bite	No	BETM intact	N	Absent	Absent
27	murugan	18	M	77696	Snake Bite	No	BETM intact	N	Absent	Absent
28	Sowmya	13	F	79273	Snake Bite	No	BETM intact	N	Absent	Absent
29	Mani	35	F	81031	Snake Bite	No	BETM intact	N	Absent	Absent
30	Easwaran	37	M	81470	Snake Bite	No	BETM intact	N	present	present
31	Haridoss	34	M	81110	Snake Bite	No	BETM intact	N	Absent	Absent
32	Chinna Ponnu	46	F	81778	Snake Bite	No	BETM intact	N	Absent	Absent
33	Venkatachalam	45	M	82725	Snake Bite	No	BETM intact	N	Absent	Absent
34	Athimohan	36	M	84679	Snake Bite	No	BETM intact	N	Absent	Absent

35	Lakshmi	21	F	84478	Snake Bite	No	BETM intact	N	Absent	Absent
36	Sakunthala	28	F	85305	Snake Bite	No	BETM intact	N	Absent	Absent
37	Mani	36	M	85717	Snake Bite	No	BETM intact	N	Absent	Absent
38	N agaraj	28	M	78184	Snake Bite	No	BETM intact	N	Absent	Absent
39	Ammainathan	35	M	87227	Snake Bite	No	BETM intact	N	Absent	Absent
40	Selvam	60	M	72117	Snake Bite	No	BETM intact	N	present	present
41	Prakash	25	M	77153	Snake Bite	No	BETM intact	N	Absent	Absent
42	Srinivasan	36	M	68419	Snake Bite	No	BETM intact	N	Absent	Absent
43	Thiru	32	M	132413	Snake Bite	No	BETM intact	N	Absent	Absent
44	Kuppu	30	F	95038	Snake Bite	No	BETM intact	N	Absent	Absent
45	Menaka	29	F	98734	Snake Bite	No	BETM intact	N	Absent	Absent
46	Sneha	12	F	68417	Snake Bite	No	BETM intact	N	Absent	Absent
47	Ajith Kumar	16	M	72417	Snake Bite	No	BETM intact	N	present	present
48	Gokul	20	M	84329	Snake Bite	No	BETM intact	N	Absent	Absent
49	Saravanan	32	M	68457	Snake Bite	No	BETM intact	N	Absent	Absent
50	Nagaraj	34	M	89117	Snake Bite	No	BETM intact	N	Absent	Absent

CONSENT FORM

TITLE OF THE STUDY: "EFFECT OF DELIBERATE INGESTION OF ORGANOPHOSPHATE PESTICIDE AND SNAKE BITE ON DISTORTION PRODUCT OTO ACOUSTIC EMISSIONS. (DPOAE)

Name of the Investigator : Dr.R.V.S. Velavan
Post Graduate ENT, UIORL,MMC

Name of the Participant:

I_____ hereby give consent to participate in the study conducted by Dr. Velavan. R.V.S, post graduate in Upgraded Institute of Otorhinolaryngology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai- 600003.

1. I hereby give consent to take part in this study.
2. I agree to share my personal details with the investigator and acknowledge that they may be used for the research purposes.
3. The information sheet was read out to me and all my doubts cleared to my satisfaction.
4. The consent form was read out to me and all my doubts cleared to my satisfaction.
5. I agree that the investigator may decide to discontinue the study at any point of time and may decide to disinclude me from the study.
6. I also give consent to attend follow up and for further Investigations should the need arise.

SIGNATURE OF THE INVESTIGATOR SIGNATURE OF THE PARTICIPANT/ATTENDER:

Place:

Date:

INFORMATION SHEET

TITLE OF THE STUDY: "EFFECT OF DELIBERATE INGESTION OF ORGANOPHOSPHATE PESTICIDE AND SNAKE BITE ON DISTORTION PRODUCT OTO ACOUSTIC EMISSIONS. (DPOAE)

Name of the Investigator : Dr.R.V.S. Velavan
Post Graduate ENT, UIORL,MMC

Name of the Participant:

- We are conducting a prospective cohort study on **"EFFECT OF DELIBERATE INGESTION OF ORGANOPHOSPHATE PESTICIDE AND SNAKE BITE ON DISTORTION PRODUCT OTO ACOUSTIC EMISSIONS. (DPOAE)** at the Upgraded Institute of Otorhinolaryngology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai- 600003.
- In this study patients who have deliberately ingested OPC Poisioning or had Snake bite or selected and using a DPOAE probe and apparatus the OAE will be measured by keeping a probe in the external auditory canal.
- At the time of announcing the results and suggestions, name and identity of the patients will be confidential.
- Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time, your decision will not result in any loss or benefits to which you are otherwise entitled.
- Taking part in this study does not involve any risks/ horn to the health of the patient in any manner
- The results of the special study may be intimidated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

SIGNATURE OF THE INVESTIGATOR: SIGNATURE OF THE PARTICIPANT/ATTENDER:

DATE:

PLACE:

சுய ஒப்புதல் படிவம்

<u>ஆய்வு செய்யப்படும் தலைப்பு</u>

கணிம பாஸ்பரஸ் பூச்சிக்கொல்□ மருந்து உட்கொண்ட மற்றும் நச்சு பாம்பு கடியால் பாதிக்கப்பட்ட நோயாளிகளுக்கு உள்காதில் [நத்தை எலும்பு] ஏற்படும் பாதிப்புகள் [நுண்ணொ□ அலைவீச்சு மாறுபாடுகள் OAE)" பற்றிய ஆய்வு.

ஆராய்ச்சி நிலையம்	:	ராஜீவ் காந்தி அரசு பொது மருத்துவமனை சென்னை மருத்துவக் கல்லூரி, சென்னை – 600 003.
பங்கு பெறுபவரின் பெயர்	:	
பங்கு பெறுபவரின் எண்	:	
பங்கு பெறுபவர் இதனை [ ] குறிக்கவும்	:	

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த கட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்மந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொளும் போது இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். என உடல் நலம் பாதிக்கப்படபட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ உடனே அதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ☐

இந்த ஆய்வில் எனக்கு இரத்தம், சிறுநீர், எக்ஸ்ரே, ஸ்கேன் பரிசோதனை செய்து கொள்ள நான் முழு மனதுடன் சம்மதிக்கிறேன். ☐

பங்கேற்பவரின் கையொப்பம் .....இடம் .....தேதி

கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்.....

ஆய்வாளரின் கையொபபம் .....இடம் .....தேதி

ஆய்வாளரின் பெயர்.....

ஆய்வு தகவல் தாள்

ஆராய்ச்சி தலைப்பு : கணிம பாஸ்பரஸ் பூச்சிக்கொள்ளி மருந்து உட்கொண்ட மற்றும் நச்சு பாம்பு கடியால் பாதிக்கப்பட்ட நோயாளிகளுக்கு உள்காதில் (நத்தை எலும்பு) ஏற்படும் பாதிப்புகள் நுண்ணொ□ அலைவீச்சு மாறுபாடுகள் (OAE)

ஆராய்ச்சாளர் பெயர் : மருத்துவர் ஆர்.வி.எஸ் வேலவன்
(காது மூக்கு தொண்டை முது நிலை மருத்துவ மாணவர்)

பங்கேற்பாளர் பெயர் :

சென்னை ராஜீவ்காந்தி அரசு மருத்துவமனைக்கு வரும் கணிம பாஸ்பரஸ் பூச்சிக்கொள்ளி மருந்து உட்கொண்ட மற்றும் நச்சு பாம்பு கடியால் பாதிக்கப்பட்ட நோயாளிகளுக்கு (நத்தை எழும்பு) ஏற்படும் பாதிப்புகள் (நுண்ணொ□ அலைவீச்சு மாறுபாடுகள் (OAE) பற்றிய ஆராய்ச்சியாகும்.

சப்த சக்தியின் தூண்டுதலால் நத்தை எலும்பு (உள்செவி) நுண்ணொ□ அலைவீச்சினை (OAE) வெளிப்படுத்துகிறது. இந்த நுண்ணொ□ அலைவீச்சு மாறுபாடுகளை அளவீடு செய்வதன் மூலம் நத்தை எலும்பு எந்த அளவு பாதிக்கப்பட்டு கேட்கும் திறன் குறைகிறது என்பதை துல்□ யமாக அறிய முடியும்.

மேற்கண்ட நோயாளிகளின் நத்தை (எலும்பு) (உள் காது) பாதிப்பு மற்றம் கேட்கும் திறனில் ஏற்படும் குறைபாடை நும்ணொ□ அலைவீச்சு மாறுபாடுகளை (OAE) அளவீடு செய்வதன் மூலம் அறிய முடியும்.

நீங்கள் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம்.

இந்த ஆராய்ச்சியின் முடிவுகளை அல்லது கருத்துகளை வெளியிடும்போதோ அல்லது ஆராய்ச்சியின்போதா தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில்தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியி□ ருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியின் முடிவுகளை ஆராய்ச்சியின்போது அல்லது ஆராய்ச்சியின் முடிவின்போது தங்களுக்கு அறிவிக்கப்படும் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

தேதி :

Certi

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

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

CERTIFICATE OF APPROVAL

To
Dr. R.V.S. Velavan,
Post Graduate in MS ENT,
Madras Medical College,
Chennai – 600003.

Dear Dr. R.V.S. Velavan,

The Institutional Ethics Committee has considered your request and approved extension of the study titled **"Effect of deliberate ingestion of organophosphate pesticide and snake bite on Distortion Product Oto Acoustic Emissions emissions. (DPOAE)"** No. 08062014.

The following members of Ethics Committee were present in the meeting held on 03.06.2014 conducted at Madras Medical College, Chennai-3.

1.	Dr. C. Rajendran, M.D.	-- Chairperson
2.	Dr. R. Vimala, M.D., Dean, MMC, Ch-3.	-- Deputy Chair Person
3.	Prof. Kalaiselvi, MD., Vice-Principal, MMC, Ch-3	-- Member
4.	Prof. Nandhini, M.D. Inst. of Pharmacology, MMC, Ch-3.	-- Member
5.	Dr. G. Muralidharan, Director Incharge , Inst. of Surgery	-- Member
6.	Prof. Md Ali, MD., DM., Prof & HOD of MGE, MMC, Ch-3.	-- Member
7.	Prof. Ramadevi, Director i/c, Biochemistry, MMC,Ch-3.	-- Member
8.	Prof. Saraswathy, MD., Director, Pathology, MMC, Ch-3.	-- Member
9.	Prof. Tito, Director, i/c. Inst. of Internal Medicine, MMC	-- Member
10.	Thiru. Rameshkumar, Administrative Officer	-- Lay Person
11.	Thiru. S. Govindasamy, BABL, High Court, Chennai-1.	-- Lawyer
12.	Tmt. Arnold Saulina, MA MSW	-- Social Scientist

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

Sd/Chairman & Other Members

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.

8/7/14

Member Secretary, Ethics Committee
Vice-Principal
Madras Medical College
Chennai-600 003.

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INTRODUCTION

OAE is a simple non-invasive and quick test that can be performed to analyse preclinical changes in the outer hair cells of patients. Studies suggest that minute sub clinical changes occurring in the outer hair cells' function can be precisely predicted with Otoacoustic emissions

Ototoxic compounds cause damage by the generation of reactive oxygen species. Snake bites and deliberate ingestion of organophosphate poisons represent an accidental exposure of outer hair cells to ototoxic compounds. The ototoxic potentials of the snake venom and organophosphate compounds has been well documented in studies. By testing the Otoacoustic emission we can estimate the outer hair cell function of normal persons after an accidental exposure to these ototoxic compounds. It is also stipulated to be the main mechanism for outer hair cell damage of the cochlea by organophosphate poisoning as well. Some of the snake venoms are neurotoxic which act by depletion of NADPH similar to the neurotoxic mechanism of organophophates.

Repeated follow up with similar testing may also help us to pick up further detoriation of the outer hair cell function. Such testing can be used to study and approximately estimate the resilience of outer hair cells to the toxic exposure of these compounds and can be thus extrapolated to other compounds which may

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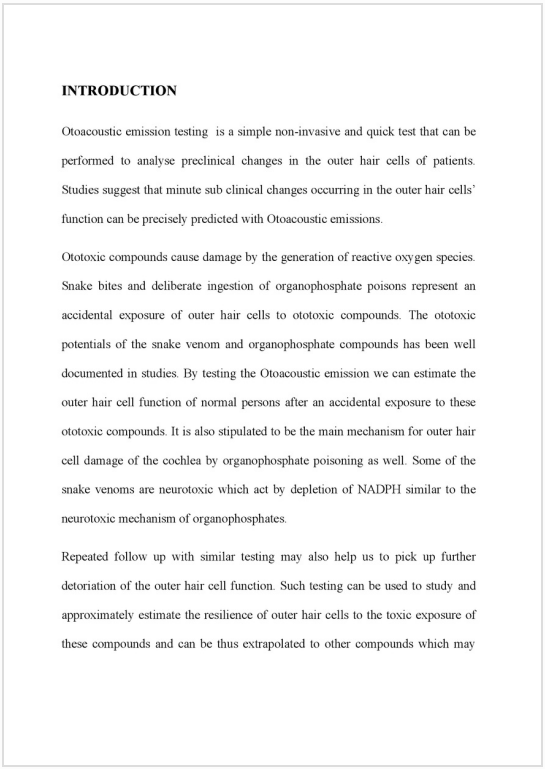

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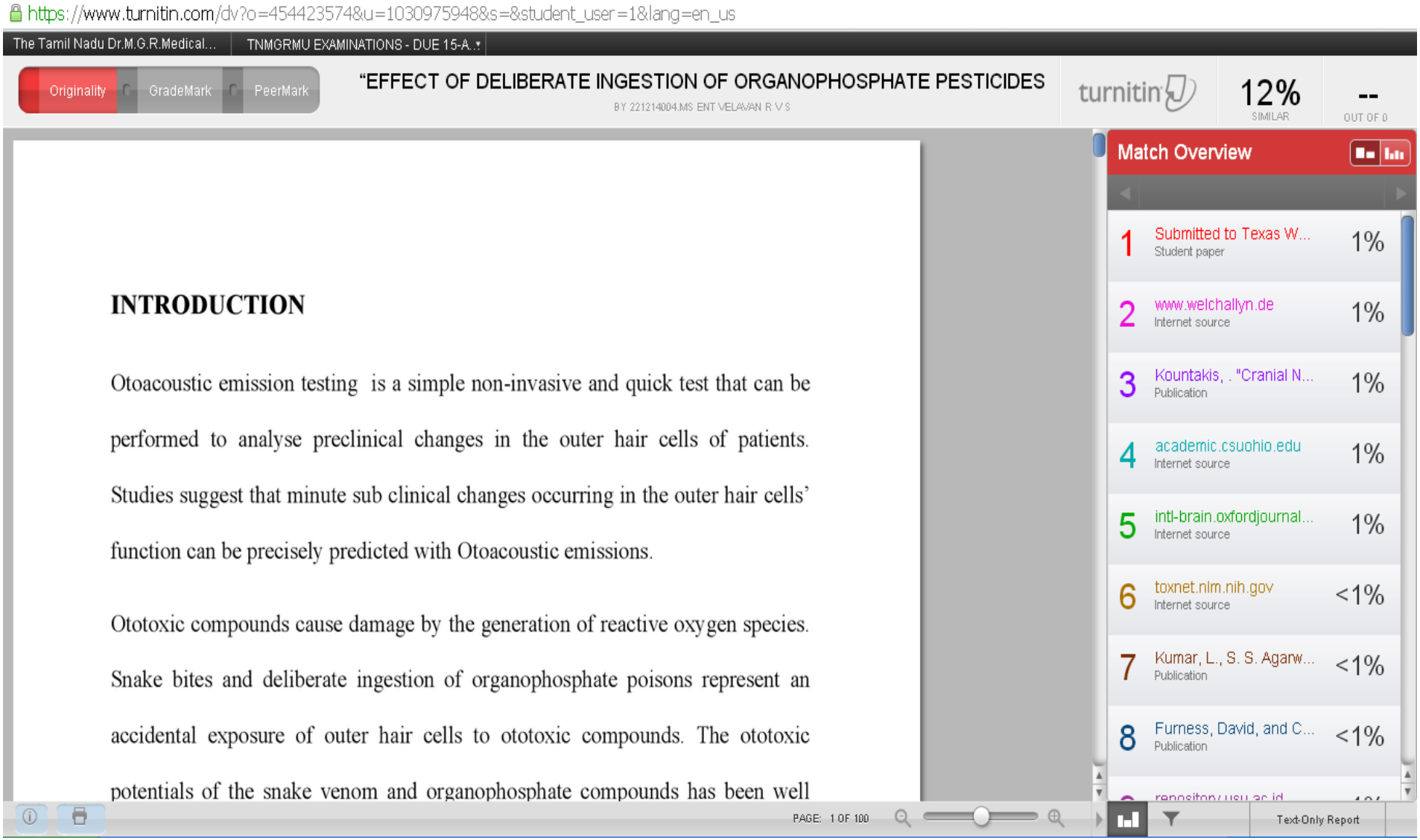
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