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Review Article

Ear, Nose and Throat Section

Middle Ear Function Changes due to the Combined Effect of Pressure along with Fluid in Middle Ear Pressure Regulation- A Review

PUJA DINKAR LANJEKAR[1], SAGAR GAURKAR[2]

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ABSTRACT

The pressure changes in Middle Ear (ME) are due to the effect of both fluid and pressure, which can be detected by tympanometry. In this review article, the mathematical and formal model of regulation of ME pressure is discussed. The air pressure in the ME chamber and the surrounding environment are the same. The auditory tube is a common connection between the ME chamber and the nasopharynx. The main functional role of the auditory tube is the ventilation of ME. When a person breathes air through an auditory tube, it enters into the ME and ventilates it. The ossicles in the ME collect sound from the tympanic membrane and transfer it to the inner ear, which requires proper ventilation of the ME. The auditory tube maintains ME pressure, the same as the external auditory canal and outside pressure. If an auditory tube is blocked, it leads to failure to ventilate ME, leading to changes in ME pressure. Swallowing and yawning allow the passive opening of the auditory tube and thus results in air flow out of the chamber. Easy and passive air exchange is allowed from the ME to the pharynx if, the pressure in the ME is higher than in the surrounding environment. ME pressure is highly variable and can change in many conditions. ME pressures increase when the body rotates from a vertical to a horizontal position because it increases the effusion of the ME mucosa due to an increase in hydrostatic pressure, which leads to an increase in the perfusion rate. Therefore, pressure increases in the case of sleeping and drowsiness. Regulation of ME pressure is a physiological process in which pressure between ME and the surrounding environment is maintained at equilibrium. The mechanism of pressure regulation is possible because of the complex sensory neural reflex pathway. A laser doppler vibrometer measures displacement of the tympanic membrane in response to sound and ME compliance is calculated by tympanometry. The movement of the tympanic membrane reduces due to the combined effect of fluid and pressure on the ME. The ME functions are altered due to the negative pressure of the fluid rather than the positive pressure.

Keywords: Auditory tube, Gas difference, Middle ear pressure, Otitis media

INTRODUCTION

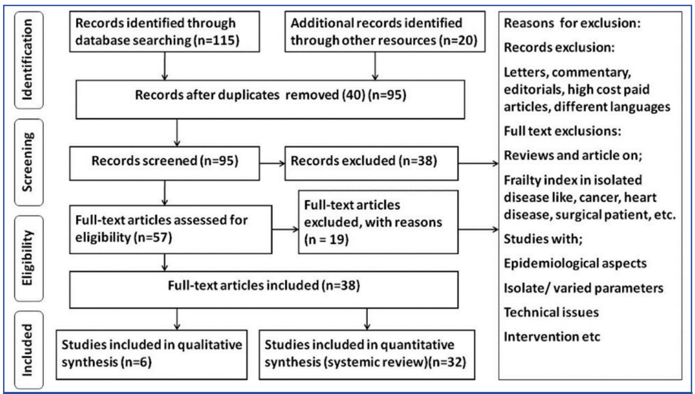
The Middle ear is a non collapsible and biotic gas chamber that is mainly closed [1,2]. The ME detects nearly continuous, low magnitude, high frequency, and variation of environmental pressure associated with sound, representing that flow as pressure-time signals for effective gas fluid coupling, which is presented to the cochlear perilymph [1,3]. The ME pressure is maintained approximately at atmospheric pressure, which is done by a sensory unit known as the tympanic membrane. Tympanic membrane functions like a diaphragm for various types of pressure sensors, and optimum signals are required so that the ME pressure is matched to the environment, that is, gas-gas coupling [3-5]. It is difficult to find fixed limits for ME pressure as it is a very dynamic chamber, and the pressure changes for many reasons [6].

The presence of fluid in ME cleft is called Otitis Media with Effusion (OME) or secretory otitis media, or serous otitis media, and the fluid is thick and visible or thin and serous, usually related to changes in ME pressure. It is due to poor function of the eustachian tube and inflammatory reaction because of acute otitis media [7]. The effusion in the ME cavity is categorised as mucoid, glue-like, and serous in various pathological conditions. OME is also called glue ear [7]. Many studies suggest that hearing loss is associated with ME effusion (fluid) [7-10]. The low-frequency hearing loss was due to reduced ME volume, and high-frequency hearing loss was caused by an increasing mass of the tympanic membrane by entrained effusion fluid [8]. In the study by Gan RZ et al., a vibration of the tympanic membrane and stapes was measured by changing the amount of fluid in the ME. The result of the tympanic membrane to the footplate of stapes displacement transmission ratio due to the effect of fluid on ME function is different between the three frequency range [10]. The ME pressure mainly decreases tympanic membrane mobility at low frequencies (f >1 kHz) [10,11]. Effusion in patients of OME is closely related to negative pressure; the negative pressure, in combination with fluid pressure, has more effect on the function of the ME than positive pressure [7]. Dai C et al., experiment combines three groups: ME pressure, fluid, and pressure-fluid combination in the human temporal bone, 0.3 mL saline solutions used as effusion, fills half of the ME cavity level above the umbo, and it produced movement in it. A displacement in response to 90dB sound load was measured by a laser doppler vibrometer, and ME compliance changes were measured by tympanometry [7]. The result of Dai C et al., shows that the displacement at the umbo (tympanic membrane) was reduced upto 17dB due to the combined effect of fluid and pressure in the ME at all frequencies, at low frequency (f <1 kHz) displacement of tympanic membrane reduce due to combined effect of fluid and pressure is more as compared to ME fluid only. Still, its value is less than only ME pressure [7].

Regulation of ME pressure is a homeostatic process that controls ME environment-pressure gradient at the optimum level; this requires normal hearing [1]. Pressure regulation in the ME is a model of the combined effect of the passive exchange of gas between the ME to the round window in perilymph, ME to the surrounding environment through the tympanic membrane, ME to topic blood vessels through mucous of the ME and most important gas transfers is via ME to the eustachian tube in the pharynx. The first three exchanges ME to perilymph, ME to local blood, and ME to the environment, are explained by using the equation of Fick's diffuse and the fourth one as the displacement of bulk of the gas governed by Loiselle's equation [1,12]. The total magnitude of a gas-pressure gradient in the ME is measured at standard ME volume, which is inversely proportional to the efficiency of normal healthy hearing [1,13,14]. ME gas pressure gradient at -300daPa along with mucosal hydrostatic pressure gradient of the ME can cause a collapse of biological gas pocket (ME) with effusion of fluid from topical blood vessels into the ME cavity [1,15-17]. This clinical condition is related to moderate to severe conductive hearing loss [1,18,19]. It is noticed that risk factors for moderate to severe conductive hearing loss are inversely proportional to ME pressure regulation efficiency [1,19-21]. The accepted explanation regarding the regulation of ME pressure is mainly related to flow; the passive diffusion of the volume of gas exchange occurs near the compartment, from the ME to the nasopharynx, through the opening of the eustachian tube [12].

SEARCH METHODOLOGY

Pubmed was used to search Medline and the Cochrane Library to search central databases. Pubmed search method was adapted to particular databases and was as {"ME pressure" (Title/Abstract)} AND {"otitis media" (Title/Abstract)} OR {"gas difference" (Title/Abstract)} OR {"auditory tube" (Title/Abstract)}. In addition, references list of potentially relevant papers for further was searched. Studies found through these electronic searches and relevant sources included in their bibliographies were examined. Original studies in English that assessed the risk factors, diagnosis and management were included [Table/Fig-1].



[Table/Fig-1]: Inclusion and exclusion criteria of the study.

THEORY OF GASES EXCHANGE

Structure of Gas Exchange System

The ME is a bony chamber, having allotted volume, with constant temperature, and filled with air. It is lined all around by mucous membrane, and it is a six (anterior wall, posterior wall, lateral wall, middle wall, roof, and floor) walled cavity like a six-sided box. It is placed in a canal in the petrous part of the temporal bone [22]. ME chambers are divided into two parts, anterior and posterior. The anterior is known as the ME proper; it continues as a single layer of epithelial cells covering a matrix of connective tissue on it and veins, arteritis, and capillary embedded into it, which is useful for metabolism at a cellular level. The posterior part is also called the mastoid air cell system, and its volume is subdivided into various hair cells by the mucous covering over the bony septa. Three ossicles in the ME (malleus, incus, and stapes) conduct pressure exerted by the tympanic membrane towards the oval window of the ME. The middle ear alone with mastoid air cell, eustachian tube, aditus, and antrum is known as middle ear cleft. The tympanic membrane forms a barrier between an external auditory canal and the ME, and it forms a lateral wall of the ME out of the six walls. In the medial wall of the ME, important structures are located; these are openings due to an oval window where the footplate of stapes is connected and a round window which is covered by a round window membrane, also called as secondary tympanic membrane located inferior and posterior to the oval window. The anterior wall has two openings: a eustachian tube at the lower end and the canal for the tensor tympani muscle at the upper end [22].

An auditory tube, also known as the eustachian tube, connects the ME chamber and the nasopharynx [20]. It goes downward, forwards, and medially it comprises one-third bony and two-thirds fibrocartilaginous parts. The bony part lies posteriorly, and the remaining fibro cartilaginous part lies anteriorly and is made up of single cartilage. Muscles associated with the auditory tube are tensor veli palatini, levator veli palatini, and salpingopharyngeus. The tensor veli palatini's medial fibres originate from the auditory tube's lateral lamina; it is a narrow and inverted triangle shape muscle [1,23]. The function of tensor veli palatini and salpingopharyngeus is to open the lumen of the auditory tube; the contraction of the fibre of muscles results in an opening of the auditory tube as in the case of swallowing and yawning [1,24,25]. For the normal healthy hearing of voice, it is required that the pressure of the ME cavity and surrounding environment pressure is equal; a change in pressure in ME, whether negative or positive, can affect hearing. Also, the passive opening of the auditory tube by creating negative pressure causes the tubular lumen to close when the ME cavity pressure is higher than the pressure inside the lumen [1,26].

Expansion of Gas Pressure

For chamber (C) carrying gas in the gas phase (G) or dissolution of gas in liquid (L) and the chamber pressure (P_{Cs}). PCs are the same as the product of molar concentration species for chamber (CCs) and the inverse capacitance coefficient for chamber β^C_s. Molar concentration species for chamber (C_{Cs}) is given by the ratio of molar (η^C_s) to a product of the volume of the chamber (V^C) [1,27].

$$P^C_s = C^C_s \div \beta^C_s = \eta^C_s \div (V^C \times \beta^C_s) ......(1)$$

PCs will never be negative except in case of negative volume, mole. The negative pressure maintains in the article is gauge pressure. The extra pressure in system relative to the environmental pressure is known as gauge pressure. The standard coefficient (β) of gases is inversely proportional to the products of the absolute temperature T^G and universal gas constant R; now, according to formula 1,

$$P^C_s = \eta^C_s \div \{V^C \div (R \times T^G)\} ......(2)$$

The coefficient, β^C_s get dissolved in water and solid. If there is more than one gas mixture, then it is calculated by using Dalton's law, as total pressure is the sum of all given pressure. Σ sums the result.

$$P^C_g = \Sigma^s P^C_s = \{(R \times T^G) \div V^C\} \times \Sigma^s \eta^C_s ......(3)$$

β^C_s, the coefficient dissolved in the blood (liquid) and perilymph, it is the same as the solubility coefficient (S_{Ls}) it depends on the total temperature T^L. Therefore, exchanging formula, 1 gives Henry's law, $P^C_s = \eta^C_s \div V^C \times S^L_s\ T^L$......(4)

In blood, some gases are free, and the rest are bound to the blood compound, therefore, molar concentration is always changing.

ACTIVITIES THAT INTERFERE WITH MIDDLE EAR (ME) PRESSURE

According to formula no 2 and 3, ME air pressure is:

$$P^{ME}_g = \Sigma^s P^{ME}_s = \{(R \times T^{ME}) \div V^{ME}\} \times \Sigma^s\ \eta^{ME}_s ......(5)$$

According to formula 5, ME cavity pressure is directly proportional to temperature and mole and is inversely proportional to volume. ME temperature is constant in organisms with constant body temperature (homeotherms). In those, minor deviation in temperature leads to poor effects on change in pressure. At constant temperature and volume and changing mole [Table/Fig-2], the formula for ME pressure is:

$$\delta P^{ME}_g = \Sigma^s P^{ME}_s = (R \times T^{ME}) \div V^{ME} \times \Sigma^s\ \delta\eta^{ME}_s ......(6)$$

Variables	Mole				Pressure			
	O_2	N_2	CO_2	H_2O	O_2	N_2	CO_2	H_2O
Atmosphere	1.2	1.2	1.2	-	2120	7946	4	67
Negative pressure	1.1	1.1	1.1	-	1547	7573	387	627
Middle Ear (ME)	1.1	1.1	1.1	-	400	8442	667	627
Blood	1.3×10^{3}	6×10^{4}	3.4×10^{2}	-	400	7639	667	627
Perilymph	1.3×10^{3}	6×10^{4}	3.4×10^{2}	-	400	7639	667	627

[Table/Fig-2]: Mole and pressure of various gases [1].

Here, in the above formula 6, the change in pressure is directly proportional to mole at constant temperature and volume. The change in mole is due to the metabolism of free gas, binding of free gas with blood components, and biological or chemical change in gas structure. ME is a solitary cavity from the adjacent chamber, it doesn't have any pore gas flow, only passive gas exchange through the auditory tube. These routes for pressure regulation in the ME are a model of the combined effect of: 1) passively exchange of gas between ME to round window in perilymph; 2) ME to the surrounding environment through tympanic membrane; 3) ME to topic blood vessels through mucous of the ME; and 4) additionally, most important gas transfers are via the ME to an auditory tube which is opened by contraction of muscles, an active and passive process in the pharynx.

The formula for the passive exchange of gas is similar to ohm's low, I = V×K hear, I is current, V is voltage difference, and K is the conductance of current which is the inverse of resistance [30]. After comparing with ohm's formula, the passive exchange of gas mole M^{C1-C2} as a current is equal to the product of pressure gradient P^{C1-C2} as a voltage and gas movement in cavity K^{m} as a conductance. Then the formula for passive gas exchange is:

$$M^{C-ME}_{s,g}=K^{m}_{s,g}\times\Delta^{PC1-ME}_{s,g}\text{......(7)}$$

Now, compared with formula 1, the effective gas exchange is,

$$\delta P^{C}_{s,g}=\delta\,\eta^{C}_{s}\div(V^{C}\times\beta^{C}_{s,g})=M^{C-ME}_{s,g}\div(V^{C}\times\beta^{C}_{s,g})\text{......(8)}$$

The exchange of gases inside the chamber and trans-barrier flux reduces the pressure gradient, which gives by,

$$\delta\Delta P^{C1-ME}_{s}\div\delta t=M^{C-ME}_{s}\div(V^{ME}\times\beta^{ME}_{s})\times(R^{\beta V(ME\div C)}_{s}+1)\text{......(9)}$$

Hear $R^{\beta V(ME\div C)}$ s is the ratio of products of capacitance and chamber volume; its value becomes zero if ME volume is infinite, as in negative pressure.

Trance Barrier Type of Exchange with the Middle Ear (ME)

Alternative for formula 7 is also relevant to gas exchange as of trance barrier, which is given by Fick's law of diffusion. A barrier Φ^{b}_{s} is 1 mole or distinct or time to create a barrier of surface area A b and coefficient D b s

$$\Phi^{b}=A^{b}\times D^{b}_{s}\times\delta\,C^{b}_{s}\div\delta\,L^{b}_{d}\text{......(10)}$$

Here, Chang in concentration C^{b}_{s} and L^{b}_{d} changes in linear distance, for ME specific formula is,

$$M^{C-ME}_{s}=(A^{b}\times\beta^{b}_{s}\times D^{b}_{s}\div L^{b}_{d})\times\Delta^{C-ME}_{s}\text{......(11)}$$

The replacement of mole between compartments causes a gradual decrease in pressure gradient and a decrease in the exchange rate.

Gas Exchange throughout Open Auditory Tube

Registration of pressure gradient results in a flow of air into the nasopharynx through an opening of an Auditory Tube (AT) is explained by poiselle's law,

$$M^{AT}_{g}=K^{AT}_{g}\times\Delta P^{ME-NP}_{g}\text{......(12)}$$

Here, k is conductance; it is the viscosity of air [25]. k an active auditory tube is measured by,

$$K^{AT}_{g}=K^{FGE}_{g}\,(V^{ME}\div RT^{ME})\text{......(13)}$$

Here, K^{FGE} is a fractional gradient of swallow, explained as changes in pressure of ME chamber for swallow. Hear, $V^{ME}\div R^{TME}$ is not changing; thus, mole is directly proposed for ME pressure. After combining formulas,

$$M^{AT}_{g}\div\Delta t^{ET}_{0}=K^{FGE}_{g}\,(V^{ME}\div R^{TME})\Delta P^{ME-NP}_{g}\div\Delta t^{ET}_{0}\text{......(14)}$$

As negative pressure has infinite gas volume, this results in changes in formula

$$\delta P^{AT}_{g}\div\Delta t^{ET}_{0}=\Delta P^{ME-NP}_{g}\div\Delta t^{ET}_{0}=(V^{ME}\div RT^{ME})\,(\Delta t^{ET}_{0}\div\delta n^{ME})\text{......(15)}$$

For post openings, ME pressure is given by,

$$P^{ME}_{g(t=i\Delta t+to)}=P^{ME}_{g(t=i\Delta t)}+\delta P^{ME-NP}_{g}\div\Delta t^{ET}_{0}\text{......(16)}$$

ME pressures change due to auditory tube opening, for pre-openings total air pressure, compared with formula 15:

$$\delta P^{AT}_{s}\div\Delta t^{ET}_{0}=(\delta\,P^{ME-NP}_{g}\div\Delta t^{ET}_{0})\times(P^{sC}_{s}\div P^{sC}_{g})\text{......(17)}$$

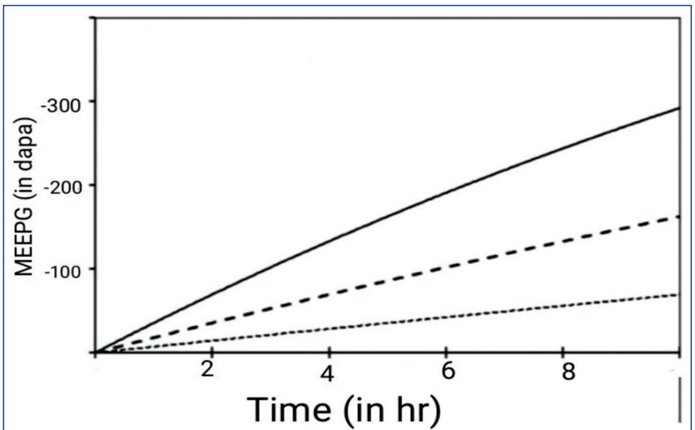
As total pressure after the opening of the auditory tube, as comparing Formula 16,

$$P^{ME}_{g\,(t=i\Delta t+to)}=P^{ME}_{g(t=i\Delta t)}+(\delta P^{ME-NP}_{g}\div\Delta t^{ET}_{0})\times(P^{sC}_{s}\div P^{sC}_{g})\text{......(18)}$$

There is no effect of auditory tube gas exchange in negative pressure.

Role of Middle Ear (ME) Mucosal Volume in the Regulation of ME Pressure

Stimulation upto 10 hour with close and inactive auditory tube and varying the frequency result in the ME to surrounding environment pressure gradient path as shown in the diagram. According to [Table/Fig-3] below, ME mucosal volume is directly proportional to rate in change in ME to surrounding environment pressure gradient. This is advisable showing gas loss in the ME by tans barrier exchange, and ME mucosal volume is one of the determinants.

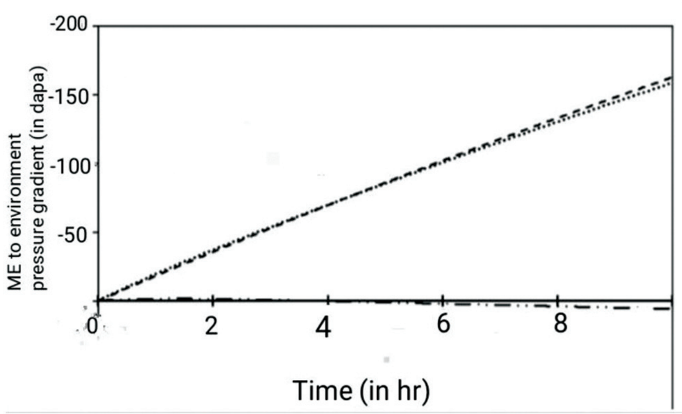


[Table/Fig-3]: Graph showing 10 hours of stimulation of the ME to the surrounding environment pressure gradient trajectory using a non functional auditory tube [1].

Here, solid line (-) is 0.1 ME mucosal volume, dotted line (---) is 0.25 ME mucosal volume, and line (......) is 0.5 ME mucosal volume. This is the graph showing 10 hours of stimulation of the ME to the surrounding environment pressure gradient trajectory using a non functional AT.

Role of Trance-Barrier Exchange in the Regulation of ME Pressure

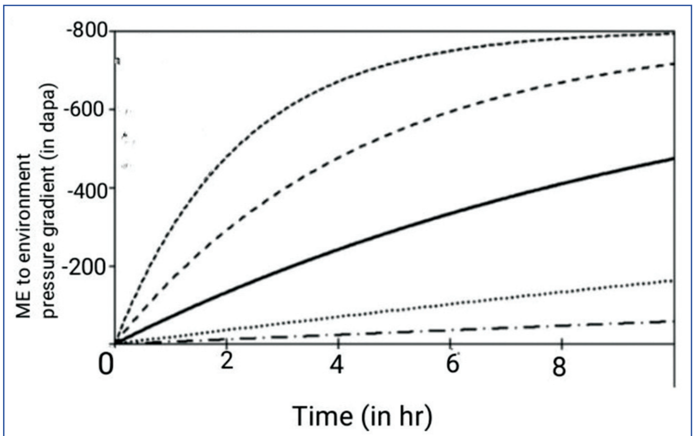
Stimulation upto 10 hours with close and inactive auditory tube and exchange across all three trans barrier paths. No trans tympanic membrane barrier exchange but ME mucosal air exchange set at standard value. Gas exchange along the membrane is also set at a standard value. The cause of ME to environment pressure gradient is given in [Table/Fig-4]; an exchange between two members barrier has little effect on pressure gradient with the slight and shallow decrease in gradient. ME to environment pressure gradient results is affected on a small scale by increasing more than one path. If only one gas is exchanged, the results are negligible and will not change by changing perilymph pressure. This is a graph showing 10 hours stimulation of ME to surrounding environment pressure gradient trajectory using a non functional auditory tube and without gas exchange between different barrier paths.



[Table/Fig-4]: Graph showing 10 hours stimulation of ME to surrounding environment pressure gradient trajectory using a non functional auditory tube [1].

Role of Perfusion Rate in Middle Ear (ME) Pressure Regulation

Stimulation upto 10 hours with close and inactive auditory tube and varying ME mucosal perfusion rate (Q). In [Table/Fig-5] ME to environment pressure gradient results at 0.02, 0.05, 0.2 and 0.5 volume/sec. Curve line of the pressure gradient is decreased at a higher perfusion rate. At a tangent, ME moles are exchanged with all chambers in a dynamic equilibrium in both liquid and gas medium. Here, Q is resident blood in volume/sec. For line (_._._) Q is 0.02; for line (.....) Q is 0.05, for solid line (_____) Q is 0.2, for line (----) Q is 0.5. This is a graph showing 10 hours of stimulation of the ME to the surrounding environment pressure gradient trajectory using a non functional auditory tube and varying ME mucosal rate.

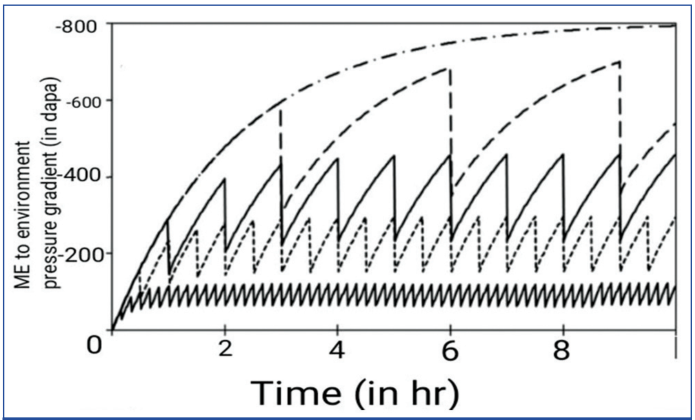


[Table/Fig-5]: Graph showing 10 hours of stimulation of the Middle Ear (ME) to the surrounding environment pressure gradient trajectory using a non functional auditory tube and varying ME mucosal rate [1].

Effect of Opening Frequency of Auditory Tube in the Regulation of Middle Ear (ME) Pressure

Changing the auditory tube opening frequency thus, stimulate the ME pressure regulation and sets the standard values of perfusion rate, auditory tube conduction rate, and auditory tube opening frequency.

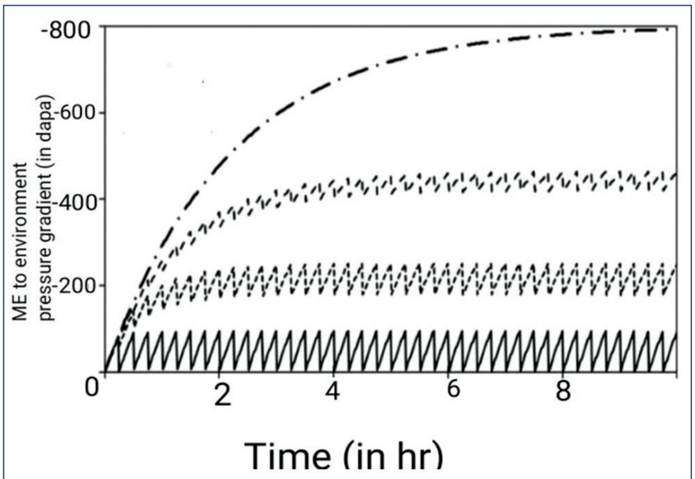
In [Table/Fig-6], ME to environment pressure gradient results at a frequency of 0.0, 0.3, 1, and 2 are shown per hours. Lesser the pressure gradient higher the opening frequency because the pressure regulation gradually increases by increasing auditory tube opening frequency. Here, F is the frequency of opening of auditory tube. For line (_._._) F is 0, for line (----) F is 0.3 for solid line (_____) F is 1 and for line (.......) F is 2. This is a graph showing 10 hour stimulation of ME to surrounding environment pressure gradient trajectory using varying functional auditory tube frequency (F).



[Table/Fig-6]: Graph showing 10 hour stimulation of Middle Ear (ME) to surrounding environment pressure gradient trajectory using varying functional auditory tube frequency (F) [1].

Effect of Gas Conduction through an Auditory Tube in Pressure Regulation

Changing the auditory tube conductance thus stimulates the ME pressure regulation and sets the standard values of perfusion rate, auditory tube conduction rate and auditory tube opening frequency. In [Table/Fig-7], ME to environment pressure gradient results for auditory tube conductance of 0.0, 0.2, 0.3 and 1, at constant auditory tube opening frequency. The total value of the pressure gradient decreases with increasing auditory tube conductance.



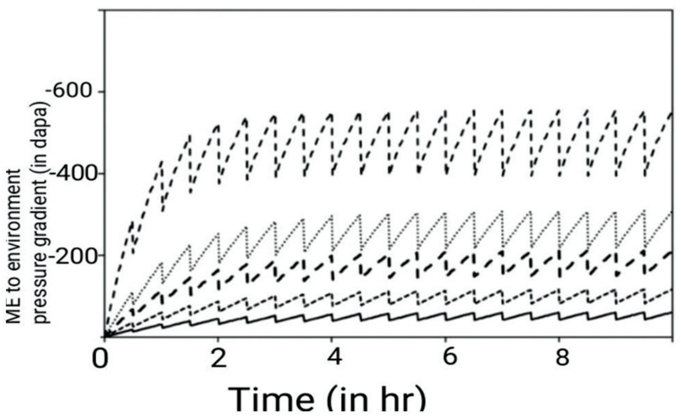
[Table/Fig-7]: Graph showing 10 hours of stimulation of the Middle Ear (ME) to the surrounding environment pressure gradient trajectory using varying functional auditory tube conductance as a fractional gradient in one swallow [1].

Here, FGE is a fractional gradient equilibrium in one swallow. For line (_._) FGE is 0; for line (----) FGE is 0.1; for line (....) FGE is 0.3 and for solid line (_____) FGE is 1. It is a graph of 10 hours of stimulation of the ME to the surrounding environment pressure gradient trajectory using varying functional auditory tube conductance as a fractional gradient in one swallow.

Association among Homeostasis Regulation and Agents Causing Stress in a Chamber

Stimulation for upto 10 hours with closed and inactive auditory tube and ME mucosal volume and perfusion rate controls the rate of trans-barrier exchange under the influence of pressure gradient. Regulations of ME pressure are affected by a condition that changes the rate of gas loss from ME, the rate of gas gain from ME, or both. This explains by ME pressure results assumed by standard with fixed auditory tube opening frequency [Table/Fig-8] and by changing the ME mucosal perfusion rate between 0.05-1 volume/sec.

Here, Q is the ME mucosal perfusion rate. For solid line (___) Q is 0.05, for line (---) Q is 0.1, for line (- -) Q is 0.2, for line(...) Q is 0.3, and for line (_-_), Q is 1. This is a graph showing 10 hours of stimulation of the ME to the surrounding environment pressure



[Table/Fig-8]: Graph showing 10 hours of stimulation of the Middle Ear (ME) to the surrounding environment pressure gradient trajectory using a functional auditory tube with a fixed frequency (F) and conductance and changing ME mucosal perfusion rate, Q [1].

gradient trajectory using a functional auditory tube with a fixed frequency (F) and conductance and changing ME mucosal perfusion rate, Q.

CONCLUSION(S)

To find out changes due to combined effect of fluid and pressure on ME function, both tympanometries with laser interferometry are used. After combining both fluid and pressure, there is a reduction of tympanic membrane (umbo) displacement at all hearing frequencies. More displacement of the umbo is detected when the negative pressure of fluid pressure is combined with the positive pressure. ME pressure due to combined fluid and pressure is determined by tympanometry. A formalised model in the form of mathematics was given to determine ME pressure flow regulation. Simple formulas of mathematics are used to well describe the physiology of all different models included in it.

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PARTICULARS OF CONTRIBUTORS:
1. Undergraduate Student, Department of ENT, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Science, Wardha, Maharashtra, India.
2. Associate Professor, Department of ENT, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Science, Wardha, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Puja Dinkar Lanjekar,
Undergraduate Student, Department of ENT, Jawaharlal Nehru Medical College,
Datta Meghe Institute of Medical Science, Sawangi Meghe,
Wardha, Maharashtra, India.
E-mail: lanjekarpuja@gmail.com

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