TECHNICAL UNIVERSITY OF CLUJ-NAPOCA

ACTA TECHNICA NAPOCENSIS

Series: Applied Mathematics, Mechanics, and Engineering
Vol. 65, Issue I, March, 2022

THERMODYNAMIC MODEL FOR MIDDLE-EAR VENTILATION - DEFINING THE *D-ORGAN* BY COMPARISON TO THE EUSTACHIAN TUBE (RE-INTERPRETATION OF A CLASSIC EXPERIMENT AND REVIEW OF LITERATURE)

Marian RĂDULESCU, Horia MOCANU, Alexandru NECHIFOR, Adela-Ioana MOCANU

Abstract: *The analysis employes Claude Bernard's physiological method of establishing the function of internal organs to reinterpret a classical experiment by Yee A.L. & Cantekin E.I. The surprising results could only be explained by the existence of the* ***D-Organ*** *(The Danaïdes Organ) which we define within the middle-ear (ME) and compare to the Eustachian tube (ET) in terms of middle-ear ventilation. Its function could only be completely defined via a physical-mathematical model. The ventilation of the middle-ear is therefore achieved by the* ***D-Organ****, a biological pump, consuming metabolic energy to move gases against pressure gradients and the F-Organ with role in passive diffusion of gas using pressure gradients, in accordance to Fick's law.*

Key words: *middle ear pressure, ventilation, gas exchange, anatomy, physiology, modeling.*

1. INTRODUCTION

The Eustachian tube is considered, at the moment, the essential element in the physiology, pathology and clinical study of the middle ear although, from an epistemological approach, this scientific truth should be questioned. The present hypothesis currently considered as the theory regarding the role of the Eustachian tube in middle-ear aeration insufficiently explains the array of phenomena for which it has been created. We aim to prove that its scientific truth is partial and therefore requires a new theory that would complete it.

The analysis of the present hypothesis should start with the method used for defining it and establishing a possible existence of a flaw in the method. This could simplify the further elaboration of a new theory. All of this could be found as early as 1855 with Claude Bernard and his lesson "Sur le role de l'anatomie dans le decouverte des fonctions" [1]. The author describes the method of "anatomical deduction" which means defining the function of an organ by simple and direct inspection of its parts. However, Claude Bernard advocates that anatomy is the consequence of physiology rather than vice-versa and establishes a *physiologic* or *functional view* which only studies a phenomenon within the living body, without prior anatomical localization and accepting only the direct results of the experiments. In other words, instead of looking for a function to attach to a studied organ, we should be looking for the organ that can perform the phenomena we study and for which we are looking for an anatomical localization.

This being said, it is most likely that the function of the Eustachian tube has been defined by *anatomical methods* using the analogy between its pipe-like shape that connects the middle-ear to the rhinopharynx and automatically choosing the physical phenomena that uses this organ – air flux to the middle-ear, originating from the nasopharynx. All following experiments, including the one from Yee A.L. & Cantekin E.I. [2] which we will be discussing, started from a pre-established anatomical

Received: 19.01.22; **Similaritie**s: 28.02.22: **Reviewed**: 11.02./21.02.22: **Accepted**:21.03.22.

localization and therefore, led to an inadequate conclusion. We should also consider that medical research can sometimes require a high degree of abstraction. [3] Using formal logic shows that what was considered analogical reasoning which should have ended in a material and theoretical physical-mathematical model is in fact a simple resemblance. This simple resemblance led to a plastic description of the phenomena as: the Eustachian tube opens by contraction of afferent muscles and air enters the middle-ear cavity. Starting from this, a number of figurative descriptions arise, but none could explain coherently and unequivocally, using a material or theoretical model, the phenomena that is the basis of middle-ear Eustachian tube ventilation.

The fundamental contradiction in the present theory is the fact that air pressure inside the middle-ear is inconsistently considered during experiments. When explaining the vibratory function of the tympanic membrane (TM) and ossicular chain (OC) the pressure is considered constant and equal to atmospheric pressure whilst in order to explain the entry of air into the ME when the ET opens, the same pressure must vary (decrease).

We maintain that by using the *physiological method*, the starting point for establishing functions to the middle ear is the clinical and experimental conclusion of identical pressure between the ME cavity and atmospheric pressure measured in the surrounding area of the patient. This conclusion is consistent with the theoretical premises of optimal vibro-mechanical function of the TM and OC.

2. METHODS USED

We have re-analyzed and commented on the 1985 classical experiment by Yee A.L. & Cantekin E.I. [2] and stated our own conclusions in comparison to other similar studies. The aforementioned experiment proves to be crucial and of extreme complexity (probably unequaled until today), uses the previously discussed physiological method on Rhesus macaque *(Macaca mulatta)* and targets the entire organism of the animal when proving, rigorously and undeniably that the pressure of the gases inside the ME (*pME*) of the animal, which for the duration of the experiment becomes a closed cavity, remains constant and equal to atmospheric pressure (E1) in spite of collapse of the ET for over 4 hours via narcosis and curarization.

$$\boldsymbol{p_{ME} = p_0 = 760 \cdot torr = const} \qquad \text{(E1)}$$

This is a fundamental condition for assessing the vibratory function of the tympano-ossicular system. However, when explaining air entering the ME by opening the ET, the same pressure *pME* must be considered variable and decreasing below atmospheric pressure (*pME < p0; p0-pME = Δp*).

The animal has been intubated and closed circuit ventilated with a mix of gases in which the fraction of O2 ($F^A_{O_2}$) varies over 5 hours, at equal intervals (1 hour each) at values of 15%, 21%, 40%, 80% and 100%.

According to the laws of respiratory exchange established by Piiper J. [4], the difference Δp (E2, E3) between atmospheric pressure and total pressure of respiratory gases dissolved in the mixed venous blood p_{MVB} varies with the partial pressure of O_2 ($F^A_{O_2}$) in the gas mix that ventilates the lungs (E2), starting from $\Delta_p = 52 \cdot mmHg$ for a 21% $F^A_{O_2}$ and up $\Delta_p = 610 \cdot mmHg$ for a 100% $F^A_{O_2}$ (pure oxygen ventilation).

$$\boldsymbol{p_{MVB} = p_{MVB}(F^A_{O_2})} \qquad \text{(E2)}$$

$$\boldsymbol{\Delta_p = p_0 - p_{MVB}} \qquad \text{(E3)}$$

However, the authors conclude, rather surprisingly, that the *pME* remains constant and at atmospheric pressure level for the entire duration of the experiment (E1) – see Table 1 & Figure 1. Consistent with the anatomical location of the Eustachian tube, the pressure was expected to decrease. Even more so, it was expected that the pressure drop would follow the graphic representation of a analytical function that was completely defined by the laws of respiratory gases exchange [4] – see Table 1 & Figure 1.

This expected pressure decrease would have occurred as a consequence of the following physiological phenomenon (according to present premises of ME physiology):

a) lack of Eustachian tube function due to muscle curarization, causing the lumen to open.
b) diffusion of gas from the middle ear to the internal environment on account of the pressure difference Δ_p^*between the total pressure of gases in the middle ear (*pME*) and the total pressure of respiratory gases dissolved in mixed venous blood (p_{MVB}) [E4].

$$\boldsymbol{\Delta_p^* = p_{Um} - p_{MVB}} \qquad \text{(E4)}$$

The gas dispersal will continue until an equilibrium is reached (E5)

$$\boldsymbol{\Delta_p^* = 0 \Rightarrow p_{Um} = p_{MVB}} \qquad \text{(E5)}$$

c) The p_{MVB} decreases from 708 torrs to 150 torrs during the experiment.
d) The pressure difference Δ_p^* (E4) rises from 52 torrs up to 610 torrs.
e) The closed Eustachian tube is the prerequisite condition for pressure balance Δ_p^*= 0 (E5) to be reached at any moment during the experiment.

The authors conclude an inexplicable result. Instead of a decreasing *pME* in accordance with the analytical function (E2), the middle-ear pressure remains constant throughout the experiment and equal to atmospheric pressure p_0 (E1) - see Table 1 & Figure 1.

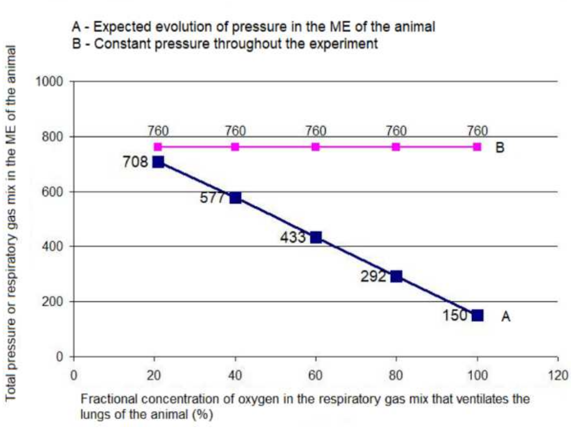

Fig. 1. Graphical representation of expected pressure decreases vs. the actual constant evolution of pressure of respiratory gas mix in the middle-ear of the experimental animal

However, their conclusions and complex explanations are still in accordance with the *anatomic method* starting point rather than to the *physiological* reasoning of Claude Bernard.

Table 1

Numerical values of fractional concentration of oxygen in the gas mix that ventilates the lungs of the experimental animal correlated to numerical values of and resulted from the Experimental laws of gas exchange

$F_{O_2}^A$ [%]	$\Delta_p^* = p_{Um} - p_{MVB}$ [E4] [torr]	p_{MVB} [torr]	$p_{U_m} = p_B$ [torr]
0,21	52	708	760
0,4	183	577	760
0,6	327	433	760
0,8	468	292	760
1	610	150	760

3. DISCUSSIONS

We propose a different approach and a theoretical thermodynamic interpretation of the experiment, following the functional method. If the conditions for a completely closed ME (protympanum, tympanic cavity, additus, antrum, mastoid cells, petrous cells) of constant volume V_ε are achieved, we define, both theoretically and experimental, a thermodynamic system ε^T consisting of the mix ε of σ types of respiratory gases saturated with water vapors at body temperature ($t_\varepsilon^0 = 37°C$or $T_\varepsilon = 310{,}15°K$).

The thermodynamic system is completely defined by its state parameters: volume V_ε [cm3], pressure p_ε [torrs] and temperature T_ε [K]:

$$\boldsymbol{\varepsilon^T = \varepsilon^T(p_\varepsilon, V_\varepsilon, T_\varepsilon)} \qquad \text{(E6)}$$

To delineate the thermodynamic system requires establishing limits and an external environment. The interface between the ε^T system and the external environment is both experimentally and theoretically defined as the non-keratinized stratified squamous epithelium of the middle ear. The external environment of the ε^T system can be considered as follows: *anatomically* - the entire body of the animal, except the middle ear epithelium; *physically* - the respiratory gases mix dissolved in the total amount of water of the body; *theoretically* (compatible to a logical – mathematical model based on the laws of thermodynamics and perfect gases) - the respiratory gases mix dissolved in the total amount of water in the body, brought to gaseous state through isobaric transformation and saturated with body temperature water vapors. According to the abovementioned statement, we can establish that the external environment of the ε^T system is yet another thermodynamic system M^T, homologous to ε^T. The system parameters of M^T (pressure p_M, volume V_M and temperature $T_M \equiv T_\varepsilon = 310{,}15°K$) are perfectly deductible from the present physiology data [4,5,6] – see Figure 2.

Thermodynamically, p_M is identical to the sum of p_{MVB} and $\boldsymbol{p_{H_2O}}$, (E7) (6) therefore p_M is equal to the total pressure of gases and water vapors in the mixed venous blood of the subject.

$$\boldsymbol{p_M = p_{MVB} + p_{H_2O}} \qquad \text{(E7)}$$

The V_M volume is a function of barometric pressure p_0 and oxygen fraction $F^A_{O_2}$ in the inhaled air (E8):

$$\boldsymbol{V_M = V_M(p_0, F^A_{O_2})}. \qquad \text{(E8)}$$

This can be proven by (E9) as part of the thermodynamic model of middle-ear ventilation:

$$\boldsymbol{V_M} = \frac{C^{MVB}\bar{F}^{\Omega}_{H_2O} m_\Omega R T_M}{\bar{F}^{MVB}_{H_2O} V_{\mu 0} \rho_{H_2O}(p_{MVB} - p_{H_2O})} = \boldsymbol{V_M(p_0, F^A_{O_2})} \qquad \text{(E9)}$$

Where:

- ✓ $\boldsymbol{C^{MVB}}$ volumetric concentration of respiratory gases, dissolved in unit volume [cm3] [STPD], p_0 and T_0= 273.15 K of mixed venous blood (MVB);
- ✓ $\boldsymbol{\overline{F^{MVB}_{H_2O}}}$ represents medium water fraction in unit volume [cm3] of mixed venous blood.;
- ✓ $\boldsymbol{m_\Omega}$ represents the actual mass of the subject [g];
- ✓ *R* represents the universal ideal gas constant;
- ✓ $\boldsymbol{\rho_{H_2O}}$ represents the water density at constant body temperatureT_M;
- ✓ $\boldsymbol{\overline{F^{\Omega}_{H_2O}}}$ represents the average partial water fraction to the body mass.
- ✓ $\boldsymbol{V_{\mu 0}}$ represents the molar volume of ideal gases in normal conditions (p_0 and T_0).

In conclusion, both the states and the processes of the thermodynamic system $M^T$are completely defined, including by numerical values of state parameters (E10):

$$\boldsymbol{M^T = M^T(p_M, V_M, T_M)} \qquad \text{(E10)}$$

By varying the O2 fraction in the gas mix ($F^A_{O_2}$) that ventilates the lungs of the subject, the authors modify, by controlled means, according to the laws of respiratory exchange (E2) [4] the pressure p_{MVB} which is equivalent to the pressure p_M:

$$\boldsymbol{p_{H_2O} = 47 \cdot torr = const} \qquad \text{(E11)}$$

This pressure p_M is the only state parameter of the thermodynamic system M^T that can be modified *in vivo* and under physiological conditions. Thus, the experiment proves that the thermodynamic system ε^T (the mix of gases and water vapors inside the middle-ear of the subject) maintains its state of thermodynamic balance - the parameters $p_\varepsilon, V_\varepsilon, T_\varepsilon$ remain constant regardless of the pressure variation in the M^T system (the external environment) which is also a thermodynamic system. In other words, the experiment proves the existence of a status quo that contradicts the universal truth of the Laws of Thermodynamic: the system ε^T acts similar to a *closed thermodynamic system* (this is just a theoretical concept, impossible in real life); the system ε^T acts like a *thermodynamically isolated and isothermal system*, incompatible with the biological field of the experiment. We maintain this statement because: biological systems are, by definition, opened thermodynamic system that exchange mater, energy and information to the environment; the interface between the systems ε^T and M^T is the epithelium of the middle-ear; this epithelium is a true biological system, and its most interesting property is permeability for the respiratory gas mix within the middle ear. Since all processes in the middle-ear are governed by the 3 Principles of Thermodynamic, the contradiction within this experiment is only an appearance and a more rigorous analysis of the process is required. The fact that the pressure p_ε remains constant although external conditions vary, and the ET has been closed for the duration, can be expressed by the following mathematical expression which is the experimental demonstration of the validity of the logical-mathematical model of middle-ear ventilation (E12):

$$\forall F_{0_2}^{A} \in [21\%, 100\%], \exists p_\varepsilon = p_{H_2O} + \sum_{\sigma=1}^{3}\left(\frac{p_{MVB_\sigma}+4\phi_\sigma RT_\varepsilon W\bar{\rho}_\Omega}{\Psi\Gamma}\right) = p_B = const \quad \text{(E12)}$$

$$W = \sqrt{m_{\Omega_x}/m_\varepsilon}$$

$$\Psi = m_{\Omega_x}/m_\Delta$$

$$\Gamma = p_{MVB} - p_{H_2O}$$

Where:

- ✓ m_{Ω_x} the mass of the considered organism (exclusively for *vertebrates - superclass Tetrapoda*);
- ✓ m_ε the mass of the thermodynamic system ε^T (see ahead);
- ✓ m_Δ the mass which is object to mechanical work between the thermodynamic systems ε^T and M^T (see ahead);
- ✓ $\bar{\rho}_\Omega$ the average density of the body;
- ✓ $\bar{\rho}_\Omega$ = 1,35 g·cm^{-3} ;
- ✓ $\phi_\sigma = \frac{p_{MVB}}{\mu_\sigma} \cdot [torr \cdot mol \cdot g^{-1}]$; where μ_σ is the molar mass of σ of gas.

Since the theoretical model of the ventilation function of the middle-ear is a completely formalized axiomatic system, we can conclude that the experiment in question is the demonstration of validity for a mathematical modelling for ME ventilation.

The constant state of equilibrium within the ε^T system (gas mix saturated by water vapors, within the ME), demonstrated by constant values of its state parameters over time (p_ε= const; V_ε= const; T_ε= const.), means that the mass m_ε corresponding to a number of mols ν_ε also remains constant (E13):

$$\nu_\varepsilon = \frac{V_\varepsilon}{V_{\mu^0}(1+\alpha_v \cdot t_\varepsilon^0)} = const, \quad \text{(E13)}$$

Where:

$\alpha_v = \frac{1}{273,15} \cdot K^{-1}$ the coeficient of isobaric dilatation of a perfect gas

$t_\varepsilon^0 = 37°C$ temperature in Celsius;

V_{μ^0} molar volume of perfect gas under normal conditions (p_0 and $T_0 = 273,15°K$);

$V_{\mu^0} = 22413,6 \cdot cm^3 mol^{-1} K^{-1}$.

We should also state that the system M^T also maintains its thermodynamic balance which is equivalent to the homeostasys of the organism of the experimental animal.

Both from an experimental and theoretical physics point of view, these two systems are in thermal contact and in thermal equilibrium and thus the systems are in thermodynamic equilibrium.

Since their temperatures are identical ($T_\varepsilon \equiv T_M$), this balance cannot be obtained via internal energy exchange (i.e., heat exchange) and it must be the result of the exchange of mechanical work. This is the fundamental conclusion of this experiment – the existence of exchange of mechanical work between the two systems, necessary and sufficient to maintain the thermodynamic balance. In order to simplify the explanation, we will use the analogy to the thermal motor. It also has two thermodynamic systems: the *hot source* (with a very high absolute temperature and high internal energy) and the *cold sink* (very low absolute temperature and internal energy compared to the first).

A function cycle of a bi-thermal cyclical irreversible machine ends once the equilibrium between the hot source and the cold sink is reached, and this is accomplished by exchange of internal energy (heat exchange). The energy that the hot source yields to the cold sink becomes the algebraic sum of mechanical work and quantity of heat and the last one determines an increase in temperature for the cold sink.

In our case the two systems have different internal energies (E14), given the difference in pressure (E15) but have the same temperature (E16):

$$U_\varepsilon = U_\varepsilon(p_\varepsilon, T) \rangle U_M = U_M(p_M, T); \quad \text{(E14)}$$

$$\Delta_p = p_\varepsilon - p_M, \quad \text{(E15)}$$

$$T = T_\varepsilon \equiv T_M. \quad \text{(E16)}$$

Given this thermic balance, it is clear that the thermodynamic balance is achieved by exchange in mechanical work, represented by the conversion of the difference between the internal energies U_ε și U_M of the two systems ε^T and M^T. The constant mass m_ε is the expressions of the exchange in mechanical work via the ME epithelium.

The mass m_Δ corresponds to a number of mols of respiratory gas mix ν_Δ which is the subject of reciprocal and simultaneous transfer between the two systems, through the ME epithelium. This is achieved by each system doing useful mechanical work L_U^D and L_U^F, equal but of opposite direction for each $\boldsymbol{\tau}$ time interval we consider (E17). (Figure 2)

$$\boldsymbol{\nu_\Delta} = \frac{\boldsymbol{V_\varepsilon \cdot \Delta_p}}{\boldsymbol{RT_\varepsilon}}. \qquad \text{(E17)}$$

Where:

- ✓ $\boldsymbol{\Delta_p}$ represets the pressure difference between the two thermodynamic systems [E14];
- ✓ $\Delta_p \in [52; 610]'[torr]$;
- ✓ R = 62362,6 [torr·cm3·mol–1·K–1] este universal constant of perfect gases.
- ✓ Vε volume of system ε^T
- ✓ Tε represents the absolute temperature in the scale of the perfect gas of the system ε^T

This entire demonstration proves that the interface between ε^T and M^T is formed of two areas corresponding to the two types of mechanical work through which the mass m_Δ is being transferred (Figure 3) and that the ME mucosa has two completely different functional areas: *the first functional area* acts identical to an element of area A^F set perpendicularly to the direction $r^{(+)}$of density variation Δ_p or pressure variation Δ_p and through which the mass m_Δ , according to Fick's law [7], passes by diffusion, from the system $\varepsilon^T$to the system M^T in a time interval τ, doing the work L_U^F in the direction $r^{(+)}$over the distance h^F; *the second functional area* acts as a biological pump that, during the interval $\boldsymbol{\tau}$ consumes the energy Q^D which it transforms, with efficiency η, into useful work L_U^D in the direction $r^{(-)}$ by which it transfers the mass m_Δ from the system M^T to the system ε^T over the distance h^D.

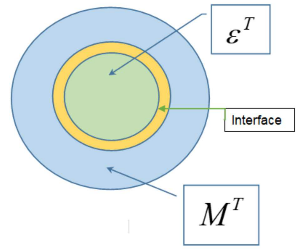

Fig. 2. Diagram for thermodynamic ε^Tsystem delimitation

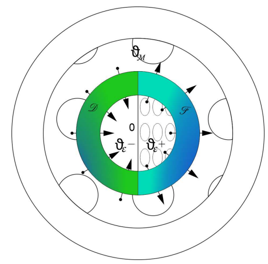

Fig. 3. Schematic representation of the two functional areas - active biological pumps (***D-organ***) vs. passive diffusion mechanism through permeable membrane (***F-Organ***) to keep middle-ear aeration. The interface between the two systems $M^T$and ε^T

A simpler, more medical approach would be: *the first functional area* is a surface of gas diffusion from the ME to the internal environment of the body, determined by gradient of partial pressures Δ_{p_σ} of respiratory gases on both sides of the epithelium (this role is currently unanimously accepted for the entire mucosa of the ME); *the second functional area* that acts as a biological pump, consuming metabolic energy, with an efficiency situated at the upper limit of a biological systems and that has dynamics and cinematics explainable by a physical-mathematical model. The ME is a chamber containing a mix of respiratory gases saturated by water vapors, at a constant temperature of 37°C and pressurized at 760 torr. The walls of this chamber are permeable for the gases within. The external environment of the chamber is an identical mix of gases but at 708 torr. A well-defined number of pumps are fitted into the walls to bring gases inside the chamber and their dynamics and cinematics is well adjusted so that their input volume is equal to the volume of diffusion through the walls. The ME cavities become a system, similar to a heart ventricle, that moves gases dissolved in the total body water by changing their state of aggregation twice, once when entering and again when exiting the ME.

We consider the cells that perform this function as an organ in its own right, which has a titanic, perpetual task that subject it to various aggression. We have named it **The Danaïdes Organ** or **the D-Organ** since, like the characters of Greek mythology, it performs a disproportionate, repetitive task that can never be completed (carrying water with a sieve).

The Eustachian tube is but a bidirectional self-regulating pressure valve, the means for a cybernetic mechanism that adjusts the pressure level within a chamber to the level of effective atmospheric pressure. Thus, it is a pipe meant to transport a mass of gas, but the physiological significance of this action is different from the present accepted theory which is a partial scientific truth.

There have been several studies performed over the last decades that concern themselves with ventilation mechanisms of the ME but none, to our knowledge, has reported the possibility of an active pump within the mucosa. We intend to pursue this theory and perform anatomic and histologic studies to prove its existence. Some of our earlier work concerning results of tympanoplasty also took into consideration the existence of a D-Organ [8]. Sade and Luntz [9] also observe de similarities between the partial pressure of gases in the ME cavities and the partial pressures of respiratory gases in the mixed venous blood and state that they were expecting similarities to the atmospheric gases. The values for partial pressures that our physical-mathematical model yields are similar to those reported in literature. [10]

A 1999 study by Ikarashi et al. revisits this important topic and concludes that there might be sufficient evidence for a bidirectional CO_2 exchange via the middle ear mucosa functions of the normal ME. However, the study speculates on the diffusion induced mechanism via partial pressure gradient rather than the presence of a specialized, active pump. A correlation between $PvCO_2$ and middle ear pressure has been suggested by several other experiments or clinical studies exchange. [11-19] Some of these even report ME negative pressure regulation without ET opening. [13]

Defining the exact role of the ET for ME ventilation is of clinical importance since a malfunctioning ET is believed to lead to numerous pathologies, all of them resulting in hypoacusis. Hearing loss represents one of the most serious afflictions confronting the world's population, with variable etiology, of which at least 50% genetic. However, WHO estimates that between 65 and 330 million individuals suffer from some form of middle ear suppuration and 50% of them suffer from hearing impairment. [20-23] The presence of an active pump, represented by the *D-Organ* would also change the paradigm of tympanoplasty and functional results since restoring sound transmission to the inner ear through reconstruction of the ossicular chain is paramount in middle ear surgery [24,25] but useless without a well-ventilated ME. The current conception is that the ME cavity is a non-ventilated type of gas pocket [26] intermittently opened to the atmosphere via the ET. Gases are absorbed continuously into the blood and the ET operates like a pressure regulator by periodically allowing air-portions into the closed ear cavity to replace the gas volumes absorbed. [27]

In 2002, Hamada et al. study gas exchange in rabbits and conclude that it occurs not only via the ET but also across the ME mucosa. [28] This supports our theoretical approach although we also maintain the existence of an active pump mechanism for this phenomenon. Marcusohn et al. conclude that the exchange of CO_2 is limited mainly by the rate of ME blood perfusion. [29] A similar study by Doyle revisits the earlier experiments of Mover-Lev at al. and provides a mathematical model for explaining why those experiments do not control for certain effects and that the time constant of the experiment was inaccurate. [30,31]

4. CONCLUSION

Middle-ear ventilation is not achieved by the Eustachian Tube but by two organs, D-Organ and F-Organ, each with a very distinctive function. The experiment we analyzed concludes on the existence of these two function areas but gives no information on the possible localization of these areas. A study based on anatomy, embryology and histology will follow to try and localize **The Danaïdes Organ** within the mucosa of the ME.

The D-Organ functions as an energy-consuming biological pump, moving gas molecules against pressure gradients whilst the F-Organ functions by passive gas diffusion pursuing pressure gradients.

The present theory on the function of the ET leads to similarities between ME air and atmospheric air, since the ladder should be the sole source of air in the ME, but we prove that this source is rather a thermodynamic system M^T homologous to the system ε^Tthat the gases within the ME form and the partial pressures of this gas are identical to those in the mixed venous blood. The theoretical model provides values for partial pressures that are similar to those reported in literature.

We can justifiably state that in a normal ME there is no atmospheric air but rather a mix of respiratory gases saturated with water vapors. This mix represents a complete thermodynamic system defined by three state parameters: pressure, volume, and absolute temperature. Atmospheric air can enter this chamber only incidentally or in an auxiliary manor to adjust the pressure and not to determine it.

The mix of respiratory gases and water vapors inside the ME on the one side and respiratory gases dissolved in the total water of the organism on the other, represent two opened thermodynamic systems which are in a state of thermodynamic balance. The latter constitutes external environment for the first. The interface of the two systems is the epithelium of the ME. The two systems are in thermal contact and equilibrium which makes heat exchange impossible. Therefore, the thermodynamic equilibrium can only be achieved by exchanging mechanical work through the interface, at the level of the two epithelial areas mentioned – D-Organ and F-Organ.

The middle-ear cavities represent a complex biological chamber that performs the following functions: delineates a physical quantity (volume V_ε) as a state parameter for a thermodynamic system ε^T; ensures via thermal contact and balance the constant value of another state parameter T_ε; the walls that separate it from the internal environment of the body have two distinct functional areas – diffusion area & pump; the work done by these two types of epithelium ensures the constant value of the third parameter of the system (p_ε); the chamber has a self-adjusting pressure valve, the Eustachian tube; the chamber contains the ossicular chain; one of its walls – the tympanic membrane – has two additional roles, integration within the tympanic-ossicular system and sensor for barometric pressure as part of the cybernetic mechanism that includes the ET.

The existence of the ε^T system is one of the prerequisites for optimal function of the tympanic-ossicular system.

The experiment by Yee & Catenkin proves the validity of our thermodynamic model and consequently the high degree of probability of our scientific hypothesis concerning the existence of the two organs within the middle-ear.

A complete, coherent, non-adversarial correspondence between the existence of the **D-Organ**, explained via a physical-mathematical model, and the pathology and clinical manifestations of the ME will be eventually possible, and it will satisfy the entire Quintilian Hexameter: Quis, quid, ubi, quibus auxiliis, cur, quomodo, quando?

5. REFERENCES

[1] Conti, F. *Claude Bernard: primer of the second biomedical revolution*. Nat Rev Mol Cell Biol; 2(9), pp.703-8, 2001.

[2] Yee, A.L. and Cantekin, E.I. *Effect of Changes in Systemic Oxygen Tension on Middle Ear Gas Exchange*. Ann Otol Rhinol Laryngol; 95(4,1), pp.369-372, 1986.

[3] Alecu, I., Mocanu, H. and Călin, I.E. *Intellectual mobility in higher education system*. Rom J Mil Med; CXX (2), pp.16-21, 2017.

[4] Piiper, J. *Physiological Equilibria of Gas Cavities in the Body*. In: Fenn, W.O., Rahn, H., Section 3 Editors. Respiration, Handbook of Physiologie, A Critical Comprehensive Presentation of Physiological Knowledge and Concepts. Washington DC: American Physiological Society 2(48), pp.1205-1218, 1965.

[5] Best, C.H. and Taylor, N.B. *The physiological basis of medical practice, A text in applied physiology*. 6th Edition, The Williams & Williams Company, Baltimore;

Part III, Chapter 31, 1955.

[6] Guyton, A.C. *Textbook of Medical Physiology*. Eight Edition, Philadelphia: WB Saunders Company, Harcourt Brace Jovanovich Inc; pp. 2,274,433-437,744,792, 1991.

[7] Felding, U.N., Banks, J.M. and Doyle, W.J. *Middle Ear Gas Exchange in the Air Phase*. Acta Oto Laryngol; 123, pp.808-11, 2003.

[8] Mocanu, H., Mocanu, A.I., Drăgoi, A.M. and Rădulescu, M. *Long-term histological results of ossicular chain reconstruction using bioceramic implants*. Exp Ther Med; 21(3), pp.262, 2021. DOI: 10.3892/etm.2021.9692

[9] Sadé, J. and Luntz, M. *Middle Ear as a Gas Pocket*. Ann Otol Rhinol Laryngol; 99, pp.529-534, 1990.

[10] Ikarashi, F., Takahashi, S., Yamamoto, Y. *Carbon Dioxide Exchange via the Mucosa in Healthy Middle Ear*. Arch Otolaryngol Head Neck Surg; 125, pp. 975-8, 1999.

[11] Buckingham, R., Stuart, D.R. and Girgis, S.J. *Experimental evidence against middle ear oxygen absorption*. Laryngoscope; 95, pp.437-42, 1985.

[12] Mover-Lev, H., Levy, D., Luntz, M., Harell, M., Ar, A. and Sadé, J. *Dependence of middle ear gas composition on pulmonary ventilation*. Ann Otol Rhinol Laryngol; 106, pp.314-9, 1997.

[13] Hergils, L. and Magnuson, B. *Regulation of negative middle ear pressure without tubal opening*. Arch Otolaryngol Head Neck Surg; 114, pp.1442-4, 1998.

[14] Shinkawa, H., Okitsu, T., Yusa, T., Yamamuro, M. and Kaneko, Y. *Positive intratympanic pressure in the morning and its etiology*. Acta Otolaryngol (Stockh); 435, pp.107-111, 1987.

[15] Doyle, W.J. and Seroky, J.T. *Middle ear gas exchange in rhesus monkeys*. Ann Otol Rhinol Laryngol; 103, pp.636-45, 1994.

[16] Sadé, J., Luntz, M. and Levy, D. *Middle ear gas composition and middle ear aeration*. Ann Otol Rhynol Laryngol; 104, pp.369–373, 1994.

[17] Luntz, M., Levy, D., Sadé, J. and Herman, M. *Relationship between the gas composition of the middle ear and the venous blood at steady state.* Laryngoscope; 105, pp.510-2, 1995.

[18] Tideholm, B., Carlborg, B., Jönsson, S. and Bylander-Groth, A. *Continuous long-term measurements of the middle ear pressure in subjects without a history of middle ear disease*. Acta Otolaryngol (Stockh); 118, pp.369-375, 1998.

[19] Yamamoto, Y. *Gas exchange function through the middle ear mucosa in piglets: comparative study of normal and inflamed ears*. Acta Otolaryngol (Stockh); 119, pp.72-7, 1999.

[20] Mocanu, H. and Oncioiu, I. *The Influence of Clinical and Environmental Risk Factors in the Etiology of Congenital Sensorineural Hearing Loss in the Romanian Population*. Iran J Publ Health; 48, pp.2301-3, 2019.

[21] Mocanu, H. *The role of perinatal hearing screening in the normal development of the infant's language*. In: Debating Globalization. Identity, Nation and Dialogue 4th Edition. Boldea I, Sigmirean C (ed.) Arhipelag XXI Press, Tirgu Mures; pp.562-569, 2017.

[22] Neagu, A., Mocanu, A.I., Bonciu, A., Coadă, G. and Mocanu, H. *Prevalence of GJB2 gene mutations correlated to presence of clinical and environmental risk factors in the etiology of congenital sensorineural hearing loss of the Romanian population*. Exp Ther Med; 21(6), pp. 612, 2021. DOI: 10.3892/etm.2021.10044.

[23] Mocanu, H. *The economic impact of early diagnosis of congenital hearing loss*. In: Debating Globalization. Identity, Nation and Dialogue 4th Edition. Boldea I, Sigmirean C (ed.) Arhipelag XXI Press, Tirgu Mures; pp. 556-561, 2017.

[24] Neudert, M., Bornitz, M., Mocanu, H., Lasurashvili, N., Beleites, T., Offergeld, C. and Zahnert, T. *Feasibility Study of a Mechanical Real-Time Feedback System for Optimizing the Sound Transfer in the Reconstructed Middle Ear*. Otol Neurotol; 39(10), pp.907-920, 2018.

[25] Mocanu, H., Bornitz, M., Lasurashvili, N. and Zahnert, T. *Evaluation of Vibrant® Soundbridge™ positioning and results with laser doppler vibrometry and the finite*

element model. Exp Ther Med 202; 21 (3), pp.262, 2021. DOI: 10.3892/etm.2021.9694

[26] Rahn, H. and van Liew, H.D. *Quoted from Studies in respiratory physiology*. WADC Tech Repet 55-357. H. Rahn and W.O. Fenn eds., 382 Wright Air Development Center, Dayton, Ohio, 1955.

[27] Ingelstedt, S. and Jonson, B. *Mechanisms of the gas exchange in the normal human ME*. Acta Otolaryngol [Suppl] (Stockh) suppl.; 224, pp.452-61, 1967.

[28] Hamada, Y., Utahashi, H. and Aoki, K. *Physiological gas exchange in the middle ear cavity*. Int J Pediatr Otorhinolaryngol; 64, pp.41–9, 2002.

[29] Marcusohn, Y., Ar, A. and Dirckx, J.J.J. *Perfusion and diffusion limitations in middle ear gas exchange: The exchange of CO2 as a test case*. Hear Res; 265, pp.11-4, 2010.

[30] Doyle, W.J. *Mathematical model explaining the sources of error in certain estimates of the gas exchange constants for the middle ear*. Ann Otol Rhinol Laryngol; 109, pp.533-541, 2000.

[31] Mover-Lev, H., Sadé, J. and Ar, A. *Rate of gas exchange in the middle ear of guinea pigs*. Ann Otol Rhinol Laryngol; 107, pp.194-8, 1998.

MODEL TERMODINAMIC PENTRU VENTILAȚIA URECHII MEDII - DEFINIREA *ORGANULUI D* PRIN COMPARAȚIE CU TUBUL EUSTACHIAN (REINTERPRETAREA UNUI EXPERIMENT CLASIC ȘI REVIZUIREA LITERATURII)

Abstract: *Lucrarea de față utilizează metoda fiziologică a lui Claude Bernard de stabilire a funcției unui organ pentru a reinterpreta experimentul clasic al lui Yee A.L. & Cantekin E.I. Rezultatele neașteptate se pot explica doar prin existența* ***Organului D (Danaid)*** *- ipoteza noastră de lucru. Autorii încearcă să demonstreze existența unui organ cu totul nou și să îl compare cu trompa lui Eustachio (ET) in ceea ce privește rolul lor în ventilarea urechii medii. Funcția acestui organ poate fi definită doar prin utilizarea unui model fizico-matematic. Ventilația urechii medii se realizează astfel prin* ***Organul D*** *ca pompă biologică, consumatoare de energie metabolică pentru a deplasa gaze împotriva gradientului de presiune și* ***Organul F*** *cu rol în difuzia pasivă a gazului prin gradiente de presiune, conform legii lui Fick.*

Marian RĂDULESCU, MD, PhD, Assistant Professor, ENT&HNS Specialist. "Carol Davila" University of Medicine and Pharmacy, Department of ENT&HNS, E-mail: focaargintie@yahoo.com, Phone: +40749098319, Address: Str. Dionisie Lupu, nr. 37, Sect. 2 020021, Bucharest, Romania. ORCID: 0000-0002-4029-7721.

Horia MOCANU, MD, PhD, Dr.med., Lecturer, ENT&HNS Specialist, "Titu Maiorescu" University, Faculty of Medicine, Department of ENT&HNS, E-mail: horia.mocanu@prof.utm.ro, Phone: +40732662268, Address: Str. Gheorghe Petrașcu, nr.67A, 031593, Bucharest, Romania. ORCID: 0000-0002-9708-8285

Alexandru NECHIFOR, MD, Assistant Professor, "Dunărea de Jos" University Galați, Faculty of Medicine and Pharmacy, Medical Clinical Department, E-mail: alexandrunechiformed@yahoo.com, Phone: +40743887349. Address: Str. Domnească, nr. 47, 800008, Galați, Romania. ORCID: 0000-0002-1481-2822.

Adela-Ioana MOCANU, MD, PhD Student, ENT&HNS Specialist, Polimed Medical Center, Department of ENT&HNS, E-mail: adela.ioana.mocanu@gmail.com, Phone: +40723400435, Address: Calea Văcărești, nr. 280, Sect. 4, 040067, Bucharest, Romania. ORCID: 0000-0003-0725-2131. – Corresponding author.