

Review Article

Genetics and Otitis Media, Role in the Occurrence, Development and Evolution to Chronicity

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Abstract

The explanatory theories of the etiopathogenesis and physiopathology of Otitis Media are many and unconvincing; however, they have remained with very few variations for decades. The therapeutic results (medical and surgical), despite scientific advances, do not fully satisfy the desired expectations. Nature is perfect. The animal and plant kingdoms are also. The human species has achieved this through evolution experienced over millions of years. Genetics, as a universal science, has taken care of this, being the only alternative capable of explaining and providing solutions to everything related to diseases. In fact, countless genetic factors that identify them have been discovered. The appearance, development and evolution of otitis media are due to predisposing genetic factors. These inflammations can be of primary or secondary origin. The path towards chronicity is directly related to the degree of pneumatic development of the tympanic cavity, especially the diameter of the tubal isthmus. The middle ear and the structures that are part of and correlated with it were conceived without errors. Considering that the security mechanism created to defend the tympanic cavity can be easily violated by neighborhood factors is to undervalue the role played by the evolution of the species. The reflections presented are intended to serve as motivation to create and perfect new effective therapeutic variants in the control and treatment of otitis media in its evolutionary course towards chronicity.

Keywords

Otitis Media, Genetic Factor, Evolution of Species, Venturi Effect, Predisposing Factors, Stephen Hawking

1. Introduction

Otitis media is the condition that perhaps most frequently affects children. Despite the scientific development achieved in the field of medical sciences, aspects of its presentation and evolution to chronicity still remain unclarified.

There are various etiological and predisposing factors that for many years have served as a guide to establish therapeutic offensives against otitis media. Various general factors are proposed that reduce the efficiency of the immune system (tuberculosis, syphilis, HIV, etc.), including, in addition, the widely accepted “immaturity of the immune system” typical

of children. Regionally, some elements are blamed for triggering middle ear infections or promoting their evolution to chronicity. Deviations of the nasal septum, adenoid hypertrophies, sinusitis and adenoiditis, among others, are mentioned. The anatomical characteristic of the Eustachian tube in the first years of life (shorter, horizontal and narrower) is another local factor that would encourage the entry of regional infections into the middle ear. Other theories consider that the poor pneumatic development of the temporal bone, particularly the middle ear, is secondary to inflammations and in-

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fections of the mucous membrane of the tube and the tympanic cavity, characteristics that would lead to the evolutionary course towards chronicity. [1-6].

The inconsistency in the results of medical-surgical treatments to eliminate some of the predisposing factors, mainly regional ones, as well as the failure to perform surgical treatments to correct certain consequences caused by both acute and chronic ear inflammations, denote that they still persist important aspects to take into account to achieve the proposed objectives.

Knowledge of the etiopathogenesis and pathophysiology of diseases has been of great importance to successfully address their treatment. However, the role assigned to the etiological factors (local, regional and general) stated to explain the pathophysiology of otitis media has been unable to reliably explain the multiple questions that have arisen.

Considering new paths to understand the predisposing factors and triggers of diseases, including otitis media, is imperative. Changes in concept generate contradiction. Many will deny them, others may accept them and for some they will be inconsequential. An ancient axiom states that "Accepting what is stated is easy, denying it is extremely difficult." The contradiction requires innumerable evidence and resources to refute what has been said. A new theoretical or practical approach or both will be the most effective way to deny what has been said by becoming another option that those interested would evaluate and can choose as the most convincing. Ours is included and also pursues this last objective.

2. Material and Method

The reflections contained in this article consist of substantiated theories arising from the contradictions emanating from the diversity of etio-pathogenic and physio-pathological criteria related to otitis media, its appearance, development and evolution, in force for decades, despite not be sufficiently explanatory or guide to expected therapeutic results. Knowledge of genetics, as a universal science that controls life in nature, has experienced rapid and immense development in recent decades; it is only capable of explaining all the principles that govern diseases. The objective of this work is to expose and defend, based on genetic concepts, all the elements that participate in the genesis, development and final evolution of otitis media. The importance of the degree of pneumatization of the temporal petrous bone in its evolution towards chronicity is emphasized and the coordinated action of the soft palate and the pharyngeal pavilion of the tube is anatomically and physiologically enhanced to defend the middle ear from the influence exerted by the traditional regional and local etiological factors. [7, 8].

3. Development and Discussion

The replacement of the medical terms "Etiopathogenesis

and Pathophysiology" with "Predisposing and triggering factors" based on genetic concepts could be more clarifying and unequivocal in everything related to the appearance, development and evolution of diseases.

Genetics is the universal science under whose control is everything related to life in the animal and plant kingdoms, both normal and pathological.

The scientific-technical development achieved in recent decades has achieved great advances in this field. Genomes, genetic map, cloning, reproduction of individual physical characteristics, diagnosis of genes that produce specific diseases, etc. are some of these advances.

The genetic information of an individual is stored in a system of codes, constituted by the set of rules that defines how a sequence of nucleotides in RNA is translated into a sequence of amino acids in a protein and thus collecting the description of hereditary profiles, current characteristics and all the information on events that may develop during the natural evolution of your life, including those related to diseases. Their actions are so complex and complete that there are no two similar individuals, healthy and pathological. From the latter arises the well-known adage: "In medicine there are sick people, not diseases."

Multiple elements and events make up genetics, consisting of: genes, RNA and DNA, mutations, nucleotides, amino acids, codons, genomes, chromosomes, genetic codes, biological rhythms, etc. (30), which together form the genetic system (GS), responsible for processing and storing all the information found in the cells, specific to each species in general and each individual in particular.

The genes identify the event, the genetic system characterizes it. Examples include: the identification of disease-producing genes such as C90RF72, responsible for the destruction of neurons in the brain of eminent scientist Stephen Hawkins (ALS); the discovery of the gene that produces the protein that is periodically released that marks the circadian rhythm of sleep, awarded the 2017 Nobel Prize in Medicine (Hall, Rosbanh and Young). In addition, there are countless biological variables regulated by time (circadian, intra- and ultra-daily cycles, circannual cycles) that show the influence of the genetic system in the programming and characterization of other events that mark the life of each individual. A very clarifying example is represented by menstrual cycles, including menarche and menopause. [9-12].

4. Predisposing Factors and Triggers of Diseases

4.1. Predisposing Factors

These genetically constituted factors identify existing diseases and determine the anatomical and functional characteristics of the affected structures. They are the elements responsible for defining everything related to the appearance,

development and evolution of diseases, and they also determine the common and individual characteristics of each of them. They record the exact period of debut (circadian) that usually occurs when encountering the specific triggering agent. Defines the exact place where it will appear and the secondary sites it will affect. It determines the quality and intensity of its clinical manifestations according to its defensive capacity (Immune System) as well as the natural evolution of the process towards healing, chronicity and even death, as the final stage of the biological cycle. These elements will be as varied as the individuals who suffer from them are different.

It is important to point out the behavior of certain diseases that occur through epidemic outbreaks. It is common to observe in some of them that of the total population exposed, a high number do not get sick. Well-known examples are in endemic epidemics, already controlled since the second half of the 20th century (measles, acute mumps, chickenpox, rubella, whooping cough, etc.), also more recently SARS-CoV-2. The epidemiological behavior is generally similar in some aspects and different especially in relation to the nature of the triggering agent. As happens in any epidemic, a part of the exposed universe developed the disease early, another portion presented it later in the late stages of the epidemic, as is being observed in the current Covid-19 pandemic that debuted at the end of 2019 and continues to be active or, as described in the aforementioned viruses of the last century, many individuals became ill in new outbreaks extended over time until advanced ages. Testimonies are reported from people who never contracted any of these infections.

In general, it can be concluded that individuals who do not develop a disease despite exposure to the triggering agent could be explained by various reasons:

- 1) They do not have a genetic predisposition to contract it (they do not have the specific gene).
- 2) They could be carriers of the predisposing factor but it is not activated (circadianly) at the time of their exposure to the triggering factor. If the activation of the genetic factor occurs in later stages when it coincides with the presence of the etiological agent, the disease would be triggered at any age.

The location of the site of debut of the disease and the other (secondary) places that it can affect respond to the programming contained and directed by the elements that make up the individual genetic system. The locations, both primary and secondary, have general similarities and particular differences.

“The considerations issued above are valid for upper respiratory tract infections in general and, in particular, with acute otitis media as a form of secondary localization of said condition.”

4.2. Disease Triggering Factors

These elements can be: physical, chemical and biological.

The interaction of these with the genetic code that represents a disease generates an antigen-antibody reaction that gives rise to the pathological process.

- 1) Physical agents are present in nature. They can be generated on our planet or from outer space. This group includes radiation, electromagnetic and sound waves, humidity, temperature, atmospheric pressure, etc.
- 2) Chemical agents are elements widely spread in nature capable of producing multiple diseases. Among them are: copper, iron, mercury, lead, magnesium, silicon, etc.
- 3) Biological agents are inferior organisms widely known and disseminated in nature. They stand out: fungi, bacteria, viruses, mycoplasmas, algae, amoebas, etc. All genetically identified.

The intensity of the clinical manifestations depends on their primary or secondary nature and the individual defensive capacity. The response of the gene to the aggression of the triggered agent occurs immediately, initiating the defensive reaction with the participation of multiple elements that constitute the immune system (IS). The defense mechanisms begin immediately as an antigen-antibody reaction that defines the response capacity individual that characterizes the clinical manifestations. The immune system fights against the development of diseases, it does not prevent or induce them, it is not immature, it is developing and is typical of each age and each individual.

Otitis media. Particularities.

Otitis media, like the rest of the diseases, are genetically identified. Their individual particularities in terms of debut, frequency, intensity, location, classification and evolution attest to this.

This condition can appear at any age, although it is more common in childhood. Its frequency of presentation is irregular. Some individuals may suffer from it repeatedly. In these patients the affected site has sometimes alternated in new episodes. The intensity of clinical manifestations can vary in different patients as well as in the same patient in different crises. There are people of advanced age who do not remember ever having suffered an otitis media crisis.

The location of the debut and secondary sites of the disease responds to the programming contained and directed by the elements that make up the individual genetic system. Each crisis has common and particular individual manifestations in relation to symptomatology and location.

Inflammations of the middle ear, depending on their origin, can be classified as primary or secondary.

Secondary otitis media appears in episodes of upper respiratory infections, commonly the common cold. This variant does not affect all patients who present episodes of this type of respiratory condition. Individuals who present repeated upper respiratory episodes do not always suffer new attacks of acute otitis media. The majority of the population has never reported acute otitis media during episodes of the common cold.

Primary otitis media is located in the middle ear from its onset. Usually of bacterial etiology. Like the other diseases,

they are genetically identified and in the same way the secondary localization sites are coded and it depends on whether or not they may appear in different patients or occur in repeated episodes in the same individual.

The evolutionary course of otitis media varies depending on the general factors involved in the process and in particular on each individual. Among these: the primary or secondary variant of the condition; the individual defensive capacity and the characteristics of the cavities of the rock.

Otitis media secondary to a common cold or influenza evolves in a few days while those located primarily in the middle ear due to bacteria (acute purulent otitis media) have a longer evolution and generally require medical treatment.

In both variants, the immune system determines the intensity and duration of the clinical manifestations.

The volume or dimensions of the structures of the tympanic cavity are the elements that determine the evolutionary course of middle ear inflammations towards healing or chronicity. The evolutionary development is also related to the type of infection and influenced by the prolongation of the process. Otitis media of viral etiology that occurs in the larger tympanic cavity, the process generally has a short evolution and does not require any treatment. If the infection occurs in boxes with greatly reduced dimensions, the obstruction of the isthmus and additus at antrum occurs early, creating a closed container that gives rise to changes that will lead through different paths to the final destination with the seal of individuality. It is necessary to highlight that the isthmus is the narrowest portion of the tube created in this way with the purpose of causing the air coming from the nasopharynx to considerably increase its speed to easily reach the tympanic cavity (physical effect described by BartolomeuVenturi). The additus at antrum, given its triangular shape, exerts a valve action isolating the mastoid antrum and the rest of the tympano-mastoid cavities from the influence of the changes experienced in the tympanic cavity, preventing the penetration of secretions and negative pressures from the cavity at the same time. that the muco-ciliary action facilitates the drainage of the secretion of the mucous glands from the antrum towards the case. [7, 8]

In order to achieve a better understanding of the dynamics of pressure changes that occur within the middle ear, we turn to the equation $P.V=k.T$, where P means pressure, V volume, k is a constant and T temperature. This formula created to determine the pressure variations of an ideal gas in a closed container, despite not being absolutely applicable in the tympanic cavity, serves to objectively evaluate the physio-pathological changes that lead to a chronic process. In the formula, P represents the intra-tympanic pressure, V is the volume of the box, k is a constant applicable to the number of gas molecules contained in the box and T is the body temperature. When evaluating the parameters that make up the equation, the degree of pneumatization of the tympanic cavity must be taken into account. The diameter of the isthmus and additus at antrum is proportional to the volume of the petrous

process cavities. The narrower these are, mainly the isthmus, the faster occlusion occurs, turning the box into a closed container. As oxygen is reabsorbed and the air inside the box becomes rarefied, the intra-tympanic negative pressure (P) increases, which in turn causes a decrease in its volume (V) favored by the congestive thickening of the mucosa, the appearance of transudation and depression of the tympanic membrane. Meanwhile, the kT parameters remain with very few variations, considering that the changes experienced by these elements are negligible.

The process that occurs within the tympanic cavity turns it into a vicious circle conditioned by the obstruction of the isthmus and the additus at antrum that begins the evolutionary process of the different stages that lead to chronicity. Individual variations in the dimensions of the tympanic cavity, the extension and thickness of the epi-tympanic membrane and its possible relationship with the bags that divide this cavity determine the type of chronic otitis media that develops from the serous accumulation rich in fibrin.: remain as a chronic adhesive process or continue to evolve until the formation of a cholesteatoma.

In episodes of primary acute otitis media, generally of bacterial cause (purulent acute otitis media), its evolution is also related to the degree of pneumatization of the petrous mass. In patients who present moderate or great pneumatic development, they generally progress towards healing, regardless of whether spontaneous or provoked perforation of the mesotympanic membrane occurs. Acute mastoiditis as a secondary location of acute otitis media occurs in well-pneumatized mastoids.

Purulent inflammations of the middle ear in rocks with little pneumatic development that cause perforation of the tympanic membrane (meso-tympanic) give rise to suppuration that can last over time, becoming a simple chronic otorrhea. All evolutionary stages are conditioned by individual variants of the degree of pneumatic development and the individual defense system, both genetically established.

The dimension of the isthmus of the Eustachian tube is the cardinal element in the evolutionary process towards chronicity. The sooner the diameter can be determined and medical or surgical action is taken, the closer the prognosis will be to a cure.

5. Conclusions

Diseases, like all living beings on planet Earth, have genetic identity. The system of elements that make up genetics determines that there are no 2 identical healthy individuals, nor with identical clinical manifestations of the same disease.

The individual genetic system predisposes to the appearance and development of diseases together with the constitutional (anatomical and physiological) characteristics of the affected region, determine its evolutionary course.

Primary acute otitis media of bacterial cause (PAOM) is located in the tympanic cavity.

Secondary acute otitis media (SAOM) appears irregularly during the course of a common cold of viral etiology.

The progression to chronicity of acute otitis media is proportional to the caliber of the tubal isthmus. In acute purulent suppurative otitis media they would evolve into simple chronic otitis media (SCOM). Acute middle ear inflammation secondary to isthmus obstruction leads to serous collection, formation of a chronic adhesive fibrous process, and possible development of cholesteatoma.

The therapeutic approach should initially focus on the permeabilization of the isthmus of the Eustachian tube. It is necessary to develop new diagnostic and therapeutic technologies for this purpose.

“Considering that the security mechanism of the entrance hole to the middle ear can be easily violated is an error in evaluating the perfection achieved by the evolution of species in their development over millions of years.” The soft palate and the pharyngeal pavilion of the Eustachian tube in coordinated action are responsible for protecting it [8].

Abbreviations

GS	Genetic System
ALS	Amyotrophic Lateral Sclerosis
PAOM	Primary Acute Otitis Media
SAOM	Secondary Acute Otitis Media
SCOM	Simple Chronic Otitis Media
IS	Immune System

Author Contributions

Cándido Adalberto Ben fez Lorenzo is the sole author. The author read and approved the final manuscript.

Conflicts of Interest

The author declares no conflicts of interest.

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