European Annals of Otorhinolaryngology, Head and Neck diseases 133 (2016) 263–268

Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

Review

Sinusology

R. Jankowski [a,*], D.T. Nguyen [a], M. Poussel [b,c], B. Chenuel [b,c], P. Gallet [a], C. Rumeau [a]

[a] Service ORL et chirurgie cervico-faciale, hôpital de Brabois, centre hospitalier régional universitaire de Nancy, université de Lorraine, bâtiment Louis-Mathieu, 54500 Vandœuvre-lès-Nancy, France
[b] Service des examens de la fonction respiratoire et de l'aptitude à l'exercice–médecine du sport, CHRU de Nancy, 54000 Nancy, France
[c] EA 3450 DevAH, développement, adaptation et handicap, régulations cardiorespiratoires et de la motricité, université de Lorraine, 54505 Lorraine, France

ARTICLE INFO

Keywords:
Paranasal sinuses
Physiology
History
Nitric oxide (NO)
Evo-devo

ABSTRACT

This paper presents a brief history of the successive anatomical, physiological and pathophysiological concepts about the paranasal sinuses. Sinusology, the science of the paranasal sinuses, is founded on scientific work on the production of nitric oxide (NO) by the sinuses and on the evo-devo theory of their formation. The paranasal sinuses seem to develop after regression of the erythropoietic marrow in the maxillary, frontal and sphenoid bones and its replacement by cavities filled with gas, which escapes into the nasal fossae through the ostium. The sinus epithelium synthesizes NO continuously. The paranasal sinus cavities form a compartmentalized reservoir of NO, which is released discontinuously in boli after an opening of the ostium. Ostium opening can be induced by sound vibration, either internal (humming) or external (an acoustic vibration added to the in-breath). NO plays the role of an "aerocrine" messenger between the upper and lower respiratory tracts, reducing pulmonary vascular resistance and facilitating alveolar oxygen transfer into the bloodstream. Its physiological role in arterial blood oxygenation could be involved in speech and singing or be activated by physiological snoring during sleep. Rhinology, the science of the nose, in which the evo-devo concept distinguishes the respiratory and the olfactory nose, is now backed up by sinusology.

1. Introduction

Sinusology is the science of the sinuses. Distinguishing it from rhinology, the science of the nose appears essential in order to guide rhinologists in the treatment of nose and sinus diseases.

The classic theory of paranasal sinus formation as cavities originating from the nose, and from the ethmoidal cells in particular, should now give way to a theory founded on the mechanisms of bone pneumatization. Classic sinus physiology, based on the ventilation and drainage functions of the ostium, is put in doubt by recent discoveries concerning nitric oxide (NO) production and storage.

This paper presents a brief history of the successive anatomical, physiological and pathophysiological concepts concerning the paranasal sinuses.

2. Anatomic sinus concepts

2.1. Highmore's antrum

The existence of the sinuses was completely unknown to the Greeks and Romans. They came to the attention of Renaissance anatomists such as Fallopius and Eustachius, but their descriptions were rough and imprecise. The first precise anatomic description of the maxillary sinus or "antrum" was made by Highmore in 1651 [1]. Highmore focused on the relations between the maxillary sinuses and the teeth, which he presented in anatomic diagrams. Subsequently, all anatomy books described the frontal and maxillary sinuses in detail, but it was yet a century before sinus pathology was recognized and became the subject of specific treatment.

2.2. Zuckerkandl's ethmoidal labyrinth

Emile Zuckerkandl's remarkable anatomy book entitled *Normale und pathologische Anatomie der Nasehöle und ihrer pneumatischen Anhäge* was published in Vienna in 1882 [2]. The ethmoidal and sphenoidal sinuses were hitherto overlooked and almost never mentioned. Zuckerkandl's book, based on numerous dissections,

* Corresponding author.
E-mail address: r.jankowski@chu-nancy.fr (R. Jankowski).

http://dx.doi.org/10.1016/j.anorl.2016.05.011
1879-7296/

provided a very complete description of the nasal cavities and surrounding air-filled cavities.

There were 8 facial sinuses, in 4 pairs on either side of the nasal cavities, with which they communicated via channels or simple orifices: the ostia. Their covering mucosa was in continuity with that of the nasal cavities, so that the sinuses appeared to be extensions of the latter.

The ethmoidal labyrinth was seen as the key part of the human sinus system. Maxillary, frontal and sphenoidal sinus pneumatization varied from side to side and from individual to individual.

The anatomic unit of the lateral structures was the ethmoidal cell, a polyhedral bone cavity of 2 to 3 mm^3. The ethmoidal cells were partitioned by denser bone laminae, Mouret's dividing roots [3], which were the roots of the main and accessory turbinates, extending from the turbinate lamina (or turbinate wall of the lateral masses of the ethmoid bone [4]) to the medial orbital wall. The dividing root of the medial turbinate separated the lateral mass into anterior and posterior ethmoidal cells.

Following Zuckerkandl, the maxillary, frontal and sphenoidal sinuses seemed to result from colonization of the respective bones by ethmoidal sinus cells under a hypothetical osteoclastic activity of the mucosa (which remains to be demonstrated [5]). According to other authors, the great sinuses formed under the mechanical action of craniofacial growth and mastication, between the beams of resistance constituted by the maxillary, frontal and sphenoidal bones and colonized by nasal mucosa secondarily [6].

2.3. *The evo-devo concept of sinus anatomy*

The origin of the maxillary, frontal and sphenoidal sinuses from the nose and from the ethmoid in particular was put in doubt in 2011 in the light of phylogenic and ontogenic findings [7], suggesting that they form in the corresponding bones by pneumatization. The radiological stages of sphenoid pneumatization in human neonates were described by Aoki in 1989 [8].

The same biological mechanism of pneumatization seems to lead to the cavitation of certain facial (maxillary, frontal) and skull-base (sphenoid, temporal) bones in humans or of the sternum and forelimb bones in birds [9]: erythropoietic marrow degenerates multifocally, leaving contiguous, confluent fatty islands, followed by gas-filled cavities with polycyclic contours [10]. The exact mechanism is unclear, but seems in humans to be able to extend beyond the usual regions to the cervical vertebrae [11] and to be able to be reactivated, generating pneumosinus dilatans [12].

Arrested pneumatization seems to result from transformation of the erythropoietic marrow into fat without being followed by the cavitation phenomenon [13]. Radiological images of arrested pneumatization in the sinuses [13] seem to corroborate an identical mechanism of formation of the sphenoidal, maxillary and frontal sinuses but not of the ethmoid [14].

In contrast to the paranasal sinuses, which develop postnatally, the ethmoid exists before birth and is simply ventilated afterward. The cartilaginous forerunner of the ethmoid actually starts to develop from the beginning of the 8th week of embryonic life, in parallel with the olfactory nose [15], and is fully developed by the end of the 1st trimester. Phylogenically, the ethmoid is actually the skull-base container of the olfactory mucosa, the developmental transformations of which lead in humans to the individualization of the lateral masses and olfactory clefts [10].

3. Physiological concepts of the sinuses

3.1. *Mute bone cavities, ventilated and drained*

According to the classical concept, whether sinuses form by means of paranasal bone excavation by the osteoclastic action of the ethmoidal mucosa or of mechanical craniofacial remodeling, sinus physiology serves to maintain homeostasis in satellite air cavities of the nose, the function of which is unknown.

Numerous hypotheses have been suggested regarding sinus function [6]: head weight reduction, thermal insulation of the brain and eyes, voice resonators, sliding planes for the internal and external bone tables during craniofacial growth, mastication shock absorbers, inspiratory air conditioning, intranasal pressure regulation – or vestigial cavities devoid of function.

Regardless of function, two factors apparently indispensable to sinus homeostasis have been studied: drainage and ventilation. Messerklinger's Austrian and Terrier's Swiss schools followed up the experimental studies by Proetz (1929–1953), Hilding (1932–1934) and Negus (1934–1949) and demonstrated the importance in humans of drainage by mucociliary motion. The French school of Flottes, Guillerm and Riu (1960) focused on sinus ventilation, and their summary conclusion is worth quoting in translation (from p. 307 of the French Society of ORL's report [16]): "The human sinuses are diverticula of the nasal cavities, with which they communicate via narrow passages, and undergo minimal ventilation and drainage. While these two functions are vital to sinus integrity, their low intensity testifies to the small role [. . .] that they play."

Ethmoidal and paranasal sinus drainage and ventilation, in the classical physiological concept, are based on the permeability of the various ostia. No particular anatomic or histologic structure is described regarding these ostia and/or channels, which feature as physiologically inert structures that are permanently open [16].

3.2. *Sinuses as producers and reservoirs of NO*

The physiological role of nitric oxide (NO) was discovered only recently, and its discoverers were awarded the Nobel Prize for Medicine in 1998. Previously, it had been seen as merely an atmospheric pollutant, with no biological role, but was then shown to be a powerful vasodilator, produced by blood vessel endothelial cells, that relaxes the smooth muscle fibers of the vascular wall. In fact, its physiological role extends to many other cell and tissue functions, notably in the respiratory, nervous and immune systems [17].

In tissue, NO is synthesized by the enzyme NO synthetase (NOS) from O_2 and the amino acid L-arginine. There are 3 isoforms of NOS. Two are constitutive: endothelial NOS (eNOS or NOS-1) and neuronal NOS (nNOS or NOS-3) present in non-adrenergic non-cholinergic nerve fibers. The third isoform (inducible NOS: iNOS or NOS-2) is induced by inflammatory cytokines (TNF, IL1β, etc.) and bacterial lipopolysaccharides and produced mainly by phagocytes (monocytes, neutrophils, macrophages). Unlike the constitutive isoforms, which produce NO by reaction and in small amounts in response to a calcium signal, iNOS production of NO is calcium-independent, large-scale (thousand-fold greater) and continuous [18].

The presence of NO in exhaled air was discovered in 1991 [19]. It seemed logical to suppose a pulmonary alveolar origin associated with respiratory gas exchange (O_2, CO_2), but the quantity exhaled in nasal respiration turned out to be far greater than in oral respiration, suggesting large-scale NO production within the nasal cavities [20]. The role of the upper airways in NO production was demonstrated by measuring exhaled NO in tracheotomized subjects at the cannula, mouth and nose: levels were low in the cannula, intermediate in the mouth and high in the nose [21]. NO is thus mainly produced in the upper airway.

Nasal administration of NOS inhibitors, however, proved not to significantly reduce production. Maxillary sinus catheterization revealed a much higher level of NO in the sinus than is exhaled in the nose, approximating indeed in some subjects the maximum authorized atmospheric concentration of 25 ppm [22,23].