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ABSTRACT
The maxillary sinus is one of four pair’s air-filled spaces that surround the nasal cavity. The majority of previously published researches considering the maxillary sinus commonly concentrated on its pathological conditions and the recent surgical or medical management procedures. However, to understand the diseases of this sinus in a better manner, it is essential to have some basic medical details. Therefore, the present review is an attempt to focus light on this sinus by doing a cosmopolitan update on its development and anatomy, besides the functional theories by searching through many well-known scientific databases including Medline, Scopus, EMBASE, PubMed Central (PMC), PubMed, Cochrane Library, and Web of Science.

In the current review, the author tried to approach, recognize and explain the fundamental data that may provide better ideas to imagine the pathological problems related to the maxillary sinus. In addition, the author did not conduct a new study on human nor animal subjects because the previously implemented articles were the chief and the only source for this review.

In conclusion, the functions and physiology of the maxillary sinus are the subjects that reflect the anatomical complexity mentioned in the most recent articles may probably show that all its functions could be a part of a large and more complicated image than that apparent nowadays.

Keywords: Human maxillary sinus development; maxillary sinus anatomy; maxillary sinus morphology; theories of paranasal sinus functions; mucous membrane (Siriraj Med J 2022; 74: 472-479)

INTRODUCTION
In the fifteenth century, drawings of Leonardo da Vinci demonstrated the human paranasal sinuses, despite some sources that regarded an Italian physician known as Berengar del Carpi as the first scientist who mentioned these sinuses in the sixteenth century. In the same century, another Italian anatomist, Vesalius reported that these sinuses containing only air and nothing more.1

In the seventeenth century, the details of maxillary sinus anatomy were recorded by Nathaniel Highmore; while in the eighteenth century, Morgagni noticed that this sinus might be absent in occasional cases. 2

In the nineteenth century, the work of two anatomists, Adolf Onodi and Zuckerkandl was the cornerstone for the modern anatomy of the human paranasal sinuses. In addition, anatomical reports done by Van Alyea and Mosher were published in the earlier years of the twentieth century, while the radiologist Zinreich was the first scientist who described paranasal sinus anatomy based on computerized tomography. 3
MATERIALS AND METHODS
Many scientific databases include; Medline, Scopus, EMBASE, PubMed Central (PMC), PubMed, Cochrane Library, and Web of Science searched. The following words and statements were searched in the title, keyword, abstract, introduction, and article heading: human maxillary sinus, maxillary sinus development, maxillary sinus pneumatization, maxillary sinus anatomy, maxillary sinus blood supply, maxillary sinus innervation, and maxillary sinus functions or functional theories. The Boolean searching strategy was used (or, and or not). All scientific articles include; original articles, case reports, systemic reviews, meta-analyses, and the references of these articles were further searched and evaluated until October 2021. No obvious limitations of this study need to be mentioned.

RESULTS AND DISCUSSION
Development of the human maxillary sinus
Human paranasal sinus develops as an invagination of the nasal fossa into its corresponding bone (frontal, maxillary, ethmoid, and sphenoid). The first sinus that undergoes development is the maxillary sinus which can be apparent on day 17th of embryonic life. The paranasal sinuses development start in the 3rd week of pregnancy and lasts into early adulthood. Ectodermal cells multiply and move medially to produce the notochord at the 4th week. The notochord forms in the embryonic disc’s caudal area and rotates to become behind the primitive for gut.4
The dorsal part of the first pharyngeal arch forms a maxillary process that extends anteriorly below the developing eye to form the maxilla. At the ending of the second month of development, the maxillary sinus demonstrated as an invagination start just superior to the inferior concha and grows to the lateral side. At the twelfth week of development, the mucous membrane evacinates in the lateral surface of the middle meatus until the nasal epithelium invades the entire maxillary mesenchyme.5

Birth, this sinus appears as a small, slit-like structure that is mostly filled with fluid and found at the medial wall of maxillary bone with its greatest dimension recorded at the anteroposterior plane with less than eight millimeters. In newly born children, through routine radiographic procedures, these sinuses are usually not visualized. Also, the rudimentary aerated sinus is about 6-8 cm³ at birth, with its maximum dimension at the anteroposterior plane.6

At the ending of the first year of life, the lateral border of this sinus projects below the medial wall of the orbit; but it extends laterally to the infraorbital fossa by the age of four years old and reaches the maxilla by the age of nine years old.7 The inferior growth usually reaches the hard palate plane by age of nine years old too. Despite the timing for the above different stages of maxillary sinus development is extremely variable but in general, they are closely related in time.8 This sinus remains to grow in a downward direction in association with the alveolar maxillary bone pneumatization to reach the nasal floor level at the age of twelve years old.9

Fig 1. Development of the maxillary sinuses. Up to the age of 12 years, growth of the maxillary sinus is predominantly in a lateral direction towards the zygoma creating the zygomatic recess (white arrow in b) and inferiorly to the level of the hard palate. Thereafter, the sinus expands inferiorly below the level of the nasal floor (white arrows in c, d).10
Ultimately, the maxillary sinus floor extends about 4-5 mm below the floor of the nose. Asymmetry in the size and shape of the sinus is common; hypoplasia may be unilateral in 7% or bilateral in 2% of adult individuals. In earlier years of human life, the complete or partial opacity recorded in the maxillary sinus may be regarded as normal.\textsuperscript{10}

The mature size of the human maxillary sinus is demonstrated at about the age of twenty years old when all permanent teeth are fully developed; therefore during adulthood, its size and shape alter particularly as a result of teeth loss. After the period of maximum growth, the sinus volume decreases in both sexes which may be due to the loss of the minerals in the matrix of the entire bony structure that surrounding the sinus in each direction to contract that sinus and decreases its volume.\textsuperscript{11}

Anatomy of human maxillary sinus

The human maxillary air sinus or antrum of Highmore (“Antron” is a Greek word meaning “a cave”) was firstly mentioned in 1651 by Nathaniel Highmore who treated a maxillary sinus empyema by extracting a canine tooth.\textsuperscript{1} It is the largest human paranasal sinus recognized as a pyramidal-shaped cavity within the maxilla body and characterized by its apex, base, and four borders.\textsuperscript{12}

A thin lateral border from the nasal cavity comprised by the maxillary sinus base to form the hiatus semilunaris in the disarticulated maxilla. However, in articulated bone this orifice is usually decreased in its size by the process of maxilla from inferior nasal concha inferiorly. While the uncinate process of the ethmoidal bone and the descended portion of lacrimal bone superiorly, and the perpendicular plate of palatine bone posteriorly.\textsuperscript{12}

The maxillary sinus extends about 4-5 mm below the floor of the nose. Asymmetry in the size and shape of the sinus is common; hypoplasia may be unilateral in 7% or bilateral in 2% of adult individuals. In earlier years of human life, the complete or partial opacity recorded in the maxillary sinus may be regarded as normal.\textsuperscript{10}

Fig 2. The maxillary sinus extending into the zygomatic process (arrows). (A) Dry skull (inferolateral view). (B) Computed tomography (axial image).\textsuperscript{13}

The maxillary sinuses are two air-filled spaces situated within the maxillary bones and may be of different shapes and sizes. The walls of these sinuses are thin, and their apex may reach the zygomatic process of the maxilla and may occupy the entire zygomatic bone.\textsuperscript{13}

Therefore, the two sinuses may occupy a great part of the maxillae bone bodies and the lateral border from the nasal cavity forms the sinus base. Whereas the orbital floor formed by the sinus roof that is ridged viaoverlaying the infraorbital canal.\textsuperscript{14}

The internal surface of the sinus may be ridged or smooth with a specific prominent bony septum and the lateral border includes grooves or canals for particular blood vessels and nerves that supply the superior posterior teeth.\textsuperscript{15}

The maxillary sinus communicates with the posterior portion of the hiatus semilunaris at the middle meatus through an orifice, the maxillary ostium on average diameter is 3-6 mm.\textsuperscript{16} In a prepared skull this opening is double, but in a recent state the posterior orifice is usually closed by mucoperiosteum and another accessory ostium sometimes is found posterior to principle one and it may be even but larger than the normal one.\textsuperscript{12} In rare cases, two or even three accessory openings may be present. The apex of the sinus is created by the zygomatic process of the maxillary bone and in some instances when the sinus is large it extends into the zygomatic bone itself. The roof of the antrum is the floor of orbit while the alveolar process is the floor of the antrum.\textsuperscript{17}

In adults, the floor of the sinus is about 1.2 - 1.5 cm under the level for the nasal cavity floor, and in most cases, the radiating bony septum is found on the sinus floor located at spaces between the particular roots of
neighboring teeth and occasionally the floor is perforated by apices of corresponded teeth.\textsuperscript{17} Due to individual variations in the air space size, the exact number of the upper teeth which roots reveal direct association with the maxillary sinus is inconstant, but the upper molar is most consistently nearby.\textsuperscript{10} Generally, the lateral and central incisor teeth roots are not found closely nearby to this sinus, besides the maxillary molars and premolars roots; however, are consistently situated under the floor of the sinus. The second molars roots are in closest proximity to this sinus floor, pursued in frequency by the first molar, second premolar, third molar, first premolar, and finally canine roots.\textsuperscript{15} The maxillary sinus floor is formed by an alveolar process; the first, the second, and the third molars with the canine roots can elevate the sinuses or can perforate their floor.\textsuperscript{12} The sinus pneumatization was identified when a maxillary posterior tooth was extracted which explains the large expansion of that sinus after the tooth extraction enveloped with the upper curving floor of the same sinus and by extraction of the second molar and some neighboring posterior teeth.\textsuperscript{9} In adults, the level of the floor is about 1.0-1.2 cm below that of the nasal cavity but in the edentulous skull, the level of the floor rises above that belongs to a nasal cavity. The two sinuses are usually equal in size but are not necessarily so, rarely one sinus is absent completely.\textsuperscript{4} The nasal surface of the maxillary body and portions of lacrimal, palatine, inferior turbinate, and ethmoidal bones are the structure that bound the medial border of the antrum.\textsuperscript{17} The existence of those bones markedly decreases the size of the orifice between the nasal cavity and antrum during life.\textsuperscript{14} The maxillary sinus is lined by a pseudostratified ciliated columnar epithelium, its cilia constantly move and sweep the mucous into a particular sinus opening and this flow process is definitive to each paranasal sinus and found even where there is an alternative orifice maybe exist. Fluids of this sinus drain by specific osteomeatal complex into the nasal cavity; if this outflow is obstructed, it leads to mucosal thickening, sinusitis, retention cyst, or polyp formation. Maxillary sinuses remain relatively larger in males than females throughout life.\textsuperscript{18} All the mentioned developmental changes may be summarized in Table 1.

**TABLE 1.** Morphological changes occur in the human maxillary sinus according to age.

<table>
<thead>
<tr>
<th>Age</th>
<th>Morphological changes</th>
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<tr>
<td>At birth</td>
<td>It filled by the deciduous tooth germ.</td>
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<tr>
<td>20\textsuperscript{th} month</td>
<td>The posterior part develops more than the anterior part.</td>
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<tr>
<td>3 years old</td>
<td>It will be about one half of the adult size sinus.</td>
</tr>
<tr>
<td>4-6 years old</td>
<td>It increases in width that associated with fast facial growth, and it locates at the second deciduous molar and the crypts of the first permanent molar teeth.</td>
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<tr>
<td>7-9 years old</td>
<td>Its growth corresponds to the eruption of the permanent teeth.</td>
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<tr>
<td>10-12 years old</td>
<td>The floor of the antrum locates at the same level of the floor of the nasal cavity.</td>
</tr>
<tr>
<td>13-15 years old</td>
<td>Its floor locates below the nasal floor, and the sinus floor is at the first molar, second molar and first premolar teeth.</td>
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<tr>
<td>≥16 years old</td>
<td>A thin layer of cortical bone left to separate between the oral mucosa and the sinus mucosa due to the continuous pneumatization process of the sinus and the reposition of the ridge. With age, the enlarging maxillary sinus may even begin to surround the roots of the maxillary posterior teeth and extend its margins into the body of the zygomatic bone. If the maxillary posterior teeth are lost, the maxillary sinus may expand even more, thinning the bony floor of the alveolar process so that only a thin shell of bone is present.</td>
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Thus the anatomical description of the maxillary sinus includes the following features; the antral roof is formed by the orbital floor and it is flat structure slopes gradually forward and laterally. On contrary, its floor is a curve structure rather than flat and formed by the alveolar process of the maxillary bone. The floor situates about 1 cm beneath the nasal floor level and closely relates to the root apices of the molar and premolar maxillary teeth. The facial surface of the maxillary bone forms the anterior wall of the maxillary sinus where the canine fossa regards as a remarkable structure at this wall. The sphenomaxillary wall forms the posterior wall of the sinus and a thin cortical bony plate separates the infratemporal fossa from the antral cavity. The lateral wall relates to the zygoma and cheeks, while its medial wall bounds by the nasal cavity. The maxillary sinus opening is closely related to its floor and situated at a higher level compared to the floor.

This sinus is supplied by branches from the maxillary artery; these include the sphenopalatine, infraorbital, posterior superior alveolar, and greater palatine arteries. While it’s venous drainage mainly into the facial vein anteriorly and the maxillary vein posteriorly and then into the internal jugular vein.

The maxillary sinus is innervated by the superior alveolar (anteriory, middle, and posterior) and infraorbital nerves from the maxillary branch V2 which is the second division of the fifth cranial nerve (the trigeminal nerve); and those alveolar nerves pass downward into the teeth that situated in the maxillary sinus walls, and they penetrate the bony structure of this sinus through delicate nervous branches to give supplement into its mucous membrane. It drains the lymph into the submandibular, deep cervical, and retropharyngeal lymph nodes.

Mucous membrane of paranasal sinuses

Each paranasal sinus is lined by a pseudostratified ciliated columnar epithelium that continues with the nasal cavity mucosa. This epithelial layer is thinner compared with the nasal epithelium. The four specific cell kinds in this epithelium are the non-ciliated columnar, ciliated columnar, goblet, and basal cells. The experiments reveal that the ciliated cells move approximately 700-850 times/minute, which moves the mucus about nine mm/minute. The non-ciliated cells have microvilli that are found on their apices aspect to increase the surface area of those cells which may facilitate the warming and humidification of the inspired air. The number of non-ciliated cells increases at the sinus orifice or ostium to about 50% compared to other sites. The basal cells are varying in shape, size, and number; their function is unknown. However, there is a theory assumed that these cells are regarded as stem cells that may be differentiated to other required cells. The glycoproteins produced by the goblet cells can be essential for the elasticity and viscosity of the mucus. These cells are innervated by the sympathetic and parasympathetic nervous stimulations.

Therefore, the sympathetic innervation increases the water concentration in the mucus secretion, while the parasympathetic innervation causes thicker mucus. The goblet cells are apocrine glands, i.e. they pour their secretion through rupture of their apical cell membrane that gets regenerated. So these goblet cells have all the criteria of synthesizing and secreting cells.

The epithelial layer supports by a delicate basement membrane, particularly lamina propria that directly adheres to the periosteum. Both, mucinous and serous glands trace downward toward its lamina propria. Previous reports reveal a general rarity of submucosal glands and goblet cells within the paranasal sinus compared to mucosa of the nose. Among the four sinuses, the human maxillary sinus contains an increased number of the goblet cells. In addition, the ostia of the anterior ethmoid, sphenoid, and maxillary sinuses show a high density of submucosal mucinous and serous glands.

The cilia of each sinus are composed of typical ‘9+2’ architecture that includes 9 outer doublet microtubules with central microtubule pair and moves in a particular direction leading the mucus flow in a specific pattern. As these sinuses may develop in an inferior and outward direction leading the mucus flow in a specific pattern. As these sinuses may develop in an inferior and outward fashion; therefore, the mucosal cilia usually move the materials such as the debris, mucous film, and even some micro-organisms against the gravity towards the exit of that sinus. In other words, the mucus formed close to the sinus ostium, when it is at the afferent border, it will move around the whole sinus cavity that is usually against the gravity before it reaches that ostium. The previous description explains the presence of an accessory ostium in situations outside the normal physiological ostium will not markedly improve the sinus drainage. In general, this feature sometimes leads to draining mucus from the natural ostium then reenters the sinus through the newly formed orifice and cycles throughout the same sinus cavity again. Therefore, the mucus of each sinus flows in a specific pattern. The stagnation phenomenon demonstrates when two ciliated borders become in contact with each other, especially occurs in osteomeatal complex region. This leads to disruption in the clearance of the mucociliary mucus and causes sinusitis so that recovery from that disease is associated with this clearance process.
Functions of the paranasal sinuses

The functions and physiology of the paranasal sinuses had been a subject for many previous articles. Unfortunately, nowadays researchers are still uncertain about all recorded functions of those sinuses. Many theories regarding the functions are present. These functions include assistance to regulate the intranasal pressure and also gas-serum pressures that subsequently delicate the ventilation, warm/humidify of the inspired air, participate in the immune response, increase the surface area of the mucosa, lighten the skull, give resonance to the voice power, absorb the head shock, and contribute to the growth of human face.

The nose is a powerful warmer and humidifier of the inspired air. It does not reach its maximum capacity to achieve this function even at 7 liters/minute of the airflow. The humidification of the nasal cavity shows a contribution of as much as 6.95 mmHg on the serum pO2. In spite of the mucosa of the nose considers as the best part that adapts to carry out this task, also these sinuses participate in the warming ability and increase the surface area of that mucosa. Several reports showed that mouth breathing has a low end-tidal CO2 that can elevate the serum CO2 and cause sleep apnea.

However, the most famous theory regards the existence of these paranasal sinuses decreases the skull weight and fixes the splanchnocranium bones mechanically. Absorption of the head shock, protection, and insulation for the neural structures and especially the brain is also assumed. Another conception suggests decreasing the nasal pressure during the mastication process; pressure control and warming of the inspired air, amplification of the voice resonance, and smell sense properties. The multiple physiological functions contribute by these air-filled spaces are thus controversial. These sinuses play an important role in heat insulation, pressure damping, voice resonance, and conditioning for the inspired air.

The sinuses contribute markedly to air filtration/immune defense achieve by the nose due to the production of copious mucous by those sinuses. The sinus and nasal mucosa are covered by cilia that move the mucus into the nasal choanae and eventually into the stomach. The thick mucus on the superficial layer of the nasal cavity mucosa acts to trap various types of bacteria and tiny particles within the substance that contains a high amount of antibacterial proteins, antibodies, and immune cells. On contrary, the underlying layer regards thinner and acts to supply a thin substrate that helps the cilia to beat. In addition, their tips principally grab the superficial layer and push it into the same direction of that beat. If there is no obstruction caused by anatomical variance or disease, this sinus moves the mucous throughout its cavity and out of its ostium into the choanae.

The formation of intranasal nitrous oxide (NO) occurs in these sinuses primarily. This substance is toxic to fungi, viruses, and bacteria at low levels (100 ppb). Its concentration at the nasal cavity may reach up to 30,000 ppb that may regard it as the principal of the theory of the sinus sterilization mechanism. In addition, this substance reveals to speed up the ciliary motility. According to previous research, the epithelial cells of the human paranasal sinuses create NO, which is prevalent within the sinus air in extremely high levels, near to the maximum allowable levels of atmospheric pollution. These observations, combined with NO’s well-known bacteriostatic properties, imply that NO plays a role in maintaining sterility inside the individual paranasal sinuses.

Theories concerning the functions of the paranasal sinuses:

Several functional theories that tried to explain the existence of paranasal sinuses have met with varying levels of acceptance among researchers:

1. Increasing resonance of the voice.
2. Humidify, warm, and filters the inspired air due to the slow air turnover process in the area.
3. Increase the mucosal surface area.
4. Absorption of the shock that applies to the head.
5. Mucus secretion to keep the nasal cavity moist.
6. Help in the growth of the face and its architecture.
7. Lightening the bones of the skull (especially the facial bones) for maintenance of proper balance.
8. Insulation of sensitive structures such as eyes and dental roots from the fast fluctuations in the temperature of the nasal cavity.

Various hypotheses are developed regarding the human paranasal sinuses but the most popular are three principal hypotheses. The first is the structural theory which depends on the following facts; lightening of skull weight to decrease the muscular efforts at the neck region. Also, optimization of the required balance between the head, as a mass, over the neck, as axis, to promote its movement in the stable upright position. In addition, plastic skull remodeling is essential for the inordinate growth between the neurocranium and splanchnocranium.

The second hypothesis is the functional or potentiation theory that includes the following facts; significant absorption of the effect forces to avoid concussions. Also, vocal resonance; however, the sinus variability and dimensions are imperfectly related with the vocal force.
Furthermore, the attenuation of the characteristic bone transmission of the sound vibrations features. Thermal insulations of the vital organs and structures. Specific enlargement of the olfactory region in human that no more exist as a hunter; these sinuses symbolize some remnants of special structures that aimed to enhance this sense; therefore, absence of this olfactory mucosa represent no significant function is exist at it. Ultimately, a supplementary activity in the defending mechanism by the mucosa of the nasal cavity throughout humidification, enrichment of preventive factors (lysozyme and IgA), and sterile secretion of diluted mucus.

The third hypothesis is the evolutionary theory which can be explained through the following historical facts. The paranasal sinuses are the outcome of water adaptation of human beings species throughout its recorded evolutionary history. During the evolution, the existence of air within the splanchnocranium supplies a hydrodynamic thrust that is necessary to retain the airways structures above the notable aquatic medium. The other ideal human characteristics that might solidify this theory include bipedalism, significant loss of the body hair, subcutaneous fat existence, various productions of tears and sweat, and Shrapnell’s membrane presence that dampens the sound waves within the above described liquid medium. Despite the fact that its actual function is ambiguous until nowadays, the evolutionary theory possibly best demonstrates the existence of large-sized and more numbered sinuses in humans compared to primates and other mammals. Another principal feature that keeps in consideration is that despite the exact function of those paranasal sinuses is vague until now, they can be the biological regard of the recurrent pathological processes. Therefore, the physiological elements that are regarded may include the following functions; mucociliary transport, ventilation, local immune response, and drainage of specific secretions.

CONCLUSION

In general, the functions and physiology of the maxillary sinus are the subjects that reflect the anatomical complexity and the most recent reports can probably show that all the mentioned functions could be a part of a big and more complicated image than that apparent nowadays.

Conflict of interest: The author notified that there are no conflicts of interest about the publication of this article.

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