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What is This?
Consequences of Evolution:  
Is Rhinosinusitis, Like Otitis Media, a Unique Disease of Humans?

Charles D. Bluestone, MD¹, Anthony S. Pagano, MPhil², J. Douglas Swarts, PhD¹, and Jeffrey T. Laitman, PhD²

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Abstract
We hypothesize that if otitis media is most likely primarily a human disease due to consequences of evolution, rhinosinusitis may also be limited to humans for similar reasons. If otitis media, with its associated hearing loss, occurred in animals in the wild, they probably would have been culled out by predation. Similarly, if rhinosinusitis occurred regularly in animals, they likely would have suffered from severely decreased olfactory abilities, crucial for predator avoidance, and presumably would likewise have been selected against evolutionarily. Thus, both otitis media and rhinosinusitis—common conditions particularly in infants and young children—appear to be essentially human conditions. Their manifestation in our species is likely due to our unique evolutionary trajectory and may be a consequence of adaptations, including adaptations to bipedalism and speech, loss of prognathism, and immunologic and environmental factors.

Keywords
evolution, rhinosinusitis, otitis media, olfaction

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Both otitis media and rhinosinusitis are common in humans, especially in infants and young children. One prospective study that enrolled 112 children (6-36 months of age) over a 3-year period identified 623 upper respiratory infections (URIs), 30% of which were complicated by acute otitis media and 8% of which had rhinosinusitis.¹ The extraordinary rate of middle-ear disease has recently been proposed to be, in part, the result of consequences of human evolution.²,³ Our hypothesis is that if otitis media is primarily a disease of humans due to evolution, rhinosinusitis could also be limited to humans for similar reasons.

Before we present our thesis that rhinosinusitis may be limited to humans, we first will summarize our previous reports on the potential impact of human evolution on the development of otitis media, since we propose that adaptations to bipedalism and speech, as well as loss of prognathism during evolution, have likely had a similar effect on both diseases.

Otitis media is associated with hearing loss, and if animals in their natural habitat developed it, they would probably have been selected out by predation. Human newborns are born relatively “early” (with anatomic and physiologic systems that must develop after, rather than before, birth) compared with many other mammals. Evolutionarily, this was likely due to initial functional constraints of bipedalism and pelvic outlet morphology, coupled with requirements of an enlarged brain (Figure 1). This early birth, compared with our ancestors, resulted in a eustachian tube that is shorter and less rigid (“floppier”) and an immature immune

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system in the first year of life when compared with older infants.\(^5\) Loss of prognathism (ie, facial flattening) and adaptation for speech resulted in a change in palate morphology, which altered the muscles of the eustachian tube (ie, tensor veli palatini, levator veli palatini) when compared with those of the monkey (\textit{Macaca mulatta}); this presumably resulted in humans having poor physiologic eustachian tube function compared with that of the monkey.\(^2\) Currently, there is no consensus among anthropologists on why the face “flattened” in humans compared with the prominent snout of monkeys and apes (\textit{Figure 2}). One theory suggests that it was the change in diet due to the acquisition of cooking almost 2 million years ago by \textit{Homo erectus} that altered the size and shape of teeth with concomitant shortening of the maxilla, mandible, and palate in \textit{Homo sapiens}.\(^6,7\) Others have suggested that the trend toward facial flattening (orthognathy) commenced even earlier among more primitive human ancestors (eg, australopith-grade hominins\(^8,9\)) that may reflect changes in social behavior (ie, canine reduction related to lower amounts of male-male competition) and earlier dietary shifts.\(^10\) Still others have related changes to respiratory-related alterations and laryngeal restructuring in the earliest members of genus \textit{Homo}.\(^11,12\)

**Does Rhinosinusitis Occur in Other Species in the Wild?**

We posit that rhinosinusitis—like otitis media—is also incompatible with survival in animals in their natural environment. Olfaction, as with hearing, is another special sense that is adversely affected when rhinosinusitis occurs.\(^13\) We propose that if animals in the wild had routinely developed sinusitis, they would have been selected out during evolution. The sense of smell is critical in most terrestrial animals for recognition, avoidance, and defense against predators.\(^14\) Odor sources from predators, identified by Apfelbach and colleagues,\(^15\) come from the whole animal or from its feces, urine, anal gland secretions, and bedding. Olfaction also aids animals in selecting safe food\(^16\) and helps animal mothers in identifying their young. Except for humans (after the neonatal age), most mammals, including our primate relatives, are habitual—obligatory in many cases—nasal breathers, and if rhinosinusitis, with its associated nasal obstruction, developed, they would not only have had poor olfactory function but also would not have been able to suckle, eat, and swallow while breathing through the nose.\(^17\) Most mammals that are “macrosmatic” (ie, largely dependent on olfaction for communication with their environment) must keep their nasal airways and olfactory epithelium open to detect the scent of predators.\(^14\) Humans—in contrast to most other mammals, including most other primates—are “microsmatic” (ie, less dependent on olfaction).\(^18\) Thus, rhinosinusitis in most other mammals in a natural setting is rare in contrast to its frequent occurrence in humans\(^18\); there have been very rare cases reported of captive primates with sinusitis.\(^19\)

### Comparative Anatomy of Paranasal Sinuses

The anatomy of the paranasal sinuses, or lack thereof, is dramatically different in nonhuman primates when compared with humans. \textbf{Table 1} shows that the superfamily Cercopithecoidae (Old World monkeys) has no sinuses except for 1 genus, \textit{Macaca} (rhesus macaque), in which only the maxillary sinus is present.\(^20,21\) \textit{Platyrrhini} (New World monkeys) exhibit variations in their sinus anatomy, with most reported having maxillary sinuses, some having ethmoids, but only homologs of the human having sphenoid and frontal sinuses; 2 genera, \textit{Saimiri} and \textit{Cacajao}, have no paranasal sinuses.\(^22\) As shown in \textbf{Table 2}, of the great apes, the gorilla and orangutan have the largest maxillary sinuses, but their ethmoids, if present, are

\begin{table}[h]
\centering
\caption{Presence or Absence of Paranasal Sinuses in Old and New World Monkeys}
\begin{tabular}{|l|c|c|c|c|}
\hline
\textbf{Taxa} & \textbf{Maxillary} & \textbf{Ethmoid} & \textbf{Frontal} & \textbf{Sphenoid} \\
\hline
\textbf{Cercopithecoidae (Old World monkeys)} & & & & \\
Most taxa—for example, \textit{Papio} (baboon), \textit{Mandrillus} (mandrill) & No & No & No & No \\
\textit{Macaca} (rhesus macaque) & Yes & No & No & No \\
\hline
\textbf{Platyrrhini (New World monkeys)} & & & & \\
Most taxa—for example, \textit{Alouatta} (howler monkey), \textit{Ateles} (spider monkey) & Yes & Yes (in some) & No\(^a\) & No\(^a\) \\
\textit{Cacajao} (uakari) and \textit{Saimiri} (squirrel monkey) & No & No & No & No \\
\hline
\end{tabular}
\end{table}

\(^{a}\)Recesses that may be homologs of sinuses are variably present.

\textit{Figure 2.} Comparison of skulls between the orangutan (\textit{Pongo}) with its prominent prognathic jaws (left) and human (right), which shows the dramatic facial flattening in the human.
rudimentary (Figure 3); ethmoids in humans have the largest volume compared with the great apes (Figure 4).

Márquez and colleagues' hypothesize that the human ethmoid sinus is not phylogenetically a “true” paranasal sinus and probably only has an olfactory function, whereas the maxillary, frontal, and sphenoid do not. They conclude that the ethmoid sinuses are “phylogenetically, embryologically, anatomically, and functionally completely different from all other paranasal sinuses, controlling their ventilation and drainage.” This configuration may have contributed to the rhinosinusitis experienced by humans. Ethmoid sinusitis is a major factor impairing olfaction, whereas maxillary, frontal, and sphenoid sinusitis is not.

Thus, animal species with rudimentary or lacking ethmoid sinuses, including the great apes, are unlikely to have compromised olfaction, because even when they are present, they are not adjacent to the cribriform plate, the outlet of the olfactory system into the nasal cavity. By contrast, the cribriform plate is in intimate contact with the ethmoid sinuses in humans. In most other mammals, the ethmoid bone is posterior to the paranasal sinuses, and the cribriform plate lies in front for optimum olfactory function; only in the human does the ethmoid bone become pneumatized and exhibit a sinus (probably related to bipedalism, in association with facial flattening/loss of prognathism) and anterior migration of the orbits, resulting in deepening of the face. As stated by Márquez and colleagues, in “humans the anterior migration of the ethmoid sinus displaced the frontal sinus superiorly which disconnected the frontal sinus from the maxillary sinus and the ethmoids migrated along with the descent of the larynx which contributed to the unique human speech apparatus.”

We conclude that similar to the effect of human evolution on the anatomy of the palate and paratubal muscles of the eustachian tube, adaptations to bipedalism and speech and loss of prognathism have had a major effect on the anatomy of the paranasal sinuses, especially the ethmoids. These likely render humans susceptible to developing rhinosinusitis when exposed to airborne irritants. Among geographically and temporally diverse human populations, indoor dwellings have been linked to the development of rhinosinusitis, as they can be poorly ventilated and contain smoke as well as viral and bacterial pathogens. The earliest evidence of maxillary sinusitis has been reported in the Neolithic period, coinciding with the appearance of huts and other free-standing structures in the archaeological record.

### Impact of Human Evolution on Drainage of Maxillary and Sphenoid Sinuses and Middle Ear

Human adaptation to bipedalism has had a significant effect on the ostia of the maxillary and sphenoid sinuses.
and the opening of the eustachian tube into the middle ear. In upright humans, the maxillary ostia are high in the medial wall, and the sinus does not drain into the nasal cavity by gravity; in quadrupeds, drainage is aided by gravity as a result of the relative anterior tilt characterizing their head position. Although not tested for drainage by gravity, similar anatomy exists in the sphenoid sinus, as the ostia are high on the anterior wall. There is a similar impact of upright posture on drainage of the middle ear, as it is less likely to drain by gravity into the nasopharynx, because the osseous portion of the eustachian tube in the middle ear is high at the level of the neck of the malleus, not in the most advantageous position in the inferior portion of the hypotympanum. In humans, drainage of the maxillary and sphenoid sinuses, as well as the middle ear, is dependent on mucociliary transport, which in the middle ear has been shown to be impaired by negative pressure and inflammation.

Functional Significance of Paranasal Sinuses

What is the functional significance of paranasal sinuses? In a review of the literature, 86 publications proposed 19 theories for the hypothesized functions of the paranasal sinuses in humans over the past 2000 years. None of these theories has achieved consensus among researchers, although production of nitrous oxide (NO) within the sinuses is the most interesting. Lundberg and coworkers propose that the source of NO in the upper respiratory tract is the paranasal sinuses and that it has a role in respiratory physiology; it enhances pulmonary oxygen uptake due to local vasodilation. This high production of NO appears to be unique in humans and most other primates but much lower in other mammals, such as dogs, rabbits, mice, and rats. In support of this hypothesis, Lewandowski and colleagues reported that baboons, which have no paranasal sinuses, were found to have marked lower concentrations of exhaled concentrations of NO than mammals with paranasal sinuses.

What remains unexplained, however, is how Old World monkeys, with the exception of Macaca, have no paranasal sinuses (see Table 1); how they have survived without sinus NO; and why other mammals that have been identified as having NO require its production from the paranasal sinuses. Also, nonprimate mammals that have paranasal sinuses (eg, dogs and rabbits) produce low concentrations of NO and have survived. If some mammals (eg, almost all Old World monkeys, some New World monkeys) can live without paranasal sinuses, the sinuses probably have no major physiologic function related to the production of NO. An alternative explanation for the variation in the presence or absence of NO is that possibly some species require its production, whereas in others, it is not necessary for survival.

One proposed function for paranasal sinuses is that they provide a biomechanical advantage, but more recently, Rae and Koppe addressed the hypothesis that sinuses arose in response to biomechanical requirements of skull architecture through dissipating masticatory stress forces related to dietary activities and concluded that the biomechanical explanation can be rejected. Among the other proposed functions are that they lighten the skull, aid in resonance to the voice, assist in regulating intranasal pressures, warm and humidify air, and are part of normal skull pneumatization. The human ethmoid sinuses, with their relatively small intranasal position, most likely do not play any role in making the skull lighter, but one could argue their position in the nasal airway may be involved in vocal resonance, in addition to the proposed olfactory function and production of NO. The other sinuses also probably do not lighten the skull in the bipedal position of humans. Most recently, a hypothesis posits that yawning may activate a ventilator system in the paranasal sinuses for selective brain cooling. At the other end of the spectrum of theories of the function, some authors have concluded that the paranasal sinuses in humans exist as “evolutionary remains of useless air spaces” (ie, primitive retentions).

Management Related to Evolution in Humans?

From our understanding of the consequences of evolution related to otitis media, we learned that differences in the anatomy and function of the muscles of the eustachian tube between the rhesus monkey and the human might improve tubal function following repair of the palate in patients with palatal clefts (ie, levator veli palatini muscle). Are there any implications for management of rhinosinusitis related to evolution? If our tentative conclusion that the paranasal sinuses are indeed primitive retentions that have no agreed upon major functional significance is correct, are there any implications for management of rhinosinusitis today? The answer to this question will have to await future research into potential safe and effective methods of prevention and treatment of rhinosinusitis.

Summary and Conclusions

Similar to otitis media, we posit that rhinosinusitis is most likely a human disease, secondary to consequences of evolution (ie, adaptations to bipedalism, speech, and loss of prognathism), which resulted in anatomic differences compared with other mammals, mainly in the ethmoid sinuses and ventilation and drainage of the maxillary and frontal sinuses. In otitis media, the associated special sense of hearing would have been diminished, making survival of animals in the wild unlikely. Similarly, if rhinosinusitis occurred, animals presumably would not have survived during evolution because of the loss of olfaction, another special sense. Humans have no doubt survived despite development of otitis media and sinusitis due to our excellent eyesight (another sense organ) and big brain along with protection from predators afforded by our family and social structure.

In conclusion, both otitis media and rhinosinusitis are most likely limited to humans and extremely common, especially in infants and young children, and consequences of
human evolution, in addition to immunologic and environmental factors.

Author Contributions

Charles D. Bluestone, substantial contributions to conception and design, drafting the article/revising it critically for important intellectual content, and final approval of the version to be published; Anthony S. Pagano, substantial contributions to conception and design, drafting the article/revising it critically for important intellectual content, and final approval of the version to be published; J. Douglas Swarts, substantial contributions to conception and design, drafting the article/revising it critically for important intellectual content, final approval of the version to be published, and provided research and figures of Pongo and human skulls and sinuses; Jeffrey T. Laitman, substantial contributions to conception and design, drafting the article/revising it critically for important intellectual content, and final approval of the version to be published.

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