

Impact of Evolution on the Eustachian Tube

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I posit that humans appear to be the only species that develops otitis media. If animals in the wild had developed middle-ear disease to any significant degree, they would have been selected out during evolution because they would not have survived their predators given the associated hearing loss. Why do humans have otitis media? Evolution has had a significant impact. It is well known that humans are born 12 months too early, which is the result of adaptations to bipedalism and our big brain that, over time, resulted in a relatively small female pelvic outlet compared with nonhuman primates. As a consequence of too early a birth, not only is our immune system immature, but the eustachian tube is too short and floppy in the first year of life. But why is otitis media still common in older individuals? What other adaptation is uniquely human? We developed speech that was associated with descent of the larynx and hyoid bone, which, along with a decrease in prognathism (i.e., facial flattening), resulted in a change in palatal morphology as compared with other primates. Comparative anatomic and physiologic studies have demonstrated significant differences between humans and monkeys, especially in the muscles of the eustachian tube. Paradoxical constriction, as apposed to dilation, on swallowing is a common tubal dysfunction in humans and certain monkey models with chronic middle-ear effusion. My hypothesis is that chronic otitis media with effusion in patients with tubal constriction is a consequence of adaptation for speech and that, most likely, the levator veli palatini muscle is the cause.

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INTRODUCTION

Apparently, humans are the only species to develop otitis media, and this disease especially afflicts many infants and young children. In a study of Pittsburgh newborns followed at monthly intervals until 2 years of age, the cumulative incidence of all episodes of middle-ear effusion was 86%, of which 42% of episodes were acute

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otitis media.¹ The disease prevalence decreases with advancing age, but is still evident in almost 10% of 7-year-old children and also occurs in adults.^{2,3}

But are humans the only species to experience otitis media? Fish are unaffected because they lack a middle ear, but once our distant ancestors advanced onto land, the middle ear developed. Because hearing loss (HL) is associated with middle-ear effusion,⁴ poor hearing would have been unfavorable for survival (i.e., because of predators) and selected out. If animals had a significant incidence of otitis media, then its complications, such as chronic suppurative otitis media (with its associated otorrhea), would be readily apparent. Thus, I posit that we humans are the only species known to have a significant degree of otitis media. The next question is, why?

Why Humans?

The comparative anatomy of the eustachian tube and its muscles between humans and our animal ancestors may aid in understanding the pathogenesis of otitis media and its subsequent management. The nonhuman primate is an ideal candidate for anatomic comparisons. The chimpanzee (*Pan troglodytes*) shares an astounding 98.4% of its genetic code with us, and if these and other nonhuman primates had HL, their natural predators (e.g., the leopard and snake) would have devoured them. The effect of a lack of modern nurturing in humans (e.g., lack of breast feeding) notwithstanding, evolution has undoubtedly played a role.

Born Too Soon

I have recently reported that humans are born approximately 12 months too early, which has had a substantial impact on diseases and disorders of the head and neck and air and food passages.⁵ When we adapted to bipedalism, the female pelvic outlet became too small to deliver newborns with our big brains, resulting in a 9-month gestation. Thus, we are “born too soon.”

It is estimated that we stood upright approximately 4 million years ago, and our brains, primarily the neocortex, grew rapidly starting approximately 2 million years ago. Nonhuman primates are ambulatory at birth, whereas we walk at approximately 1 year of age. During the first 12 months of life, when the incidence of otitis media is quite high, not only is our immune system immature, but the eustachian tube is also too short and floppy (i.e., with increased compliance).⁶

Thus, one consequence of adaptation to bipedalism and our big brain is a birth that is too early, resulting in

otitis media in the first year of life. Still, an immature tube in the young infant does not explain the persistence of the relatively high incidence of otitis media in many older humans, including adults.

Adaptation to Speech

What else, other than our bipedalism and big brain, is unique to humans? We developed speech. Even though other animals are able to communicate with their vocal tract, our speech is unique in the animal kingdom. Our vocal tract becomes elongated with the descent of the larynx, which begins slowly at approximately 3 months of age and reaches the level of the adult larynx by approximately 3 years of life; neonates can suckle while breathing. In almost all other mammals, the epiglottis approximates the palate, which facilitates swallowing and breathing.

It was previously thought that the descent of the larynx in the human over the course of evolution was unique in the animal kingdom, but this assumption was the result of the study of dead animals. Recently, Fitch and Reby,⁷ using cineradiography and magnetic resonance imaging (MRI) in live animals, reported that some animals, such as dogs, goats, and pigs, dynamically lower their larynx during vocalization, but the larynx is not permanently descended in the pharynx. Our larynx is permanently lower after the neonatal period, which contributes to our unique (e.g., particulate) speech.

Contrary to the previously held notion that humans are the only primate that has a permanently descended larynx, Nishimura et al.,⁸ using MRI in chimpanzee (*Pan troglodytes*) infants, recently reported that the larynx also permanently descends in these animals. In a later report from the same group, they found that the hyoid also descended, which was also thought to be uniquely human; they postulated that this adaptation was probably related to the enhancement of swallowing as opposed to speech.⁹ But how is the descent of the larynx possibly related to development of otitis media in humans?

As described by Nishimura et al.,⁹ it appears that the human supralaryngeal vocal tract develops to form a unique, two-tube configuration. This configuration contributes greatly to the development of speech in the human and is dependent on the reduced growth of the palate. Prognathism (facial flattening) is also likely a major factor in the development of human speech caused by changes in the morphology of the palate.

As can be appreciated on the MRI-derived comparison of images of the human and chimpanzee (Fig. 1),¹⁰ there is reduction in prognathism, and the palate is shorter in the human as compared with the chimpanzee.¹¹ This difference in palatal size probably aids in the production of vowels and consonants in humans. Thus, the adaptation to speech has altered the morphology of the palate in the human.

But how is adaptation to speech with subsequent changes in the palate related to development of otitis media? Because the two major muscles associated with the function of the eustachian tube (the tensor veli palatini and the levator veli palatini) are palatal muscles, they may not be anatomically or physiologically the same in the human as compared with the nonhuman primate. I posit that a consequence of adaptation to speech has contributed to our susceptibility for middle-ear disease as caused by changes in the paratubal musculature.

Comparison of Structure and Function of Eustachian Tube in Rhesus Monkeys (*Macaca mulatto*) and Humans

Unfortunately, we do not have information on the anatomy and physiology of the eustachian tube and its paratubal muscles in the chimpanzee or any other animals in its family (the *Pongidae*, great apes), but we have extensively studied the structure and function of the eustachian tube in the rhesus monkey, a primate member of a related family (the *Cercopithecidae*, Old World monkeys). As described by Doyle and Rood,¹² the anatomic

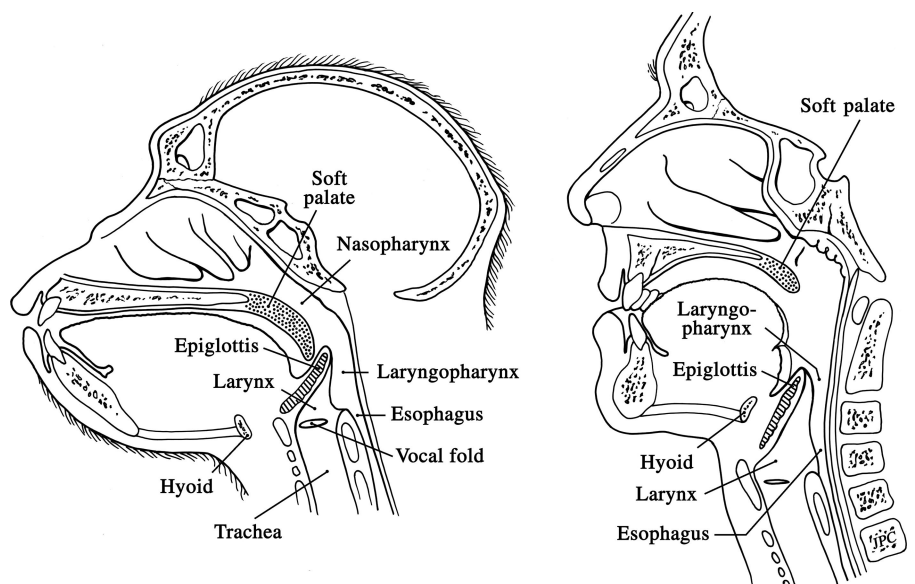


Fig. 1. Midsagittal magnetic resonance images of *Pan troglodytes* (chimpanzee) and *Homo sapiens* (human). Note facial flattening and shorter palate in the human as compared with the chimpanzee. Modified and with permission from Fitch, 2002.¹⁰

structures of the rhesus monkey are similar to humans, and thus the rhesus monkey is suitable as an experimental surrogate for humans, prompting us to use this animal in our laboratory. Nevertheless, there are some notable differences that may influence functional efficiencies between these two species. These differences may help explain why we have never observed naturally occurring otitis media in hundreds of rhesus monkeys (or cynomolgus monkeys, *Macaca fascicularis*) in our laboratory in over 30 years.

The rhesus monkey's genome has recently been mapped, revealing a 97.5% similarity to humans. Even though the anatomy of the eustachian tube is essentially similar in the two species, the tube's length in the rhesus monkey is two thirds within bone (intrabullar) and one-third cartilaginous (extrabullar). In the human, the order is reversed; one third is osseous, and two thirds is cartilaginous. This difference implies that the rhesus tube is stiffer (less compliant) than the human tube. Indeed, we have reported that the human eustachian tube is highly compliant (floppy), especially in infants.¹³ In a comparative study of eustachian tube function between the rhesus monkey and humans, we concluded that the monkey tube is stiffer than in humans.¹⁴ A floppy eustachian tube would be more susceptible to otitis media than one that is stiff.

Also, the morphology of the tensor veli palatini muscle is distinctly different between the two species. In both the monkey and in humans, this muscle has been shown to be the only dilator of the tube during swallowing, which equilibrates middle-ear pressure with ambient pressure.¹⁵ It primarily inserts into the lateral cartilaginous lamina of the tube. In the monkey, it attaches to the entire length of the tubal cartilage, whereas in humans, the muscle's insertion is much shorter.¹² This difference may explain the remarkable ability of the monkey in our laboratory to equilibrate applied negative middle-ear pressure, even when the pressure is suddenly applied. By contrast, we humans (some more than others) have difficulty equilibrating applied middle-ear negative pressure,¹⁶ especially when the negative pressure within the middle ear is sud-

denly applied, such as during descent in an airplane or when scuba diving.

Flisberg et al.,¹⁷ in studies using a pressure chamber, described the "locking" mechanism of the eustachian tube in healthy human volunteers; when middle-ear negative pressure between -30 and 50 mm Hg was applied in the chamber, the tube locked, and the subjects could not open it by swallowing. In a recent comparison study of eustachian tube function between the monkey and humans in our laboratory, the duration of tubal dilation (i.e., opening) was more efficient in the monkey than in the human,¹⁸ which can be attributed to the comparative anatomic differences (described above) between the two species.¹²

From these studies and our observations, we see that humans have relatively poor function in opening the eustachian tube compared with the monkey. This inefficient tubal opening is most likely related to the frequent finding of middle-ear negative pressure, effusion, and even acute otitis media during a viral infection in experimental nasal challenge studies in adult volunteers, especially in individuals who had preexisting tubal dysfunction.¹⁹

Another important anatomic difference between the rhesus monkey and the human is the levator veli palatini muscle. This muscle is not thought to aid in tubal opening. A convincing study of this was our assessment of eustachian tube function after excision of the levator veli palatini muscle in the palate of monkeys, which demonstrated that this muscle is not a dilator of the eustachian tube.²⁰ It most likely acts to support the inferior portion of the tube, in addition to its velopharyngeal valve function. In humans, this muscle has a rounded belly and does not attach to the tube but abuts the inferior portion of the tubal lumen. In the monkey, the muscle bundle is less well rounded, with some fibers attached to the tube's lateral membranous wall, and the physical separation between the muscle and inferior portion of the tube is greater in the monkey than in the human (Fig. 2).¹² These differences in the anatomy of the levator veli palatini muscle between the human and monkey may explain our finding on eustachian tube function testing of paradoxical "constriction," as opposed to opening, of the eustachian

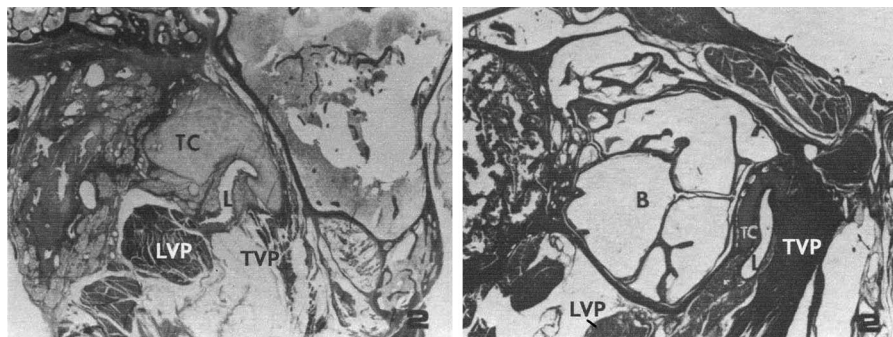


Fig. 2. Coronal view of the left eustachian tube and related structures in the temporal bone specimen from a 13-year-old human female (left) compared with a coronal view of the left eustachian tube in a temporal bone specimen from a rhesus monkey (right). Note that in the human, the levator veli palatini muscle has a rounded belly and closely approximates (abuts) the inferior portion of the tubal lumen. In the monkey, this muscle is more sparse and there is a distinct separation between the muscle and the tube's lumen. Also, note the robust belly of the tensor veli palatini muscle in the monkey compared with the human. TC = tubal cartilage; L = tubal lumen; TVP = tensor veli palatini muscle; LVP = levator palatini muscle; B = bulla of monkey. With permission from Doyle and Rood, 1980.¹²

tube during swallowing in patients with chronic middle-ear effusion and some of our monkey models of otitis media, as described below.

Etiology of Constriction of the Eustachian Tube

We recently reported the study of eustachian tube function in 38 older children, adolescents, and adults who had had chronic otitis media with effusion and had tympanostomy tubes in place. When compared with normal individuals, dysfunction of the tube was documented in all; the most common abnormality was high tubal resistance during swallowing, which implied constriction of the tube.²¹ This dysfunction was diagnosed when performing forced-response function testing, as depicted in Figure 3.

Even though we did not appreciate the possible significance of constriction in the past, we have observed this dysfunction in studies of children and adults who had had otitis media and who had tympanostomy tubes in place or a perforation of the tympanic membrane.²²⁻²⁴ We also reported this dysfunction in infants with an unrepaired cleft palate who had had tympanostomy tubes inserted for chronic middle-ear effusion.²⁵ However, we did not find constriction during function testing in six normal adults with traumatic perforations²² or in a more recent study of eight adult volunteers with no past history of otitis media and normal-appearing tympanic membranes who were tested after a myringotomy.

Animal studies we conducted in the past are now most revealing, when re-examined, with regard to constriction. We identified tubal constriction when we transected or excised the tensor veli palatini tendon at the hamulus of the pterygoid bone²⁶ and after we clefted the monkey's palate.²⁷ However, in contrast to observing constriction in these experiments, we did not find constriction of the eustachian tube after injection of botulinum into the belly of the tensor muscle.²⁸

In retrospect, most informative was the experiment conducted with six rhesus monkeys in which these two paratubal muscles were electrically stimulated and eustachian tube function assessed.²⁹ Stimulation of the tensor veli palatini muscle did not result in constriction, but when the levator veli palatini muscle was stimulated, we did observe constriction.

These experiments in monkeys give rise to the hypothesis that constriction observed in humans with otitis media is secondary to an abnormality of the levator veli palatini muscle. This hypothesis is further supported by the distinct differences in the anatomy of this muscle in relation to the eustachian tube between the two species, as described above. Constriction of the tube would prevent equilibration of middle-ear pressure with ambient pressure and result in middle-ear underpressures and effusion. We have documented this sequence of events in animal experiments.¹⁵ This series of middle-ear outcomes did not occur when we excised the palatal portion of the levator veli palatini muscle in the monkey.²⁰ Ghadiali³⁰ has suggested from computer modeling that asynchronous firing sequence of the two paratubal muscles (the levator veli palatini and tensor veli palatini) may interfere with physiologic dilation of the tube, with resultant constriction.

Thus, I conclude that constriction of the eustachian tube is most likely secondary to abnormal structure or function, or both, of the levator veli palatini muscle and is involved in the pathogenesis of chronic middle-ear effusions in humans. Constriction of the tube may or may not be involved in the pathogenesis of recurrent acute otitis media and is an issue to be answered by future studies. Increased tubal compliance may be a more important abnormality in recurrent middle-ear infection, especially in infants. Also, during an upper respiratory tract infection that can compromise tubal function, the relatively short

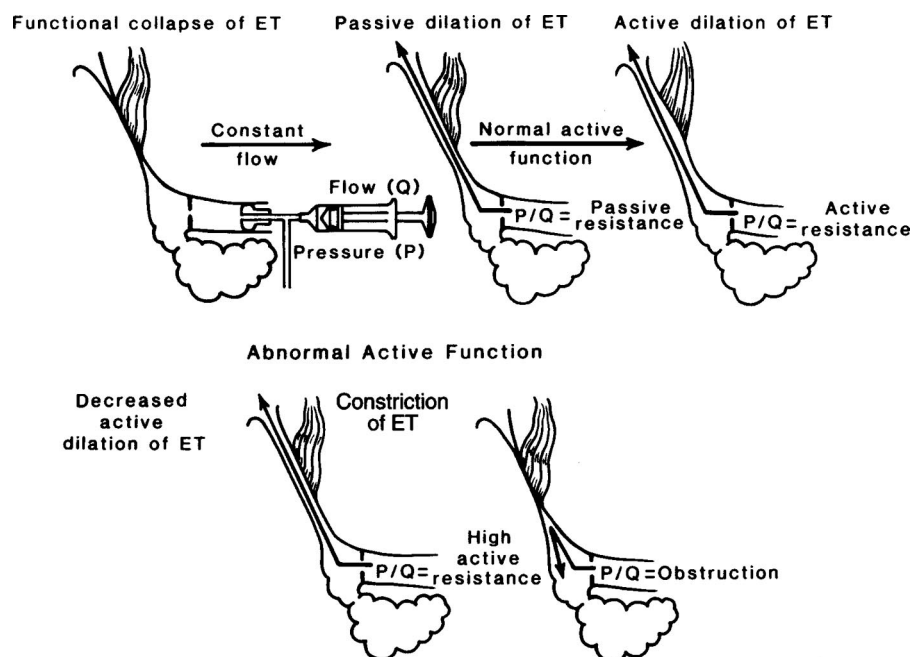


Fig. 3. Cartoon showing the elements of forced-response eustachian tube function testing when the tube normally dilates on swallowing (above) compared with an abnormal tube that constricts during swallowing (below). ET = eustachian tube; P = pressure; Q = flow. From Bluestone, 2005.⁶

tensor veli palatini insertion ratio in humans could result in middle-ear under-pressures followed by acute middle-ear disease, as discussed below.

Nature and Nurture Related to Pathogenesis and Management

At what period in the descent of humans did otitis media appear as a common disease? There is evidence from fossil records of prehistoric *Homo sapiens* to document that otitis media is an ancient disease.³¹ In contrast, I have not uncovered any reports of fossil records of middle-ear-mastoid disease in animals. Most likely, prehistoric humans with otitis media survived their many predators because of the cultural differences between humans and animals; our ancestors in the clan would have protected their young offspring with HL.

Not all humans have, or have had, otitis media. In a viral nasal challenge study, Buchman et al.³² found that individuals who had preexisting abnormal eustachian tube function were more likely to develop middle-ear under-pressures and effusions than subjects who had normal function prior to the challenge. Casselbrant et al.³³ reported a genetic predisposition to the disease, but the genetic origin of this susceptibility has yet to be uncovered. It is possible that the genetic susceptibility is related to variation in the anatomy of the skull base and maxillofacial complex, with resultant impingement of the levator veli palatini muscle on the anteroinferior portion of the tube.

Thus, nature is an important component of the disease. But what role does nurture play in the pathogenesis?

The heading of this section is nature *and* nurture as opposed to nature versus nurture because the etiology and pathogenesis of otitis media is usually related to both. Today, the consequences of modern child care, including a lack of breast-feeding, day-care attendance, and use of pacifiers, as well as exposure to passive smoking, have been designated as risk factors for the disease.³⁴ These factors are potentially preventable, but the possible underlying anatomic factors posited earlier have yet to be confirmed.

As a consequence, management options directed at correction remain hypothetical. It is unlikely we can alter our comparatively inefficient eustachian tube dilation in the near future, but the levator veli palatini can potentially be altered, especially in the infant with an unrepaired cleft palate, at the time of surgical correction of the palate. Future research should focus on factors involved in constriction of the eustachian tube and methods to eliminate it.

CONCLUSION

Otitis media is a human condition related to the consequences of evolution (adaptations to bipedalism, a big brain, and speech) and other factors related to heredity and nurture.

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