The evolutionary reason for the need to secure the airway in anesthesiology

Biro, P

The Evolutionary Reason for the Need to Secure the Airway in Anesthesiology

Peter Biro MD DESA

Institute of Anesthesiology, University Hospital Zurich, Zurich, Switzerland

KEY WORDS: evolution, pharyngeal crossing, airway anatomy, securing the airway

IMAJ 2011; 13: 5–8

The recently celebrated 200th anniversary of the birth of Charles Darwin may be good reason to consider a question that is disconcerting for anesthetists, even though it is obviously of evolutionary origin. I am referring to the anatomic and functional crossing between the airway and the digestive tract at the level of the pharynx, what I call "the pharyngeal crossing." The traffic analogy is intentional: just as road crossings are the most frequent site for accidents, the same is true for the anatomic region in the pharynx at the level of the glottis in terms of securing the airway during anesthesia.

"Accidents" at this location constitute the most feared anesthesiological complications – inability to intubate, failure to secure the airway, aspiration of gastric content, and difficulty to maintain oxygenation – all life-threatening conditions. About 5% to 10% of intubations are known to be difficult, one intubation in about 1500 attempts persistently fails and can lead to considerable morbidity and mortality, and about one-third of anesthesia-related deaths are caused by inability, for various reasons, to maintain oxygenation [1]. Systemic anesthetics, as used for general anesthesia and sedation, and neuromuscular relaxants interfere in a dose-dependent manner with the physiological and protective functions of the laryngo-pharyngeal system and usually have a detrimental effect on both spontaneous breathing and the subtle neuromuscular control of the airway. This is why most airway-related devices in anesthesiology – particularly the tracheal tube – are designed to bridge the airway branch of the pharyngeal crossing and ensure safe and unhindered ventilation [2]. A far more radical means of disengagement of the crossing is tracheostomy, which is simply an artificially created parallel alignment of the two tracts that become partially or totally separated.

Apart from this narrow anesthesiological viewpoint, there are several other medical conditions that are linked to the existence and malfunction of this crossing, such as dysphagia or foreign body aspiration; also, mishaps in daily life may occur, for example, choking on an object. The question is why humans, as well as other mammals and reptiles including birds, have this anatomic configuration that allows or even causes so many problems?

THE CROSSING AT THE LEVEL OF THE PHARYNX

The pharyngeal crossing can best be described when viewing a longitudinal section of the upper body in sagital plane [Figure 1]: the airway begins at the nostrils and the nasal cavity is located cephalad to the mouth. When stretching the neck by retroflecting the head, this dorsal orientation can also be viewed as posterior. The digestive tract begins at the lips and the oral cavity is placed caudal of the airway, which in a stretched head position can be seen as anterior. So the first segments of the two tracts are clearly orientated as a combination of a posterior airway and an anterior digestive tract. The two tracts are separated by the palate, but they converge at the level of the mesopharynx, thus representing a common entity – which is also the center of the crossing. At the level of the hypopharynx the two tracts divide again, but this time in an opposite direc-

Figure 1. Sagital cross-section through the head/neck region illustrating the crossing between the gastrointestinal (black) and respiratory (white) tracts. The hashed section represents the critical intersection region.

tion, to an anteriorly located airway (larynx and trachea) and a posterior digestive tract segment (the esophagus) – separated by the esophagotracheal membrane.

Evolutionary transformations include a functional/adaptive component and one would expect that highly complex and 'problematic' morphologies would be avoided when possible, or if occurring for a transitorily specific reason, even eradicated. With that in mind, it is somewhat astonishing that this pharyngeal crossing has been preserved in humans, mammals, reptiles and birds from our ancestors in geological deep time. There are many grossly differing variants of it, including the air nostrils of marine mammals (which although appearing to be located on the back of the animal, in fact are anterior from the brain), but all have the pharyngeal crossing at various levels in front of the cervical spine.

In humans as well as in all mammals, birds and reptiles, the upper airway crosses the gastrointestinal tract at the level of the pharynx, a circumstance that might cause hypoventilation and loss of protective airway reflexes when anesthetics are administered – this in turn represents the necessity to secure the airway by tracheal intubation

The inevitable question then is why are these two tracts not aligned in a parallel fashion, e.g., with an oral cavity above the nasal cavity (or vice versa), and in this manner are completely separated all the way down through the thorax? Instead of establishing such a simple and functionally undemanding configuration, this system with the crossing requires sophisticated means of avoiding the above mentioned problems and, in real life, potentially possible mishaps like choking. Obviously, the evolutionary process has not resulted in an anatomic configuration suitable for anesthesia, but one adapted for unhindered feeding, breathing and protected airways. For this reason various anatomic features such as the epiglottis and vocal cords became parts of a complex system, and certain protective functions and reflexes were established such as swallowing and coughing. The number of nerves and muscles involved in the control and maintenance of a functioning pharyngeal and laryngeal system is large and requires sophisticated neurological surveillance. And all this has evolved to separate the breathed air from the swallowed food and to ensure that everything moves on the right path. But why do these two tracts have to cross each other? The establishment of such a complex and vulnerable system instead of the hypothetic parallel tracts version mandates a good reason.

The existence of the "pharyngeal crossing" in all tetrapods can be traced back to its evolutionary origins when the lungs developed from the swim bladder of Devonian fishes

FROM ONTOGENY TO PHYLOGENY

To answer a question regarding phylogeny, or more precisely in this case, why evolution has led to the establishment of a pharyngeal crossing, a clue is found in the embryonic ontogeny of air-breathing vertebrates. This describes the individual development of the embryo from the fertilized egg to its mature form before birth. Of course, ontogeny is not simply a reproduction of phylogeny in all its ramifications. But the major trends in the stepwise development of the digestive tract and the adjacent airway segments mirror quite well the main evolutionary steps taken by the involved organs. At first, one can discern that the much older digestive tract is generated first and runs uninterrupted from the mouth to the anus (third week of gestation). Then, a bud-like protuberance begins to spread from the ventral wall of the proto-pharynx anteriorly (fourth week of gestation), thus marking the development of the trachea, bronchi and lungs. With this we already have the lower branch of the airway, but not yet the crossing. The latter is established only when the epipharynx and the nasal cavity separate from the dorsal wall of the proto-pharynx posteriorly (12th week of gestation), which in the event that it is incomplete leads to malformations such as cleft lift and palate. When this upper segment is developed, the pharyngeal crossing is established [3].

When we transpose these steps of the ontogenic evolution to the phylogeny of higher air-breathing vertebrates, the assumption would be that the lungs developed as an anterior appendix of the digestive tract, and the nasal-epipharyngeal system segregated itself as a posterior entity from the cranial end of the oral-lingual-mesopharynx system. All these components were aligned in the midline of the sagital plane and comprise the pharyngeal crossing where they emerged from the proto-digestive tract [4]. However, this rather complex morphology came into being for a very compelling external reason, which forced the organisms to adapt this way, obviating more simple alternatives (e.g., the above mentioned two separate parallel tracts). To find this "very compelling external reason" we must first identify the origin of the proto-lung, which is the key to the answer.

The best approach to this is found in those creatures that are considered phylogenetically closest to the first air-breathing animals. Some amphibians still have gills (at least during their pre-metamorphic life) and/or gas exchange through their body surface [5,6]. These ancillary gas exchange surfaces are necessary because their lungs in the evolutionary sense did not reach the more advanced efficacy of terrestrial animals. In particular, carbon dioxide elimination, ions and acid-base regulation remain partially dependent on gills, while oxygen uptake remains mainly concentrated in the lungs [7,8]. A closer look at these proto-lungs reveals their phylogenetic origin as the commonly known gas bladder in fish (also known as swim bladder or fish maw). In fish the gas bladder usually does not have anything to do with gas exchange; it plays a role in adjusting the specific weight of the animal in order to control its buoyancy. For this reason, it contains variable amounts of gas that are occasionally adjusted by the gulping of air through the mouth and by gas exchange with a specific capillary vessel system. In lungfish and amphibians the gas bladder increasingly became a simple unilobar or bilobar lung-resembling extension, and in later forms a substitute for the receding gills [9,10]. For this reason, exchanging its gas content with the ambient air had to be done by swallowing and regurgitating air, which is nothing other than a primitive form of breathing [11].

The evolutionary reason for the existence of the "pharyngeal crossing" is a direct consequence of the development of an anteriorly orientated proto-lung while the atmosphere was located posterior of the animal

Astonishingly, there are fish with a gas bladder that emanates dorsally from the esophagus; these include the garpike (*Atractosteus lepisosteus*), the carp (*Cyprinus carpio*) and the perch (*Perca fluviatilis*) [Figure 2A]. The garpike even uses it for ancillary gas exchange; however, this promising model did not evolve further to more advanced terrestrial forms. The reason why the ventral and not the dorsal variant evolved exclusively to the lung of tetrapods is not known. If the reverse was true, the dorsal lung position could have resulted in a parallel and separate alignment of the two tracts, which would be more practical from an anesthesiological perspective. Our ancestors missed this opportunity, since they derived from that group that had a ventrally oriented gas bladder [Figure 2B], which is preserved in the present-day bichir (*Polypterus bichir*) and lungfish (*Protopterus dolloi*) [11]. The vascularized gas bladders of our common ancestor – that is, of ourselves and of the contemporary lungfish – can be viewed as the homologous precursor of the lungs in all later evolved tetrapods [12] [Figure 3]. Of course, the proto-lung inhalation and exhalation of these creatures occurred in the cranial segment of the digestive tract, which is the oral cavity. Only later, in less water-dwelling and more land-dwelling amphibians such as frogs, the nasal cavity separated from the oral cavity and became located posteriorly [Figure 4]. The very simple reason for this cephalad shift is that the atmosphere was above – i.e., posterior, while the water in which the animal spent most of its life (and found its food) was ventrally located, or anterior.

AN ACCIDENTAL DEVONIAN LEGACY

The transition from a predominantly aquatic to terrestrial dwelling probably occurred during the Devonian period, approximately 380 million years ago. The trigger for this intricate construction, the above mentioned "very compelling external reason" was nothing other than the physical stratification of the two-layer environment of these creatures deployed horizontally: the water of the shallow seas at the bottom (anterior) and the atmosphere above (posterior). The cause for this development is not known; eventually a temporary rise in atmospheric oxygen concentration expanded the opportunity to conquer yet unoccupied terrestrial habitats. The opening from the nasal sac into the roof of the mouth occurred early in the evolution of tetrapods, even earlier than

Figure 2. In fish, the orientation of the swim bladders as related to the esophagus is possible in two variants: **[A]** dorsal orientation as in garpike, carp and perch, and **[B]** ventral orientation as in bichir and lungfish. It was the second variant from which the gas bladders evolved to lungs in amphibians and land-living tetrapods.

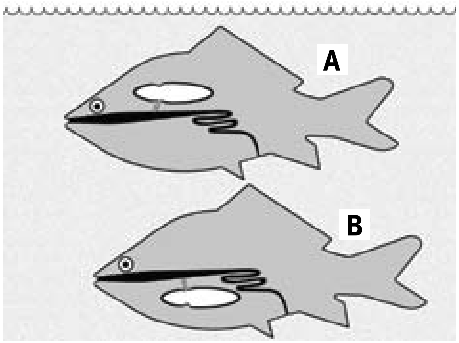


Figure 3. In lungfish, the proto-lungs may be aligned parallel and even dorsal from the esophagus, but essentially, the trachea emanates from the hypopharynx ventrally, thus representing the precursor of a crossing, which is a T-intersection at this stage.

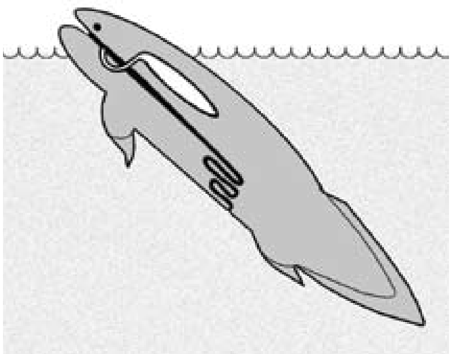
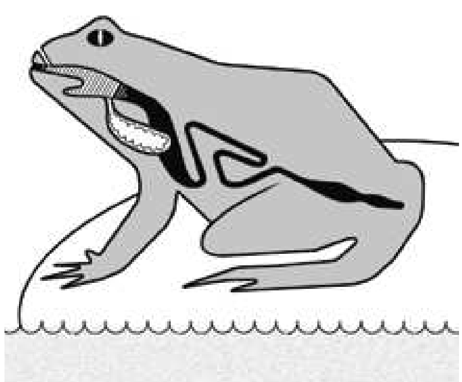


Figure 4. In the frog, the intersection between the gastrointestinal (black) and respiratory (white) tracts is fully developed and in principle not different from humans. The critical overlap between the two tracts comprises the pharynx (hatched)



the limbs [13,14]. The palate separated the anterior part of the two cavities, while further behind, the pharyngeal crossing came into being. Folds from the upper lips developed, segregated as nostrils and moved cephalad, thus establishing the external ends of the nasal cavity. This was located posterior of the mouth, while the trachea and the lungs were forced to point in a ventral direction since they derived from the anteriorly oriented gas bladders. Hence the crossing was unavoidable.

Whenever anesthetists make efforts to secure an airway, what we are doing is struggling to fix an evolutionary mishap, which without doubt was caused by biological and environmental conditions some hundred million years ago. However, the existence of the pharyngeal crossing yielded certain benefits as well. The necessity to control the 'traffic' at the level of the pharyngeal crossing caused the creation of a gate-like structure to open and close the airway – the glottis and the vocal cords. This organ in turn enabled the terrestrial vertebrates to produce noise, ultimately leading to phonation and in our case to the amazing (and in the evolutionary context quite peculiar) human capabilities of speaking and singing.

Corresponding author:
Dr. P. Biro
Dept. of Anesthesiology, University Hospital Zurich, Raemistr. 100, CH-8091 Zurich / Switzerland
Phone: (41-44) 255-1111
Fax: (41-44) 255-4409
email: peter.biro@usz.ch

References

1. Peterson GN, Domino KB, Caplan RA, Posner KL, Lee LA, Cheney FW. Management of the difficult airway: a closed claims analysis. *Anesthesiology* 2005; 103: 33-9.
2. Weksler N, Klein M, Weksler D. The argument for the laryngeal mask airway. *IMAJ Isr Med Assoc J* 2004; 6: 240-5.
3. Moore KL, Persaud TVN. The Developing Human. Philadelphia: WB Saunders, 1998.
4. Laurin M. Tetrapod phylogeny, amphibian origins, and the definition of the name tetrapoda. *Syst Biol* 2002; 51: 364-9.
5. Anderson JS. Focal review: The origin(s) of modern amphibians. *Evol Biol* 2008; 35: 231-47.
6. Anderson JS. Incorporating ontogeny into the matrix: a phylogenetic evaluation of developmental evidence for the origin of modern amphibians. In: Anderson JS, Sues H-D, eds. Major Transition in Vertebrate Evolution. Bloomington: Indiana University Press, 2007: 182-227.
7. Brauner CJ, Matey V, Wilson JM, Bernier NJ, Val AL. Transition in organ function during the evolution of air-breathing; insights from Arapaima gigas, an obligate air-breathing teleost from the Amazon. *J Exp Biol* 2004; 207: 1433-8.
8. Farmer CG. Evolution of the vertebrate cardio-pulmonary system. *Ann Rev Physiol* 1999; 61: 573-92.
9. Coates MI, Clack JA. Fish-like gills and breathing in the earliest known tetrapod. *Nature* 1991; 352: 234-6.
10. Graham JB, Lee HJ. Breathing air in air: in what ways might extant amphibious fish biology relate to prevailing concepts about early tetrapods, the evolution of vertebrate air breathing, and the vertebrate land transition? *Physiol Biochem Zool* 2004; 77: 720-31.
11. Liem KF, Bemis WE, Walker WF, Grande L. Functional Anatomy of the Vertebrates. An Evolutionary Perspective. 3rd. edn. Fort Worth: Harcourt College Publishers, 2001.
12. Ahlberg PE, Smith MM, Johanson Z. Developmental plasticity and disparity in early dipnoan (lungfish) dentitions. *Evol Dev* 2006; 8: 331-49.
13. Shubin N. Your Inner Fish: A Journey into the 3.5-Billion-Year History of the Human Body. New York: Pantheon, 2008.
14. Zhu M, Ahlberg PE. The origin of the internal nostril of tetrapods. *Nature* 2004; 432: 94-7.

Capsule

New therapies that prevent or inhibit metastases

Tumor metastases are a major cause of death from solid tumors. Evidence from preclinical models suggests that tumor cells do not metastasize alone but rather are assisted by specific host cells that modify the microenvironment of the target organ so that it can support the survival and growth of newly arriving tumor cells. Two independent studies of lung metastasis in mice converge on this theme. Kowanetz et al. (*Proc Natl Acad Sci USA* 2010; 107: 21248) show that tumor cells secrete granulocyte colony-stimulating factor, a protein that expands and mobilizes bone marrow cells of a specific type called $Ly6G^{+}Ly6C^{+}$ granulocytes and facilitates their homing into the lung before the arrival of tumor cells. Upon accumulation in the lungs, these granulocytes then secrete proteins that enhance the invasive properties of tumor cells, including matrix metalloproteinases and Bv8, a protein that stimulates tumor cell migration. Duda and team (*Proc Natl Acad Sci USA* 2010; 107: 21677) provide evidence that the stability of circulating metastatic tumor cells is enhanced when they "cotravel" with stromal cells derived from the primary tumor, such as fibroblasts. Once these cellular clumps reach the lung, the stromal cells appear to provide an early growth advantage to the tumor cells. Further exploration of the cells and signaling molecules identified in these studies could lead to therapies that prevent or inhibit metastases.

Eitan Israeli

"I'm sure that someday children in schools will study the history of the men who made war as you study an absurdity. They'll be shocked, just as today we're shocked with cannibalism"

Golda Meir (1898-1978), Israeli Prime Minister. Israel's first and the world's third woman to hold such an office, she was described as the "Iron Lady" of Israeli politics years before the epithet became associated with British prime minister Margaret Thatcher. Former prime minister David Ben-Gurion used to call Meir "the best man in the government."