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Neuroanatomy of the pharynx and larynx

Jonathan Cheetham
Cornell University Hospital for Animals, Box 25, Cornell University, Ithaca, New York 14850, USA.

Learning objective: To understand the relationship between equine performance and structure of the equine upper airway

At maximal exertion, Thoroughbred and Standardbred racehorses have a maximal oxygen uptake (VO$_{2\text{max}}$) of approximately 160 ml/kg bw/t/min which is 40 times the value at rest (Evans and Rose 1988; Morris 1991). The delivery of oxygen for this uniquely high rate of consumption requires a number of specific neuroanatomical respiratory adaptations.

Respiratory minute volume (V$_{\text{E}}$) in horses is approximately 67 l/min at rest, rising 27-fold to 1800 l/min at exercise (Butler et al. 1993). At low speeds (up to 6 m/s), this is mainly due to an increase in respiratory frequency (R$_{\text{f}}$) which rises from 14 breaths/min to 120 breaths/min (Butler et al. 1993; Ducharme et al. 1994). Tidal volume (V$_{\text{T}}$) is approximately 5 l at rest and this increases to 14–18 l at maximal exercise (Butler et al. 1993; Tetens et al. 1996).

This means that at high speed the horse must move 14 l of air approximately 1.5 m in 0.25 s through the airway to the alveoli, then stop it and return it to the environment. This generates very high peak flows of approximately 65–80 l/s at exercise (Butler et al. 1993; Connally and Derksen 1994; Tetens et al. 1996; Radcliffe et al. 2006). These high flow rates are associated with high tracheal pressures both during inspiration and expiration. The greatest drops in airway pressure occur at the nostrils and the rostral aspect of the nasopharynx during inhalation (Rakesh et al. 2008a). This area is susceptible to collapse during inhalation, as it receives only muscular and not bony support. During expiration, airway pressure is greatest over the dorsal surface of the soft palate (Rakesh et al. 2008a).

The normal pharynx is a tubular structure extending from the caudal end of the nasal cavity to the larynx, which can constrict or dilate to facilitate breathing and swallowing. In horses, the soft palate divides the pharynx into nasopharynx dorsally and oropharynx ventrally and terminates caudally at the confluence of the caudal pillars to form the palatopharyngeal arch that covers the oesophageal orifice. Dysfunction of the structures that support the pharynx can lead to small changes in airway geometry and as airflows are high this can lead to profound changes in performance.

The caudal border of the soft palate lies ventral to the rostral body of the epiglottis, except during deglutition, resulting in obligate nasal breathing. In approximately 10–20% of horses the soft palate becomes displaced dorsal to the epiglottis during high speed exercise (Rehder et al. 1995; Martin et al. 2000; Parentle et al. 2002; Ducharme 2006; Lane et al. 2006). This results in dorsal displacement of the soft palate (DDSP), an expiratory obstruction that is often associated with stertor (Haynes 1983; Morris and Seehermar 1990; Holcombe et al. 1998; Ducharme et al. 2003).

The investigation of DDSP has focused on the neuromuscular function of 2 groups of muscles. Those that control the palate and those that control the position of the hyoid apparatus. The control of the soft palate is determined by 4 pairs of muscles: Tensor veli palatini, levator veli palatini, palatinitus and palopharyngeus (Table 1). These muscles form the lateral wall of the nasopharynx. Finally, the stylopharyngeus muscle is innervated by the glossopharyngeal nerve and tenses the dorsal wall of the nasopharynx at exercise (Tessier et al. 2004). The aetiology is closely linked to pharyngeal lymphoid hyperplasia in young horses as the pharyngeal branch of the vagus nerve runs through the floor of the guttural pouch which is also the roof of the pharynx. Thus inflammation of the dorsal pharyngeal wall can lead to dysfunction of the pharyngeal branch of the vagus nerve and so DDSP.

The larynx is suspended from the pterous temporal bone by a chain of paired hyoid bones, the stylohyoid, ceratohyoid, single basihyoid bone, and thyrohyoid which articulates with the rostral aspect of the thyroid cartilage. The strap muscles (sternohyoid, sternothyroid and omohyoid) contract during exercise and pull the larynx caudally. Transection of the sternothyrohyoid muscle produces an inspiratory obstruction at exercise (Holcombe et al. 1994). The paired thyrohyoid muscles, which attach to the caudal border of the thyrohyoid bones and run to the ipsilateral thyroid lamina, may prevent caudal retraction of the larynx at exercise. Bilateral resection of these muscles produces DDSP at slow speed exercise (Ducharme et al. 2003).

The rostral hyoid muscles (genioglossus, geniohyoid and styloglossus) pull the larynx rostrally through their direct or indirect attachments to the hyoid apparatus and are all innervated by the hypoglossal nerve (Sawczuk and Mosier 2001; Fogel et al. 2005; Guinery et al. 2005). The hypoglossal nerve runs just lateral to the ceratohyoid bone and it is possible to use a nerve location technique to deliver local anaesthetic and induce nerve dysfunction. Bilateral blockade of the hypoglossal nerve at this level results in DDSP at high speed exercise with an expiratory obstruction of airflow (Cheetham et al. 2009). As the hypoglossal nerve innervates muscles which control laryngohyoid position this finding led us to evaluate the relationship between racing performance and laryngohyoid position.

Table 1: Function and innervation of the intrinsic palate musculature

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Function</th>
<th>Innervation</th>
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<tbody>
<tr>
<td>Tensor veli palatini</td>
<td>Tenses rostral aspect of soft palate</td>
<td>Trigeminal–mandibular branch</td>
</tr>
<tr>
<td>Levator veli palatini</td>
<td>Elevates the palate</td>
<td>Vagus–pharyngeal branch</td>
</tr>
<tr>
<td>Palatinus</td>
<td>Shortens and depresses the palate</td>
<td></td>
</tr>
<tr>
<td>Palatopharyngeus</td>
<td>Shortens and depresses the palate</td>
<td>Vagus–pharyngeal branch</td>
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Laryngeal function is also susceptible to the high negative pressures produced during inspiration. The sole abductor of the arytenoid cartilage is the dorsal cricoarytenoid muscle, which is innervated by the recurrent laryngeal nerve. The equine DCA consists of 2 neuromuscular compartments (NMC). The lateral NMC is multi-penate caudally, with fibres running at an oblique angle to the sagittal ridge. These fibres converge at a superficial rostral tendon and insert on the dorsolateral aspect of the muscular process of the arytenoid cartilage. The medial NMC inserts on the dorsomedial aspect of the muscular process of the arytenoid cartilage, and no tendon is present. The functional significance of this neuromuscular specialisation will be discussed. 

References
Available on request.
Upper airway disease is a common cause of poor performance in the horse (Morris and Seeherman 1991; Martin et al. 2000). Nasopharyngeal and laryngeal evaluation is important when examining horses for poor performance with upper airway signs. Currently, endoscopy is the most common method to evaluate the equine upper airways. Recurrent laryngeal neuropathy (RLN), aryepiglottic fold entrapment, chondritis and dorsal displacement of the soft palate (DDSP) are all causes of poor performance related to the upper airway (Lane et al. 1987; Morris and Seeherman 1991; Martin et al. 2000). Videendoscopy is commonly used to evaluate the function and the stability of the equine upper airway either at rest or during treadmill exercise (Hackett et al. 1991; Ducharme et al. 1991; Dart et al. 2001; Parente et al. 2002). Laryngeal grading systems based on endoscopic findings have been described and are used to assist in clinical decision making and prognostication (Dart et al. 2001; Dixon et al. 2003). Yet videendoscopy has a number of limitations. The upper airway anatomy can only be assessed from the lumen and thus nonluminal structures including the intrinsic and extrinsic laryngeal musculature and hyoid bones are not evaluated. Thus, although the function of the larynx can be determined, many anatomic components of the larynx and related structures are largely not assessed except by gross palpation. For some conditions, such as DDSP videendoscopy at rest has been found to have a poor correlation with the diagnosis of DDSP made during treadmill exercise, and therefore the latter is often required to make a definitive diagnosis (Parente et al. 2002). This procedure requires appropriate facilities and carries some risk of injury to the horse. Based on these limitations, we have investigated a potential role for ultrasonography as a complimentary diagnostic tool for the equine upper airway in the unsedated standing horse.

An ultrasonicographic scanning technique for the equine larynx including useful acoustic windows and the normal ultrasonographic appearance at each site has been described (Chalmers et al. 2006). Ultrasound allows visualisation of portions of the hyoid apparatus, laryngeal cartilages and associated soft tissues (including intrinsic and extrinsic laryngeal musculature) that are not seen using endoscopy (Chalmers et al. 2006). Additionally, real time ultrasound allows observation of the movement of the vocal folds and of the arytenoid cartilages during respiration (Chalmers et al. 2006). Ultrasonography offers several advantages including that it is noninvasive, can be performed on the standing horse, and is widely available.

The laryngeal ultrasound technique involves evaluating the throat region from 5 established acoustic windows. The 3 ventral windows allow easy visualisation of the basihyoid bone including the lingual process, the strap muscles of the neck, the tongue, and the ventral aspects of the thyroid cartilage, cricoid cartilage, trachea. Also from the ventral window, portions of the cartohyoid and thyrohyoid bones can be seen close to their articulation with the basihyoid bone and the broad rostral insertion of the thyrohyoid muscle can be seen. When compared to endoscopy in the assessment of the equine airway, ultrasonography allows assessment of nonluminal structures, including laryngeal musculature, the hyoid bones, and surrounding tissues such as the strap muscles of the neck.

Imaging of the vocal folds from the cricothyroid notch is reliably achieved and is facilitated by obstruction of the nasal passages and by patient cooperation. In standing horses, imaging of the vocal folds from this window is readily achieved, and the thoracolaryngeal reflex (‘slap’) test facilitates evaluation of vocal fold function. From the lateral windows, arytenoid movement can be assessed. The movement of the arytenoids can be increased by occlusion of the nasal passages or by using the slap test. In all horses, patient cooperation has an impact on ability to adequately assess arytenoid movement from the lateral window.

Since the introduction of this technique, our investigations of the use of ultrasonography in the laryngeal region has expanded to the evaluation of clinical cases with upper airway abnormalities including dorsal displacement of the soft palate, recurrent laryngeal neuropathy, and arytenoid chondritis. The ultrasound findings in each of these conditions will be discussed with a view to establish the utility and limitations of laryngeal ultrasound in the clinical work-up of horses with poor performance.

Selected references
Update on recurrent laryngeal neuropathy: Pathogenesis

Paddy Dixon
Royal (Dick) School of Veterinary Studies, University of Edinburgh, Easter Bush Veterinary Centre, Midlothian EH25 9RG, UK.

A precise cause for unilateral laryngeal dysfunction is only found in a minority of horses, for example due to damage to the recurrent laryngeal nerve by guttural pouch mycosis, perivascular irritant injections or nerve trauma during neck surgery. Mechanical reasons for unilateral laryngeal dysfunction can also be identified in horses with laryngeal dysplasia (4-BAD syndrome). The aetiology of bilateral laryngeal dysfunction can usually be found, such as when it occurs secondary to hepatic encephalopathy or immediately following general anaesthesia. However, the vast majority of cases of unilateral laryngeal dysfunction, either partial paralysis (hemiparesis) or total paralysis (hemiplegia), have no obvious aetiology and consequently these cases are usually diagnosed as suffering from recurrent laryngeal neuropathy (RLN) (synonyms: idiopathic laryngeal hemiplegia, ‘roaring’, ‘whistling’), which is one of the most important upper airway disorders of horses.

Recurrent laryngeal neuropathy, which is invariably unilateral, left-sided and primarily affects taller horses can cause airway obstruction, abnormal respiratory noise and reduced exercise performance, especially in horses exercising at maximal effort such as Thoroughbred racehorses. However, in its most severe form, RLN can affect horses working at slow speeds, such as draught horses. RLN may be a progressive disease and clinical signs may develop in adulthood. Despite its enormous importance, studies on the aetiology, pathogenesis and likely hereditary nature of RLN have received only limited and intermittent attention to date. More recently, the Havemeyer workshop on RLN, which brought together workers from many disciplines concerned with RLN, appears to have stimulated renewed interest in the study of this important disorder (Anon 2003).

The aetiology of RLN still remains unknown, and the many hypotheses include mechanical causes such as tension and stretching of the recurrent laryngeal nerve and/or its local blood supply during neck movement, especially in taller horses, although animals with much longer necks such as giraffes do not suffer from recurrent laryngeal nerve dysfunction. Other proposed causes of RLN include ingested neurotoxins or alternatively nerve damage caused by vitamin deficiencies but these mechanisms would be expected to cause generalised neurological dysfunction leading to generalised muscular dysfunction including megaesophagus, generalised muscle weakness or tetraparesis, whereas the clinical signs in RLN are clinically restricted to dysfunction of the left larynx i.e. are those of a mononeuropathy. There is a significant body of evidence that RLN is inherited, for example, the offspring of RLN-affected stallions are more likely to be affected with RLN than offspring of unaffected stallions. The mechanisms and mode of likely inheritance remain unclear at this time, but it is thought likely to be a polygenic trait (Marti and Ohnesorge 2002).

The lesions in the recurrent laryngeal nerves of RLN-affected horses have been well described microscopically (Duncan et al. 1991) and latterly also by teased nerve fibre examinations. The pathological changes in affected recurrent laryngeal nerves appear to be axonal in nature and are characterised by a proximal to distal decrease in large myelinated fibres, most marked in the distal aspects of the nerves. The lesions in the laryngeal muscles innervated by the recurrent laryngeal nerve (both adductory and abductory) are also characteristic of neurogenic atrophy (muscle fibre atrophy and angulation, fibrous and fat replacement) and have been very well characterised in RLN. Although RLN is invariably clinically and endoscopically unilateral, similar but milder pathological lesions are also often present in the right recurrent laryngeal nerve although RLN cases extremely rarely have evidence of right sided laryngeal dysfunction. Despite RLN clinically presenting as laryngeal adductor dysfunction, (i.e. of stridor and reduced exercise performance) as compared to a laryngeal adductor dysfunction (i.e. dysphagia) laryngeal muscle atrophy is in fact most severe in the laryngeal adductor muscles (Cahill and Goulden 1986a; Collins et al. 2009).

Although pathological changes have been reported in other long peripheral nerves in some RLN cases (Cahill and Goulden 1986b), age-related pathological changes can also be found in the distal limb nerves of some older horses not suffering from RLN (Wheeler and Plummer 1989). Recently, Hahn et al. (2008) compared lesions in laryngeal nerves and other long peripheral nerves in RLN affected cases and found the neurological and muscle changes confined to the recurrent laryngeal nerves and laryngeal muscles, respectively, showing that RLN is not a polynuropathy and thus confirming that it is a mononeuropathy. Clarification of this aspect of RLN pathology suggests that RLN is a unique neurological disease as compared to inherited neuropathies in other species, that are invariably polynuropathies. However, vocal cord involvement can be the first manifestation of Charcot-Marie-Tooth disease (the most common family of inherited motor and sensory human peripheral neuropathies) (Aboussouan et al. 2007) where the precise genetic causes of many of its types have now been determined, and animal models have been generated. Different gene mutations can cause clinical signs ranging from a severe generalised polynuropathy to a syndrome in which only nerves exposed to local trauma are affected (i.e. hereditary neuropathy with pressure palsies). A similar inherited vulnerability factor could explain the apparent predisposition of the recurrent laryngeal nerves to develop stretch-related lesions in affected horses.

References
Recurrent laryngeal neuropathy (RLN) is a major cause of poor performance in racehorses and affects 5–8% of Thoroughbreds (Lane et al. 1987; Dixon et al. 2001). The current gold standard for treating recurrent laryngeal neuropathy (RLN) in horses is still a prosthetic laryngoplasty, with or without vocal cordectomy or ventriculectomy (Hawkins et al. 1997; Kidd and Sione 2002; Dixon et al. 2003; Kraus et al. 2003). The frequent and significant loss of arytenoid cartilage abduction seen in the immediate post-surgical period is one limitation of this technique (Dixon et al. 2003; Brown et al. 2004). This loss of abduction leads to a reduction in cross-sectional area of the rima glottidis and the return of exercise intolerance and abnormal respiratory noise (Schumacher et al. 2000; Dixon et al. 2003; Brown et al. 2004). This loss of abduction may also contribute to the modest 48–68% post-operative success rate observed in racehorses (Russell and Sione 1994; Hawkins et al. 1997; Strand et al. 2000; Davenport et al. 2001; Kidd and Sione 2002; Radcliffe et al. 2006).

This lecture will provide an update on a number of strategies being used attempt to improve the success rate associated with treatment of recurrent laryngeal neuropathy in horses. It was recently suggested that curettage of the cricoarytenoid joint might induce fibrosis of the joint and reduce loss of abduction in the post-operative period (Parente 2004), however, we have observed loss of abduction in clinical patients that had curettage. One disadvantage of this technique is that loss of abduction often occurs in the early stages post-operatively and may precede fibrosis. Work using an in vitro laryngeal model has shown that placement of polymethylmethacrylate (PMMA) in the left cricoarytenoid joint (CAJ) provides resistance to arytenoid collapse at physiological flows and pressures in both static and dynamic (cyclic flow) conditions (Cheetham et al. 2008). These data also show that PMMA injected into the CAJ reduces the force experienced by the laryngoplasty suture in vitro. One disadvantage of PMMA used clinically is that it promotes bacterial adherence (Kendall et al. 1996), we suggest that antibiotics should be incorporated into PMMA in studies evaluating its clinical efficacy for CAJ stabilisation. The rapid curing of the PMMA means that the laryngoplasty suture should be pre-tied before the bone cement is injected into the joint and the arytenoid ab ducted. This method has been used in a small number of clinical cases in conjunction with a traditional laryngoplasty suture(s).

Flow modelling studies have identified a focal area of increased negative inspiratory pressure on the medial aspect of the contralateral aryepiglottic fold (AEF) in horses with RLN (Rakesh et al. 2008). This has led to excision of the AEF in clinical cases presenting for laryngoplasty. One limitation of the laryngoplasty suture is the laryngeal is always ‘tied back’. It is a static solution. The ideal treatment for RLN would be a dynamic solution that would open the rima glottidis only when physiologically appropriate, that is during maximal exercise. A neuroprosthesis is an electrical stimulator that generates a signal whose amplitude, frequency, pulse duration and pulse characteristic can be controlled. Early investigation in laryngeal neuroprosthesis demonstrated that reanimation of the arytenoid cartilage and vocal fold was possible in dogs (Sanders et al. 1991; Zeal ar et al. 1994). More recently positive results were reported in humans in a small clinical study (Zealar et al. 2003).

We have initially focused on the motor limb of neuroprosthesis. In experimental horses, when the pacing electrode was placed on the recurrent laryngeal nerve, stimulation resulted in full arytenoid cartilage abduction but also had medial bowing of the vocal cord due to stimulation of the vocalis muscle. This necessitated pacing of the recurrent laryngeal nerve after transection of its adductor branch in order to achieve correct physiological function.

Stimulation of the entire recurrent laryngeal nerve after transection of the abductor branch of the recurrent laryngeal nerve resulted in various degrees of arytenoid cartilage abduction: full abduction was obtained in horses with laryngeal grade I or II (n = 7) and laryngeal grade III (n = 2), while poor abduction was obtained in long-standing (>1 year) grade IV horses (n = 2). Constant stimulation of the recurrent laryngeal nerve for 60 min led to full abduction without evidence of muscle fatigue (n = 2). Complications associated with the procedure was cuff displacement and this occurred as late as 14 months after implantation.

These complications have lead to the need to explore intramuscular stimulation. The intramuscular course of the recurrent laryngeal nerve and the location of the CAD motor endplates have been identified using Schiller’s and acetylcholinesterase staining (Cheetham et al. 2008).

Intramuscular pacing was then used in the CAD muscle only. These electrodes and their location in the lateral compartment of the CAD yielded also good abduction of the arytenoid cartilage. Complications such as late electrodes dislodging was noted in some horses until the design of the electrodes and the surgical technique was refined.

We are currently optimising design of the intramuscular electrode and the parameters for stimulation.

Selected references


Pharyngeal collapse (PC), also referred to as nasopharyngeal obstruction or dynamic pharyngeal collapse, is a cause of upper respiratory noise and exercise intolerance in athletic horses. It has been observed endoscopically during high speed treadmill examinations in both racehorses and sport horses referred for clinical evaluations of reduced athletic performance. Dynamic PC is characterised by ventral displacement of the dorsal pharyngeal wall, and/or axial displacement of the lateral pharyngeal walls and/or may also include dorsal displacement of the pharyngeal floor (soft palate or epiglottis). It has also been described as potentially being a precursor to, or part of the condition of dorsal displacement of the soft palate. It typically occurs during inspiration and end-expiration.

The exact mechanism(s) causing this condition are not fully elucidated, but it is thought to be related at least partly to weakness in the stylopharyngeus muscle, exacerbated by the negative inspiratory pressures generated in the nasopharynx during inspiration at high speeds. The stylopharyngeus muscles originate from the axial surface of the stylohyoid bones and extend to the roof of the nasopharynx, acting to dilate the dorsal nasopharynx. The condition can be worsened by ventral or dorsal flexion of the neck.

Pharyngeal collapse may be the primary cause of poor performance, or it may be present as part of a constellation of other upper airway abnormalities, or it may appear in combination with other body system abnormalities such as significant lower airway disease, cardiac disease or musculoskeletal abnormalities. When it occurs in combination with other upper airway obstructions, it is observed more frequently than when it is seen as the sole cause of reduced athletic performance. In one study, dynamic PC was diagnosed as the sole cause of poor performance in 6% of the cases seen on a high speed treadmill examination (49/828), whereas it was present in combination with other problems in 20% of the population (172/828).

Similar to other upper airway obstructions, dynamic PC may result in abnormalities of gas exchange, characterised by decreased exercise PaO2 and increased exercising PaCO2. In an earlier retrospective study, PC was the most frequently diagnosed single upper airway abnormality, and correspondingly the most frequent cause (50%) of abnormal exercising blood gas values. In addition, the most severe gas exchange deficits occurred in horses with PC (whether alone, or in combination with other abnormalities). Therefore, dynamic PC, whether alone or in combination with other abnormalities, may affect gas exchange during exercise, and this may be sufficient to affect athletic performance. More recently, Boyle et al. reported that 37% of the cases with a primary diagnosis of PC as the cause of poor performance had abnormalities of gas exchange reflected by a low PaO2, and 27% had an abnormally elevated PaCO2. Horses with abnormalities of gas exchange had a moderate or severe grade; none were of mild severity.

Unfortunately, no definitive treatment exists for dynamic PC. Recommendations include extended rest, and therapy aimed to decrease inflammation such as nonsteroidal anti-inflammatory drugs and systemic, as well as inhaled, corticosteroids. It is not known if there is a connection between inflammation of the lower airways and PC; however, subjectively, some horses seem to improve clinically after inhaled anti-inflammatory therapy for lower airway disease. In addition, management may increase the likelihood of performance success. Management suggestions include adjusting the frequency of strenuous training and/or racing, and potentially decreasing the length of the races. Different head carriages, if possible, may also decrease the presence or severity of PC.

Future performance may be affected by PC. One study showed that while there was no statistically significant difference in earnings in racehorses before and after the diagnosis of PC (n = 24) (pre, $2920 ± 3796 vs. post, $1823 ± 2907), if horses aged ≥4 years were separated (n = 15), earnings were significantly decreased after diagnosis (pre, $3371 ± 4514 vs. post $1010 ± 921, P = 0.003). Therefore, older horses may be less likely to return to their previous level of performance. Horses with a Grade 3 and 4 dynamic PC also had a significant decrease in earnings relative to other grades, and thus a guarded prognosis for return to successful competition.

Suggested reading