

# Aryepiglottic fold augmentation as treatment for late-onset dysphagia following surgical treatment of recurrent laryngeal neuropathy

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## Keywords

Horse, dysphagia, recurrent laryngeal neuropathy

## Summary

**Objective:** Coughing and dysphagia have been described following prosthetic laryngoplasty (LP) with or without ventriculectomy/ventriculocordecotomy (VE/VCE) for the treatment of recurrent laryngeal neuropathy. All previous case descriptions include patients with acute onset of clinical signs after surgery that persisted. The authors observed a late-onset of dysphagia and coughing months to years after LP ± VE/VCE. The condition was always associated with an abnormality of the aryepiglottic fold (AEF). Treatment options for those patients are limited. We suggest augmentation of the AEF as treatment for affected horses. The goal of the study was two-fold: Firstly, to describe a new condition of late-onset dysphagia in horses following LP ± VE/VCE associated with an abnormal appearance of the AEF, and secondly, to offer a minimally invasive and successful treatment for those patients. **Material and methods:** Six horses were presented because of dysphagia and coughing with an onset of months to years after LP ± VE/VCE. Endoscopically, the AEF always appeared thinner and more flaccid to a varying degree. The food path was traceable along the AEF into the trachea using dyed molasses. An initial injection of hyaluronic acid (HA) into the AEF led to immediate improvement of the dysphagia. The procedure was performed in the standing sedated horse. The needle was placed through the cricothyroid ligament and the injection performed under endoscopic guidance. **Results:** All horses tolerated the injection well. Injection of HA was successful only in the short term in all cases and repeated injections were needed for permanent resolution using either cross-linked HA, polyacrylamide hydrogel or platelet rich plasma. **Conclusion and clinical relevance:** Horses may develop dysphagia and coughing months to years after LP ± VE/VCE as a late-onset complication. The condition seems to be associated with an abnormal appearance and function of the AEF. Successful treatment is possible by augmenting the AEF. However, careful patient selection is mandatory.

## Schlüsselwörter

Pferd, Dysphagie, Hemiplegia laryngis sinistra

## Zusammenfassung

**Gegenstand und Ziel:** Husten und Dysphagie sind bekannte Komplikationen nach therapeutischer Laryngoplastik (LP) mit oder ohne Ventrikulektomie/Ventrikulocordecotomie (VE/VCE) zur Behandlung der einseitigen Kehlkopflähmung. Bei den bisher beschriebenen Fällen trat die Störung jedoch unmittelbar nach der Operation auf. Die Autoren beobachteten Patienten, bei denen die Dysphagie Monate bzw. Jahre nach der LP ± VE/VCE erstmalig auftrat. Gleichzeitig wurde ein abnormales Erscheinungsbild der Plica aryepiglottica (PAE) festgestellt. Da keine zuverlässige Therapie für diese Patienten beschrieben ist, empfehlen die Autoren die Augmentation der PAE. Ziel der Studie war einerseits die Neubeschreibung der verzögert auftretenden Dysphagie bei Pferden nach chirurgischer Behandlung der Hemiplegia laryngis sinistra und andererseits deren minimalinvasive Behandlung mittels Augmentation der AEF. **Material und Methoden:** Sechs Pferde wurden Monate bzw. Jahre nach erfolgter LP ± VE/VCE wegen Dysphagie und Husten vorgestellt. Bei der endoskopischen Untersuchung erschien die PAE in unterschiedlichem Ausmaß dünner und schlaffer als normal. Durch gefärbte Melasse ließ sich eine abnormale Futterpassage entlang der PAE bis in die Trachea nachweisen. Initial wurde Hyaluronsäure (HS) in die PAE injiziert. Dies führte zur unmittelbaren Verbesserung der Dysphagie. Am stehenden, sedierten Pferd wurde die Kanüle durch das Ligamentum cricothyroideum in das Kehlkopflumen eingeführt und die Injektion in die PAE dabei endoskopisch kontrolliert. **Ergebnisse:** Bei allen Patienten verlief die Injektion komplikationslos. Die HS-Injektion brachte jedoch nur kurzzeitig Erfolg. Zur dauerhaften Behandlung der Dysphagie waren erneute Injektionen notwendig, entweder mit kreuzvernetzter HS, Polyacrylamid-Hydrogel oder thrombozytenreichem Plasma. **Schlussfolgerung und klinische Relevanz:** Pferde können auch Monate bis Jahre nach einer LP ± VE/VCE eine Dysphagie entwickeln. Die Störung scheint mit einem abnormalen Erscheinungsbild und einer gestörten Funktion der PAE einherzugehen. Eine erfolgreiche Behandlung mittels Augmentation der PAE ist möglich, setzt jedoch eine sorgfältige Patientenauswahl voraus.

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## Augmentation der Plica aryepiglottica zur Beseitigung spät auftretender Dysphagie nach chirurgischer Behandlung der Hemiplegia laryngis sinistra

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## Introduction

Prosthetic laryngoplasty (PL) was firstly described by Marks et al. (26) as a surgical treatment for horses with recurrent laryngeal neuropathy (RLN) and it is probably the most commonly performed therapy for athletic horses with RLN presented with exercise intolerance. The procedure has been combined with ventriculotomy (VE) or ventriculocordectomy (VCE) particularly to alleviate noise production and to a lesser degree to improve performance (12).

Complications following surgery, primarily coughing and/or dysphagia were described consistently in the past (9, 11). Some authors distinguish between short-termed occurrences during hospitalisation or prolonged manifestation. The reported prevalence of chronic cough varies between 57% in older publications (13) and less than 20% in the current literature (21, 33). Few authors explicitly describe nasal discharge during feeding as a long-term sequel (9, 13, 15). However feed material contaminating the nasopharynx has been described as an incidental finding discovered during resting endoscopic examination (4, 8). Recently, with the advent of dynamic endoscopy, oesophageal reflux of saliva or food material into the nasopharynx has been observed following PL (2, 4, 23). This was seen during exercise only, except in one case (2) and it was termed upper oesophageal incompetence. All previous descriptions of dysphagia associated with PL include cases of continuous clinical signs following surgery or no overt clinical signs. We are not aware of a case publication specifically reporting a delayed onset of dysphagia accompanied by coughing following PL with or without VE/VCE. The authors observed dysphagia following PL  $\pm$  VE/VCE in a small number of patients at rest with an onset several months after surgery. It was always associated with a visible abnormality of the left aryepiglottic fold (AEF). The only other abnormality of the AEF previously published is an axial deviation of the AEF observed during high speed endoscopic evaluation (20). The abnormality seen in the present cases occurred at rest.

Regarding the treatment for coughing and or dysphagia, clinical signs often subside with time, usually within 4 weeks (10). Alternatively, loosening or removal of the prosthesis has been suggested (9). Endoscopic implant injection into the dorso-axial aspect of the left arytenoid has also been reported in four horses as being successful treatment for continuous dysphagia following PL (29). Treatment for axial deviation of the AEF includes fold resection or rest (20, 23).

The aim of the present report is two-fold: Firstly, to describe a new condition of late-onset dysphagia in six horses following PL  $\pm$  VE/VCE associated with an abnormal appearance of the AEF, and secondly, to offer a minimally invasive and successful treatment for those patients.

## Material and methods

### Medical history

The six Warmblood horses (two mares, four geldings; 6–13 years old) were presented between 2004 and 2013. All horses had undergone PL surgery 9 months to 6 years previously. Two horses were operated on by the first author (Nos. 2 and 5), four by other surgeons (► Table 1). The author used a routine surgical technique for PL and unilateral VCE via laryngotomy (12). Preoperatively and for 3 consecutive days the horses received procaine penicillin-streptomycin (23 mg/kg i.m. once daily; Veracin® compositum, Albrecht, Aulendorf, Germany) and flunixin (1.1 mg/kg i.v. once daily; Flunidor® RPS, cp-pharma, Burgdorf, Germany). The degree of abduction after surgery was considered moderate (grade 3 [9]). The horses were stall confined for 3 weeks. Limited hand walking was initiated at the beginning of the second week and regular training was resumed 6 weeks after surgery. The remaining four horses also had PL and VCE as assessed by endoscopic appearance during subsequent endoscopy. Exact description of the technique was not available except for case 4, which had an identically per-

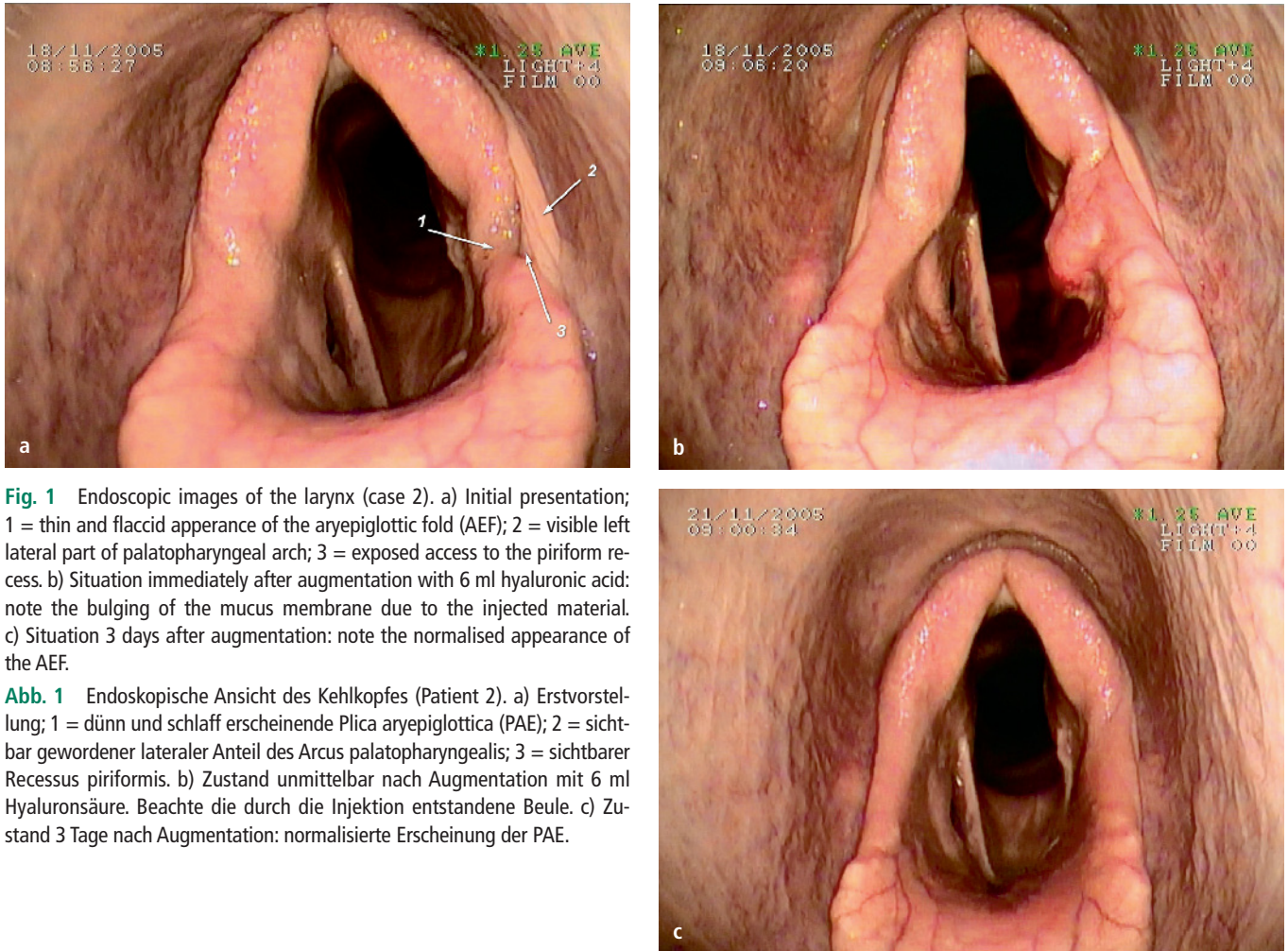
**Table 1** Case details of six horses with late-onset dysphagia.

**Tab. 1** Angaben zu den sechs Pferden mit zeitlich verzögert aufgetretener Dysphagie

Case no.	Age at first presentation for dysphagia	Time since laryngoplasty	Abduction after laryngoplasty*	Abduction at presentation for dysphagia*	Augmentation			Follow-up after last treatment
					First	Second	Third	
1	8 years	> 3 years	unknown	2/5	sodium HA	cross linked HA	cross linked HA	6 months
2	10 years	1.5 years	3/5	3/5	sodium HA	cross linked HA	cross linked HA	6 years
3	13 years	3.5 years	unknown	2/5	sodium HA	PRP	–	1 year
4	11 years	5 years	unknown	2/5	sodium HA	PRP	–	5 years
5	6 years	9 months	3/5	3/5	sodium HA	PRP	PRP	4 years
6	11 years	6 years	unknown	2/5	sodium HA	PAH	–	1 year

\* Degree of abduction according to Dixon et al. (9)

HA = hyaluronic acid, PAH = polyacrylamid hydrogel, PRP = platelet rich plasma



**Fig. 1** Endoscopic images of the larynx (case 2). a) Initial presentation; 1 = thin and flaccid appearance of the aryepiglottic fold (AEF); 2 = visible left lateral part of palatopharyngeal arch; 3 = exposed access to the piriform recess. b) Situation immediately after augmentation with 6 ml hyaluronic acid: note the bulging of the mucous membrane due to the injected material. c) Situation 3 days after augmentation: note the normalised appearance of the AEF.

**Abb. 1** Endoskopische Ansicht des Kehlkopfes (Patient 2). a) Erstvorstellung; 1 = dünn und schlaff erscheinende Plica aryepiglottica (PAE); 2 = sichtbar gewordener lateraler Anteil des Arcus palatopharyngealis; 3 = sichtbarer Recessus piriformis. b) Zustand unmittelbar nach Augmentation mit 6 ml Hyaluronsäure. Beachte die durch die Injektion entstandene Beule. c) Zustand 3 Tage nach Augmentation: normalisierte Erscheinung der PAE.

formed surgery and postsurgical management as described for the author's two cases.

All owners reported a symptom-free period after surgery. The current complaint was an intermittent cough as the first symptom, which worsened in an inconsistent manner over several weeks. All horses had been treated unsuccessfully with antibiotics and expectorants by referring veterinarians.

### Initial presentation

At presentation the horses were bright, alert and responsive and vital signs were within normal limits. Coughing was pronounced during feeding and subsided to a lesser degree during resting times. Food material came out of their nostrils during feeding in variable amounts. Horses were sedated for upper airway endoscopy using detomidine (0.008–0.012 mg/kg i.v.; Domosedan®, Vetoquinol, Ravensburg, Germany). On endoscopic examination the nasopharynx, larynx, and trachea were found to be contaminated with food particles. To estimate the degree of dysphagia and food path 50 ml of molasses dyed with methylene blue were adminis-

tered orally with a syringe and the horses re-evaluated endoscopically. Blue colour was traceable along the left AEF and all the way into the upper part of the trachea. Abduction of the left arytenoid cartilage was considered moderate and good (grades 3 and 2 [9]) in all horses. Notably, the left AEF appeared thinner and more flaccid compared to the right side (► Fig. 1a), the extent varying between horses. Presumably due to the abnormally flaccid appearance of the fold, the left side of the palatopharyngeal arch and the piriform recess became more visible. There were no other abnormalities seen on endoscopic evaluation. The guttural pouches were not inspected in all cases.

### Surgical treatment

Preoperatively the horses received flunixin and antibiotics. Trimethoprim-sulfadiazine (15 mg/kg p.o.; Synutrim®, Vetoquinol) was used during the first surgery and procaine penicillin-streptomycin was applied in all subsequent procedures. Surgeries were performed in the standing horse sedated with detomidine (0.012 mg/kg i.v.; Domosedan®, Vetoquinol) and butorphanol



**Fig. 2** Endoscopic image of the larynx (case 3) during injection of sodium hyaluronic acid into the axial aspect of the aryepiglottic fold. Note the food contamination within the larynx.

**Abb. 2** Endoskopische Ansicht des Kehlkopfes (Patient 3) während der Injektion von Hyaluronsäure in die axiale Seite der Plica aryepiglottica. Beachte die Futterreste im Lumen des Kehlkopfes.

(0.012 mg/kg i. v.; Alvegesic®, cp-pharma). Sedation was prolonged as required. Extended head-neck position was facilitated by placing the head forward on a table. The area ventral to the larynx was clipped and prepared aseptically for surgery. The flexible endoscope was placed transnasally to visualise the larynx. An 18 G, 15 cm long spinal needle (Mila International, Erlanger, USA) was advanced at the midline through the cricothyroid ligament. Care was taken to place the needle as cranially as possible at the V formed by the palpable edges of the thyroid cartilage. Entry of the needle into the lumen was observed endoscopically. A volume of 10 ml lidocaine (Lidocainhydrochlorid 2%, bela-pharm, Vechta, Germany) was sprayed onto the axial surface of the AEF using the ventrally placed spinal needle, this being followed by a single submucosal injection of 0.5 ml lidocaine. For the ensuing augmentation, the needle was placed submucosally again in the axial aspect of the AEF, approximately 5 mm ventral to the AEF attachment on the arytenoid cartilage (► Fig. 2). The substance of choice was injected as a single depot. Various products were used for injection over time, but in all horses the initial treatment consisted of 6 ml sodium hyaluronic acid (HA; Recosyn®, Recordati Pharma, Ulm, Germany).

Following the first augmentation the trimethoprim-sulfadiazine application was continued once daily for 10 days to prevent lower airway infection due to the existing tracheal food contamination. The horses were re-evaluated endoscopically 3 days after surgery and subsequently discharged. It was advised for patients to refrain from strenuous exercise for 2 weeks.

## Subsequent presentations and follow-up

Symptoms of dysphagia re-occurred in all six horses after 4–6 weeks. For the second injection either 6 ml (n=2) of cross-linked HA (Alpha Ionic, Zilina, Slovakia), 6 ml (n=3) of platelet rich plasma (PRP; E-PET, Pall Corporation, Port Washington, USA) or 6 ml (n=1) of polyacrylamide hydrogel (Arthramid® Vet, Contura International, Soeborg, Denmark) were used. For the third augmentation (required in three horses only) cross-linked HA (n=2) or PRP (n=1) were used. After the second and third augmentation, procaine penicillin-streptomycin was administered once daily for 3 days. Horses were again discharged on the third day after surgery with the recommendation that exercise should be reduced for 2 weeks.

All clients were contacted by telephone between 6 months and 6 years after the last injection to obtain information about recurrence of dysphagia, coughing or any other complications.

## Results

### Surgical treatment

All injections were carried out without complications and were tolerated well by the horses. Additional sedation was needed in case 3 only (0.008 mg/kg detomidine and butorphanol, respectively). Considerable swelling at the submucosal puncture site on the AEF was noticed immediately after the injection due to the placement of the augmenting material of choice (► Fig. 1b). All horses were re-examined endoscopically daily and after 3 days a normalised appearance of the AEF was observed (► Fig. 1c).

Clinically, signs of dysphagia had improved in all cases immediately after surgery and there was noticeably less coughing. However, 4–6 weeks after the first surgery the symptoms re-occurred in all cases. After a second injection three horses had no re-occurring symptoms. In the other three horses, a third injection was performed 3 months later, finally successfully.

### Follow-up

According to the owners, symptoms of dysphagia or a cough did not re-occur. Owners of the two horses with the shortest follow-up period (6 months and 1 year in cases 1 and 3, respectively) were lost for a longer follow-up. The other owners were approached up to 6 years after surgery. One horse experienced an upper hind limb fracture 6 years later and another horse was euthanized due to intestinal strangulation 5 years later, but both were used for their intended activity up to this time. Two horses were still in use for pleasure riding and medium level dressage 1 and 4 years after surgery, respectively.

## Discussion

In this report we describe our observation of dysphagia and coughing as a possible late-onset complication following PL  $\pm$  VE/VCE in six horses. Additionally, the authors offer a minimally invasive and successful treatment for the affected patients.

Coughing and dysphagia are well documented sequels after PL (9, 11, 21). The exact causes of these symptoms are not known and are possibly multifactorial. It has been shown that food and water entered the laryngeal cavity in horses after experimentally induced or natural RLN and PL (14). Foremost excessive arytenoid abduction has been associated with an increased incidence of coughing (9). It is perceivable that the incomplete seal of the laryngeal aditus during swallowing, caused by a mismatch of the permanently fixed arytenoid cartilage and the epiglottis, allows food and saliva to enter the trachea. In horses with dysphagia after PL an insufficient occlusion of the rima glottis at the dorsal inner surface of the left fixed arytenoid was documented. Retrograde laryngoscopy, where the endoscope is placed through a small tracheotomy and directed cranially, was used to observe the laryngeal opening from caudal during feeding (16, 29, 32).

Loosening or replacing the prosthesis has been suggested as a treatment option for dysphagia or coughing (15). In some horses the abduction does decrease with time as do the symptoms of coughing and dysphagia (9). However some horses, with the degree of abduction considered good can also show signs of coughing and dysphagia for no apparent reason (11). Damage to intrinsic laryngeal muscles either during surgery or as a result of denervation, or even reactive fibrosis due to the prosthesis were also considered potential causes for pharyngeal dysfunction (14). In the present case series, the surgeries were performed by various clinicians. To draw conclusions from a specific surgical technique or material therefore was not possible. Furthermore, any type of swelling after the upper airway surgery might affect deglutition, as drainage of a seroma on the surgical site stopped coughing in one horse (9). Recently, laryngeal fistula formation has been described as a complication following PL, which was also associated with coughing (5). Additionally, a disposition for palatal dysfunction with an unknown aetiology has recently been described following PL (3).

The horses in the present case series developed the clinical signs months to years following the initial surgical treatment for RLN and after a long symptom-free period. A delayed onset of dysphagia and coughing months to years after surgery was mentioned in a German standard equine textbook (16) and a review article (1), both without citation. Ahern and Parente (1) reported that "mobilisation of the muscular process is required" to treat these cases, however, with the downside of a subsequently inadequate glottis opening.

Notably, we observed in all horses of the present case series that the left AEF appeared thinner and more flaccid. Consequently, the left lateral portion of the palatopharyngeal arch and the ipsilateral piriform recess were more exposed than normal. This was parti-

cularly obvious when making direct comparison to the right unaltered side. The cause for this AEF abnormality is unknown since no histological examination was performed. We speculate that the AEF may have become atrophied over time. The normal AEF in horses extends between the epiglottis and the base of the corniculate process of the arytenoid cartilage (27) and consists of two layers of mucus membranes only (22). The AEF in humans additionally contains several layers of collagenous fibres and also a few muscle fibres, the latter of which do not attach to the epiglottis (31). Muscular or ligamentous components are not described in the equine AEF, though information is scarce.

The only other abnormality described for AEF is axial deviation of the AEF, a condition causing dynamic obstruction of the upper respiratory tract during maximal exertion. This diagnosis of axial deviation of the AEF can be made during dynamic endoscopy only, and no abnormality on the fold itself was described at rest (7, 8, 19, 20). Axial deviation of the AEF has been found in horses without preceding upper airway surgery (20) or following PL  $\pm$  VE/VCE (4, 7, 8). There was no significant association between the degree of arytenoid abduction and AEF deviation (7). Leutton and Lumsden (23) observed this entity right-sided only in 37% of their patients with RLN before PL surgery and in 48% of their patients after surgery, also including bilateral cases. In total, AEF axial deviation appears to be mainly bilateral or slightly more right-sided (7, 20). The main clinical complaints were noise and exercise intolerance; dysphagia and coughing were not described (7, 8, 20, 22). It can also be an incidental finding (4). It was categorised as mild, moderate and severe (4) and was often associated with other upper airway abnormalities like palatal instability or dorsal displacement of the soft palate (22). As treatment, excision of the collapsing tissue was recommended by some surgeons. Success rate after laser excision was 75% if the axial deviation was the only abnormal finding and 50% of the horses improved after rest only (20). These authors suspected immaturity or fatigue as being possible causes for this condition; others suspected abnormal stretching of the fold (22).

Other unusual causes of dynamic upper airway obstruction include the dynamic ventro-rostral displacement of the dorsal laryngeal mucosa seen during dynamic endoscopy (30) or fourth branchial arch defects (4-BAD) leading to rostral displacement of the palato-pharyngeal arch (22). Very recently a new complication, termed oesophageal reflux or upper esophageal incompetence, was seen in horses after PL. In the aforementioned horses presumably saliva was seen emanating from the upper esophageal opening. In some horses food material was seen in the nasopharynx or even nostrils. This was observed in almost all horses during exercise only (2, 4, 23).

The rationale for the injection technique used in our study as treatment for the presented cases with late-onset dysphagia was the appearance of the laryngeal opening, specifically the thin and flaccid AEF. Also, the blue dyed molasses along the AEF led to the fold being the potential structure for food leakage. We suspected that AEF augmentation would re-establish a more morphological

### Conclusion for practice

The present report describes six horses with late-onset (months to years) dysphagia and coughing after prosthetic laryngoplasty with or without ventriculectomy/ventriculocordectomy and with a thin and flaccid appearance of the AEF. In all horses the food path was traceable along the aryepiglottic fold into the trachea using dyed molasses and in all horses the initial injection with hyaluronic acid led to immediate improvement of the dysphagia. The described augmenting injection technique is straightforward, minimally invasive and, depending on the injected material, cost efficient. Though we were successful in treating these six horses, application in a larger group of patients is needed to validate the recommended technique.

normal situation. The development of this technique is based on previous work by several other clinicians (16, 29, 32). Augmentation of upper airway structures in horses, specifically of the epiglottis (34) or the soft palate (28), has been described using a ventral laryngotomy approach under general anaesthesia or was performed endoscopically in standing horses. Ohnesorge et al. (29) published a technique where horses with dysphagia following PL were injected with either poly-L-lactic acid or cross-linked HA. The material was injected medio-dorsally under the mucus membrane of the arytenoid using custom-made tubing with a fitted needle passed through the working channel of the endoscope or attached externally to the endoscope. We modified this technique in three ways: 1) a ventral approach through the cricothyroid ligament, 2) a different injection site within the larynx (AEF) and 3) using alternative solutions for augmentation. The shorter, ventral approach appears safer to us during potential sudden deglutition, requires less augmenting agent to fill the long tubing and enables the convenient triangulation technique to be used.

In all our cases sodium HA was used for the first course of treatment. In all cases it was only successful short term and failure was attributed to resorption of the HA. However, the immediate success proved the feasibility and efficiency of the injection technique itself. We therefore consider this initial injection to be an important diagnostic step. There are multiple other upper airway pathologies and short-term failure of this initial injection demands further diagnostics and a different treatment approach.

The subsequent choice of augmenting agents was based on the availability at the time. Cross-linked HA, a product used in the human cosmetic industry and recently described in an equine tenectomy model, is a chemically modified HA with extended residence time (17). However the high costs prohibit its application in most cases. The rationale for using PRP was to stimulate healing of the AEF tissue; however, based what is known about the equine AEF, the only tissue to stimulate is the mucosa or submucosa. Polyacrylamid hydrogel has been used for years in human plastic and cosmetic surgery as a soft tissue filler (6, 25). It has been described in horses as a treatment for osteoarthritis (18) as well. Polyacrylamide hydrogel consists of 97.5% sterile water and 2.5%

polyacrylamide and it is highly biocompatible and non-biodegradable. Other tissue fillers previously applied in equine cases are polytetrafluorethylene (28, 34) or collagen (28). Based on our limited experience we currently advise polyacrylamide hydrogel as an augmenting agent, but further studies are required to optimise the augmenting agent and volume to be injected. In human patients with unilateral vocal fold paralysis, injection laryngoplasty is one of the most widely used treatment modalities (24, 35). Various commercially available tissue fillers for aesthetic procedures are among the proposed injection materials for this human glottis insufficiency. However, it was concluded that more research is needed for comparing viscosity and predictability of the surgical deposition of injected substances (24).

### Conflict of interest

The authors declare not to have any conflict of interest.

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