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Review Article

Evolving concepts of laryngeal paralysis

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Abstract

Accepted concepts of the pathophysiology and treatment of laryngeal paralysis have changed over the years. It has long been observed that symptoms of laryngeal paralysis vary greatly, both between patients and over time. There have been various theories to explain these differences. This article reviews how these ideas have changed over time as research has produced new information. Currently, the most popular view is that the laryngeal nerve regenerates after injury, albeit incompletely and inconsistently, and that variations in symptoms and laryngeal posture can be accounted for by muscle activity.

Key words: Larynx; Paralysis; Surgery

It was not possible to diagnose laryngeal paralysis until the development of mirror laryngoscopy. This technique was introduced during a meeting of the Royal Society of Medicine in 1854 by a singing teacher, Manuel Garcia.[1] Subsequently, unilateral laryngeal paralysis became recognised as a fairly common cause of hoarseness.

However, other questions arose concerning the causes of certain peculiarities which were commonly observed then and are still encountered today.[2]

Firstly, the symptoms of laryngeal paralysis vary greatly. Some patients are quite hoarse, or even aphonic, while others are moderately 'breathy' or only slightly hoarse. Occasionally, laryngeal examination reveals a paralysed vocal fold in an individual with no vocal symptoms whatsoever.

Additionally, the 'position' of the paralysed vocal fold usually changes over time in a given patient. Immediately after sudden onset of paralysis, the vocal fold has been noted to lie in a lateral, cadaveric position, with poor closure during phonation. However, after a few months, the paralysed vocal fold tends to move medially, with improved glottal closure and voice. In a patient with bilateral paralysis, stridor increases over time, due to medial migration of the vocal folds.

Finally, it is commonly observed that a paralysed vocal fold lies laterally after vagus nerve injury, but moves to a paramedian position after recurrent laryngeal nerve (RLN) injury. The physiological explanations for these phenomena have been hotly debated, and have shifted over the years since Garcia's presentation to the Royal Society of Medicine. Our current knowledge of the pathophysiology of laryngeal paralysis has important implications for the treatment of paralytic dysphonia.

Until the mid-twentieth century, there was no accepted therapy for restoring voice in patients with unilateral laryngeal paralysis. Jackson and Jackson stated that the primary consideration in the management of a patient with laryngeal paralysis was the identification and treatment of the cause, since there was no effective treatment for laryngeal dysfunction.[3] Later, injection laryngoplasty proved to be effective in improving the voice in many (but not all) patients with unilateral paralysis. In particular, injection of the paralysed vocal fold with Teflon® enjoyed widespread acceptance, for a time, as the treatment of choice for unilateral laryngeal paralysis.[4] With time, it became apparent that Teflon could produce unacceptable granulomatous reaction. Therefore, Teflon injection has largely been supplanted by laryngeal framework surgery, which uses an externally placed implant to medialise the vocal fold.[5] However, neither injection nor medialisation laryngoplasty is successful in all patients. In particular, these procedures are much less effective in patients with a paralysed vocal fold that lies in a lateral position. And so, the question as to why vocal folds vary in position has therapeutic relevance.

The debate as to the cause of variation in vocal fold position has been particularly heated in many medical meetings, within the UK Royal Society of Medicine and across Europe in general. Felix Semon espoused a theory that is commonly referred to as 'Semon's law'. He proposed that the reason a paralysed vocal fold assumes the median position is that the nerve fibres supplying the posterior

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cricoarytenoid muscle (the only abductor of the larynx) are more sensitive to injury than the nerve fibres to the adductor muscles.[6] This theory had much to commend it; it seems logical that, with some innervation remaining in adductor muscles, the vocal fold would be pulled medially.

However, there are two problems which discredit this theory. First, this theory would predict that in a progressive nerve injury, the paralysed vocal fold would eventually move from medial to lateral, as first the abductor and then the adductor muscles are weakened. However, this is precisely the opposite of what is observed. Second, subsequent research has demonstrated that, in the RLN, the abductor and adductor nerve fibres are not compartmentalised, but commingled within the nerve.[7] Thus, the chance of a selective injury to one type of fibre is slim.

A competing theory, which held sway until recent years, was termed the 'Wagner–Grossman hypothesis'.[8] The central physiological assumption of this hypothesis was that action of the cricothyroid muscle is responsible for pulling the vocal fold medially in patients with a RLN injury. The rationale was that the RLN supplies all intrinsic laryngeal muscles except the cricothyroid muscle. This theory seemed very parsimonious, as the cricothyroid muscle would be paralysed after transection of the vagus nerve. Thus, it is very appealing to suppose that the action of this muscle is what accounts for the clinical differences in patients with RLN and vagus nerve injuries.

However, research on the physiology of the cricothyroid muscle has cast considerable doubt on the Wagner–Grossman hypothesis. The cricothyroid muscle does behave as an accessory muscle of respiration, increasing its activity during inspiratory loading, by increasing activity in response to respiratory stimuli such as increased airway resistance or breathing of CO_2. However, simultaneous measurement of transglottal resistance and laryngeal electromyography (EMG) has failed to document any effect of increased cricothyroid activity on glottal area or vocal fold position.[9,10] Moreover, animal experiments comparing vocal fold position after chronic RLN injury versus RLN injury plus cricothyroid denervation have also failed to demonstrate any effect of cricothyroid denervation.[11] Finally, experiments in human cadaver larynges tested the mechanical effects of simulated contraction of the cricothyroid muscles. Cricothyroid contraction significantly tenses and lengthens the membranous vocal fold, but does not adduct the vocal fold.[12] Thus, in patients with laryngeal paralysis, the variations of vocal fold position and vocal function cannot be attributed to the cricothyroid muscle.

Subsequent clinical studies have strengthened this position.[13] In a series of EMG measurements in 114 patients with a fixed vocal fold, Hirano *et al.* found some EMG activity in 65 per cent.[14] They noted that the position of the paralysed vocal fold did not correlate with the innervation status of the cricothyroid muscle. In fact, they found that the vast majority of patients had EMG activity in the thyroarytenoid muscle, and that the position of the paralysed vocal fold correlated with the number of motor units detected by EMG in the thyroarytenoid muscle, with more units in more medially located vocal folds. Blitzer *et al.* also noted laryngeal activity in most patients with RLN injury, and reported that the vocal fold was less flaccid and had less tendency to droop in a patient with more EMG activity.[15]

An unexpected finding of laryngeal nerve injury research has been a very strong propensity for the transected RLN to regenerate, even after purposeful resection of a segment of the nerve. In my own experiments, I created 2 or 3 cm long defects in the RLN of cats, and on re-exploration found that the nerve had regenerated across this gap. Transection of this regenerated nerve caused an immediate lateralisation of the paralysed vocal fold, with simultaneous increase in transglottic resistance.[11] Experiments in dogs have confirmed the strong propensity of the RLN to regenerate.[16–18] Evidence that this nerve also regenerates in humans can be found in the results of surgical exploration of patients with recurrent spasms after RLN transection for spasmodic dysphonia.[19] The nerve was found to regenerate, despite ligation by sutures or surgical clips.[20] As noted above, Hirano *et al.* and Blitzer *et al.* both reported significant levels of laryngeal EMG activity in patients who had sustained RLN injury.[14,15]

Today, most laryngologists believe that, in most cases, a paralysed vocal fold is not completely denervated. The dissenting voice comes from Damrose and colleagues, who performed intra-operative evoked EMG on patients undergoing medialisation thyroplasty, and found no evidence of RLN innervation.[21] The reason for this conflicting finding could be related to the severity of glottic insufficiency in the patients selected for surgery.

Impaired vocal fold motion and variability of function after RLN injury and have been attributed to synkinetic reinnervation.[22] Reinnervating nerve fibres are scrambled and do not reach the appropriate muscles. Synkinesis is known to occur after facial nerve or extremity nerve injury.[23] In addition, inappropriate reinnervation of laryngeal muscles after RLN transection and repair has been documented in rats as well as in guinea pigs.[24,25] Crumley has advocated the classification of sykinesis as 'good', when it results in a favorable vocal fold position and vocalis muscle bulk, or 'bad', with, maintains muscle bulk, so that the vocal fold is not thin and atrophic, with dysfunctional motion and sometimes episodic spasm.[22] Recurrent severe airway obstruction, due to episodic laryngospasm, is a severe but rare late complication of RLN injury.[26]

Synkinesis also explains why efforts to surgically reinnervate a paralysed vocal fold have to date failed to restore normal function. Numerous investigators have attempted to reinnervate the larynx, most with the goal of restoring respiratory abduction in patients with bilateral laryngeal paralysis.[27–31] Reanastomosis of the main RLN trunk results in reinnervation of laryngeal muscle with restoration of tone, but no purposeful motion. Some respiratory motion has been reported in animal experiments wherein nerve fibres

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from the diaphragm have been directed to the posterior branch of the RLN, or directly implanted into the posterior cricoarytenoid muscle.[32,33] The best motion is achieved when such surgery is performed immediately after RLN transection. Results are poor with delayed attempts to reinnervated.

Laryngeal synkinesis clearly occurs, and is responsible for abnormal motion after nerve injury. However, it cannot account for vocal fold immobility in the face of considerable EMG activity. This would require the opposing muscle actions to have exactly equal force vectors that cancelled each other out, which would have a very low probability of occurring.

I recently reported results of experiments that appear to clarify some of these issues. I resected segments of either the RLN or vagus nerve in cats, and then after a few months performed endoscopy, EMG and histological evaluation of the laryngeal muscles. I found that the RLN consistently regenerated within four to six months.[34] I also noted preferential reinnervation of the thyroarytenoid muscles compared with the posterior cricoarytenoid muscles. I concluded that the paramedian position and fairly normal bulk of the vocal fold was due to robust reinnervation of the thyroarytenoid muscle, and that immobility was due to deficient abductor activity of the posterior cricoarytenoid muscles. In contrast, after vagus nerve injury, there was essentially no EMG activity in either the thyroarytenoid muscle or the posterior cricoarytenoid muscle on the involved side, and the paralysed vocal fold was flaccid and abducted. Histology of the RLN in those animals revealed no axons whatsoever. I concluded that the median position of the vocal fold after RLN injury is analogous to a flexion contracture in a stroke patient, with unopposed muscle activity holding the vocal fold in an adducted position. In contrast, there is little or no reinnervation of the larynx after a vagus nerve injury, so that the vocal fold is flaccid and lies in a cadaveric position. This explanation could account for both the medial shift of the vocal fold over time after RLN injury, and the observed clinical differences between patients with RLN and vagus nerve injuries. It does not preclude the occurrence of other abnormalities after nerve injury, such as those involving sensory aberrancies, adductor function during inspiration, or episodic spasm.

The reason for preferential reinnervation of laryngeal adductor muscles remains to be determined. It may be simply a numbers issue, with many more adductor than abductor muscle and nerve fibres. It may be that the posterior cricoarytenoid muscle is further away from the regenerating nerve stump. It may also be that the two types of muscles differ in their response to denervation, in terms of local production of growth factors that attract regenerating axons, or in their capacity to be reinnervated. However, preferential reinnervation of adductor muscles, with inadequate abductor activity, sounds eerily like the 'law' proposed by Semon many years ago.[6] It is likely that he astutely observed the phenomenon of abductor weakness in many patients. However, he proposed that the reason for airway obstruction in patients with bilateral RLN paralysis was that the nerve fibres supplying the abductor muscles were more sensitive to injury than those nerve fibres supplying the adductor muscles. No plausible reason for a differential sensitivity could be identified. Therefore, because his proposed mechanism did not predict clinical behaviour, both the mechanism and his observations were ultimately rejected. This is perhaps a good example of 'throwing out the baby with the bathwater'.

Another issue in managing patients with laryngeal paralysis is the common observation that vocal fold medialisation procedures, such as vocal fold injection augmentation, or type I thyroplasty, are often ineffective when the vocal fold lies in a lateral position. This is best understood by considering the mechanics of laryngeal motion. All motion of the vocal fold is caused by the actions of muscles on the cricoarytenoid joint. The vocal ligament is attached to the vocal process of the arytenoid cartilage. As the arytenoid cartilage rotates internally or externally, it drags the vocal fold along with it, to close or open the glottis. However, the arytenoid does not just rotate in an axial plane. As the vocal folds adduct, the vocal process moves in and down, and with abduction, it moves outward and upward.[35] When the vocal fold lies just a short distance from the midline, as in paramedian paralysis, its vocal process is in nearly the same axial plane as the opposite vocal process during phonation, and the vibratory edge of the paralysed vocal fold can be moved to a favourable position by exerting medial force, such as that achieved by injection or thyroplasty. However, when the vocal fold lies laterally, it is most often displaced in a vertical dimension as well. Thus, a simple medial-directed force does not correct the displacement in the vertical dimension. The arytenoid adduction procedure, as described by Isshiki, controls the position of the vocal process by simulated adductor muscle contraction, and is usually quite effective in closing a posterior laryngeal gap.[35] In a review of 20 cases of patients who had unsatisfactory results from a thyroplasty undertaken for laryngeal paralysis, Woo *et al.* found a persisting posterior gap in 12. In each of these patients, arytenoid adduction was successful in restoring a good voice.[36]

The actions of laryngeal muscles have been studied in a cadaver model, placing radiopaque markers on various landmarks and performing computerised axial tomography at rest and with simulated contraction of individual laryngeal muscles.[37,38] The axis of rotation by adductor muscles is oblique, lying in a somewhat vertical axis in the coronal plane but with an antero-posterior tilt in the saggital plane. In contrast, the posterior cricoarytenoid muscle rotates the arytenoid about a nearly horizontal axis that is oblique in the axial plane.[38] As a result, adductor and abductor forces are not completely orthogonal. This means that contraction of the posterior cricoarytenoid muscles and elevation of the vocal process does not preclude rotation about the vertical axis. Phonatory activation of the posterior cricoarytenoid muscles has long been observed.[39] The difference in the axes of rotation explains how such activation of the posterior cricoarytenoid muscles can provide

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tension and posterior support, without forcibly abducting the vocal folds.

Knowledge of the mechanics of the cricoarytenoid joint has been applied in developing two modifications of arytenoid adduction, both of which utilise a suture to mimic action of the posterior cricoarytenoid muscles. A suture is placed in the muscular process of the arytenoid and then anchored under tension to the inferior cornu of the thyroid cartilage. Cadaver studies have indicated that this results in a rotation similar to that effected by contraction of the posterior cricoarytenoid joint.[40] This posterior suspension suture is a useful adjunct to arytenoid adduction in patients with the flaccid paralysis often observed after a vagus nerve injury. The suspension suture provides posterior support to the arytenoid, restoring some tension to a flaccid vocal fold, and also corrects inferior displacement of the vocal process. A posterior suture can also be used alone to relieve airway obstruction in many patients who have stridor and obstruction due to bilateral RLN injury.[41] Although these patients often have considerable adductor activity, there is insufficient abductor function to move the vocal folds to an open position during inspiration. A posterior suspension can be used to abduct one vocal fold. Because this does not abolish adduction in the axial plane, some phonatory adduction is still possible. Thus, the procedure appears to restore dynamic function, with the glottis closing during phonation and springing open again when phonatory activation ceases. This procedure can improve the airway significantly, without the same degree of voice impairment that is encountered with static enlargement of the glottis.

Conclusion

Our concepts of the pathophysiology of laryngeal paralysis have evolved considerably in the past century and a half. We now understand that paralysis is not an 'all or nothing' phenomenon, and that patients with clinical laryngeal paralysis differ greatly in the position and function of the affected vocal folds. We also understand that vocal fold motion is three-dimensional, and that surgical procedures to reposition the vocal fold must take this into account. The ideal treatment for laryngeal paralysis would be to restore normal innervation, and research should continue toward that goal. It may be that many concepts that we now firmly espouse could eventually prove false. Or, as in the case of Semon's law, our observations may be accurate, but the mechanisms may differ from our current speculations.

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