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ORIGINAL ARTICLES

Management of common voice problems: Committee report

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OBJECTIVE: **This report provides the reader with a state-of-the-art update on a number of common voice problems that require phonosurgical intervention.**

STUDY DESIGN AND SETTING: **This multiauthor review is not a position statement of the American Academy of Otolaryngology–Head and Neck Surgery (AAOHNS) and may reflect institutional preference and/or bias. It arose from a panel discussion at the AAOHNS meeting in 2000.**

RESULTS: **We provide a review of the genesis and management of papillomatosis, dysplastic glottal epithelium, arytenoid granulomas, Reinke's edema, and vocal-fold paralysis.**

CONCLUSIONS AND SIGNIFICANCE: **In the past decade, there has been a dramatic expansion of knowledge regarding a variety of voice disorders and associated treatment. There has been a convergence of basic science investigations in anatomy, physiology, and pathology with clinical trials of treatment, both surgical and nonsurgical. This information should provide the reader with current insight into critical management issues of the aforementioned disorders.** (Otolaryngol Head Neck Surg 2002;126:333-48.)

Laryngology developed as a medical and surgical specialty in eastern Europe in the late 1850s[1,2] as a result of Garcia's[3] investigations into singing phonation. Management of the human voice has

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been an enduring and crucial area of investigation throughout laryngologic history. The importance of a reliable human voice has become increasingly evident during the development of the communication age of the 20th century and will become even more critical in the 21st century.[4] Vocal impairment can result in loss of productivity in the workplace and become a psychosocial problem. Surgical research and investigations into the physiologic function underlying human laryngeal voice production have led to a watershed of operations designed to restore and improve the quality of the human voice.

The term *phonosurgery* was developed by von Leden in the early 1960s and refers to surgical procedures that maintain or improve the human voice. Phonosurgery includes (1), phonomicrosurgery, or endoscopic microsurgery of the vocal folds, (2) laryngoplastic phonosurgery, or open neck surgery that restructures the laryngeal cartilage framework and soft tissues, (3) injection techniques, which include the placement of medications as well as synthetic and organic biological substances, and (4) neural reinnervation of the larynx.

Successful management of the human voice typically requires the use of laryngeal stroboscopy. This device, which was perfected in 1895,[5] allows for clinical assessment of vocal fold vibration and oscillation, a fundamental component of voice production. The widespread use of stroboscopy hallmarked the instillation of physiologic principles of laryngeal sound production into the design of new surgical procedures. This resulted in paradigmatic shifts in the medical and surgical management of voice disorders during the past decade. The procedural innovations have been fueled by international collaboration and driven by improved understanding of the physiologic function of vocal fold oscillation.

Recent successes have led to enthusiasm for future developments, similar to the nascent era of laryngology in the middle nineteenth century. Laryngeal and voice problems are universal throughout the world regardless of age, gender, or social stratification. The inability to communicate vocally can be crippling to the teacher as well as the parent, laborer, or performing artist. The larynx has the most complex voluntary motor function in the human body; the delicacy of interdependent management is sustained by surgeons, speech language pathologists, singing-voice teachers, and family members. Tremendous advancements have been achieved during the past 10 years, and the early part of the twenty-first century should bring many more promising accomplishments.

RECURRENT RESPIRATORY PAPILLOMATOSIS

Background

Recurrent respiratory papillomatosis (RRP) of the upper airway and digestive tract is a severe and potentially fatal disease that frequently is a complex management problem for both the patient and the otolaryngologist.

RRP can occur on any mucosal surface of the upper aerodigestive tract, but it most commonly occurs in the larynx. Recently, there have been significant advancements in the understanding of molecular mechanisms underlying RRP as well as in the clinical treatment of the disease. Improvements in DNA-testing technology, specifically Southern blot methodology, have facilitated definitive identification of the human papilloma virus (HPV) as the etiologic source of RRP.[6] This scientific progress is encouraging for the future enhanced care and treatment of patients with RRP.

The most common HPV types involved in RRP are HPV-6 and HPV-11. It is important to note that the HPV infection occurs in epithelial cells and is not located in any layer deeper than the epithelium. This, of course, plays an important role when it comes to surgical removal of RRP. Equally important regarding the surgical treatment for RRP is a study by Steinberg et al[7] that identified the HPV in normal-appearing mucosa in patients with RRP. This finding had the impact of directing the surgeon to not use the axiom that "more is better" when treating RRP surgically.

Clinical Presentation

When the diagnosis of RRP, juvenile or adult, is made, it is important to establish thorough lines of communication with the patient and/or the family regarding the nature of the disease and future treatment. The involved individual(s) should be offered comprehensive education regarding background

knowledge of RRP, including information regarding RRP support groups, specifically, the Recurrent Respiratory Papillomatosis Foundation (www.rrpf.org). The importance of this type of patient education and investment of time and energy cannot be overemphasized.

Patients with RRP are tremendously challenging. When aggressive recurrent disease is encountered, the surgeon and patient must delicately balance airway safety, the effects of multiple general anesthesia procedures, and quality of life and employment disturbance from the vocal dysfunction and procedural disability. This often requires extensive communication to ensure that the patient's and surgeon's goals are mutually aligned.

Patients who have respiratory papillomatosis of the glottis most frequently present with hoarseness. Commonly, the glottal disease is confined to the musculomembranous region, although it is not unusual to find extension in the interarytenoid region, ventricle, and subglottis. Exophytic disease can lead to stridor and airway compromise, especially in children.

Treatment

It is important to remember that RRP is typically not cured with surgical removal of the disease. Thus, a more aggressive resection does not result in an improved chance for a cure or a decreased chance for recurrence. The general behavior of the disease usually leads to eventual recurrence. Therefore, all surgical treatment, regardless of the methodology of the removal, should be based on the principles of precise, conservative removal of the disease. The importance of gentle, precise surgical debulking/removal is paramount to the surgical management of RRP.

Ideally, surgical intervention should be done by individuals with high-level expertise in microsurgical procedures of the larynx. Successful management is dependent on skilled operating room supporting staff, communication with anesthesiology colleagues, and availability of current microsurgical instrumentation. This includes current laryngoscopes[8] and hand instruments as well as angled telescopes.[9] It is crucial that the surgeon be facile with several surgical techniques to remove the disease because the different regions of laryngeal mucosa often require different surgical approaches and instrumentation (CO_2 laser, microsurgical cold steel, and microdebrider).

Approaches for surgical removal of RRP are controversial; instrumentation should be individualized and selected with care to optimize precision. It must be emphasized that RRP is an epithelial disease and that it is critical to preserve the underlying superficial lamina propria (SLP) and other vital structures, such as anterior commissure tendon and vocal process. Furthermore, the natural history of RRP is that it recurs, which usually necessitates multiple procedures in the lifetime of a patient. These factors must be omnipresent in the surgeon's mind because the preservation of normal laryngeal tissue will facilitate optimal function for the future, since a medical solution will ultimately be conceived. At present, the preferred treatment technique of glottic RRP is microsurgical cold steel excision[10] using phonomicrosurgical treatment equipment and techniques (Fig 1A to D).

Microlaryngoscopy for RRP should be performed with the largest possible laryngoscope for optimal visualization of the disease and surgical removal.[8] An important adjunct for evaluating and subsequently treating patients with RRP during microlaryngoscopy is the use of angled telescopes through the suspended laryngoscope.[9] The 30° and 70° telescopes are of special importance for visualizing the undersurface of the true vocal fold, ventricle, anterior commissure, and posterior glottis. The telescopes can also be helpful during RRP resection and are important for establishing the adequacy of treatment at the completion of each surgical session.

Subepithelial infusion[11] enhances phonomicrosurgical management in a number of ways. The infusion positions the disease toward the center of the laryngoscope, which improves visualization and precise surgical removal. In addition, the disease is separated from important, delicate underlying layered microstructures (SLP), which should be preserved during surgical removal of the RRP.

Adjunctive treatment options for RRP have been appealing for years, especially given the recalcitrant and recurrent nature of the disease. This is especially true because of the conceptual understanding that RRP is an infectious process, a

viral infestation of the upper aerodigestive tract mucosa, that surgery does not fully eradicate. Adjunctive treatments are all presently done on an experimental basis.

Photodynamic therapy has been studied extensively; however, to date there is no conclusive evidence demonstrating either a high degree of success or a cure.[12] Furthermore, side effects with earlier, older photosensitizing agents have been severe. Research is being done with newer agents that will, it is hoped, be effective and have minimal side effects. More recently, pulsed-dye laser photoangiolysis of the microcirculation associated with papillomatosis offers an exciting new surgical treatment that may allow for clinic treatment of selected patients and enhanced vocal outcomes.[13]

Indole-3-carbinol (I3C) has been used for RRP with moderate success.[14] I3C is a chemical found in high concentration in cruciferous vegetables (cabbage, broccoli, cauliflower, and Brussels sprouts) and has been found to be active in modulating estrogen metabolism that affects HPV activity. In addition, I3C has been shown in the laboratory to suppress RRP growth in vitro, as well as to reduce RRP growth in an animal model. A prospective, open-label clinical study demonstrated significant reduction of RRP new growth in one third of patients with no adverse side effects. I3C is taken orally and appears to successfully suppress new papilloma growth in a significant portion of patients with RRP.

Intralesional injection of cidofovir is the most recent adjunctive/experimental treatment for RRP.[15] Cidofovir is a known antiviral agent that is approved by the Food and Drug Administration for cytomegalovirus retinitis. Preliminary experience with intralesional injection of the RRP disease with cidofovir has been highly favorable. However, no long-term results with respect to side effects, complications, and cessation of treatment have been demonstrated. A multicenter, prospective randomized trial is planned in the near future for this promising treatment option.

RRP continues to be an extremely challenging disorder for patients, their families, and clinicians. However, significant advances in HPV viral research and the subsequent adjunctive treatments hold great promise for the future. At present, surgical management must be regarded as primarily palliative, and this has been greatly enhanced by using techniques of modern-day phonomicrosurgery for precise and conservative microsurgical removal of papilloma disease. Advancement of the field of experimental/adjunctive treatment for RRP is dependent on future research funding efforts and the ethical use of new methods. Specifically, experimental treatments should be applied in a systemic and methodic fashion as opposed to anecdotal and trend-based options.

MANAGEMENT OF THE WHITE VOCAL FOLD LESION

Background

When confronted with a white lesion on the vocal fold, the surgeon is often confronted with a myriad of management dilemmas. Is the lesion malignant? Should the lesion be biopsied or just followed closely? If a biopsy is performed, should it be a complete excision or a random biopsy? If the pathology report is consistent with a nonmalignant diagnosis, how should the patient be managed? Are there any medical options to reduce the frequency of recurrence? Adding to the confusion is the natural tendency for these lesions to partially or completely regress, stabilize without further progression, or progress to malignant degeneration. Furthermore, white lesions may be found in association with a variety of other benign laryngeal lesions including vocal fold polyps, nodules or cysts, laryngeal papillomas, and granulomas.

Clinical Presentation

There have been a variety of clinical terms to describe white lesions of the vocal fold: *leukoplakia, hyperkeratosis, keratosis, pachydermia,* and *epithelial hyperplastic lesion.* However, it is very difficult to accurately predict which white lesion will progress into carcinoma based solely on clinical appearance. Studies have shown that the surface appearance bares little correlation with the underlying histopathology.[16] Simple hyperplasia, dysplasia, and/or carcinoma can all coexist in the same lesion. Despite this, there are a few clinical signs that are suggestive of invasive carcinoma. Furthermore, stroboscopy has not been a reliable method of determining the presence of cancer or

the depth of invasion if cancer is known to be present.[17] In decreasing order of importance, ulceration, erythroplasia, surface granularity, increased keratin thickness (verrucous appearance), increased size, recurrence after excisional biopsies, and long duration have all been associated with carcinoma.[16]

Histopathologically, white lesions on the vocal fold may be classified as hyperplasia, metaplasia, or dysplasia. Dysplasia has been further classified as being mild, moderate, or severe. In mild dysplasia, one sees simple hyperplasia with a more or less extended keratosis but without actual dysplastic changes or mitotic figures and cellular atypia. In moderate dysplasia, there is hyperplasia with or without keratosis but with cellular atypia. With severe dysplasia, there is significant cellular atypia present in various epithelial layers without extension beyond the basement membrane (as seen in carcinoma in situ).

There have been a number of recent studies examining whether histopathologic and/or immunohistochemical factors can predict progression from dysplasia toward infiltrative carcinoma. Eventual progression to carcinoma has been reported in approximately 2% to 12% of mildly dysplastic lesions, 9% to 33% of moderately dysplastic lesions, and 13% to 44% of severely dysplastic lesions.[18,19] In addition, recent studies with immunohistochemical markers, such as the Ki-67 nuclear protein, Langerhans cell density, proliferating cell nuclear antigen (PCNA), *p53* suppression gene, and CD44 glycoprotein tumor immunohistochemical analysis, have shown future potential in accurately predicting progression to carcinoma.[20-22] However, further study on a larger series of patients is warranted before any firm recommendations can be made regarding the use of these markers on a routine clinical basis.

Treatment

The initial management of a patient with a white lesion on the vocal fold should begin with a determination of whether this is a low- or high-risk lesion based on history and physical examination. Tobacco and ethanol abuse, occupational risk factors, diet and vitamin deficiency, irradiation exposure, viral exposure (ie, HPV), and laryngotracheal reflux have all been[23,24] epidemiologically associated with laryngeal carcinogenesis. Therefore, the patient needs appropriate counseling regarding these risk factors as part of the overall treatment plan.

A 1-month trial of conservative measures is reasonable in the absence of any worsening of vocal symptoms, an enlarging lesion, or clinical signs suggestive of invasive carcinoma. Conservative measures include instructing the patient on proper hydration, reduction of dehydrants (ie, caffeine and alcohol), and elimination of any vocal abuse tendencies. The patient is also strongly advised to stop smoking and/or to seek treatment for their ethanol abuse. Other risk factors, such as laryngotracheal reflux, also need to be addressed at this time.

Chemoprevention with retinoids, selenium, and other agents is still controversial. However, a recent report evaluated the clinical response to retinol palmitate for laryngeal hyperplasia with an induction dose of at least 300,000 IU followed by a maintenance dose of 150,000 IU.[25] There was a complete response in 75% of the patients and a partial response in the remainder. None of the lesions progressed to cancer.

One principal drawback to using retinoids is that the lesions tend to recur when treatment is discontinued. Also, there may be significant side effects due to mucocutaneous toxicity. In addition, recent reports suggest an increased incidence of lung cancer when beta-carotene was used for primary cancer prevention in heavy smokers.[26,27] Therefore, patients need to be cautioned regarding potential adverse side effects.

Radiation therapy has not been shown to prevent the progression of dysplastic lesions to carcinoma; in fact, it may even precipitate malignant degeneration. Therefore, radiation therapy should be reserved for carcinoma in situ or invasive carcinoma.

If the patient does not improve with conservative measures, then an excisional biopsy is performed (Fig 2A to D). Due to the multicentricity of cancer in hyperplastic lesions, random biopsies are discouraged. Excisional biopsy is performed with special emphasis on preserving the structural integrity of the deeper uninvolved layers of the vocal fold and surrounding normal mucosa.[16] Routine "vocal fold stripping" is not advised.

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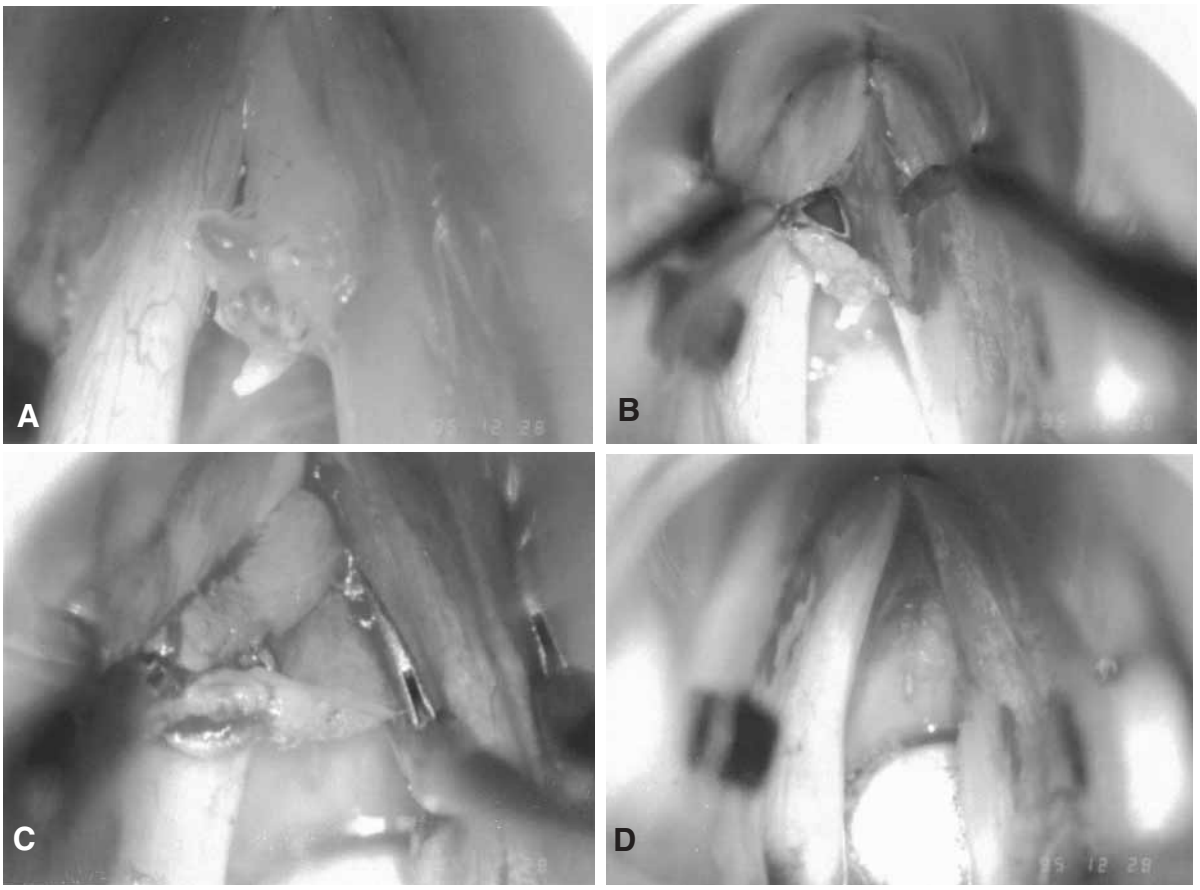

Fig 1. **A,** An exophytic single focus of papilloma on the right vocal fold is seen subsequent to subepithelial infusion of saline solution and 1:10,000 epinephrine into the superficial lamina propria. **B,** The lesion is retracted as a microflap, and a dissector is used to sweep the superficial lamina propria from the basement membrane back to the patient. Note the lack of bleeding secondary to the infusion. **C,** The microflap containing the lesion is retracted, and an upturned scissors is used to complete the excision. **D,** The lesion has been completely resected.

In the absence of carcinoma, most hyperplastic lesions occur on the superior or ventricular surface of the vocal fold.[16] Therefore, dissection onto the phonating edge of the vocal fold is often not necessary for complete excision. The lesion is carefully dissected off the deeper layers of the lamina propria using precise phonosurgical technique. This minimizes the chances of adversely affecting vocal function due to extensive vocal fold fibrosis. At the completion of the surgical procedure, the specimen is labeled and sent for serial section to avoid missing a focus of carcinoma.

Difficulty in dissecting the lesions off the deeper layers of the lamina propria or vocalis muscle suggests an invasive carcinoma or significant fibrosis from prior surgery. With carcinoma in situ or invasive carcinoma, a more generous resection of mucosa and/or underlying ligament and muscle may be necessary (ie, a cordectomy). However, the patient has to be advised that the degree of permanent vocal fold dysfunction is proportional to the amount of vocalis muscle removed. Also, anterior commissure involvement may adversely affect oncologic outcome with transoral endoscopic resection if the lesion cannot be adequately exposed.[28] Therefore, in this scenario, radiation therapy may be more advisable.

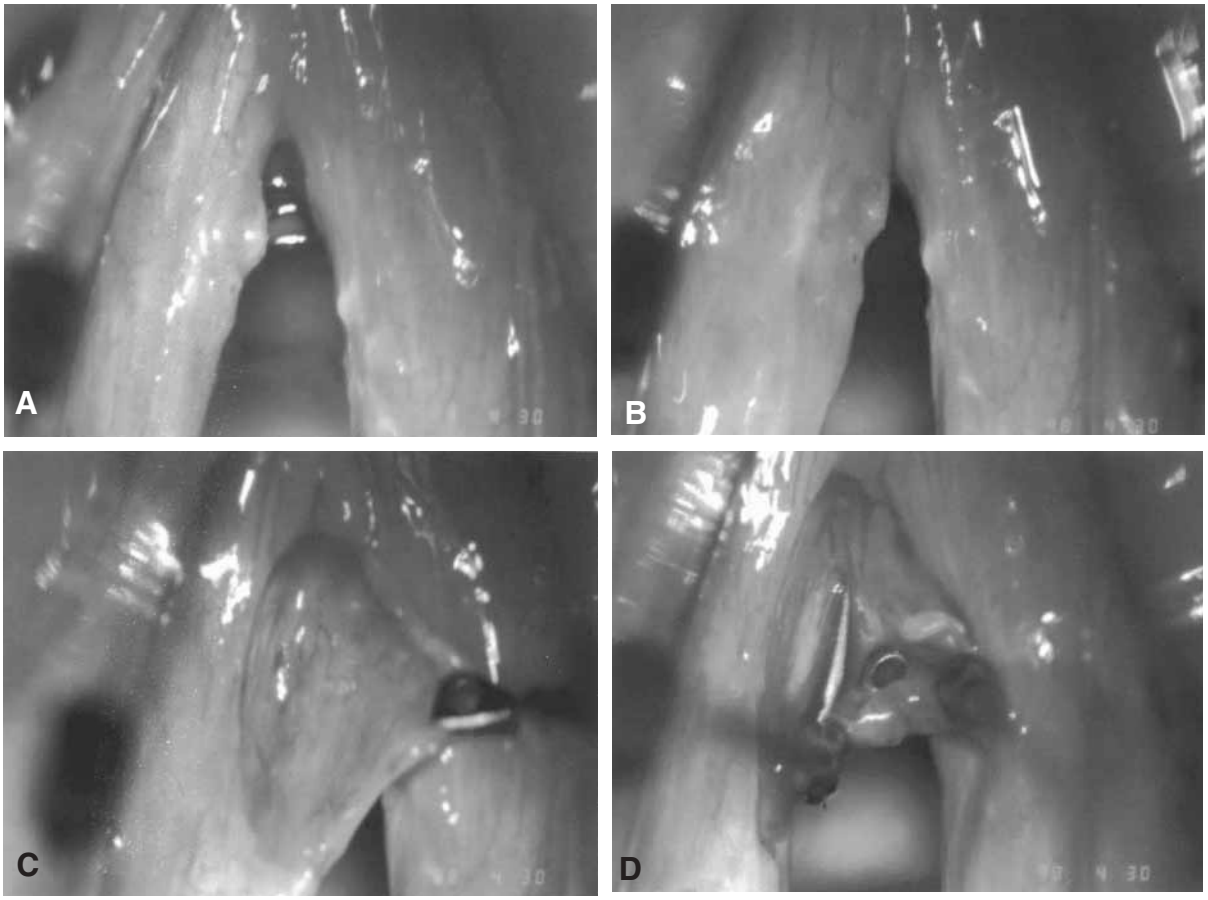

Fig 2. **A,** There are bilateral irregular lesions of the superior and medial surface of the vocal folds. There is a T1, N0, M0 squamous cell carcinoma on the left and keratosis with atypia on the right. **B,** A subepithelial infusion of saline solution and epinephrine has been placed on the left. **C,** The dissection within the normal superficial lamina propria is performed to encompass the entire left lesion. The dissection on the medial and subcordal surface has not begun yet. **D,** The microinvasive carcinoma is excised at its caudal margin with an upturned scissors.

ARYTENOID GRANULOMAS

Background

Contact ulcers and granulomas were the first laryngeal conditions to be related to reflux disease.[29] In addition to laryngopharyngeal reflux, authors writing on the topic have implicated many other etiologic factors, including vocal trauma/abuse, chronic throat clearing, endotracheal intubation, and vocal fold paresis.[30-32] In most cases, the etiology of granulomas is multifactorial, and several underlying etiologic factors may be present in an individual patient. Vocal fold granulomas are common and relatively recalcitrant to therapy, and surgery alone is seldom effective.[32] To achieve successful long-term outcomes, each of the underlying causes needs to be identified and corrected.

Clinical Presentation

For patients with granulomas, the history is important and should focus on the onset of symptoms and findings. Pain and odynophonia are more common than significant vocal change. Did the granuloma occur after intubation, trauma, or viral infection? The granuloma patient should be routinely evaluated for signs and symptoms of laryngopharyngeal reflux and for glottal closure problems. Symptoms associated with the latter are effortful phonation, vocal fatigue, breathiness, and odynophonia. At Wake Forest Medical Center,

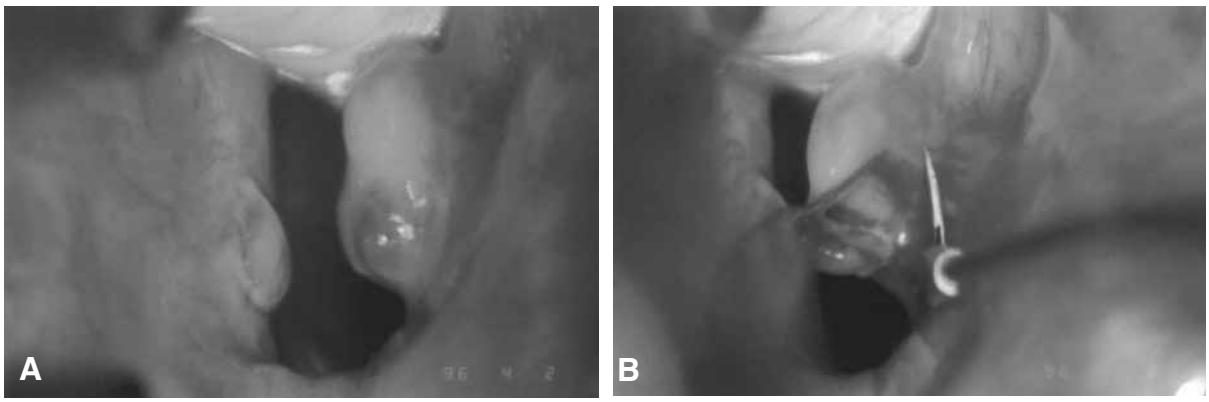

Fig 3. A, Bilateral granulomas are seen. The endotracheal tube is positioned anterior to the laryngoscope. **B,** Subsequent to a subepithelial infusion, the granuloma is retracted and an upturned microscissors is used to resect the lesion without disturbing the arytenoid perichondrium.

most granuloma patients now undergo a complete medical evaluation that includes (1) fiberoptic laryngoscopy, (2) acoustical (voice laboratory) analysis, (3) laryngeal electromyography, and (4) reflux (pH) testing.

Fiberoptic laryngoscopy is important to evaluate for subtle movement disorders consistent with a diagnosis of vocal fold paresis. In addition, laryngeal biomechanics are assessed to determine the potential role of abusive vocal behaviors. Acoustical analysis is performed primarily to rule out vocal fold paresis. In many cases of paresis, closure on electroglottography in the unloaded phase will drop into the 30% to 40% range. This is characteristic of glottal insufficiency, regardless of the cause.

With increasing frequency, we perform laryngeal electromyography on granuloma patients. Finally, ambulatory double-probe (simultaneous esophageal and pharyngeal) pH monitoring is performed. When this comprehensive diagnostic battery is used, we have found that many patients have more than one underlying cause for their granulomas.[32]

Treatment

Treatment options include voice rest, voice therapy, antireflux therapy, surgical removal (Fig 3*A* and *B*), botulinum toxin injections, and medialization laryngoplasty.[32-35] The remainder of this section is devoted to the Wake Forest algorithm for management of arytenoid granulomas.

Most patients with granulomas will show signs and symptoms of laryngopharyngeal reflux. With or without reflux testing, if such signs and symptoms are present, we recommend use of a double-dose proton pump inhibitor, with the first dose being given in the morning before breakfast and the second in the afternoon before the evening meal. Many patients with granulomas will have resolution on antireflux treatment alone; however, it is not unusual for such granulomas to take 6 to 8 months to resolve.[32] Patients with granulomas are seen in the clinic approximately every 2 months, and if there is no improvement based on the laryngeal examination, the dose of proton pump inhibitor is increased. (We have used doses of omeprazole as high as 40 mg 4 times a day in some patients with granulomas.) At high doses, if treatment still seems to be failing, repeat pH testing is carried out to evaluate drug efficacy, and in some cases fundoplication is recommended. The key to successful antireflux management in this group of patients is to not assume or expect resolution within the first few months of treatment.

Some patients exhibit chronic throat clearing and abusive vocal behaviors. In these cases, voice therapy by a trained speech-language pathologist is indicated. In addition, patients who have persistently abnormal biomechanics should be evaluated for vocal fold paresis. It has been our experience that many such patients have underlying vocal fold paresis and that the abnormal biomechanics are

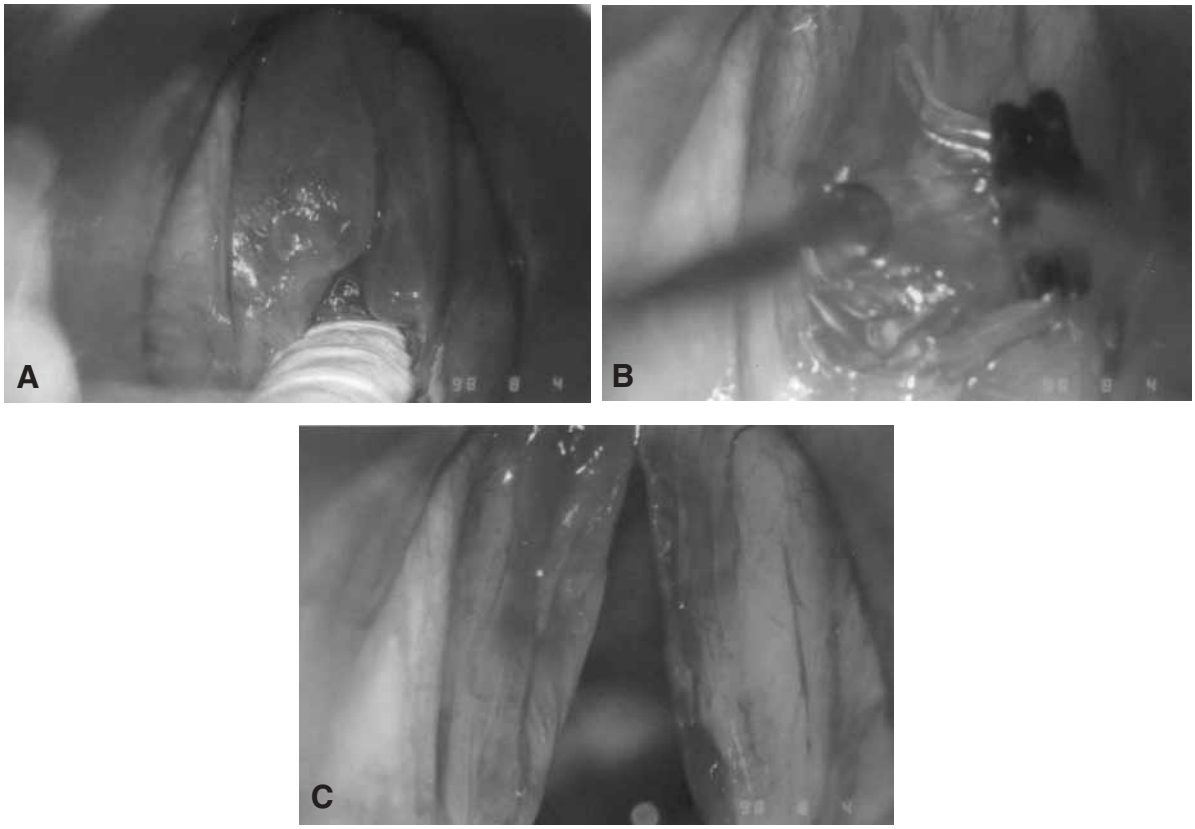

Fig 4. A, This patient presented with severe polypoid corditis ("Reinke's edema"). She had laryngeal sleep apnea, as well as a fundamental frequency of approximately 90 Hz. **B,** A microsuction is used to remove the relatively acellular swollen tissue for more normal contouring. **C,** The image in **B** at a higher magnification. There is excellent apposition of the epithelial edges, and the vocal folds are more appropriately contoured. (All images are courtesy of Singular/Thompson Learning.)

compensatory for an underlying hypokinetic laryngeal condition.[33]

It has been recommended that botulinum toxin injection be used for recalcitrant granuloma cases.[34] We have used this treatment and found it to be effective in selected cases. It is, however, still important to attempt to identify each of the underlying etiologies; otherwise, granuloma recurrence is likely. For patients who appear to have chronic abusive behaviors wherein repeated trauma is believed to be a crucial factor in a recalcitrant granuloma, we use 15 IU of botulinum toxin in the ipsilateral thyroarytenoid muscle. Others use low-dose (2.5 IU) bilateral injections. We wish to emphasize that the routine use of botulinum toxin injection as a primary treatment is not appropriate.

The most controversial area of granuloma management is surgical removal. In our opinion, there are 4 indications for surgery: (1) airway obstruction, (2) to rule out carcinoma (in selected cases), (3) when the granuloma matures and becomes a fibroepithelial polyp, and (4), on rare occasions, to restore the voice in a patient who needs prompt voice restoration.[32] When surgical removal is performed, it is important to avoid reinjury to the perichondrium. In addition, for granuloma surgery, we recommend using jet ventilation so that endotracheal intubation may be avoided.

We do not use intralesional depo-steroid injections, because such injection may delay epithelialization. Once a granuloma is removed, a race is on between granulation, which comes from the depths of the wound, and epithelialization, which occurs

from the edges of the wound. Although it has been debated whether cold knife versus laser is preferable, we usually use the laser to excise these relatively vascular lesions without any apparent problems.

Within the past decade, we have identified a number of patients with recurrent vocal process granulomas that have underlying vocal fold paresis. In some of these cases, unilateral and/or bilateral medialization laryngoplasty has been carried out with a successful resolution of the granulomas.[36] In one notable case, the patient had had granulomas removed 7 times over a 3-year period. We performed bilateral medialization laryngoplasty for bilateral vocal fold paresis 5 years ago, and there has been no recurrence of granuloma since that time.

In summary, arytenoid granulomas are common, have a multifactorial pathogenesis, and often are recalcitrant to therapy. Identification and management of each of the underlying factors are important to achieve successful treatment outcomes.

REINKE'S EDEMA

Background

Reinke[37,38] described the potential space that bears his name in 1895. Its anteroposterior boundaries are the anterior commissure tendon and arytenoid vocal process, whereas the vocal ligament is deep to Reinke's space. Hirano[39] referred to this region as the SLP, which is underlying the vibratory epithelium. Excessive swelling of this space is known as *Reinke's edema, polypoid corditis, polypoid laryngitis,* or *polypoid degeneration.*

Histopathologic analysis of the tissue reveals that decreased amounts of fibronectin, collagen, and elastin are evident in the basement membrane and lamina propria. The vocal fold is more deformable.[40] Thickening of the epithelial basement membrane, edematous lakes, and increased vessel wall thickness are also seen.[41] The initiating trauma leading to the edema is thought to be injury to the capillary endothelium with subsequent extravasation of fluid into the potential space.

Clinical Presentation

Individuals with polypoid corditis describe the gradual onset of a rough and abnormally low-pitched voice (females, < 130 Hz; males, < 110 Hz) because the mass-loaded folds oscillate at an inordinately low frequency. Females present more frequently than do men and undergo phonomicrosurgical management more frequently because of the greater discrepancy from their normal fundamental frequency (180 to 230 Hz).

Typically, Reinke's edema presents as extensive swelling that is situated on the superior surface of the musculomembranous vocal fold. It has a multifactorial genesis; these patients typically smoke extensively, have laryngopharyngeal reflux, and demonstrate vocal hyperfunction.[42] Hypothyroidism must also be ruled out. The swelling probably occurs from the increased aerodynamic pressures that drive vocal fold mucosal oscillation in a general environment of glottal mucositis, which is secondary to smoking and reflux. The swelling is typically bilateral but often asymmetric in volume. Airway symptoms are unusual if the arytenoids abduct normally, because the edema is confined to the anterior glottal aperture. Epithelial pliability and mucosal wave characteristics vary greatly between patients and are dependent on the viscoelasticity of the pathologic SLP. Some individuals have hyperdynamic pliable waves, and others, who have sustained severe phonotrauma, demonstrate poor pliability and mass motion of the epithelium and pathologic SLP. When the edema is extensive, it can potentially obscure an occult malignancy.

Treatment

Treatment of Reinke's edema begins with elimination of predisposing risk factors. These individuals should discontinue smoking, have their reflux controlled, and undergo preoperative vocal therapy before undergoing a procedure.[42,43] Systemic steroids are not routinely used to treat Reinke's edema, and topical beclomethasone has not been shown to be effective.[44] Patients should be advised that if they continue to smoke, the problem will not resolve without surgery and will likely recur subsequent to surgical resection.[43] Many surgeons will not operate on patients with Reinke's edema if they continue to smoke unless there is concern that cancer may coexist with the polypoid condition. However, extensive edema may obscure the identification of an early malignancy in the office, so

that some individuals will undergo earlier microlaryngoscopic intervention if keratosis is noted.

Surgery has been the mainstay of treatment for Reinke's edema. Vocal-fold stripping[46] was designed as a one-handed, unmagnified treatment for Reinke's edema by means of a monocular laryngoscope and without general anesthesia. Unfortunately, this procedure is imprecise, and frequently, excessive SLP and epithelium are removed. This can result in a prolonged period of healing and, often, stiff scarred vocal folds. Although the vocal folds appear normal by means of a mirror or fiberoptic examination, stroboscopy reveals loss of epithelial pliability and lack of vibration.

In 1985, Hirano et al[47] described a more precise technique that involves incising the epithelium lateral to the polypoid area, elevating the mucosa as a flap, reducing the gelatinous matrix within the SLP that forms the bulk of the abnormal vocal fold, redraping the flap, and trimming the excess mucosa (Fig 4A to C). A microscissors is used for the initial incision unless there is prominent subepithelial vascular injection, in which case the CO_2 laser[48] can be advantageous. The gelatinous hypertrophied SLP should then be carefully contoured and reduced to a more normal volume. This can be done by suctioning or by direct removal. Great care must be taken not to overreduce the SLP, which results in an inordinately stiff vocal system.[42] The vocal ligament should never be visualized directly. Overreduction of the SLP can result in a severely strained harsh voice, because these individuals already use high subglottal pressures to drive their floppy mass-loaded folds. Vocally, it is preferable to leave a larger fold than to create a visually pleasing smaller fold.

Once the SLP has been reduced, the epithelium is redraped and trimmed appropriately. There are varied opinions as to whether both vocal folds should be worked on simultaneously. Exuberant resection of epithelium and SLP anteromedially may leave 2 opposed raw surfaces at the anterior commissure, which can lead to web formation. If the incisions and dissection are confined to the superior surface of the vocal folds, bilateral procedures were not associated with complications.[28,42]

Microflap cytoreduction avoids removing excessive amounts of mucosa, and healing time is therefore shortened.[49] If leukoplakia/keratosis or another suspicious process involves the mucosa, that tissue should also be removed for pathologic examination. This may cause a defect to be present that will lengthen the healing time. After an initial period of vocal rest of about 10 days, patients should receive vocal therapy and be monitored closely. Preventing recurrence is dependent on modification of the predisposing factors, especially smoking.

Control of the medical factors along with surgical resection will usually elevate the fundamental frequency of female patients to approximately 150 Hz, which is commensurate with the normal fundamental frequency for female smokers.[42] Patients should also undergo a course of voice therapy postoperatively because the biomechanics of the glottal sound production has been radically altered and they have become accustomed to phonating with excessive subglottal pressure.[42] Courey et al[50] and Zeitels et al[42] demonstrated that normal mucosal waves are rarely restored despite the use of Hirano's microflap technique.

In summary, Reinke's edema has a multifactorial genesis and the majority of surgical procedures are performed on women due to the fact that they sustain greater discrepancy from normal phonatory characteristics. Successful management requires control of risk factors: smoking, phonotrauma, and reflux and precise surgical technique.

UNILATERAL VOCAL FOLD PARALYSIS

Background

There is currently a vast array of treatment options for unilateral vocal fold paralysis (UVFP), although fundamentally these options fall into 1 or more of 4 categories: (1) voice therapy, (2) injection laryngoplasty, (3) laryngeal framework surgery, or (4) reinnervation or pacing. The many treatment options are a testament to the diligence with which laryngologists, speech pathologists, and others have pursued rehabilitation of this clinical problem. They are also a reminder that the ideal treatment for UVFP, the ability to reconstitute physiologic vocal fold movement, is not yet established.

Advances in recent years have come primarily in the form of refinements or modifications to existing procedures, but there are some notable

examples of truly pioneering investigation. The following brief review of recent literature is divided according to the broad treatment categories stated above and focuses on voice restoration.

Clinical Presentation

Vocal fold paralysis has been one of the omnipresent laryngologic management problems since the origin of the specialty. Patients present with varied vocal function and accompanying aerodynamic dysfunction. This has stimulated a large body of literature over the past 140 years that attempted to explain this variability. At present, the observed inconsistent resting position of the arytenoid and, in turn, the musculomembranous vocal fold is believed to be secondary to (1) residual innervation,[51] (2) unpredictable reinnervation and synkinesis,[52] and (3) atrophy (described in 1872[53]) and fibrosis of denervated muscles.[54] These factors also determine the final position, contour, length, mass, and aerodynamic viscoelasticity of the vocal fold.

Treatment

Voice therapy. Recent literature continues to reflect the fact that laryngologists and speech pathologists believe voice therapy plays a significant role in the treatment of patients with UVFP. In particular, many patients with less severe dysphonia or better glottic closure have favorable outcomes with voice therapy alone, and preoperative or postoperative voice therapy can help facilitate voice recovery in more severely dysphonic patients who are treated surgically.[55] Indeed, Isshiki[56] recently said that "Phonosurgery sometimes works as pump-priming to facilitate the voice therapy that follows."

Injection laryngoplasty. Although recent clinical trends reflect that there is an increasing use of laryngeal framework surgery over injection techniques for treating UVFP, there continues to be a role for injectable implants in the temporary and permanent less common treatment of this problem. Both the technique of injection and the nature of the injected material have received attention in current literature.

Several authors have demonstrated the value of blending the old with the new by performing indirect injection laryngoplasty using topical anesthesia on the awake and upright patient with modern video laryngoscopy equipment together with traditional injection devices.[57-59] Efficiency, cost, avoidance of anesthetic risks, and the ability to actively monitor voice in a relatively normal phonatory posture are some of the proposed advantages of indirect techniques.

In the canine vocal fold, Stein et al[60] explored the histopathologic and migratory properties of 4 different injectable alternatives for vocal fold medialization: Teflon (Polytef Paste; Mentor Inc, Norwell, MA), autologous fat, silicone suspension, and hydroxylapatite cement. The silicone suspension caused the most intense inflammatory response, whereas Teflon resulted in chronic inflammation with detectable regional lymph node migration. The authors did not see significant inflammation with hydroxylapatite or fat, and the fat was preserved at 6 months from injection. Issues with the persistence of viable fat do remain, however, as Saccogna et al[61] found no significant graft survival 12 months after lipoinjection into the feline vocal fold. Research continues with a variety of injectable substances, such as autologous collagen[62] or fascia.[63]

Laryngeal framework surgery. The type I thyroplasty or medialization thyroplasty, explored in detail originally by Isshiki et al[64] has received much attention in recent years. It continues to be the most commonly used laryngeal framework procedure and most frequent intervention for paralytic dysphonia. Implant composition, development of standardized kits, pediatric application, and treatment outcomes were some of the areas of recent interest.

Cummings et al[65] designed the VoCom System (Smith and Nephew Richards, Memphis, TN), which uses preformed hydroxylapatite prostheses for medialization of the musculomembranous region of the vocal fold, and Montgomery et al[66] developed the Montgomery Thyroplasty Implant System (Boston Medical Products, Westborough, MA) with preformed wedge-shaped Silastic prostheses.[66] Limited tissue reactivity and implant stability are proposed features of the VoCom System,[67] whereas the Montgomery implant was specifically designed with an extended posterior

flange to medialize the vocal process of the arytenoid cartilage.

A bioimplant with a long history of use in cardiovascular surgery, expanded polytetrafluoroethylene (ePTFE [Gore-Tex]; W.L. Gore & Associates, Inc, Flagstaff, AZ) has also been used in medialization thyroplasty[68,69] and was recently described in conjunction with arytenoid adduction.[69,70] These groups describe favorable voice results, a straightforward surgical technique, and the safety of an implant material that has stood the test of time in other surgical disciplines.

Recently, type I thyroplasty was reported in the pediatric population,[71] and it was indicated that standard methods for determining the vocal fold level and window placement in adults were not accurate in children. These authors found that implants were frequently placed too high if adult guidelines were used, and they suggested an intraoperative method for determining vocal fold level using visualization of needles passed through the thyroid ala. They concluded that pediatric type I thyroplasty is an evolving procedure.

Using aerodynamic and acoustical data, Lundy et al[72] compared short- versus long-term voice results with type I thyroplasty. Although preoperative versus postoperative data showed significant differences, they found no statistically significant differences between the 1-month versus the >1-year postoperative assessment points. A validated voice outcomes tool, the Voice-Related Quality of Life measure was also recently used to assess outcomes with the type I thyroplasty. Dramatic differences in Voice-Related Quality of Life were seen when patients with untreated UVFP were compared with patients who had undergone a type I thyroplasty.[73] A survey conducted by Rosen[74] struck a cautionary note about the surgical learning curve, as major complications were more frequent for surgeons who had performed <10 procedures in their career.

Surgical manipulation of the arytenoid cartilage itself is likely the second most commonly performed laryngeal framework procedure. Originally described by Isshiki et al,[75] many authors favor arytenoid adduction for closing large posterior glottal gaps. Noordzij et al[76] used an excised canine larynx model to study the biomechanics of arytenoid adduction and concluded that it medialized and lowered the vocal process of the arytenoid but did not increase vocal fold stiffness in the middle musculomembranous region. In keeping with this finding, most recent literature has primarily discussed the use of arytenoid adduction in conjunction with other procedures such as medialization thyroplasty that act more on the musculomembranous vocal fold.[69,70,77,78] Indeed, it has become commonplace in the literature to refer to an anterior subunit consisting of the musculomembranous vocal fold and a posterior subunit consisting of the arytenoid cartilage and attached muscles.

Citing the fact that arytenoid adduction does not simulate the synchronous agonist-antagonist function of each of the intrinsic laryngeal muscles, Zeitels[69] introduced the adduction arytenopexy as a new procedure effecting favorable arytenoid position in UVFP. This operation involves opening the lateral aspect of the cricoarytenoid joint and manually medializing the arytenoid on the cricoid facet. The arytenoid cartilage is thus drawn posteriorly, superiorly, and medially and is fixed precisely with a suture. The authors combine this procedure with medialization thyroplasty to address both anterior and posterior subunits and more recently have incorporated cricothyroid joint subluxation as an adjunctive procedure.[69,79] The cricothyroid subluxation procedure is the sole static reconstructive procedure for UVFP that is primarily designed to adjust for tension in the denervated musculature, which has a different resonant frequency for optimal vibration. With this innovation, most patients will obtain 2 octaves of dynamic frequency range.[79] Woodson et al[80] also appreciated the importance of agonist-antagonist muscle activity in arytenoid position and noted improvement in arytenoid posture after arytenoid adduction, which included a supplemental posteriorly oriented anchoring suture.

Laryngeal reinnervation or pacing. The quest for methods to functionally reinnervate the paralyzed larynx continues. Nerve transfer procedures are currently the most widely used reinnervation operations, although reinnervation in general is much less commonly used than laryngeal framework surgery.

Very good voice results with the ansa cervicalis to recurrent laryngeal nerve transfer, a procedure originally reported by Fisher[81] and subsequently popularized by Crumley,[82] have been presented recently by several authors.[83,84] Using perceptual and acoustic analyses, Olson et al[84] concluded that results were excellent for patients with isolated laryngeal paralysis but suboptimal for patients with coexistent nonparalytic laryngeal pathology or extralaryngeal pathology that may affect vocal quality.

Exciting new work is under way in attempting to apply gene-based therapy to the problem of UVFP. Flint et al[85] recently reported success in limiting damage to laryngeal neuronal and muscular tissues after denervation using a novel, non–viral-mediated insulin-like growth factor I (IGF-I) gene transfer system. A plasmid containing the human IGF-I gene sequence was locally transferred into denervated rat laryngeal muscle fibers, inducing IGF-I production. Compared with control denervated animals, IGF-I–transfected animals had a significant increase in the lesser diameter of muscle fibers, a significant decrease in motor endplate length, and a significant increase in the percentage of endplates with nerve contact. They were unable, however, to determine whether the increase in neural elements observed in treated animals was due to preservation of original nerve fibers or to regeneration and nerve sprouting.

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