Five years after successfully completing the world’s first total larynx transplant, The Cleveland Clinic continues to explore differing means of expanding the procedure to a greater range of patients. Protocols for the current procedure require life-long immunosuppression. Chronic immunosuppression carries significant morbidity and mortality risks and has limited laryngeal transplants to selected patients.

The induction of either partial or complete immunological tolerance to grafted tissue would alleviate, perhaps eliminate, both the burden and risks of chronic immunosuppression. Two separate efforts in this direction arrived at two separate findings. The first experiment involved treating the graft recipient with an immosuppressant and a monoclonal antibody immediately prior to the transplant and for five days following the procedure. The results of this experiment suggest that a functional tolerance that obviates the need for long-term immunosuppression can be induced in animals and deserves further exploration to assess its clinical potential. This work has been accepted as a Rapid Communication for publication in Transplantation.

The second experiment attempted to explore the utility of donor-specific transfusion (DST) in the rat model of laryngeal transplants. This protocol involves introducing the graft recipient’s immune system to allograft antigens prior to the transplant and for five days following the procedure. The results of this experiment suggest that a functional tolerance that obviates the need for long-term immunosuppression can be induced in animals and deserves further exploration to assess its clinical potential. This work has been accepted as a Rapid Communication for publication in Transplantation.

Experiments Indicate Immune System Can Be Induced To Accept Laryngeal Grafts

Marshall Strome, M.D.
From the Chairman

Dear Colleagues:

The Cleveland Clinic Department of Otolaryngology and Communicative Disorders has experienced tremendous growth during the past few years. Our professional staff has grown to 32 full-time faculty, representing one of the largest otolaryngology programs in the United States.

As we continue to build upon a foundation of excellence in the science and practice of otolaryngology, our goal remains to provide the highest quality care for adult and pediatric patients with routine or complex ear, nose and throat problems.

During the past year, the demand for services grew, resulting in an increase in patient visits and surgical procedures. Despite the increased clinical activity, faculty members contributed nearly 100 scientific publications to peer-reviewed medical journals, were appointed to offices in national societies and journals, received numerous awards and grants, and served frequently as visiting professors.

Our commitment to research as the foundation for innovative patient care and the future development of our specialty was exemplified when one of our residents was recognized by our national academy for submitting the best overall research grant in 2002.

This issue of Otolaryngology Advances details only a small subset of the work and accomplishments of our esteemed faculty. We are delighted to share this publication with our colleagues and friends across the country.

Sincerely,

Marshall Strome, M.D., M.S., F.A.C.S.
Chairman & Professor, Department of Otolaryngology and Communicative Disorders

Immune System Can Be Induced To Accept Laryngeal Grafts

continued from page 1

ings indicate that immunological tolerance is limited locally to the transplanted larynx. This tolerance, albeit localized, mitigates the need for chronic immunosuppression. This is believed to be the first report of induced functional tolerance without extensive recipient preconditioning in a laryngeal model.

The work with induced immunosuppression is proceeding. The mechanisms of localized immunologic acceptance need to be described, as the potential clinical implications of the phenomenon are substantial.

Awards/Honors/Offices...

Marshall Strome, M.D.
President, Society of University Otolaryngologists
One of a group recognized as International Scientists of the Year

Daniel Alam, M.D.
Jack Anderson Award, AAFPRS
(Highest board exam score in the nation)

Martin J. Citardi, M.D.
Board of Directors, American Rhinologic Society

Ramon Esclamado, M.D.
President, Northeast Ohio Society of Otolaryngology — Head and Neck Surgery

Catherine Henry, M.D.
Past President, American Medical Women’s Association

Keiko Hirose, M.D.
Eugene I. Derlacki Award from the American Hearing Research Foundation

Peter Koltai, M.D.
Secretary, American Society of Pediatric Otolaryngologists

Donald Lanza, M.D.
President, American Rhinologic Society

Craig Newman, Ph.D.
Associate Editor, Journal of the American Academy of Audiology

Peter Weber, M.D.
Board of Directors; Board of Governors Executive Committee; Co-chairman, Cherry Blossom Conference; American Academy of Otolaryngology — Head and Neck Surgery
Editor, American Journal of Otolaryngology
The Use of Endoscopic Anterior Skull Base Resections for Sinus Malignancy

Donald Lanza, M.D., Martin Citardi, M.D. and Pete Batra, M.D.

Recently we reported a growing experience using the minimally invasive approach for the surgical management of sinus cancers. In combination with radiation and, occasionally, chemotherapy, early survival rates are comparable to more traditional techniques.

Sinus cancers are relatively rare but when they do occur, they can have a devastating impact on life and may include disfiguring treatments. Due to the proximity of the paranasal sinuses to vital structures (eye and brain), these cancers are often impossible to remove with wide surgical margins. Traditional management of these lesions has typically required open removal during combined surgery with both a neurosurgeon and otolaryngologists performing an anterior craniofacial resection.

Now, we are able to endoscopically resect the cribiform plate (skull base) through the nostril without any facial or scalp incisions. Computer-aided surgery has become an integral part of these procedures. Using small portions of cartilage from the septum and ear, the skull base is reconstructed to prevent the brain from herniating down into the nasal cavity. Postoperatively, many patients go on to radiation therapy. Success with these techniques is very promising as discussed in a portion of this abstract presented to the American Rhinologic Society in September 2002:

In conjunction with a colleague from the University of Pennsylvania (William E. Bolger, M.D.), we reported on 15 patients who fulfilled the study criteria and had a minimally invasive endoscopic approach with or without combined neurosurgical resection. The 15 patients included the following types of cancer:

- Squamous cell carcinoma (SCCa) – five
- Malignant melanoma – two
- Adenocarcinoma – two
- Adenosquamous carcinoma – one
- Meibomian gland carcinoma – one
- Leiomyosarcoma – one
- Chondrosarcoma – one
- Ethesioneuroblastoma – one
- Spindle cell carcinoma – one

The mean age was 60.4 (26-78) years and mean follow-up period was 24.8 months. Combined XRT with or without CTx, pre- or postoperatively was given to 13/15 patients. Ten patients were resected solely with an endoscopic approach, and five patients in combination with neurosurgery. There were no peri- or postoperative deaths. The local recurrence was 20.0% (3/15) including 2 patients with malignant melanoma and one patient with SCC who died due to cavernous sinus invasion. The distant metastatic rate was 20.0% (3/15) including 2 patients with malignant melanoma and one patient with leiomyosarcoma. Overall survival was 80.0% (12/15) at mean follow-up duration of 29.5 (4-74) months. Eleven patients remain free of disease (73.3%, 11/15) by clinical, endoscopic, and radiographic (CT or MRI) surveillance. Their mean duration of follow-up was 30.5 months.

Minimally invasive endoscopic resection of sinonasal malignancies, with or without combined neurosurgery, and in combination with adjunctive therapies yields improved morbidities as well as local recurrence, overall survival, and disease-free survival rates that are comparable to traditional anterior craniofacial approaches in combination with adjuvant therapies. We can now report five-year survival employing an endoscopic approach.

Introducing New Staff

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Intracapsular Partial Tonsillectomy Effective in Removing Large Tonsils

Cleveland Clinic physicians have developed a new power-assisted technique for intracapsular partial tonsillectomy, which shaves away a portion of the tonsils rather than completely excising them. The procedure results in less pain and quicker recovery. This procedure is performed primarily on children whose tonsils are so large that it disrupts their breathing, causing sleep apnea, rather than those who have frequent throat infections.

Peter Koltai, M.D., head of the Section of Pediatric Otolaryngology of The Children’s Hospital at The Cleveland Clinic, developed the technique, wherein he uses a micro-debrider to shave away tonsil tissue.

During the procedure, most of the tonsil is trimmed, leaving a small amount of tonsil tissue and the capsule that separates the tonsil from the muscle beneath. There is a lower incidence of bleeding and the rapid recovery means children can return to school and activities sooner.

A study of intracapsular “partial” tonsillectomy by Drs. Koltai, Tom I. Abelson, M.D., head of Cleveland Clinic Beachwood Otolaryngology, and others was recently presented at a national meeting. The study found no significant differences in complications—both operations were effective in correcting sleep-disordered breathing. But, children who had partial tonsillectomy had significant less postoperative pain and a more rapid recovery.

Section of Pediatric Otolaryngology Update

Keiko Hirose, M.D.

To respond to increasing demand for services, the Section of Pediatric Otolaryngology is adding staff and space. Paul Krakovitz, M.D., who recently completed a fellowship in pediatric otolaryngology at the Clinic, has been appointed to the staff. Plans are underway to create a new pediatric otolaryngology clinic, complete with child-friendly waiting and surgical scheduling areas and easy access to audiology.

Development of new technology to diagnose and treat pediatric otolaryngology problems as well as researching causes of these problems continues to be a focus of the Section.

Peter Koltai, M.D., is working on a new ultrasonic probe to assist in the diagnosis of middle ear effusion in children. The probe is being developed to distinguish the difference between an aerated middle ear and a fluid-filled middle ear. Preliminary studies have demonstrated its effectiveness; a phase two study will involve more subjects to validate its use in clinical practice. (See the article about Dr. Koltai’s power-assisted intracapsular partial tonsillectomy procedure on this page.)

My research continues to focus on the role of inflammatory mediators in hearing loss after cochlear damage. We have found that while the inner ear has often been considered a region of immune privilege, it appears that inflammatory cells do enter the ear after cellular damage. It is likely these cells play an important role in the outcome of the cochlea. By understanding the role inflammation has on inner ear damage, we hope to someday intervene with agents that address the specific mechanism of hearing loss in children with acquired hearing loss.

Tinnitus Management Clinic Provides Patients with Coping Strategies

Craig Newman, Ph.D. and Sharon Sandridge, Ph.D.

When severe tinnitus interferes with a patient’s ability to cope with everyday life, staff members in the Tinnitus Management Clinic at The Cleveland Clinic offer a variety of management approaches to provide relief. The goal of the Clinic, staffed by a team of otolaryngologists, audiologists and psychologists, is to move patients from an intolerant to a tolerant state of tinnitus.

The first step is to rule out health conditions requiring medical or surgical intervention. Following clearance by an otolaryngologist, the patient is referred to audiology for interventional rehabilitation.

The program begins with a 90-minute group education session during which a variety of topics are discussed. Patients learn how the hearing mechanism works, the prevalence of tinnitus, possible causes, common reactions and treatment options.

When needed, individual follow-up appointments are scheduled with audiologists and psychologists. Audiologists assess tinnitus impairment (actual perception of the tinnitus signal), as well as disability and handicap. A variety of psychoacoustic and self-reporting methods are used to evaluate the quality and dimensions of the tinnitus by assessing pitch, loudness, maskability and residual inhibition. A standardized, self-reporting test developed at The Cleveland Clinic, known as the Tinnitus Handicap Inventory, is used to obtain a baseline measurement against which treatment outcomes can be evaluated.

The main focus is intensive counseling using strategies borrowed from tinnitus retraining therapy and tinnitus masking. Sound therapy intervention may be performed using assistive devices, hearing aids and/or sound generators. For selected patients, treatment options include biofeedback therapy and cognitive-behavioral therapy.

How to Refer Patients

Physicians can schedule appointments for their patients in the Cleveland Clinic Department of Otolaryngology and Communicative Disorders by calling 216/444-6691 from 7 a.m. to 11 p.m., seven days a week, or toll-free at 800/553-5056.

Visit our Web site at clevelandclinic.org/otol/
Adult Subglottic Stenosis Responds To A Modified Pediatric Procedure
Isaac Eliachar, M.D. and Nathan Sautter, M.D.

The Cleveland Clinic's Section of Laryngotracheal Reconstruction is pioneering a minimally invasive treatment for adult subglottic stenosis that preserves the voice, stabilizes the airway, and may substantially reduce the need for the retreatments that are common to other approaches.

Adult subglottic stenosis is challenging. Both endoscopic resection with dilation and open laryngotracheal reconstruction, the two primary treatment approaches carry risks, are associated with complications and often require retreatment. Minimally invasive endoscopic resection and dilation are effective for mild to moderate subglottic stenosis but benefits are often temporary. Open laryngotracheal reconstruction with cartilage grafting is a common approach to moderate to severe stenosis. The procedure is extensive and is associated with large incisional scars, voice changes and extended recovery. Many patients harbor co-morbidities that contribute to unsatisfactory results, high complication rates and failures.

The ideal treatment would be minimally invasive, preferably endoscopic, voice preserving and reversible. The procedure would burn no bridges.

The Clinic has extensive experience with an approach that meets these criteria but that experience has been confined to pediatric patients. Success with the ‘cricoid split’ procedure in managing pediatric subglottic stenosis induced the Laryngotracheal Reconstruction Section to tailor the approach to adults. Preliminary results of an adult anterior cricoid split procedure with placement of a silicone spacer graft are promising.

Maximal narrowing is most frequently encountered at the level of the cricoid ring. The cricoid cartilage is the only fully circumferential ring in the laryngotracheal complex (or skeleton). It is also the most resistant to treatment by dilation.

The procedure begins with a small horizontal skin incision made over the cricoid arch. The cricoid cartilage is split vertically with the integrity of the inner perichondrium being preserved. The undermining of the mucoperichondrium is extended laterally for a few millimeters on inner margins of the split cartilage to allow the insertion of a specially designed spacer graft. The graft, which resembles a railroad track, is inserted to expand the circumference of the cricoid arch (see illustration). The procedure may be accompanied by endoscopic injections of long-acting steroids and topical application of Mitomycin-C.

The split incision of the cricoid ring allows the stenosed segment of the larynx to be dilated gently with progressive, monitored balloons or conical dilators. The cricoid ring’s circumference can be expanded to a greater extent than is permitted with other procedures. Retreatments are less frequent. It is possible that they may be eliminated. If followup treatment is indicated, it is anticipated that dilations will be more effective due to the expanded cartilaginous skeleton.

Three patients with moderate to severe subglottic stenosis have undergone this procedure with excellent and stable results. None has required repeated dilations with followups ranging from five to 12 months. Postoperative CT scans confirm silicone graft stability with no evidence of migration, rejection, or damage to the cricoid arch cartilage. There have been no inflammatory responses within the laryngeal wall. The patients’ voices have been preserved. The silicone spacer does not incorporate into the cartilage and appears to be amenable to future treatments if indicated. The small scar is easily hidden.

This minimally invasive method may find its place as a preferred treatment for adult subglottic stenosis. Although not a cure, the treatment stabilizes the airway at physiologically safe and comfortable levels for extended followup periods. Research is continuing.

For information, contact Dr. Isaac Eliachar, Head, Section of Laryngotracheal Reconstruction, 216-444-8231 or by email: eliachar@ccf.org.

Skin incision exposes the cricoid arch which is split down to the inner perichondrium

Dilatation of the subglottic stenosis

Undermining of inner perichondrium followed by placement of spreader stent

After drain placement, wound is closed in layers
Meet Our Staff

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Reflux, whether gastroesophageal, laryngopharyngeal, or nasopharyngeal, has been associated with a multitude of laryngeal symptoms and findings such as reactive airway disease, otitis media with effusion and sinusitis. A myriad of laryngeal signs, including posterior commissure bar, arytenoid erythema, postcriocoid edema, true vocal cord lesions, obliteration of the ventricles and pseudosulcus, and others have been attributed to injury from reflux.

Close collaboration between the Cleveland Clinic Department of Gastroenterology (Michael Vaezi, M.D., and Joel Richter, M.D.) and Otolaryngology (Douglas Hicks, Ph.D., Tom I. Abelson, M.D. and Claudio Milstein, Ph.D.) is producing a plethora of data which, when complete, will hopefully help elucidate the specificity and sensitivity of laryngeal findings in relation to reflux.

In a recently published study in the *Journal of Voice* (16:4, 564-579, 2002), with Dr. Hicks as lead author, 86 percent of normal subjects without laryngeal symptoms of reflux had findings attributed to reflux. Thus the traditional attribution of hypopharynx irritation signs to reflux is challenged: the need for improved diagnostic specificity is highlighted. A comprehensive review of the subject, discussing pH studies (including pharyngeal pH), impedance studies, and animal work will be published soon in the *Journal of Clinical Hepatology and Gastroenterology* with Dr. Vaezi as lead author.

Data are now being analyzed from a large group of patients referred with hypopharyngeal findings and symptoms of laryngopharyngeal reflux (LPR). These patients have had recorded laryngeal endoscopy and pH monitoring, followed by four months of treatment with b.i.d. proton pump inhibitor followed by repeat recorded endoscopy. An important aspect of the above work is the inclusion of both inter-observer and intra-observer comparisons of the endoscopic exams.

With a combination of animal studies, carefully documented human protocols, evaluation of rater reliability and very close cooperation between the departments of Gastroenterology and Otolaryngology, we hope to help to delineate when reflux is, in fact, the cause of otolaryngologic complaints and findings.

Normal larynx and hypopharynx.

Appearance in GERD patient.