Dendritic cells in laryngeal transplantation

In 1998, Marshall Strome, M.D., and his team at Cleveland Clinic successfully performed a total laryngeal transplant in a human laryngeal trauma victim. Many other patients have lost their larynges too — not just to trauma, but also to cancer. While most patients are potential and willing laryngeal allograft candidates, the increased risk of malignancy associated with post-transplant immunosuppression remains problematic.

Dendritic cells (DC) are potent antigen presenting cells that may be the prime instigators of allograft rejection. They exist in virtually every tissue in the body, both lymphoid and nonlymphoid. Little is known about their resting distribution in the larynx, let alone what their role is following laryngeal transplantation. In theory, they make up a portion of the classically described “passenger leukocyte” population that is inevitably transferred from donor to recipient with any type of allograft. Under the guidance of Dr. Strome, and in collaboration with the Cleveland Clinic Lerner Research Institute Imaging Core, otolaryngology resident Aaron Friedman, M.D., took some preliminary steps toward unshrouding the mystery behind these crucial cells.

First, the location of DC within an animal model was assessed carefully. Advanced techniques for \textit{in situ} cell identification including immunofluorescence, confocal microscopy and computerized image analysis were employed to enumerate these cells within epithelial, subepithelial, and previously unanalyzed regions of the rat laryngotraheal complex (Figure 1). Next, using Dr. Strome’s extensively studied rat laryngeal transplantation model, allografts were performed and the patterns of DC migration during the immediate postoperative period were quantified. The application of simultaneous monoclonal antibodies allowed the investigators to track DC originating from donor vs. recipient animals (Figure 2).

It was discovered that DC are concentrated near the airway lumen. Mucosal densities slightly exceeded submucosal values. Only minimal quantities were found in other previously unexplored sites such as the parathyroid gland, thyroid gland, paraglottic fat and intrinsic laryngeal musculature. Moreover, no DC were identified within cartilage. As antigen-presenting cells, the proximity of DC to the airway is somewhat expected given their immune surveillance role and the constant exposure of the respiratory tract to inhaled antigens. Knowledge of such a distribution may allow the use of aerosolized vehicles for influencing DC responses to airway infection, asthma or laryngeal transplantation.

\textbf{Fig. 1: Confocal fluorescence image of rat subglottis, 3-D reconstruction.} Nuclei (blue), dendritic cells (red), elastin autofluorescence (green). $E = \text{epithelium, } BM = \text{basement membrane, } SE = \text{subepithelium.}$

Continued on page 3
TRIBUTE TO MARSHALL STROME, M.D.
By Tom I. Abelson, M.D., Medical Editor, Otolaryngology Advances

This space always has been filled with a yearly update from Marshall Strome, M.D., Chairman of the Head and Neck Institute. Dr. Strome announced last year he would step down from this position, and Michael S. Benninger, M.D., has been chosen to be the institute’s next Chairman (see back cover). It is with sadness over Dr. Strome’s departure and pride in his accomplishments that both this column and the entire issue of Otolaryngology Advances are dedicated to him.

After Dr. Strome joined Cleveland Clinic’s Department of Otolaryngology and Communicative Disorders in August 1993, the department grew dramatically and eventually earned the designation Head and Neck Institute. The growth has been manifested in sections specifically designed to encompass the breadth and depth of staff expertise, which allow both productivity and mentoring of junior faculty. The institute has been a model for the four cornerstones of Cleveland Clinic’s mission: patient care (clinical and hospital), research and education.

Below is a summary of some of Dr. Strome’s accomplishments, but he would probably say that he is most proud of his family and the family of people who work in the institute. And he knows the people. He knows the names of the custodial and maintenance staff and most others whose faces frequent our floors. He has actively supported and promoted the careers and professional development of his physician and research staff, as well as nurses and other support staff.

During Dr Strome’s tenure, the staff has increased from seven to 32. There are now 133 people working within the institute.

One of the cornerstones of Dr. Strome’s mission for the institute focused on research by residents, faculty and dedicated researchers. One year of the residency has been dedicated entirely to research, and our residents have won the most prestigious research awards in the country. Many of them later sought careers in academic medicine. In addition, Dr. Strome initiated a competitive resident research day as part of the two days of events during graduation ceremonies each spring.

In the last two years, members of the institute have produced 240 publications, and the faculty has had more than 1,000 academic contacts, including publications, courses, visiting lectureships, professorships, awards and honors.

Dr. Strome is especially proud of having expanded the Otolaryngology Regional Practice staff, opening offices in Cleveland Clinic family health centers in six Cleveland suburban locations and in Florida. His successful integration of faculty from these facilities to the main campus is a model for Cleveland Clinic.

Dr. Strome’s professional accomplishments are well-known. He performed the first laryngeal transplant, developed many other significant innovations, authored more than 200 scientific publications, received a multitude of national and international awards and led many professional organizations and meetings.

While we will miss the prodigious scientific and leadership qualities that Dr. Strome possesses, it is Dr. Strome the caring, engaged person that the Cleveland Clinic family will miss the most.
DC also were distributed in an increasing craniocaudal gradient, with tracheal values exceeding supraglottic densities. The glottis, however, exhibited dramatically fewer DC. This may explain why croup is clinically confined to specific regions of the airway.

Following laryngeal transplantation in rats, donor DC migrated to recipient cervical lymph nodes as early as 12 hours postoperatively and reached a nadir within 3 to 5 days. These cells also were identified in cervical lymph nodes of recipient animals from 12 hours to 5 days postoperatively, ensuring that migration (rather than cell death or loss of cell surface markers) was occurring. Conversely, recipient DC infiltrated the laryngeal allograft, reaching a maximal density by day 7. The timing of these events helps to explain the investigators’ previously documented result that a week-long course of postoperative immunosuppression followed by no additional anti-rejection medication prevents significant laryngeal allograft rejection in rats for several months. This data, in turn, may translate into more optimized immunosuppression regimens for future human laryngeal transplant patients.

In the setting of head and neck malignancy, however, laryngeal transplantation following total laryngectomy will only take root if systemic immunosuppression can be minimized or if donor-specific immunosuppression can be achieved. Dr. Strome and his research team are continuing in these efforts. Now that the early kinetics of postoperative DC migration have been elucidated, steps toward manipulating this process can begin. By inhibiting donor DC efflux, preventing recipient DC influx, or perhaps a combination of the two, laryngeal allograft tolerance in the absence of generalized immunosuppression may become a reality. Moreover, the culture and preoperative administration of donor DC to the recipient has shown promise in other allograft systems, and adaptation into the laryngeal model is currently under way.

Figure 2: Immunofluorescence (IF) staining of 3 monoclonal antibodies in laryngotracheal allograft recipients sacrificed at 12 hours and 7 days postoperatively. Co-staining of cells allowed for differentiation of donor vs. recipient-derived DC. Hematoxylin and eosin (H & E) stained slides are 16 μm away from the corresponding IF slide. Images shown are from tracheal ring 4.

**Key Points:**

- Dendritic cells (DC) are potent antigen-presenting cells that may be the prime instigators of allograft rejection.
- Laryngeal transplantation following total laryngectomy will only take root if systemic immunosuppression can be minimized or if donor-specific immunosuppression can be achieved.
- By inhibiting donor DC efflux, preventing recipient DC influx, or perhaps a combination of the two, laryngeal allograft tolerance in the absence of generalized immunosuppression may become a reality.
Genetic Testing and Counseling are Now Available for Patients with Head and Neck Paraganglioma

Physicians caring for patients with head and neck paraganglioma are encouraged to refer them to Cleveland Clinic for genetic testing. At most, a positive result can be lifesaving because it will tell caregivers that a patient’s relatives may be at risk for familial paragangliomas — including vagal paragangliomas and glomus jugulare, glomus tympanicum and carotid body tumors. At the least, a negative result can put a family’s mind at ease. In either case, the benefit is worth the effort.

“The point of this simple blood test is to look for specific genetic mutations that are associated with hereditary paragangliomas,” says Robert Lorenz, M.D., Section Head of Head and Neck Oncologic Surgery. “When we find such a mutation in a patient, we can alert his or her family members that they may be at risk. If the relative is also positive, we can begin a monitoring program. If the relative does develop the disease, we will be able to detect it at the earliest possible moment.”

Dr. Lorenz and colleague Charis Eng, M.D., Ph.D., Head of Cleveland Clinic’s Genomic Medicine Institute, established the screening program in spring 2007, and they have received a favorable response. Says Dr. Lorenz, “Patients have thanked us and told us things like, ‘I never knew this test existed. I’ve been living in fear that my kids will get this tumor, too.’ Well, there’s no point in fearing the unknown. It’s better to know for sure.”

“For people who test positive, we can set up a schedule for regular magnetic resonance imaging scans, urine screens, other follow-up tests and family screening,” he continues. “On the other hand, people who test negative won’t ever have to worry about this again, nor will their children.”

So far, Drs. Lorenz and Eng have screened 20 patients or family members of patients, and they have identified a positive result in 6.

All testing includes counseling

Counseling is an integral part of the screening process. Before any blood is drawn, the individual meets with Dr. Eng and a genetic counselor. Another meeting takes place when the results become known.

“Pre- and post-test counseling are crucial,” says Dr. Lorenz. “You should never just perform a test and disclose the results without having adequately prepared a patient. You need to have a qualified person lead them down the road. A counselor makes the patient aware of all the possible outcomes and the implications of each. When a test is negative, the counselor can explain exactly what that means. When a test is positive, the counselor can initiate the long-term monitoring process.”

Drs. Eng and Lorenz examining MRIs of a patient with multiple head and neck paragangliomas.
The nature of the mutations

The mutation responsible for paragangliomas occurs in one of the genes that encodes certain succinate dehydrogenase (SDH) subunits. SDH is an enzyme involved in the mitochondrial respiratory chain complex II, and it has four subunits (A, B, C, and D). Mutations in three of these subunits (B, C, and D) have been reported in individuals with hereditary paragangliomas and pheochromocytomas. These tumors may also be seen in association with syndromes caused by mutations in the VHL, RET, or NF1 genes.

While a standard history may identify only 10% of patients with hereditary paraganglioma, studies have shown that testing for the SDH gene will demonstrate a mutation in up to 28% of cases. In addition, patients positive for a mutation in SDH subunit C are at increased risk for thyroid and kidney cancer at a young age.

These mutations are passed on in families by autosomal dominant transmission. As a result, each child of a carrier has a 50% chance of inheriting the abnormal copy. A maternal imprinting effect has been observed in families with SDH subunit D mutations, so the children of a woman with an SDH-D mutation will not be at increased risk of developing a paraganglioma, even if they inherit the mutation and can pass it on to their own children.

Expanding the database

As part of a research project, Drs. Lorenz and Eng are also offering genetic testing to more than 400 untested paraganglioma patients who were previously treated at the Cleveland Clinic Head and Neck Institute.

“If you have a patient with a paraganglioma and you don’t know if it’s hereditary or not, please give us a call,” says Dr. Lorenz. “This is especially important if your patient is younger than 50 or has multiple tumors.”

Key Points:

- Genetic testing for patients with head and neck paraganglioma can be lifesaving.
- Pre- and post-test counseling are an integral part of the screening process.
- Testing for the SDH gene will demonstrate a mutation in up to 28% of cases.
Hot-and-Cold Running Success: Laser/Cryoablation Procedure is Superior to Traditional Treatment for Early Glottic Carcinoma

Thanks to a combined procedure, patients undergoing treatment for early-stage glottic carcinoma enjoy significantly better and quicker voice restoration.

The procedure, which was pioneered by Marshall Strome, M.D., Chairman of Cleveland Clinic Head and Neck Institute, involves the addition of cryoablation to standard CO2 laser resection. Data accumulated thus far reveal that patients treated with the combination procedure experience less perioperative inflammation, less scarring and less deposition of collagen. What’s more, the collagen that is present is less dense and histoarchitecturally amenable to vocal fold mobility. As a result, patients end up with more pliable vocal folds and better phonation. Moreover, the incidence of anterior glottic web formation in patients with anterior commissure involvement is lower. Finally, cure rates are comparable to those of laser therapy alone and radiotherapy (~90%).

The addition of cryoablation adds only a few minutes to this outpatient procedure. “First, the tumor is lasered endoscopically until negative margins are confirmed by frozen-section biopsies,” says Claudio F. Milstein, Ph.D., a speech-language pathologist at Cleveland Clinic Voice Center. “Then the cryoprobe is applied to the tumor bed and slightly beyond. The tissue freezes instantly and thaws shortly thereafter. Patients are sent home with no restrictions on eating or speaking.”

An unexpected benefit

“Dr. Strome initially developed this combined procedure thinking that it would result in better disease control,” Dr. Milstein continues. “But we were pleasantly surprised to discover that the cryoablation resulted in a quicker recovery and better voice quality than we had expected. We started seeing excellent clinical outcomes, but the reason was not clear.”

To understand the mechanism behind these findings, Dr. Strome and colleagues conducted an experiment on 12 dogs. In each animal, one vocal fold was treated with laser therapy alone and the other was treated with laser and cryotherapy. Then histologic samples were analyzed and compared.

“What we found was very interesting,” Dr. Milstein says. “In the cryoablated tissue, we saw less inflammation, less keratinization, and more deposition of hyaluronic acid than we saw in the tissues treated with laser alone. Also, we found that freezing alters the histoarchitecture of the collagen fibers, as they are more organized—that is, cross-linked in a basket-weave pattern. These are key findings that revealed why the pliability of the vocal fold tissue is enhanced and less scar formation is observed.”

“As a result of our animal study, we started to understand why our surgical outcomes were so good. The combination of less inflammation, less collagen deposition, less-dense collagen and cross-linked fibers are all important for vocal fold vibration, mucosal waves and the resulting voice quality.”
Postoperative assessments

For 1 year postoperatively, patients are scheduled for follow-up every 2 months because if a recurrence does develop, it is most likely to do so within the first year. Thereafter, patients are seen every 3 or 4 months through year 4, and then twice a year during year 5.

“We keep a close eye on all our patients,” Dr. Milstein says. “Follow-up assessments are critical for early detection of possible recurrences. Even those patients who live outside the Cleveland area are asked to make a commitment to return for regular follow-ups.”

The postoperative assessments include videostroboscopy, a perceptual voice evaluation, and a patient self-rating:

- During the videostroboscopic examination, clinicians look for minute changes in vibratory patterns and mucosal waves.
- During the perceptual assessment, the patient’s voice quality is evaluated by staff clinicians.
- Finally, patients rate their own voice quality.

Findings are compared with preoperative baseline values, and the results are also tracked by serial evaluations throughout the course of follow-up.

Follow-up study

Thus far, the combined procedure has been performed on 48 patients—45 men and three women, aged 46 to 96 years (mean: 66.2). Of this group, eight patients (16.7%) had already failed previous radiation treatment. Also, 17 patients (35.4%) had involvement of the anterior commissure, which is noteworthy because these patients generally fare poorly with the traditional laser procedure. Ten patients (20.8%) had carcinoma in situ, 19 patients (39.6%) had category T1a disease, six patients (12.5%) were at category T1b, and 13 patients (27.1%) had a category T2 tumor. Follow-up ranged from 3 to 118 months (mean: 23).

Results

The greatest improvement in subjectively appraised voice quality occurred between months 3 and 6, and improvement continued for up to 18 months in some cases. On the self-rating, 36 patients (75.0%) said their voices were “much better” and seven (14.6%) said they were “somewhat better” than they were before the procedure. Only three patients (6.3%) reported “no change,” and two (4.2%) said they were “somewhat worse.” “Overall,” says Dr. Milstein, “patient satisfaction has been very high.”

The subjective findings mirrored the results of videostroboscopy. At 3 to 6 months, vocal fold vibrations and the resulting mucosal waves were much improved. Very little improvement was seen prior to the 3-month mark.

The recurrence rate with combined laser/cryotherapy is consistent with the rates for both laser alone and radiation alone. Five of our patients (10.4%) experienced a recurrence. All of these developed within the first year postoperatively, and all patients were re-treated with the same therapy. All five remain tumor-free today. It is noteworthy that none of these recurrences arose in any of the eight patients who had previously failed radiation therapy.

Finally, only two of the 17 patients (11.8%) with involvement of the anterior commissure developed an anterior glottic web, and one of those patients was already predisposed to keloid formation. “This is a significant finding because the literature shows that most patients with anterior commissure involvement who undergo laser surgery alone tend to develop a web,” says Dr. Milstein.

“Our finding that cryotherapy is associated with a dramatic reduction in anterior glottic webs is yet another important advantage of combination treatment.”

“In conclusion,” he says, “the combined procedure is not just a viable alternative to laser ablation alone or a 7-week course of radiotherapy. We believe that it will eventually become the primary modality for treating early glottic carcinoma.”

Key Points:

- The addition of cryoablation to laser surgery results in better and quicker voice restoration than does treatment with laser surgery alone or radiation.
- Combined laser/cryotherapy is available only at Cleveland Clinic.
- Not only are voice outcomes better, disease-control rates are comparable to those of traditional treatments.
- The incidence of anterior glottic web formation in patients with anterior commissure involvement is much lower with the combined procedure.
Researchers at the Cleveland Clinic Head and Neck Institute (HNI) have been studying the links between asthma and sinusitis during the last few years. Projects related to sinonasal polyposis have sought to uncover inflammatory pathways known to be active in asthma. Steven Cannady, M.D., Pete Batra, M.D., and Martin Citardi, M.D., collaborated with Serpil C. Erzurum, M.D., of the Cleveland Clinic Lerner Research Institute.

The effort represents the first such collaboration between the HNI and Pathobiology and Pulmonary, Allergy and Critical Care Medicine Departments. “This project was a unique opportunity to take the lessons learned from intensive research into the mechanisms of asthma inflammation and apply them to our field,” says Dr. Cannady. Dr. Batra added, “With this project, we have begun to narrow the gap in understanding between the asthmatic airway and the chronic inflammation associated with sinus disease.”

One airway hypothesis

Asthma is a major public health problem with a long history of research funding that has allowed a legacy of important discoveries into its pathophysiology. More recently, basic research into the mechanisms of inflammation in the chronic sinusitis sufferer has been conducted. It has long been recognized that asthma and chronic nasal conditions such as rhinitis, sinusitis and nasal polypsis occur together more frequently than by chance. In addition, many of the standard treatments for asthma mirror those utilized in chronic sinus disease. It stands to reason that some of the mechanisms that initiate and sustain asthmatic airway inflammation could be active in sinusitis. Proving the presence in nasal polyps of molecular signaling cascades present in asthma is an important initial step in linking the two diseases.

“The identification of common inflammatory mechanisms in asthma and sinusitis is paramount to understanding the nasal airway’s response to infection, chronic inflammation, and the origins of sinusitis,” says Dr. Citardi.

Translational research approach

Through NIH funding obtained by Drs. Cannady, Citardi and Batra through the Cleveland Clinic General Clinical Research Center, and an institutional grant, a translational research project was conducted. Healthy volunteers were recruited and compared with nasal polyp patients. Clinical data, laboratory studies and tissue samples were collected and compared on all patients enrolled in the study.

“Translational research is a great way to apply science from the lab bench to help understand patient disease in the clinic,” says Dr. Erzurum. “Given the large population of patients suffering from chronic sinusitis and followed at the Head and Neck Institute, this type of project was bound to result in some interesting data.”

More than 20 patients with chronic rhinosinusitis and nasal polyps were enrolled, as well as 10 healthy volunteers. Each patient enrolled was subjected to the sinonasal outcomes survey, had routine blood testing including tests for allergy, and underwent nasal brushings, lavage and biopsy (of polyp tissue or middle turbinate for disease and volunteers, respectively).

New findings uncovered in nasal polyposis

Signal transducers are responsible for translating a cell’s reaction to its environment into gene expression. As such, the Signal Transducers Activated on Transcription (STAT) class of transducers are a relatively new family found to be important in the body’s inflammatory and anti-proliferative response. STAT1 is a relatively specific responder to infection and cytokines linked to infection. It was found to be upregulated in the tissue of nasal polyp patients when compared with healthy nasal tissue. Immunostaining localized this expression to the epithelium and endothelium of polyps, suggesting that inflammation is active at the mucosa-air interface, and the site of inflammatory cell recruitment-blood vessels (Figure).

“STAT1 has previously been shown to be expressed at high levels in asthmatic airways, and in patients with cystic fibrosis. As a central signaling event, its activation results in gene expression and protein translation of inflammatory chemokines and cytokines found to be present in nasal polyposis. In some ways, it represented the discovery of the most upstream event in the polyp inflammatory cascade discovered to date,” says Dr. Cannady.

From there, a thorough investigation into downstream events was conducted, representing the first complete evaluation of these pathways in polyp tissue. Highlights of the findings included confirmation of low nitric oxide (NO) in polyp irrigations despite high iNOS enzyme production.
The paradox represented by low NO in the setting of activated machinery to produce the gas has always puzzled researchers in this field. Thus, we sought to determine why,” says Dr. Batra.

The substrates required for NO production were analyzed for the first time in nasal polyp tissue and found to be comparable to the levels in healthy volunteers.

“Once we established that the reason for low NO was not a supply problem, we needed to assess what was happening to the NO produced that could contribute to its low measured values,” Dr. Citardi says.

Expanding upon previous work by Dr. Citardi, nitrotyrosine, a marker of nitrosative damage to amino acids, was found to be elevated in polyps. In addition, superoxide dismutase (SOD), a critical enzyme for deactivation of reactive gases such as NO, was decreased in polyps. These findings comprised a plausible explanation for low NO despite STAT1 activation and iNOS expression. The NO gas was causing oxidative damage to the tissue of the nose with unchecked ability to counteract it with SOD.

“It is very interesting just how similar the findings uncovered during Dr. Cannady’s time in my laboratory are with those we have found in asthma. They are nearly mirror images,” says Dr. Erzurum.

“Interestingly, loss of NO by any mechanism has been associated with cell proliferation, and at least on the surface, could explain some of the proliferative phenotype seen in polyposis,” says Dr. Cannady.

**Significance of findings**

Identification of an upstream event such as STAT1 activation is an exciting finding. Not only does it provide evidence for similar biologic mechanisms in asthma and sinonasal polyposis, it provides a potential target for therapy.

“More specific therapy for sinonasal polyposis is on the horizon. The identification of STAT1 activation is one event that may allow us to target therapy in a more specific manner for airway inflammatory diseases,” Dr. Citardi says.

With the basic understanding afforded by this research, a clearer picture of the abnormalities involved in chronic nasal inflammation has emerged. “Other studies have identified portions of the pathway we have defined, but have not examined all factors that may affect it in one study. This was lacking in the literature up until now,” Dr. Cannady says.

Future studies are currently planned to assess whether external factors activate STAT1 or whether the transducer is activated constitutively. “The next set of studies of polyyp tissue will seek to understand if STAT1 represents a response of mucosa to its environment now, or a change in cellular mechanics that occurred distantly in the past,” says Dr. Batra.

“In asthma, one hypothesis of the disease pathogenesis is that of perfectly timed viral insult can alter cell signaling and setting up a perpetual inflammatory environment. The same could be true of sinus sufferers,” says Dr. Erzurum.

Regardless of what is found next, the findings already uncovered have unlocked a new avenue of investigation for rhinologists seeking to understand the pathogenesis of sinus disease.

**Key Points:**

- The Signal Transducers Activated on Transcription (STAT) class of transducers are a relatively new family found to be important in the body’s inflammatory and anti-proliferative response.
- Nitrotyrosine, a marker of nitrosative damage to amino acids, was found to be elevated in polyps. Superoxide dismutase, a critical enzyme for deactivation of reactive gases such as NO, was decreased in polyps.
- The identification of STAT1 activation may allow us to target therapy in a more specific manner for airway inflammatory diseases.
- Future studies are currently planned to assess whether external factors activate STAT1 or whether the transducer is activated constitutively.
Treatment of Benign Paroxysmal Positional Vertigo Continues to Evolve and Improve

According to Judith White, M.D., Ph.D., Section Head of Vestibular and Balance Disorders, office maneuvers to diagnose benign paroxysmal positional vertigo (BPPV) have improved. The Dix-Hallpike maneuver is now routinely performed with little or no neck extension. This technique improves tolerance by older patients who may have cervical arthritis or other limitations. Alternately, the “side-lying” test may be used, which is the first position in the Semont maneuver. The patient lies on his side and points his nose to the ceiling. No neck extension is needed and good stimulation of the posterior semicircular canal of the undermost ear is achieved. Visualization of the nystagmus can be aided by the use of infrared video or optical Frenzel lenses, which eliminate visual fixation.

Lateral canal involvement is more frequently recognized

The lateral (horizontal) canal is the second most common canal affected by BPPV. Lateral semicircular canal benign paroxysmal positional vertigo (LSC-BPPV) is characterized by nystagmus provoked by supine bilateral head turns and beating toward the undermost ear. There are two distinct subtypes of LSC-BPPV based on the direction of horizontal nystagmus during supine head turns: geotropic and apogeotropic. Geotropic LSC-BPPV beats toward the undermost ear on supine positional testing and is characterized by short latency and prolonged duration of horizontal nystagmus with poor fatiguability. Apogeotropic LSC-BPPV is characterized by similar short latency and prolonged duration horizontal nystagmus, but the nystagmus beats away from the undermost ear on supine positional testing. These two types may reflect the position of the otoconial debris in the lateral canal (Figures 1 and 2).

The diagnosis of lateral canal BPPV is improved by performing supine head turns. While Dix-Hallpike positioning is highly sensitive to posterior semicircular canal BPPV, it lacks sensitivity in LSC-BPPV. Positioning testing should include both Dix-Hallpike and supine positional testing in the head-centered supine, right-ear-down and left-ear-down positions. We generally perform the supine testing first, because the nystagmus observed when initially lying supine may be very helpful in identifying the affected canal. The head is then turned to the left and right while supine, and then the patient returns to sit and the Dix-Hallpike positioning is performed. The Dix-Hallpike alone was entirely negative in two published patient reports where horizontal nystagmus with lateral supine head turns reached 12 d/s and 16 d/s due to LSC-BPPV.

The identification of the involved ear in lateral semicircular canal BPPV can be especially difficult because the canals are coplanar, and nystagmus is seen in both lateral supine positions. Order effect and head tilt may affect the direction of nystagmus. In geotropic LSC-BPPV, the nystagmus is worse with the affected ear down. Treatment for geotropic LSC-BPPV consists of 360° roll maneuvers toward the unaffected ear beginning

Fig. 1: In left lateral geotropic semicircular canal benign paroxysmal positional vertigo, horizontal nystagmus beats toward the undermost ear in supine head turns.
According to Judith White, M.D., Ph.D., Section Head of Vestibular and Balance Disorders, office maneuvers to diagnose benign paroxysmal positional vertigo (BPPV) have improved. The Dix-Hallpike maneuver is now routinely performed with little or no neck extension. This technique improves tolerance by older patients who may have cervical arthritis or other limitations. Alternately, the "side-lying" test may be used, which is the first position in the Semont maneuver. The patient lies on his side and points his nose to the ceiling. No neck extension is needed and good stimulation of the posterior semicircular canal of the undermost ear is achieved. Visualization of the nystagmus can be aided by the use of infrared video or optical Frenzel lenses, which eliminate visual fixation.

with the patient in the supine position with the head flexed 0 to 30° and laterally rotated toward the affected ear, and proceeding in 90° increments every 30 to 60 seconds toward the unaffected ear. The Gufoni maneuver is also highly effective and is performed with the patient beginning in the sitting position and lying quickly to the unaffected side and then rotating the head 45° downward, maintaining the position for two to three minutes as described in Casani.

**Treatment for apogeotropic LSC-BPPV consists of a variety of maneuvers**

Identification of the affected ear can be more challenging in apogeotropic LSC-BPPV. Nystagmus is usually worse with the affected ear uppermost, and nystagmus is occasionally seen on assuming the supine position, which usually beats toward the involved side. The modified Gufoni maneuver can be performed with the patient beginning in the sitting position and lying quickly to the affected side and then rotating the head 45° upward, maintaining the position for 2 to 3 minutes, as described by Appiani. Anterior semicircular canal BPPV is a controversial entity. Some investigators suggest that torsional nystagmus has a downbeat component, in contrast to posterior canal, which has an upbeat component. Since the same maneuvers used to treat posterior canal BPPV appear effective for possible anterior canal involvement, the question may have more theoretical than clinical relevance, and has rarely been a consideration in our clinical practice.

Central nystagmus may be positional. Several cases of multiple sclerosis have presented to the vestibular section with paroxysmal downbeat nystagmus in supine testing. MRI studies revealed the diagnosis. Central pathology should always be a consideration in atypical, vertical nystagmus or in patients with persistent BPPV despite multiple repositioning attempts. In another case, persistent apogeotropic horizontal positional nystagmus was associated with an acoustic neuroma.

**Recurrence common after successful canalith repositioning for BPPV**

Treatment is commonly effective in eliminating the current episode, but does not prevent additional episodes. Although the average recurrence rate is approximately 15% per year, reported rates have ranged from 5% per year to 45% at 30 weeks. Recurrence usually affects the same ear as the original BPPV. Conversion between canals can occasionally occur, usually between posterior and lateral canals when the patient is retested with Dix-Hallpike positioning after canalith repositioning has been performed. It is heralded by the development of brisk horizontal nystagmus, and responds well to an immediate supine head roll maneuver toward the unaffected side.

Several studies have suggested that post-procedure instructions to keep the head elevated do not increase treatment efficacy, although conflicting reports are also published. Numerous centers continue to recommend post-procedure restrictions based on anecdotal experience.

*For references, please e-mail the editor.*

**Key Point:**

- Office maneuvers to diagnose BPPV have improved, along with treatment efficacy.
Studying Novel Techniques for Detection of HPV Infectivity in Squamous Cell Carcinoma Patients without a History of Alcohol or Tobacco Use

Tobacco and alcohol use are well-known and established risk factors for head and neck squamous cell carcinoma (HNSCC). However, there is a subset of HNSCC patients who do not report a history of tobacco or alcohol use. These patients comprise a unique population, and other etiologies for their HNSCC have been investigated. One such area of research is the role of human papillomavirus (HPV).

A recent article in the *New England Journal of Medicine* has shown HPV to be a risk factor for HNSCC. Furthermore, numerous reports have demonstrated a survival outcome advantage in patients with HPV-positive tumors. With the recent approval of the HPV multivalent vaccine for cervical cancer, research is ongoing as to the utility of such a vaccine against HNSCC in this patient population. Rapid and accurate diagnosis of patients with HPV-associated HNSCC will be critical to any therapeutic intervention targeting the virus.

HPV serotypes that have been associated with cancer development are 16 and 18. The incidence of these patients with HPV varies widely. Across published reports, HPV positivity varies from 20-90%. This variation may be due to the variety and sensitivity of the methods used to identify HPV. One of the most common methods is polymerase chain reaction (PCR). However, this method is known to be sensitive to contamination, and may be prone to false negatives. If accurate investigation of HPV-associated tumors is to be done, then it will be necessary to provide an accurate and sensitive method of determining HPV involvement.

Walter Lee, M.D., and colleagues in the Department of Pathology and the Head and Neck Institute, have recently presented research on detecting HPV using a new method in surgical samples at an international meeting in Barcelona, Spain. A series of 22 patients without a history of alcohol or tobacco use underwent detection of HPV using novel and newly available well-validated low-and high-risk probe sets (Ventana Medical Systems, Tucson, Ariz.). Both low- and high-risk serotypes were screened in pathological specimens. This technique allows for accurate and rapid detection of HPV infectivity in pathological samples. Furthermore, it allows for direct visualization of HPV in HNSCC cells. The high-risk Family 16 probe cocktail has an affinity to high-risk HPV genotypes 16, 18, 31, 33, 35, 39, 51, 52, 56, 58, and 66. The low-risk Family 6 probe cocktail has an affinity to HPV genotypes 6 and 11. The slides were examined for the presence of integrated HPV using light microscopy. Positive signal is indicated by dark blue staining. Copy number can be estimated by comparison to the controls, which are xenograft controls that have known copy numbers. Internal negative controls were examined for each tissue section.

There were a total of 22 patients in this series. Three patients had multiple samples due to persistent or recurrent tumor and, thus, the total number of samples tested was 25. There were 14 males and 8 females. The average age of the patients was 64 years. In no case did the multiple samples have a different HPV status. The most common anatomic sites included tongue (8 cases), tonsil (7 cases) and larynx (7 cases). The Tumor (T) staging of these 25 samples was: T1=5, T2=8, T3=4 and T4=5. The Neck (N) staging was: N0=17, N1=2, N2b=5, N2c=1. 24 samples were M0 while one sample was stage M1. Two of 22 (10%) patients had positive detection for high risk HPV probes. Both of these samples were tonsillar tumors, thus resulting in 29% of tonsil samples having high-risk HPV. No tumors were positive for low-risk HPV.

The study demonstrates the utility of new, commercially available, well-validated probe sets for low- and high-risk HPV determination that can be used in clinical paraffin embedded tissue samples. The significant advantages of the ISH technique are visualization and localization of HPV and a high sensitivity that is coupled with a high specificity.

For references, please e-mail the editor.

**Key Points:**

- Detection of HPV in head and neck squamous cell cancer may be critical in some patients without a history of tobacco or alcohol use.
- A new technique available at Cleveland Clinic provides for accurate and rapid detection of HPV infectivity.
The Hearing Implant Program (HIP) to date has done approximately 80 bilateral cochlear implants; approximately 25 have been simultaneous and the rest sequential, according to Peter Weber, M.D., Co-Director of HIP.

The advantages that bilateral cochlear implantation provide are superior hearing in conditions where background noise is prevalent, as well as better hearing in situations where there is quiet. In addition, a significant number of patients are able to obtain sound localization skills and the squelch effect is averted. The squelch effect occurs when the head blocks sound coming from the opposite side (i.e., the side that does not have the microphone for the cochlear implant attached). Thus, the patient has to constantly turn his/her head in the direction of the sound in order for the microphone to pick it up.

Every adult patient who has undergone a bilateral implant in a sequential fashion has demonstrated significant improvement in hearing abilities when wearing both implants. The same is true for children who are old enough to test. Interestingly, the vast majority of adult patients actually do better with the new implant than with their old implant. Part of this result may be due to new technology or we may be implanting the “dominant ear.” This includes patients who had their first implant up to 11 years before their second implant. Our simultaneous group is demonstrating impressive results with scores and testing abilities that far outpace what we expect from a single implant user and, in some instances, outpacing children with normal hearing.

We are proud that one of our patients, whom we implanted on her first birthday, will be one of the subjects featured in a new movie about bilateral implants.

We also have evaluated surgical complications associated with bilateral cochlear implants and have not seen any significant complications. Surgical complications evaluated were facial paralysis (0 instances), vertigo (about 5% incidence - only transient for few days postop, no long-term problems) dysguesia (0%), TM perforations (0%), infection including meningitis (0%), long-term pain or headache (0%), and bleeding (0%). Increased time of surgery for simultaneous bilateral CI was on average about 60 minutes; this increase did not necessitate any other treatment such as placement of a Foley catheter. Thus, we are demonstrating the significant advantages of bilateral cochlear implantation as well as the relative safety of this implantation.

H & E stain of squamous cell carcinoma of the tonsil.

Positive ISH for high-risk HPV in same sample. The blue demonstrates HPV in situ.

**Key Points:**

- Bilateral cochlear implantation provides superior hearing in conditions where background noise is prevalent, as well as better hearing in situations where there is quiet. In addition, a significant number of patients are able to obtain sound localization skills and avert the squelch effect.
- We have not seen any significant surgical complications associated with bilateral cochlear implants.
Researchers in Cleveland Clinic’s auditory neuroscience laboratory have recently demonstrated a new association between the role of inflammation and the effect of ototoxic drugs on hair cell survival and hearing. This work represents the first study in which inflammation has been shown to play a role in the outcome after drug toxicity in the ear.

In the case of ototoxicity, the primary determinants of cell survival or cell death are likely due to direct effects of the drug on hair cells and their function. Studies in aminoglycoside ototoxicity have demonstrated that hair cells do uptake the drug, the drug is incorporated in lysosomes of the hair cells, and proapoptotic pathways are initiated via activation of oxygen-free radicals and stimulation of caspase-mediated cell death pathways. However, it is possible that other influences that are derived from outside the cochlea also play a role in determining which cells eventually recover and which cells succumb to toxicity. This is the first study that shows that inflammation in the cochlea can adversely affect cell survival after ototoxic injury.

“We used a transgenic mouse that expresses green fluorescent protein in the place of an important signalling molecule called fractalkine receptor,” says Keiko Hirose, M.D., Section Head of Pediatric Otolaryngology. Fractalkine receptor, abbreviated CX3-CR1, is expressed in monocytes, macrophages, microglia, some T cells and NK cells. CX3CR1 was found to be important in protecting hair cells and in preserving residual hearing after kanamycin exposure in mice. The cells that express CX3CR1 are the cochlear inflammatory cells, called cochlear macrophages. These macrophages have been observed in the past in the cochlea in various types of damage including noise damage and drug-induced damage. Macrophages are primarily seen in the structures of the cochlea called the spiral ligament and spiral limbus, sites known to manifest cellular loss following a number of different hearing insults.

The discovery of the protective role of this receptor carried by macrophages suggests that hair cell damage and hearing loss can be rendered far worse by a poorly regulated inflammatory response after primary insult to the ear.

Immunohistochemistry has shown that the population of green fluorescent CX3CR1-expressing cells are best described as macrophages for the following reasons: one, they express other surface markers consistent with tissue macrophages, and two, they are observed engulfing particles of cellular debris that result from the primary tissue damage exerted by the ototoxic medication. Both immunostaining and detailed light microscopic studies have confirmed these two aspects of the inflammatory cell population in the cochlea. The recruitment of these inflammatory cells may in part be a means to clear the cochlea of toxic substances unleashed by dead and dying cells. The inflammatory cells could be capable of exerting some protective effects or may be laying the foundation for repair.

“Based on our recent studies, it is clear that when inflammatory cells lose their ability to signal through CX3CR1, these cells can exacerbate the primary damage mediated by ototoxic drugs such as kanamycin, an antibiotic, and furosemide, a diuretic,” Dr. Hirose says. “If inflammation plays an important role in the repair process after destructive hearing loss, we may be able to intervene with agents that modulate the inflammatory response and thereby prevent or perhaps attenuate loss of hearing.”

This research was presented at the International Meeting of Neuroimmunology in Nagoya, Japan.

**Key Points:**

- If inflammation plays an important role in the repair process after destructive hearing loss, we may be able to intervene with agents that modulate the inflammatory response and thereby prevent or perhaps attenuate loss of hearing.
Head and Neck Institute Staff Directory

Chairman

Marshall Strome, M.D., M.S., F.A.C.S.
Professor and Chairman, Head and Neck Institute
Clinical Interests: head and neck surgery with special interest in laryngology; thyroid and parotid surgery
Ph: 216.444.6691 FX: 216.445.9409

Audiology

Craig Newman, Ph.D.
Main Campus
Vice Chairman and Section Head
Clinical Interests: adult audiologic rehabilitation; tinnitus; evoked potentials; hearing aids; outcomes research
Ph: 216.444.6691 FX: 216.445.9409

Donald Goldberg, Ph.D.
Hillcrest Hospital Atrium
Co-Director, Hearing Implant Program
Clinical Interests: audiologic (aural) management/treatment; cochlear implants; auditory-verbal therapy; pediatric and educational audiology; communication assessment of children and adults who are deaf or hard of hearing
Ph: 440.312.3681 FX: 440.312.8810

Sharon Sandridge, Ph.D.
Main Campus
Director, Audiology Clinical Services
Clinical Interests: electrophysiologic assessment; state-of-the-art amplification options including assistive listening devices and digital hearing aids; tinnitus and older adults
Ph: 216.444.6691 FX: 216.445.9409

Community Otolaryngology

Robert Katz, M.D.
Solon Family Health Center
Section Head
Clinical Interests: pediatric otolaryngology; otology; head and neck surgery; general otolaryngology
Ph: 440.519.6950 FX: 440.519.1364

Tom Abelson, M.D.
Beachwood Family Health and Surgery Center
Solon Family Health Center
Clinical Interests: voice medicine; pediatric otolaryngology; sinus disease; general otolaryngology
Ph: 216.839.3740 FX: 216.839.3749

Steven Ball, M.D.
Strongsville Family Health and Surgery Center
Clinical Interests: adult and pediatric general otolaryngology; chronic sinusitis and sinus surgery; thyroid and salivary gland surgery; adult and pediatric neck masses
Ph: 440.878.2500 FX: 440.878.2666

Edward Fine, M.D., Ph.D.
Westlake Family Health Center
Clinical Interests: laryngology; sinonasal disease; facial cosmetics and reconstruction
Ph: 440.899.5630 FX: 440.899.5636

Richard Freeman, M.D., Ph.D.
Westlake Family Health Center
Clinical Interests: general otolaryngology; head and neck surgery; sinonasal disease
Ph: 440.899.5630 FX: 440.899.5636

Daniel Knott, M.D.
Hillcrest Hospital Atrium
Clinical Interests: general otolaryngology; facial plastic and reconstructive surgery
Ph: 440.312.3681 FX: 440.312.8810

Center for Surgery Research

Suyu Shu, Ph.D.
Main Campus
Research Interests: cellular immunology; cancer immunotherapy; molecular biology
Ph: 216.445.3800 FX: 216.445.3805
George Ozvardakci, M.D.  
Lorain Family Health and Surgery Center  
Clinical Interests: sinus problems; hearing loss; hearing aids; snoring; sleep apnea; tonsils and adenoids  
Ph: 440.204.7400 FX: 440.204.7396

Facial Aesthetic and Reconstructive Surgery

Daniel Alam, M.D.  
Main Campus, Beachwood Family Health and Surgery Center  
Section Head  
Clinical interests: plastic and reconstructive surgery; facial plastic surgery; head and neck microvascular reconstruction; facial paralysis; rhinoplasty  
Ph: 216.444.6691 FX: 216.445.9409

Michael Fritz, M.D.  
Main Campus, Independence Family Health Center  
Clinical Interests: pediatric and adult facial plastic surgery; functional and cosmetic rhinoplasty; soft tissue and bony facial reconstruction for complex head and neck wounds following surgery or trauma; microvascular reconstruction  
Ph: 216.444.6691 FX: 216.445.9409

General Otolaryngology

Alan Kominsky, M.D.  
Main Campus, Beachwood Family Health Center  
Vice Chairman and Quality Review Officer  
Clinical Interests: adult and pediatric general otolaryngology; sleep apnea; snoring; sinonasal disease  
Ph: 216.444.6691 FX: 216.445.9409

Catherine Henry, M.D.  
Main Campus  
Clinical Interests: chronic cough; reflux disease; medical management of sinus disease; hearing loss; balance disorders  
Ph: 216.444.6691 FX: 216.445.9409

Head and Neck Surgery

Robert Lorenz, M.D.  
Main Campus  
Section Head  
Clinical Interests: vocal cord paralysis; head and neck oncology; laryngotracheal reconstruction; skull base tumors; benign and malignant tumors of the neck, thyroid and salivary glands  
Ph: 216.444.6691 FX: 216.445.9409

Walter Lee, M.D.  
Main Campus  
Clinical Interests: salivary gland tumors; oral cavity lesions; laryngeal tumors; immunotherapy research  
Ph: 216.444.6691 FX: 216.445.9409

Joseph Scharpf, M.D.  
Main Campus  
Clinical Interests: head and neck cancer and reconstructive surgery; general adult and pediatric otolaryngology  
Ph: 216.444.6691 FX: 216.445.9409

Marshall Strome, M.D.  
Main Campus  
Clinical Interests: head and neck surgery with special interest in laryngology; thyroid and parotid surgery  
Ph: 216.444.6691 FX: 216.445.9409

Benjamin Wood, M.D.  
Main Campus  
Clinical Interests: head and neck benign and malignant tumors; thyroid and parotid tumors; sinus tumors and chemodecetomas  
Ph: 216.444.6691 FX: 216.445.9409

Marshall Strome, M.D.  
Main Campus  
Clinical Interests: head and neck surgery with special interest in laryngology; thyroid and parotid surgery  
Ph: 216.444.6691 FX: 216.445.9409

Martin Citardi, M.D.  
Main Campus, Beachwood Family Health and Surgery Center  
Section Head and Associate Residency Program Director  
Clinical Interests: revision sinus surgery; frontal sinus surgery; sinonasal neoplasia; computer-aided sinus surgery; endoscopic orbital decompression; endoscopic CSF leak repair  
Ph: 216.444.6691 FX: 216.445.9409

Laryngology

Nasal and Sinus Disorders
Pete Batra, M.D.
Main Campus, Beachwood Family Health and Surgery Center
**Clinical Interests:** revision endoscopic sinus surgery; medical and surgical management of sinonasal polyposis; sinonasal tumors; CSF leak repair; endoscopic orbital and DCR surgery; image-guided surgery; inhalant allergy
Ph: 216.444.6691  FX: 216.445.9409

Gordon Hughes, M.D.
Main Campus, Hillcrest Hospital Atrium
**Section Head**
**Clinical Interests:** ear surgery for deafness and infection; facial paralysis; immunology of the ear; pediatric ear diseases; vertigo diagnosis and management; tumors of the ear
Ph: 216.444.6691  FX: 216.445.9409

Peter Weber, M.D.
Main Campus, Hillcrest Hospital Atrium, Beachwood Family Health and Surgery Center
**Co-Director, Hearing Implant Program Residency Program Director**
**Clinical Interests:** surgery for pediatric and adult ear disease including cochlear implants; implantable hearing aids; infectious cholesteatomas; acoustic neuromas; ear tumors; skull bone lesions; facial nerve disorders and vertigo
Ph: 216.444.6691  FX: 216.445.9409

Keiko Hirose, M.D.
Main Campus
**Section Head, Pediatric Otolaryngology**
**Clinical Interests:** pediatric ear surgery; hearing loss evaluation; cochlear implantation; basic science research in causes of deafness; general pediatric otolaryngology
Ph: 216.444.6691  FX: 216.445.9409

Chris Discolo, M.D.
Main Campus, Hillcrest Hospital Atrium
**Clinical Interests:** pediatric otolaryngology; diagnosis and management of complex airway problems; head and neck masses; speech and swallowing disorders; management of children with cleft lip and palate
Ph: 216.444.6691  FX: 216.445.9409

Paul Krakovitz, M.D.
Main Campus, Beachwood Family Health and Surgery Center, Independence Family Health Center
**Clinical Interests:** malignant head and neck disease; pediatric and adult thyroid/parathyroid disorders; voice surgery and velopharyngeal insufficiency; general pediatric otolaryngology
Ph: 216.444.6691  FX: 216.445.9409

Douglas Hicks, Ph.D.
Main Campus
**Section Head, Voice Center**
**Director, Voice Center**
**Clinical Interests:** voice science; voice disorders; care of the professional voice
Ph: 216.444.6691  FX: 216.445.9409

Claudio Milstein, Ph.D.
Main Campus
**Clinical Interests:** voice disorders; care of the professional voice; aerodigestive tract disorders; laryngeal physiology; functional dysphonia; vocal cord dysfunction
Ph: 216.444.6691  FX: 216.445.9409

Judith White, M.D., Ph.D.
Main Campus, Beachwood Family Health and Surgery Center
**Section Head**
**Clinical Interests:** vestibular disorders; dizziness and balance; hearing problems; ear disease; vertigo
Ph: 216.444.6691  FX: 216.445.9409
Beachwood Ph: 216.839.3740

Gilberto Alemar, M.D.
Weston
**Clinical Interests:** surgery of the nose and sinuses; sinusitis; voice and swallowing disorders; head and neck tumor surgery; sleep apnea and snoring; surgery for airway reconstruction
Ph: 954.659.5786  FX: 954.659.5787

Eloy Villasuso III, M.D.
Weston
**Clinical Interests:** Hearing loss; dizziness/balance disorders; chronic ear infections; pediatric ear disease; acoustic neuromas; lateral skull base tumors; facial nerve disorders; cochlear implants; otosclerosis
Ph: 954.659.5178  FX: 954.659.5787
U.S. News Ranks Cleveland Clinic
One of America’s Top Hospitals
Head and Neck Institute Ranked Among Top 10

Cleveland Clinic has been ranked among America’s top hospitals since U.S. News & World Report began its annual survey of “America’s Best Hospitals” in 1990. The 2007 survey recognized Cleveland Clinic as one of the nation’s best hospitals overall, ranking the hospital as No. 4 in the country. The magazine’s “America’s Best Hospitals” survey ranks our otolaryngology program among the top 10 in the nation. For more details, visit clevelandclinic.org.

New Staff

Daniel Knott, M.D.

Daniel Knott, M.D., recently joined the staff of Cleveland Clinic’s Head and Neck Institute. Dr. Knott specializes in general otolaryngology and facial plastic and reconstructive surgery.

Dr. Knott earned his medical degree from the University of California San Diego School of Medicine. He has a bachelor of arts in international politics and economics from Middlebury College in Middlebury, Vermont. Dr. Knott completed a general surgery internship and a residency in otolaryngology/head and neck surgery at Cleveland Clinic. He completed his fellowship in facial plastic and reconstructive surgery at UCLA Medical Center in Los Angeles.

Dr. Knott recently won the American Head and Neck Society’s Robert Maxwell Byers Award for his evaluation of hardware-related complications in vascularized bone grafts with locking mandibular reconstruction plate fixation. He has received several additional awards and honors during his education and residency.

Dr. Knott has authored numerous papers and given presentations across the country. He has applied for a patent, along with several co-inventors, for tyramine-based hydrogels for vocal cord repair and augmentation.

Dr. Knott is seeing patients at Hillcrest Hospital. His appointment number is 440.312.3681.

Staff Awards

Keiko Hirose, M.D., is First Recipient of George Adams Award

Keiko Hirose, M.D., Head of Pediatric Otolaryngology, is the first recipient of the George Adams Award for general research. The Triologic Society presented the award and honored Dr. Hirose in recognition of her dedication to academic medicine and research in otolaryngology. George L. Adams, M.D., who passed away last year, was the Chair of Otolaryngology at the University of Minnesota. His wife created the award in his memory. Dr. Hirose was nominated by Cleveland Clinic Head and Neck Institute Chairman Marshall Strome, M.D.

Section of Audiology Awarded for Program

The Audiology Foundation of America recently awarded the Excellence in Education Award to the Section of Audiology in the Head and Neck Institute at Cleveland Clinic. The award was presented for the Doctor of Audiology (Au.D.) program as part of the Northeast Ohio Au.D. Consortium (NOAC). NOAC is a joint program of Cleveland Clinic, The University of Akron and Kent State University that allows students to gain experience and education through an internationally recognized healthcare provider and at universities recognized nationally for strong audiology programs.

Craig Newman, Ph.D., Receives Presidential Award

Craig Newman, Ph.D., Head of Audiology, received the Presidential Award at the recent meeting of the American Academy of Audiology in Denver. The award was presented to him for his service to the academy and to the profession of audiology.
Outcomes Data Available

The latest edition of outcomes data from the Cleveland Clinic Head and Neck Institute is available. Our outcomes booklet also offers summary reviews of medical and surgical trends and approaches. Charts, graphs, and data illustrate the scope and volume of procedures performed in our department each year. To view outcomes booklets for the Head and Neck Institute, as well as many other Cleveland Clinic medical and surgical disciplines, visit clevelandclinic.org/quality.

Visit Us Online

To learn more about Cleveland Clinic’s Head and Neck Institute, including information about our research and educational programs, visit our Web site: clevelandclinic.org/headandneck.

Online Access to Your Patient’s Treatment Progress

Whether you are referring from near or far, our eCleveland Clinic service, DrConnect, can streamline communication from Cleveland Clinic physicians to your office. This new online tool offers you secure access to your patient’s treatment progress at Cleveland Clinic. With one-click convenience, you can track your patient’s care using the secure DrConnect Web site. To establish a DrConnect account, visit eclevelandclinic.org or e-mail drconnect@ccf.org.
Otolaryngology Advances

FALL 2007

Otolaryngology Advances offers information from Cleveland Clinic otolaryngologists, speech pathologists and audiologists about state-of-the-art medical, surgical and rehabilitative techniques. It is written for physicians and should be relied upon for medical education purposes only. It does not provide a complete overview of the topics covered, and should not replace the independent judgment of a physician about the appropriateness or risks of a procedure for a given patient.

© The Cleveland Clinic Foundation 9/2007

Tom Abelson, M.D.
Medical Editor
Christine Harrell
Managing Editor
Irwin Krieger
Art Director
Dino Rhodes
Marketing Manager

PLEASE DIRECT CORRESPONDENCE TO:
Head and Neck Institute/A-71
The Cleveland Clinic Foundation
9500 Euclid Avenue
Cleveland, Ohio 44195

In addition to providing general adult and pediatric otolaryngology services, the Cleveland Clinic Head and Neck Institute offers highly specialized tertiary care services including audiology, facial aesthetic and reconstructive surgery, head and neck surgery, laryngotracheal reconstruction, voice disorder treatment, nasal and sinus disorders treatment, otology-neurotology, speech-language pathology, and vestibular and balance disorders treatment. The Head and Neck Institute is part of Cleveland Clinic, an independent, not-for-profit, multispecialty academic medical center.

Michael S. Benninger, M.D.

Michael S. Benninger, M.D., has been appointed Chairman of the Head and Neck Institute, effective January 1, 2008. Marshall Strome, M.D., Chairman of the Head and Neck Institute since 1993, announced last year he would be retiring from his position.

Dr. Benninger is the Chair of the Department of Otolaryngology-Head and Neck Surgery and is the Cummings-Brush Chair in Surgical Education for the Henry Ford Health System in Detroit. He is the Chair of the Board of Governors of the Henry Ford Medical Group and Hospital. He serves as Director of the hospital’s Medical Center for the Performing Artist and is Co-Director of its Professional Voice Clinic.

In addition to his work at the hospital, Dr. Benninger has been involved in regional, national and international medical organizations. He serves on the Board of Directors of the American Academy of Otolaryngology-Head and Neck Surgery, and has been a former Vice President and Chairman of the Board of Governors of that organization. He is a Past-President of the American Rhinologic Society and the Michigan Oto-Laryngological Society. He is the past Editor-in-Chief of Otolaryngology-Head and Neck Surgery. He is the Treasurer and on the Executive Council of the American Laryngologic Association. Dr. Benninger is on the Board of Directors of the Voice Foundation and the International Association of Phonosurgeons, and has recently been on the Executive Council of the Triological Society. He has served on the Residency Review Committee for Otolaryngology and as a member of the Medical Advisory Board for WebMD. He is the Past-Chairman of the Steering Committee for the Sinus and Allergy Health Partnership.

Dr. Benninger has authored or edited five books, including his most recent, The Performer’s Voice. He also has written numerous book chapters and scientific articles, focusing primarily on voice care and laryngology, nasal and sinus disease and healthcare management. He has lectured extensively across the country and throughout the world.

A graduate of Harvard University, Dr. Benninger received his medical degree from Case Western Reserve University in Cleveland. He completed his residency at Cleveland Clinic.