NEWYORK–PRESBYTERIAN
Ear, Nose & Throat

Affiliated with **COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS and SURGEONS** *and* **WEILL MEDICAL COLLEGE OF CORNELL UNIVERSITY**

Fall 2006

Cochlea Damage May Be Eased With Gene Rx

Patients undergoing chemotherapy for testicular cancer or head and neck cancers are often treated with *cis*-platinum, an antineoplastic drug that can cause damage to the cochlea when taken in chemotherapeutic doses. NewYork-Presbyterian Hospital/Weill Cornell Medical Center's Samuel H. Selesnick, MD, has taken a novel approach to combating this damage: He has begun investigating gene therapy as a means of protecting the cochlea.

"Ototoxins like *cis*-platinum are a good model to investigate, since, unlike aging, we can control dosage and the degree of damage to the inner ear, especially in an animal model," Dr. Selesnick explained. "We are partnering with Michael Kaplitt, MD, of the Department of Neurosurgery. Through him, we are getting access to different types of gene therapy vectors." Dr. Kaplitt, whose focus is on the neural axis, is a venerated gene therapy researcher, working with both animals and humans.

Dr. Kaplitt uses an adenoassociated virus (AAV), a tiny, nonpathogenic virus that is currently considered one of the best options for gene therapy because it infects nondividing cells and provokes only a mild immune response. Once genes are inserted into its DNA, the altered virus is used to treat the subject.

For this study, the AAV was inserted into the ear of a rodent. "We take rats and treat them with a specific gene called *XIAP*, the X-linked inhibitor of

see Gene Rx, page 4

Full-Spectrum Clinical Care Addresses Baby Boomers' Increasing ENT Needs

Demand for otorhinolaryngology clinical services is at an all-time high at NewYork-Presbyterian Hospital, where the focus of the ENT programs at both NewYork-Presbyterian/Columbia and NewYork-Presbyterian/Weill Cornell is full-spectrum patient care.

At NewYork-Presbyterian/Columbia, the ENT department benefits from the presence of Morgan Stanley Children's Hospital of NewYork-Presbyterian, and boasts two full-time pediatric otolaryngologists; Lanny Garth Close, MD, predicts a third surgeon will be added over the coming year. The department is renowned for its expertise in airway reconstruction, as well as its evolving cochlear implant program.

As an example of the depth and breadth of the department at NewYork-Presbyterian/Columbia, Spiros Manolidis, MD, Director of the Otology & Skull Base Surgery Divisions, brings additional expertise with his research on cochlear implant electrode insertion dynamics. Jeffrey M. Ahn, MD, Director of the Division of Facial Plastic and Reconstructive Surgery, and Director, Sleep Disorder Surgery, was among the first U.S. surgeons to use the harmonic scalpel to perform uvulopalatopharyngoplasty; he also collaborates with colleagues in the departments of Neuropathology and

Michael G. Stewart, MD, MPH, examines a patient at NewYork-Presbyterian/Weill Cornell.

Neuroanatomy on research for new therapies for patients with facial nerve paralysis. Hector P. Rodriguez, MD, conducted the initial research and development of somnoplasty and was the first surgeon to perform it.

Also at NewYork-Presbyterian/Columbia is the renowned Voice and Swallowing Center, where physicians and researchers have either developed the technology and techniques, or have published extensively on them. For example, Jonathan Aviv, MD, together with Thomas Murry, PhD, invented the endoscopic air-pulse laryngeal sensory testing technology known as FEESST (Flexible Endoscopic Evaluation of Swallowing with Sensory Testing).

"We are developing an optical transesophageal probe to allow direct visualization of the structures of the throat," said Dr. Close. Moreover, he recently hired Columbia-trained Eli Grunstein, MD, with special expertise in airway

see ENT Expertise, page 3

INSIDE STORY

NewYork-Presbyterian
The University Hospital of Columbia and Cornell

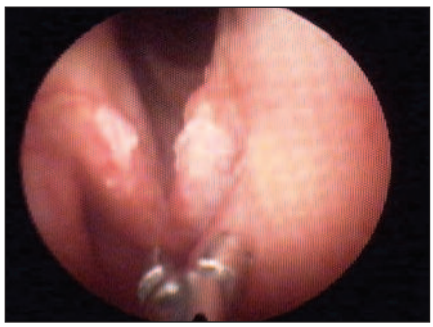
In-Office Throat Diagnostics Reduce Risk Of Contamination and Speed Recovery

Jonathan E. Aviv, MD, has transformed his practice with the help of a piece of plastic: an inexpensive, disposable sheath that covers a standard flexible endoscope and provides a channel for instruments. "It [the EndoSheath] transforms a $4,500 endoscope into a $15,000 biopsy and therapeutic tool," he explained. "Endoscopes with built-in channels are very difficult to clean effectively, so there's tremendous risk of cross-contamination. The disposable sheath eliminates that risk."

Dr. Aviv and his colleagues at NewYork-Presbyterian Hospital/Columbia University Medical Center primarily use the EndoSheath for in-office biopsies of vocal fold tumors, cysts, polyps, and masses, bypassing the need for operating rooms and general anesthesia. Using only local anesthetics, with the patient awake and sitting upright in a chair, Dr. Aviv places the endoscope through the patient's nose, allowing him to examine the throat and perform the biopsy using a tool that goes through the channel located within the sheath. "If I were to do a vocal cord biopsy in the operating room, it would take 2 hours," he said. "Now it takes 15 minutes, maybe 20, to perform the identical procedure more safely and efficiently in the office."

Dr. Aviv cited one case in which a patient had a vocal cord tumor so large that the biopsy would ordinarily have required a tracheotomy. The need for surgery was eliminated by performing the diagnostic procedure via transnasal endoscopy using the disposable sheath and channel.

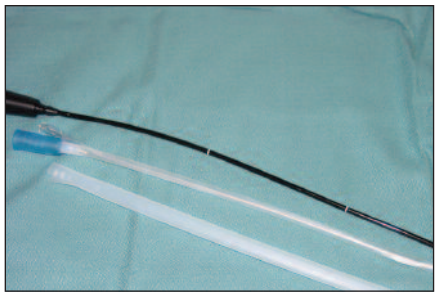
The disposable sheath also improves the range of treatment options. "There are certain cysts that can be decompressed with this technique by opening the cyst and then sending a suction catheter down through the sheath



Stretching exercises can improve vocal fold healing

channel to suction it out," Dr. Aviv said. "You can send laser fibers down the channel and vaporize small tumors. This technology and these techniques are translatable to urology, pulmonology, and gastroenterology."

Dr. Aviv's colleague, Thomas Murry, PhD, uses information from these in-office diagnostic procedures to help patients such as singers, executives, and others who depend professionally on their voices. He also examines patients via videostrobolaryngoscopy, the use of a stroboscopic light that makes the rapid motion of the vocal folds appear slower. "In a soprano, the vocal folds can vibrate as much as 1,400 times a second, but this slows down the image to 6 to 8 vibrations a second so that we can see how the folds move, if the left and right move in synchronicity, if there's any injury on the top or bottom edge, and whether there's any stiffness," he explained. "All of the examinations



The disposable sheath eliminates the risk of cross-contamination

are now done in the office with a little scope that goes over the back of the tongue and shines down on the vocal folds while the patient sustains a tone."

Dr. Murry noted that small hemorrhages in the vocal folds are increasingly common as a result of overuse of dietary supplements. "We have seen some people with bleeding in the vocal folds due to excess doses of vitamin E, of aspirin or aspirin-related products, or of herbal medicines that have been popular in low doses. We are very careful about monitoring the herbal supplements that people take because they can be as dangerous as they can be helpful." This has led Dr. Murry to investigate stretching exercises—the equivalent of physical therapy—to help improve healing after a vocal fold injury. "When you wound the vocal folds, say with a little hemorrhage, it leaves a little scar, and that scar is stiff. We are learning more about how those tissues heal and how to help them heal," he said.

Jonathan E. Aviv, MD, is Professor of Otolaryngology and Head and Neck Surgery, Columbia University College of Physicians and Surgeons, and Director, Division of Laryngology, and Medical Director of the Voice and Swallowing Center, NewYork-Presbyterian Hospital/Columbia University Medical Center.
E-mail: javivmd@aol.com.
See also www.voiceandswallowing.com.

Thomas Murry, PhD, is Professor of Clinical Speech-Language Pathology in Otolaryngology/Head and Neck Surgery, Columbia University College of Physicians and Surgeons, and Clinical Director of the Voice and Swallowing Center, NewYork-Presbyterian Hospital/Columbia University Medical Center.
Email: tm2103@columbia.edu.

ENT Expertise

continued from page 1

reconstruction, speech and swallowing problems, to join long-time Director of Pediatric Otolaryngology, Joseph Haddad, Jr., MD.

New Facility at Weill Cornell

The ENT Department at NewYork-Presbyterian/Weill Cornell Medical College also offers the full range of otorhinolaryngological services, with a neonatal and pediatric ICU ready to care for its youngest patients. "We are currently researching the use of hyperbaric oxygen in sensorineural hearing loss, treatment of cerebrospinal fluid leak, the role of fluid intake after adenotonsillectomy, and the study of ciliary function in neonates," explained Michael Stewart, MD.

Physicians and researchers at NewYork-Presbyterian/Weill Cornell are also studying novel techniques for treatment of epistaxis, genetic analysis of patients with chronic sinusitis, novel approaches to endoscopic skull base surgery, and the effect of sinus surgery on voice parameters. In addition, Dr. Stewart said, "We have developed collaborative research programs with many departments, including Neurology and Neuroscience, Neurological Surgery, Radiology, Medical Oncology, and Pulmonary Medicine."

In January 2007, the ENT department will be moving across York Avenue into the new Weill Cornell Ambulatory Care and Medical Education Building, a 16,000-square-foot state-of-the-art facility that will have more space for outpatient procedures, more comfortable waiting rooms for patients, improved patient flow, and room for additional interdepartmental clinical collaborations. Immediate plans call for allergy testing and treatment, expanded hearing testing, and the availability of hearing aides and amplification devices for purchase on site.

"We are also working with colleagues in Pulmonary Medicine to create a joint Sinus and Asthma clinic," said Dr. Stewart. "The new building will facilitate clinical collaboration with our colleagues in many other disciplines, including Ophthalmology, Genetics, and Plastic Surgery."

By far the largest patient demand comes from aging Baby Boomers—some 76 million strong—who have high standards for health and wellness. They are seeking care for such otorhinolaryngological issues as sleep disorders, especially obstructive sleep apnea; problems with voice, speech and swallowing; hearing loss; and cancers of the head and neck.

Columbia University, which is renowned for its work on swallowing disorders, otitis media, nerve regeneration, and hearing rehabilitation, has two fully-funded NIH-supported basic research laboratories for Hearing and Head and Neck Cancers.

Hearing research at Columbia University is headquartered at the venerated Fowler Memorial Laboratory, in use for more than 30 years. Fowler is currently run by Elizabeth Olson, PhD, whose co-PI is Shyam M. Khanna, PhD. They are currently researching the role of the external ear and tympanic membrane in reception of acoustical signals, using time-averaged holography to study tympanic membrane vibrations. Their research also focuses on the function of the middle ear, the micro-mechanics of the inner ear (including the development of an optical sectioning microscope to visualize cellular details), and on coding of the auditory signal in the neural spike train.

Dr. Close recruited Gloria Su, PhD, from Johns Hopkins to run the Molecular Oncology laboratory. Dr. Su's expertise is in the molecular genetics of head and neck squamous cell carcinoma (HNSCC) and pancreatic ductal adenocarcinoma, as well as mouse modeling (because they mirror human tumorigenesis) for both types of cancer. Dr. Su has found that while both cancer types share some common oncogenes and tumor-suppressor genes (e.g., p16 and p53), each has its unique targeted mutations (e.g., Cyclin D1 for HNSCC and K-ras for pancreatic cancer). The lab is also analyzing tissue-specific knock-out mice based on the genetic profiles of human ductal pancreatic cancer and HNSCC. Dr. Su and colleagues hope to reveal new prognostic markers, discover tumor markers for early detection analysis, and develop chemopreventive and therapeutic treatments that target tumor-specific pathways.

Joint Residency Training Program

Recently, the joint residency training program for Columbia University College of Physicians and Surgeons and Weill Medical College of Cornell University received approval from the Residency Review Committee/Accreditation Council for Graduate Medical Education to permanently increase the yearly complement of residents from 3 to 4, thereby making NewYork-Presbyterian Hospital's program one of only a handful in the country that train four residents per year.

"Dr. Stewart and I worked together to present a very strong proposal for expansion of the training program to four residents each year on a permanent basis," said Dr. Close. "It's a remarkably powerful program to have two Ivy League medical schools and Memorial Sloan-Kettering as your training base."

"There were educational opportunities at both campuses that we couldn't take advantage of with fewer residents," said Dr. Stewart. "The demand for our physicians in both departments is tremendously high, and now we are going to be able to avail ourselves of the opportunities to train the next generation in our specialty," he added.

Lanny Garth Close, MD, is Chairman and Howard W. Smith Professor of Otolaryngology at Columbia University College of Physicians and Surgeons, and Director of Service, Department of Otolaryngology/Head and Neck Surgery, NewYork-Presbyterian Hospital/Columbia University Medical Center. Email: lgc6@columbia.edu.

Michael G. Stewart, MD, MPH, is Chairman of the Department of Otorhinolaryngology and Professor of Otorhinolaryngology and Public Health, Weill Medical College of Cornell University, and Otorhinolaryngologist-in-Chief, NewYork-Presbyterian Hospital/Weill Cornell Medical Center. Email: mgs2002@med.cornell.edu.

Gene Rx

continued from page 1

apoptosis, a gene that at least theoretically could help protect the inner ear from the damage caused by toxins, in this case *cis*-platinum," said Dr. Selesnick. "We go on to give the *cis*-platinum and see whether the vector is getting into the inner ear, and if it is, whether it is producing the gene product that protects the inner ear. We found that this was indeed the case—we were able to protect these rats' ears from *cis*-platinum with the altered AAV."

The use of gene therapy for inner-ear treatment is "at the leading edge of basic science in otolaryngology," Dr. Selesnick noted. He and Dr. Kaplitt presented the results of their study at the 2006 national meeting of the American Otological Society, prompting significant interest. Dr. Selesnick emphasized, however, that this is only the first step. "Now we are taking this further and looking at doses of *cis*-platinum—not just large doses but a series of small doses [similar to what] human cancer patients would receive during chemotherapy. We want to reduce side effects as much as possible while still retaining the efficacy of the drug, and that is often done through adjusting doses over time, so we're starting to look at that in a rodent model," Dr. Selesnick said. Once safety and efficacy are demonstrated in the murine studies, the goal is to perform trials in humans. Dr. Selesnick acknowledged that such trials are at least one year away.

Within the Department of Otorhinolaryngology, long-term research projects such as these are somewhat unusual. "Most of what we have published in the past decade has been clinical in nature," Dr. Selesnick said. "We've been looking at treatment for some frustrating disorders, such as sudden sensory neural hearing loss, which affects up to 20 individuals per 100,000 per year. A number of patients, sometimes up to half, don't do well with conventional treatments, so we have done some studies looking at the use of hyperbaric oxygen. We found some success, but not nearly what we had hoped for, so we are continuing to investigate other avenues of treatment. We are also starting to offer transtympanic therapy, injecting medications through the eardrum into the inner ear. There have been a number of studies looking at this over the past few years," Dr. Selesnick said. "It is still not clear how efficacious the treatment is, but we'll be looking into it."

Samuel H. Selesnick, MD, is Professor of Otorhinolaryngology in Neurology and Neurological Surgery, Weill Medical College of Cornell University, and Vice-Chairman, Department of Otorhinolaryngology, and Director of Otology, Neurotology and Skull Base Surgery, NewYork-Presbyterian Hospital/Weill Cornell Medical Center.
E-mail: shselesn@med.cornell.edu.

NEW YORK–PRESBYTERIAN Ear, Nose & Throat

Lanny Garth Close, MD
Chairman and Howard W. Smith Professor of Otolaryngology
Columbia University College of Physicians and Surgeons
Director of Service, Department of Otolaryngology/Head and Neck Surgery
NewYork-Presbyterian Hospital/Columbia University Medical Center
Email: lgc6@columbia.edu

Michael G. Stewart, MD, MPH
Chairman, Department of Otorhinolaryngology
Professor of Otorhinolaryngology and Public Health
Weill Medical College of Cornell University
Otorhinolaryngologist-in-Chief
NewYork-Presbyterian Hospital/Weill Cornell Medical Center
Email: mgs2002@med.cornell.edu

Related Links:

www.CornellENT.org

www.ENTColumbia.org

Fall 2006

NewYork-Presbyterian Hospital
525 East 68th Street
New York, NY 10021

NONPROFIT ORG.
U.S. Postage PAID
Permit No. 566
Utica, NY