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EDITORIAL ADDENDUM

# Summary: International Tinnitus Forum Annual Meeting, September 23, 2000, Washington, DC

**Chairman, Abraham Shulman, MD**
**Coordinator, Barbara Goldstein, PhD**

## PRESENTATIONS

The International Tinnitus Forum is a forum dedicated to reflecting ongoing basic and clinical scientific efforts for understanding and managing tinnitus. It provides a network for exchange of information among professionals involved in both diagnosis and treatment of tinnitus. The forum originated in 1982 as the International Tinnitus Study Group sponsored by Dr. J. Shea, Jr. Since that time, it has been an annual event prior to the start of the annual meeting of the American Academy of Otolaryngology–Head and Neck Surgery. From 1982 to 1995, support was provided by the Lionel Hampton Ear Research Foundation and the American Tinnitus Association. Since 1995, the forum has been sponsored as an educational effort by the Martha Entenmann Tinnitus Research Center, Incorporated. It has presented state-of-the-art, dynamic exchanges of scientific advances in the study of tinnitus.

The September 2000 meeting was the eighteenth annual gathering of the organization now called the *International Tinnitus Forum*. The focus was on neuroprotective therapy and drug delivery to the inner ear as components in the attempt to control inner ear complaints highlighted by tinnitus. *Neuroprotection* refers to processes that protect and improve neuronal function and prevent further impairment after injury has occurred.

The concept of neuroprotective therapy for disorders of the central nervous system characterized by stroke, neurodegeneration, trauma, and hemorrhage is considered to be applicable to complaints regarding the hearing and balance systems, both peripheral and central. Symptoms are manifested clinically in affected patients by hearing loss, vertigo, ear blockage, or tinnitus.

The program was divided into two sections. First, the basic science section included presentations of advances in treatment and understanding of tinnitus from the perspectives of biochemistry, nuclear medicine, brain imaging, and cochlear physiology. The guest of honor was Dr. Steven K. Juhn, otolaryngology professor and director of the biochemistry laboratory in the department of otolaryngology at the University of Minnesota, Minneapolis. Second, a clinical section included presentation of results of different drugs and drug delivery systems for treating inner ear symptoms of hearing loss, tinnitus, and vertigo, with an emphasis on the symptom of tinnitus.

The transactions were recorded. Presenters were requested to submit manuscripts for publication in the *International Tinnitus Journal*, the official journal of the International Tinnitus Forum. (The Web site for the *International Tinnitus Journal* is www.tinnitusjournal.com.)

Prof. Albert Stracher, chairman of the department of biochemistry and distinguished professor at the Health Science Center at Brooklyn, State University of New York (HSCB/SUNY), presented his experience with the cellular protease calpain and its inhibitor, leupeptin, and their neuroprotective actions to counter the ototoxic effects of gentamicin in an animal model. Significant are the past efforts of his group, which have continued for 10 to 15 years and have focused on the use of leupeptin in both animals and humans for providing neuroprotection and reversal of symptoms for conditions of sectioning of a nerve and muscular dystrophy.

Dr. Michael D. Seidman, director of the otolaryngology research laboratory and of otologic and neuro-otologic surgery and cochairman of the complementary and alternative medicine initiative at the Henry Ford Health System, presented results in animals of the experimental use of leupeptin in the inner ear, which originated with and was sponsored by the Martha Entenmann Tinnitus Research Center. The work of Drs. Stracher, Shulman, and Seidman supports the clinical investigation—for the first time in humans—of the neuroprotective effects of leupeptin in patients with a predominantly cochlear and severely disabling type of

tinnitus. Completion of this study is slated for 2000 or 2001 at HSCB/SUNY. The results will be shared with investigators who have been selected for a multicenter study of neuroprotection with leupeptin for tinnitus relief in this population.

Dr. Abraham Shulman, professor emeritus in clinical otolaryngology at HSCB/SUNY, presented a preliminary brain study of the γ-aminobutyric acid (GABA) benzodiazepine deficiency syndrome in a central-type tinnitus using $^{123}$I-labeled Iomazenil with single-photon emission computed tomography (SPECT). SPECT, a nuclear medicine–imaging technique, was performed in six patients at HSCB/SUNY by Dr. Arnold M. Strashun, director of the department of nuclear medicine, and at the Neurospect Center, Yale University Medical School, by Dr. John P. Seibyl, director.

The study hypothesis was that some tinnitus patients may have a deficiency in the GABA-A benzodiazepine receptor, which may be the basis for development of a tinnitus of the severe disabling type. In this preliminary report, all six patients demonstrated a deficiency in this receptor. For the first time, a neural substrate (i.e., the medial temporal lobe system of brain) in patients with tinnitus, particularly of the severe disabling type, was demonstrated to be deficient in GABA-A receptor density. This receptor is considered to be a biochemical marker for this type of tinnitus and, as such, provides a basis for the development of a neuropharmacologic approach to tinnitus control.

Guest of Honor Dr. Steven K. Juhn presented "Blood Labyrinth Barrier and Fluid Dynamics of the Inner Ear." This study provided a basis for understanding the underlying function of the inner ear and factors that must be considered in introducing medication for inner ear perfusion in attempting control of such symptoms as hearing loss, tinnitus, vertigo, and ear blockage, either individually or in combination.

The second part of the meeting, moderated by Dr. Michael D. Seidman, provided an exchange of clinical experiences using various methods of drug delivery to the inner ear. The contributors focused on the symptom of tinnitus, either as the primary complaint or as an accompanying complaint for hearing loss and vertigo.

Dr. H. Zenner, professor and chairman of the department of otolaryngology at the University of Tubingen, presented a summary of his efforts in developing a pump implantable in the mastoid portion of the temporal bone in an attempt to control inner ear symptoms of hearing loss, tinnitus, vertigo, and ear blockage, either alone or in combination. After implantation within the ear, a touch-sensitive device would allow delivery of various drugs to the inner ear for control of inner ear symptoms (including tinnitus) when the tinnitus is disturbing to an affected patient. The device has been under development for the last 5 years and now is in clinical trials. It is expected to be introduced clinically within the next 2 years.

Dr. H. Silverstein, president of the Florida Ear and Sinus Foundation and clinical professor of otorhinolaryngology and head and neck surgery at the University of South Florida School of Medicine, Tampa, presented his clinical experience with a device that he developed (called the *Microwick*) for medication self-delivery into the inner ear by affected patients. In an office-based procedure, a wick of absorbable material is inserted through the eardrum to make contact with a structure called the *round window*. Drops placed by the patient into the ear with a dropper find their way into the round window for entrance into the inner ear. Excellent results were reported for control of both vertigo and tinnitus in patients with a clinical diagnosis of Ménière's disease.

The remaining presentations were of significant results for tinnitus relief with a drug delivery system called *intratympanic drug delivery* for inner ear complaints of hearing loss, tinnitus, and the like. The medical diagnoses were Ménière's disease, sudden loss of hearing, and subjective idiopathic tinnitus of the severe disabling type. The technique is not new and had its origins in the 1930s. It was reintroduced by Prof. E. Sakata, chairman of the department of otolaryngology at Saitama University, Saitama, Japan, in 1982. Since then, Prof. Sakata has reported excellent results in more than 2,500 patients. The drugs used have been steroids and lidocaine (Xylocaine) for the complaint of vertigo in patients with Ménière's disease. Dr. H. Sakata of the University of Tokyo reported an update of the experience with lidocaine therapy.

Dr. John J. Shea, Jr., director of the Shea Clinic and professor of otolaryngology at the University of Tennessee, Memphis, reported excellent results for intractable tinnitus using this technique in combination with intravenous Xylocaine. Dr. M. Hamid, director of the Cleveland Hearing and Balance Center; clinical professor of ear, nose, and throat medicine at the Medical College of Virginia; and clinical professor at Air Shams University, Egypt, reported excellent results with steroids using this technique for the symptom of vertigo in patients with Ménière's disease.

The drug delivery technique of placing a catheter internally into the space behind the eardrum to the round window membrane and connecting it externally to a pump was presented as a means for diagnosing sudden loss of hearing and tinnitus. Dr. D. Morrison, in private practice in North Carolina, reported excellent results of using this method for tinnitus control, in both the short and long terms. Dr. M. Hoffer, LCDR, U.S. Navy, San Diego, presented the application of this drug delivery system for patients with sudden hearing loss and ver-

tigo associated with Ménière's disease. Excellent results were reported for control of vertigo and associated tinnitus in such patients, but results for hearing improvement overall were reported to be poor.

Dr. John Epley, professor of otolaryngology in the department of otolaryngology at the University of Oregon, Portland, presented intratympanic tests for managing intratympanic drug therapy using lidocaine and steroids. This report was significant, because it provided to physicians who are considering this intratympanic drug therapy technique a basis for patient selection. Very good to excellent short- and long-term results were reported for the symptom of vertigo in patients with Ménière's disease and for such patients with either an associated or chief complaint of tinnitus.

## CONCLUSIONS

Surgical treatment is available to patients receiving a clinical diagnosis of predominantly cochlear-type tinnitus. The complications, as reported by the aforementioned presenters, include occasional perforation of the eardrum and additional hearing loss.

The key to efficacy of any method attempting to provide relief to patients with severe disabling tinnitus depends on the establishment of an accurate diagnosis of the symptom of tinnitus. Patients are advised to work with their otologist or neurootologist and an audiologist to identify their tinnitus as predominantly of a cochlear type.

Presentations at this meeting support expectations for the development of a group of drugs called *calpain inhibitors*. They may offer neuroprotection to the hearing and balance system and may result in relieving the symptoms of hearing loss, tinnitus, vertigo, and ear blockage, which occur alone or in combination.

Other neuroprotective agents (e.g., steroids) may achieve a degree of tinnitus relief when delivered by various systems. The ability of such drug delivery systems to penetrate the middle ear for perfusion of the inner ear has altered significantly the therapeutic management both of the symptom of vertigo associated with the diagnosis of Ménière's disease and of predominantly cochlear-type tinnitus. The key to increased efficacy for tinnitus relief using such systems depends on establishing an accurate diagnosis of this disorder.