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# Abstracts of the Twenty-Fifth Ordinary Scientific Congress of the Neurootological and Equilibrimetric Society

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## TINNITOLOGY, TINNITOGENESIS, NUCLEAR MEDICINE, AND THE TINNITUS PATIENT

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Since the 1970s, clinical interests in otolaryngology and audiology for the symptom of tinnitus for both its diagnosis and treatment have witnessed the evolution of a new discipline—tinnitology. Tinnitology is an integrated discipline of basic sciences, neuroscience, and clinical medicine for the understanding of aberrant auditory phenomena unrelated to an external source of sound. Nuclear medicine techniques of positron emission tomography and single-photon emission computed tomography provide to patients with subjective idiopathic tinnitus (1) correlation of structure and function, which improves the accuracy of the tinnitus diagnosis; (2) a monitoring system for determining the efficacy of modalities of therapy attempting tinnitus relief; and (3) information about neuroreceptors and neurochemistry in brain involved in underlying or accompanying basic mechanisms of tinnitus production for specific clinical types and subtypes of tinnitus. Case reports will demonstrate the development and application of clinical neuropharmacology protocols for tinnitus treatment, highlighted by neuroprotective drug therapy to control tinnitogenesis, an auditory epileptiform phenomenon.

## CALPAIN INHIBITORS AS NEUROPROTECTIVE AGENTS IN NEUROGENERATIVE DISORDERS

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It seems plausible to hypothesize that in all forms of neurodegeneration or other forms of tissue degeneration, a com-

mon pathway exists that, when deciphered, could lead to our understanding a variety of diseases, rests in tissue necrosis, and could offer potential for therapeutic intervention. In recent years, progress toward elucidating this common pathway has been accelerated through the studies of a number of laboratories, including our own, on the role of the protease calpain in this process. Thus, in a variety of such disorders as stroke, spinal cord injury, traumatic nerve injury, Parkinson's disease, amyotrophic lateral sclerosis, Alzheimer's disease, muscular dystrophy, and cataract formation, unregulated calpain proteolysis, initiated via dysregulation of calcium ion homeostasis, participates in the pathogenesis of these diseases and is a potentially unifying mechanistic event. Calpains are a homologous family of  $\text{Ca}^{2+}$  activated proteases, of which the two most common forms are ubiquitous and constitutively expressed.

A relatively recent interest of ours has been the role of neurodegeneration in hearing loss and tinnitus, particularly that associated with noise. These studies grew out of early discussions originating with Professor Abraham Shulman of the Department of Otolaryngology, State University of New York Health Science Center at Brooklyn, and leading to a collaboration with Dr. Richard J. Salvi of the Center for Communication Disorders and Sciences, Hearing Research Laboratories, State University of New York at Buffalo. Further studies in this very promising area of research are continuing for noise-induced hearing loss protection and tinnitus control. A brief review of calpain will be presented.

## LEUPEPTIN PROTECTS AGAINST ACOUSTIC OVERSTIMULATION\*

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Calpains are calcium-activated proteases that are present in most vertebrate cells, including neurons. During the early stages of neuronal injury, calpain levels are markedly elevated by the influx of calcium, leading to the selective proteolysis of cytoskeletal and membrane proteins, kinases, phosphatases, and transcription factors. Previous studies have shown that some neural pathologies can be significantly attenuated calpain inhibitors. The purpose of the present study was to determine whether leupeptin, a tripeptide calpain inhibitor known to protect against peripheral nerve degeneration, would protect sensory hair cells from acoustic overstimulation.

Hearing loss in the left and right ear was estimated from local evoked potentials recorded from electrodes implanted bilaterally in the inferior colliculus. Leupeptin was infused into scala tympani in the basal turn of the cochlea using an osmotic pump and catheter (1 mg leupeptin per milliliter in HBSS; flow rate, 0.5 ml/hr for 14 days). Baseline hearing levels measured during the first 4 days after implantation of the pump were within normal limits, suggesting that the pump, leupeptin, and carrier solution had no adverse effect on cochlear function. After baseline measures of hearing were completed, the animals were exposed at either 100 dB SPL or 105 dB SPL for 48 hours to an octave band of noise centered at 4 kHz. Hearing losses were typically 5–25 dB lower in the leupeptin-treated ear than in the untreated control ear during the first 7 days postexposure; however, this protective effects sometimes dissipated by 14 days postexposure. At the end of the experiment, the animals were sacrificed and their cochleas processed as a flat surface to allow estimation of the amount of inner hair cell (IHC) and outer hair cell (OHC) loss as a function of position in the cochlea. The noise-induced OHC and IHC lesions were almost always substantially smaller in the leupeptin-treated ears than in the untreated control ears. Moreover, the hair cell losses in some of the leupeptin-treated ears were negligible, despite more than 2 weeks of cochlear infusion. These results suggest that leupeptin may be a potent otoprotective agent. In addition, the lack of damage in several leupeptin-treated ears suggest that the long-term infusion of this calpain inhibitor has no obvious ototoxic effects on the sensory hair cells.

\*This work was supported by the Martha Entenmann Tinnitus Research Center, Brooklyn, NY.

## SENSOLOGY AND TINNITUS

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Tinnitus and hypoacusia are complaints of neurootological patients that frequently are accompanied by vertigo and dizziness. Very often, these combined signs form the basis for a referral to the neurootologist, who then completes a functional differential diagnosis and plans lesion-oriented differential therapy. When combining sensorimotor tests with suprathreshold evoked responses of the acoustic type, it is possible not only to discriminate peripheral inner ear lesions of the cochlear and vestibular type, but also to differentiate central pa-

thology on the different levels within the map of the central statoacoustic system.

Besides our extensive history charts NOASC, classic threshold and suprathreshold audiometry, acoustic discomfort thresholds, tinnitus masking, and impedanciometry are applied during our comprehensive neurootometric workup.

For our neurootological topodiagnostic network analysis at our Bad Kissingen neurootological research laboratory, we regularly use polygraphic electronystagmography, visually evoked potentials, and computer-analyzed ultrasound cranio-corpography, together with transitory otoacoustic emissions and acoustical brainstem and cortically evoked responses, for objectively recording the responses within various neurosensory pathways. The vestibular evoked potentials together with brain electrical activity mapping still are restricted to the Würzburg neurootology laboratory for tinnitus investigations.

An anatomical plan in sagittal and coronal cerebral section from the vertex toward the foramen magnum, with a display of important neuroanatomical structures (CNS-driven) regulating the hearing as well as the equilibrium control, demonstrates how closely interrelated are the spatioacoustic processors. Furthermore, telencephalic and diencephalic supervisory loops are modulating the activity in this area. To our knowledge, the range-of-motion functions of the basal ganglia play an important role for establishing driving patterns for various neurosensory internal and external transitions.

Therefore, a modern concept of tinnitology must take into consideration that afferent hearing comprises at least three very important information chains: (1) acoustic space control, (2) acoustic modulations of individuals and social emotions, and (3) acoustic transfer of intellectual (verbal) information.

The first and second of these information chains especially possess pathways in common with other neurosensory functions and structures, which must be studied for a broader concept of modern tinnitus therapy in the sense of competitive sensology. Preliminary results of this therapy, for instance, through common sensology-based whole-body expressions (Just and Dehler, Kaute, 1998) seemingly open a whole new field in tinnitus therapy.

## A NEUROPHARMACOLOGY FOR TINNITUS

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Various models of the generation of subjective tinnitus have been developed to find therapeutic strategies. There is strong evidence of a prevalent peripheral generation of subjective tinnitus in the cochlea (Ehrenberger et al., 1983; Eggermont, 1990). According to our working hypothesis, tinnitus is generated mostly at the synapses between inner hair cells and their afferents (cochlear-synaptic tinnitus). The pathophysiology of cochlear-synaptic tinnitus is compatible with a wide range of inner ear diseases: presbycusis, sound-induced hearing loss, or sudden hearing loss. Following the well-known pathophysiological model of the glutamatergic neurotoxicity and because glutamate is likely to act as the neurotransmitter in the afferent cochlear synapse, we assume that cochlear-synaptic tinnitus is a glutamate receptor-linked inner ear disease. Neuropharmacological modulation of the differ-

ent activities of the glutamate receptor subtypes referred to afferent cochlear neurotransmission may make possible causal tinnitus treatment.

Microiontophoretic animal experiments in guinea pigs have shown that the quinoxaline derivative caroverine acts as a specific reversible antagonist of glutamate receptor subtypes of the cochlear afferents. Caroverine is clinically available as a spasmolytic drug in some countries. After a pilot study with caroverine in 72 patients suffering from cochlear-synaptic tinnitus, we performed a single-blind, parallel, placebo-controlled study according to GCP guidelines to test the effect of a single infusion of caroverine in 60 patients with cochlear-synaptic tinnitus. For evaluation of the tinnitus, a subjective rating and a psychoacoustic measurement (tinnitus matching) were performed before, immediately after, and 1 week after the infusion therapy. Therapeutic success was defined as improvement in the subjective rating and in the tinnitus matching. The dosage of caroverine depended on the effect of subjective tinnitus reduction and had to be chosen individually for each patient. Of 30 caroverine-treated patients, 19 (63.3%) showed a relevant tinnitus reduction (according to our definition of success) immediately after the infusion. After 1 week, the effect was stable in 48.3% of the patients treated. The results of our blind study demonstrate that selective glutamate receptor antagonists such as caroverine generally promise to be effective tools in tinnitus treatment.

#### ELECTROPHYSIOLOGICAL TESTING IN THE TINNITUS PATIENT

**Nasser Hassan, Abraham Shulman, and Barbara Goldstein** Martha Entenmann Tinnitus Research Center, Brooklyn, NY, USA

This is a preliminary report of electrophysiological recording of auditory short, middle, and late responses with brain electrical activity mapping (BEAM) in a normal and tinnitus patient population. The parameters of identification between the two populations include comparison of evoked responses and frequency spectral analysis (two- and three-dimensional BEAM) for latency, phase-frequency, and frequency-amplitude. Significant differences between the 2D and 3D mapping techniques include (1) increased accuracy of correlation of anatomical location with the electrophysiological recording; (2) greater correlation of all electrodes with cortical areas of hyperelectrical and hypoelectrical activity; (3) identification of the Z axis in 3D, which allows identification of depth of the electrical dipole generators; (4) information about both the time and frequency domains in 3D; and (5) increased accuracy of mapping with 3D, using fewer electrodes than are needed with 2D recordings. Differences between normal and tinnitus patient populations are highlighted by the following: (1) P300 increased latency variability response; (2) increase in late responses of up to 800 msec; (3) alteration of parameters of spectral analysis for phase and frequency for P300 and late responses; and (4) reversal of polarity of P300 in the tinnitus patient. Early results of this preliminary study suggest that increasing indices examination may prove to be a useful

and sensitive tool for identifying electrophysiological correlates in tinnitus patients.

#### ROLE OF THE VESTIBULAR SYSTEM AND VESTIBULAR TESTING FOR THE TINNITUS PATIENT

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Frequently, tinnitus is combined with such neurootological symptoms as vertigo, nausea, and hearing loss. Especially in patients older than 40, the sign of tinnitus is increasingly found. Based on the original concept of Shulman and Seitz (1981) that tinnitus arises in some cases from a site of vestibular dysfunction, Parmentier (1988) has suggested such an approach for vestibular analysis using computerized rotation and a pursuit tracking test. Such an approach seems to be logical, taking into consideration the very broad connections and representations of the vestibular analyzer within the central nervous system.

Since 1990, we have used the technology of brain mapping of the electrical activity during angular accelerations in the Neurootology Department at the University ENT Clinic, Würzburg. We have succeeded with the registration and analysis of the vestibular evoked potentials (VestEP), obtained from scalp-located electrodes during repetitive short-lasting accelerations. Hence, in the present study, we have aimed to analyze the modifications in the principle VestEP components in patients suffering from tinnitus as a main complaint. We have tried to deduce some basic considerations about the nature and generating sites of the symptom of tinnitus. Owing to our comparative brain electrical mapping findings, the character of the electrographic VestEP changes in our group of tinnitus patients is of an irritative type.

#### TINNITUS IN HEREDITARY MENIÈRE'S SYNDROME

**Carlos A. Oliveira, Roberta Bezerra, and Mercedes F.S. Arafijo** Department of Otolaryngology, University of Brasília, Brazil

In 1997, the authors described a large family with classic Menière's syndrome and migraine inherited as an autosomal dominant trait. Using a special questionnaire for all the affected members of this family, true migraine was well demonstrated preceding or following the Menière's attacks in the majority of family members. We now have used another questionnaire designed to characterize the natural history of tinnitus and have asked these questions of all affected and unaffected members of this family. We have thought to obtain a clear description of tinnitus regrading loudness, intensity and degree of annoyance, time of onset and duration, variations over time, and so forth. Finally, we tried to establish the relations of tinnitus with the other Menière's symptoms and with the migraine complex of symptoms. The findings of this survey will be reported and commented on in this communication. Only headache appears more often than tinnitus in these patients, and the latter is the only symptom that is present all the time with some variation during the crisis.

## THE MEDICAL AUDIOLOGIC EVALUATION OF THE TINNITUS PATIENT

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We outline our routine approach to tinnitus patients underlying the different aspects of our examination—namely, the clinical history; objective ear, nose, and throat and general examination; and audiovestibular testing. We highlight the interest in testing not only the cochlear but the vestibular function of the inner ear. From our point of view, this is of paramount importance for the cochleovestibular system as a unit. All these data are stored in a database bank. Then we show our preliminary results. We currently have 83 patients suffering from tinnitus, and the results in them are presented statistically. We characterize the population in terms of its gender distribution and mean age. The localization and characteristics of tinnitus and associated symptoms also are noted. The results of the audiovestibulometric examinations—pure-tone audiometry, vocal audiometry, and brain evoked response audiometry, CCG, and electronystagmography—are discussed. We conclude that many tinnitus patients, even those who had no vestibular symptoms, showed some disturbances in the vestibular test. This fact highlights the need for a complete cochleovestibular investigation of all patients who complain of tinnitus.

## NUTRITIONAL ASPECTS AND TINNITUS CONTROL

**Wallace Rubin** Louisiana State University, New Orleans, LA, USA

Biochemical mechanisms are a significant factor in neurootological problems. Investigation of biochemical causes of neurootological problems is warranted and can be cost-effective. Dietary, nutritional, chemical, immunological, and stress factors are directly involved as tinnitus-causative mechanisms and must be evaluated and considered when one designs the treatment regimen.

## SURGERY AND TINNITUS CONTROL

**Jack L. Pulec** Pulec Ear Clinic, Los Angeles, CA, USA

The majority of patients who suffer with tinnitus can now be successfully treated by specific conservative medical therapy, surgical therapy, or masking techniques. A thorough neurootological examination, including blood tests and imaging to establish the site of the lesion and the specific etiology, is necessary. Appropriate surgical techniques include an endolymphatic subarachnoid shunt operation for idiopathic Menière's disease, repair of a perilymphatic fistula, decompression of a stenotic internal auditory canal, or cervical rhizotomy in the case of neurogenic cervical vertigo. In addition, such procedures as stapedectomy, tympanoplasty, or myringotomy with a ventilating tube may be required. Excision of acoustic tumors and other lesions of the cerebellopontine angle can be curative. Objective tinnitus can often be relieved by severing the stapedial or tensor tympani tendon. Vascular tinnitus sometimes requires obliteration of the jugular bulb, carotid endarterectomy, or removal of an arteriovenous shunt or abnormality. In patients with intractable aural tinnitus or

tinnitus coming from the cochlear nerve, the excision of the cochlear nerve either by the translabyrinthine or middle cranial fossa approach offers a high degree of success. The implications of the use of these procedures will be described.

## CLINICAL EVALUATION OF THE PERSONALITY OF TINNITUS PATIENTS

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Subjective tinnitus is a physiological or pathophysiological phenomenon. It is caused by a lesion of the hair cells (often) or in the ascendant parts of the auditory pathway (rarely). Physiological parameters of tinnitus can be measured, although by subjective means only. The following parameters commonly are evaluated: match for intensity, match for frequency, masking with pure tones, and noise, and residual inhibition.

For the clinical evaluation, the psychological parameters are equally important: loudness, annoyance, and interference with activities. These parameters can be evaluated by questionnaire with surprising reproducibility in cooperating patients. However, the examination of tinnitus patients should include the entire tinnitus patient protocol (Shulman, 1981). The correlation between the physiological and psychological parameters is fairly low. This fact implies that the evaluation of psychological parameters is extremely important as an estimate of the patients' experience of their tinnitus. Among tinnitus patients, only a few (approximately 1 in 20) do not adapt to the tinnitus and desire long-term treatment. This group is composed of patients with different results in their physiological tests. However, patients with extremely intense tinnitus that is very difficult to mask are mainly involved in this group. No generally accepted explanation has yet been given for why some patients adapt to tinnitus less well than do others. The general state of patients' health, their personality traits and mood, their approach to their health problems, self-esteem of their output requirements on health from the social environment, and their social functioning in general probably influence their psychic adaptation to tinnitus. No "tinnitus-specific" personality exists. However, tinnitus patients with maladaptive personality traits tend to suffer more from their tinnitus. This fact can be understood as a constitutional lower threshold for stress, generally. Other psychological factors are more variable in time; they have more character of state. They have special importance in the critical period of adaptation (stadium II, according to Smolík-Hahn). This period falls usually in the first half year after the onset of the tinnitus.

Psychical adaptation to the presence of tinnitus is mainly spontaneous. However, according to the clinical praxis, some support of the physician can be very useful: Patients should be told repeatedly, in connection with the necessary examinations, that their tinnitus is not a serious symptom. Patients should be given time to accept that the tinnitus is not curable. It is better for patients—especially patients with signs of lowered stress threshold, those affected by other strong stressors, patients whose adaptation to the tinnitus is poor or delay (>3



months), and those for whom special care is necessary—to be told this fact by the doctor. The following aspects must be taken into account: gender, age, and physiological critical periods; other somatic diseases and difficulties, especially pain; conflict between the tinnitus and the self-perception of personal health; interference of tinnitus with professional life, requirements, and expectations; and other social stressors.

A patient's care should open the way for adaptation to the tinnitus by reducing the total amount of stress on the patient. This should be achieved by solving the patients' apparent and hidden problems. The use of psychopharmacology should be limited to very severe cases or to patients with a certain diagnosis of major depression. Different thresholds to stress, according to an individual's personality, mental and social state, and general somatic health, must be taken into account.

#### ELECTRICAL TINNITUS SUPPRESSION

**Jun-ichi Matsushima,<sup>1</sup> Noboru Sakai,<sup>1</sup> Shigeki Miyoshi,<sup>2</sup> Noribiro Uemi,<sup>2</sup> and Thoru Ifukube<sup>2</sup>** <sup>1</sup>School of Medicine and <sup>2</sup>Hokkaido Research Institute for Electronic Science, Hokkaido University, Sapporo, Japan

We treated tinnitus patients with various types of electrical stimulation at an outpatient clinic. The area of electrical stimulation comprises the external tragus, external ear canal, and middle ear. We used direct current or a 10-kHz sinusoidal wave modulated by 100 Hz. We implanted an electrical tinnitus suppressor in the mastoid in seven patients, such that they were treated at home. Major aims of our electrical stimulation are to make tinnitus patients feel relaxed and to improve sleep disorders, eventually resulting in improved attention. Longer residual inhibition, improved word perception, and hyperacusis and improved balance were attained as a result of improved attention.

#### ACOUSTIC TUMOR SURGERY AND TINNITUS

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Since 1981, using an enlarged middle cranial fossa approach to the cerebellopontine angle without destruction of the labyrinth or cochlea, the author has operated on 311 unilateral acoustic neurinomas. Tumor sizes ranged between 3 mm for intrameatal lesions and 35 mm for lesions within the cerebellopontine angle. Complete tumor removal was accomplished in 98% of cases. Postoperatively, two deaths occurred, and neurological complications were seen only rarely. Excellent function of the facial nerve was obtained in 92% of cases (in small- and medium-size neurinomas, 98% House I and II), and severe paralysis persisted in only 2%. Preservation of hearing was possible in 69% of patients with small tumors and in 45% of the total group. The hearing function was usually stable over years. A few patients developed hearing impairment on the operated side. Interestingly, the tinnitus disappeared or decreased in approximately 40% of the cases, especially in patients in whom hearing function could be preserved. Only in a few cases did this symptom occur or intensify postoperatively.

#### INDIRECT METHODS OF DISCERNING COCHLEAR AQUEDUCT PATENCY

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Cochlear aqueduct (CA) patency is believed to be a key factor in patients suffering from symptoms of perilymphatic fistula. Study of the CA is difficult because of its size and position. Even when the CA is partially or completely viewed on a computed tomography scan, one cannot be sure that it is functionally patent. It cannot be filled with radioactive dye, such as Hypaque, in the way that one can fill the internal auditory meatus. Even if the bony CA appears completely open, there may be no "free flow," or the flow may be too slow to permit any filling with dye. In recent years, Dr. Robert Marchbanks has developed a means of measuring minute changes in tympanic membrane displacement caused by an inward or outward movement of the stapes footplate in response to sound. It is believed that tympanic membrane displacement will occur only in the presence of a patent CA. In that Marchbank's device is not yet available in the United States, alternative strategies have been attempted. These strategies (1) performing pure-tone audiometry while the patient is sitting and in the Trendelenburg position and recording changes in pure tones and degree of tinnitus, (2) performing audiometry and simple neurological resting (Rombergism) before and after performing a lumbar puncture with the drainage of a small amount of spinal fluid, (3) performing transtympanic ECOG with the patient both relaxed and straining and occasionally seeing an increase in the SP with straining, and (4) in one case injecting a radioactive tracer by way of a lumbar puncture and measuring increased radioactivity in fluid emanating from the ventilation tube placed in the tympanic membrane. Our observations will be presented in a case report format.

#### HYPERINSULINEMIA: A MERGING HISTORY WITH THE IDIOPATHIC NEUROOTOLOGY OF TINNITUS, VERTIGO, AND HEARING LOSS

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To have an appreciation of hyperinsulinemia and its merging relationship with idiopathic neurootology, mainly tinnitus, vertigo, and hearing loss, one must begin with an appreciation of the history of neurootology and the history of diabetes mellitus. Both have their earliest recognition by the ancient Egyptians. The polyuric conditions resembling diabetes mellitus and "humming in the ear," now known as tinnitus, were described. In the chapter, History of Tinnitus Research, in Abraham Shulman's classic text, *Tinnitus—Diagnosis and Treatment* (1991), Shulman traces tinnitus from its very earliest recognition. The early history of diabetes mellitus revealed no relationship per se to neurootology. However, Yallow's refinement of a radioimmunoassay (RIA) for insulin (1969) demonstrated increased insulin (hyperinsulinemia) in a known diabetic following a 100-g glucose load. This technology introduced a new analytical chemistry technique to clinical medicine.

In our laboratories, the RLA of insulin applied to the 100-g glucose tolerance test (1972) not only corroborated Yal-

low's findings of hyperinsulinemia but identified specific hyperinsulinemia patterns of the non-insulin-dependent diabetic state. Our database of more than 15,000 glucose-insulin tolerances has statistically confirmed standards for euinsulinemia, hypoinsulinemia, and hyperinsulinemia. It also has confirmed that hyperinsulinemia precedes hyperglycemia. Hyperinsulinemia with normal glucose tolerance thereby becomes the earliest identification of glucose intolerance.

The first major impact of hyperinsulinemia in the clinical arena was in the discipline of neurootology. In 1977, Updegraff identified hyperinsulinemia with idiopathic Menière's disease. The cases were an intermix of normal, impaired, or diabetic (non-insulin-dependent diabetes mellitus) glucose tolerance (or all combined). All who had maintained nutritional management compliance experienced sustained clinical response.

Updegraff's studies subsequently were substantiated by others. Mangabeira-Albemaz, Fukuda, Proctor, and Brookler independently identified hyperinsulinemia as the major diagnostic factor in their cases of idiopathic dizziness and tinnitus. The relationship of hyperinsulinemia and subjective idiopathic tinnitus was specifically addressed by Proctor. The limited utilization of RIA technology and the potential availability of enzymatic immunoassay presents a practical and precise alternative to RIA hyperinsulinemia identification. The merging relationship of idiopathic neurootology with hyperinsulinemia has been established. The identification or exclusion of hyperinsulinemia by cost-effective technology in clinical neurootology is warranted.

#### EPILEPSY AND TINNITUS

**Christo Kolchev** Medical University of Sofia, Alexander Hospital, First Neurology Clinic, Sofia, Bulgaria

Tinnitus as a distortion of sensory perception does not represent a clinical entity but a variety of tinnitus syndromes. In a specially designed study, using the method of brain electrical activity mapping (BEAM) of vestibular evoked potentials (VbEP), we established that the group of tinnitus patients demonstrates three main findings: shortening of the latencies of the first and second VbEP components; increase of the amplitude of the III/IV peak-to-peak component; and a DC shift of all the VbEP components toward negativity. The same BEAM-VbEP pattern is registered from epileptic patients. Both epilepsy and tinnitus syndromes are elicited by hypersensitization of specific cortical areas (due to basic neurophysiological pathomechanisms) or by hyperactivation of those areas by an external afferent input.

According to our trigger-target concept, the brain cortex is invariably the target of pathological influences that produce the so-called transient perceptual aberrations (vertigo, sensory, epilepsy, tinnitus, headaches and facial pains, hallucinosis, phobias, etc.). As triggers serve focal lesions within a variety of intracerebral, intracranial, and corporeal structures, as well as environmental factors. The activity of such triggers results in rapid (phasic) or slow (tonic) shifts in the membrane excitability. These processes take a microportion or macroportion of time and are related to the depolarization shift of the neuronal membranes. A specific epileptogenic event is the

paroxysmal (phasic) depolarization shift. Probably, tinnitus perception is related to a mild (nonexcessive) degree of cortical disinhibition, with a slow appearance (sustained, or tonic, depolarization shift) and diffuse (nonfocal, lobar) distribution of the excitation.

Despite the fact that the majority of tinnitus syndromes are nonepileptic events, they have a common mechanism of cortical disinhibition. Tinnitus and epilepsy are similar but not identical syndromes. There exists one exception: sensory epilepsy manifested by auditory seizure. According to a tinnitus definition, such epileptic manifestations as auditory aura and complex partial seizure with auditory contents can be considered as short-lasting repetitive or transient tinnitus events.

#### ROLE OF HIGH-FREQUENCY AUDIOMETRY IN THE ASSESSMENT OF THE TINNITUS PATIENT

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Tonal audiometry is usually the first test performed on patients with subjective idiopathic tinnitus. Some of these patients show hearing thresholds within normal limits. However, conventional audiometry assesses hearing only up to 8 kHz, and information about the hearing in frequencies above this is not assessed. Human hearing can reach 20 kHz in young subjects, and this upper limit decreases with advancing age. If hearing thresholds in the frequencies exceeding 8 kHz are not assessed, it is not possible to know whether the hearing of a patient is within normal limits. These high frequencies are almost irrelevant for speech understanding, but their importance lies elsewhere.

Tinnitus matching is performed with an audiometer. If this equipment cannot match the frequency of tinnitus above 8 kHz, high-frequency tinnitus will not be matched. Moreover, the audiologic assessment of the tinnitus patient is not complete without the measurement of hearing thresholds in all frequencies that the patient can hear. We discuss the importance of high-frequency threshold assessment in tinnitus patients. Results are presented from our experience with this method of exploration in tinnitus patients.

#### OUR CLINICAL EXPERIENCES OF STEROID-TARGETING THERAPY TO THE INNER EAR FOR CONTROL OF TINNITUS

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The treatment of tinnitus has been the topic of many articles and journals. Even special meetings of scientific societies have devoted their attention to this symptom. However, the best therapeutic modality for tinnitus has not yet been established. Our clinical trial of an inner-ear drug delivery system (DDS) for control of vertigo, tinnitus, and hearing loss started in 1974 (Sakata et al., 1976). Inner-ear DDS was performed by transtympanic perfusion of medicine to the round window via the middle ear. One or one-half milliliter of 4% lidocaine hydrochloride was used to alleviate distressing symptoms of tinnitus and vertigo at the beginning of our clinical trials for inner-ear diseases, especially Menière's disease. Although the

injection of 4% lidocaine hydrochloride is very effective for control of vertigo and tinnitus, the patients complained of vertigo for 1-5 hours after the injection of lidocaine. Consequently, in 1981 we began to use 2 or 4 mg of dexamethasone for inner-ear DDS as steroid-targeting therapy to the inner ear (Sakata et al., 1983). The procedure of our therapeutic modality has been reported elsewhere. We summarized our long-term clinical experiences with inner-ear DDS for control of inner-ear dysfunction, especially for tinnitus. Therapeutic results of steroid-targeting therapy to the inner ear were evaluated in 3,041 patients (3,978 ears) with tinnitus. The overall positive results on tinnitus were 75% immediately after intratympanic dexamethasone perfusion and 68% after 6 months.

The danger of perforating the eardrum and of discomfort of vertigo resulting from the transtympanic injection of dexamethasone is minimal. We believe that the transtympanic injection technique is an effective DDS for control of inner-ear diseases and may be performed by any neurootologist in the outpatient clinic.

#### TREATMENT OF TINNITUS BY INTRATYMPANIC INJECTION WITH LIDOCAINE

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In 1985, intratympanic injection of lidocaine 2% was tried in 28 patients suffering from Menière's disease and had a dramatic effect on the vertigo and dizziness. The tinnitus in those patients disappeared in 10.7% and was alleviated in 57.1%. On the basis of those results, we injected intratympanic lidocaine 2% in 52 patients suffering from idiopathic subjective tinnitus. The injections were performed through a tympanostomy tube at 1-week intervals. Only nine patients who underwent five instillations of lidocaine intratympanically benefited from the procedure. In our opinion, the repeated intratympanic instillations of lidocaine are effective in the long run and, with patience and assurance to the patients, the results can be truly rewarding.

#### INTRATYMPANIC DRUG THERAPY, ELECTRICAL STIMULATION, AND TINNITUS CONTROL

**Thomas Lenarz** Department of Otolaryngology, University of Hannover, Hannover, Germany

Tinnitus control can be achieved by drug therapy and electrical stimulation. However, owing to the nonspecific action of several drugs in the central nervous system and the high rate of side effects, local therapy seems to be a possible approach to achieve a better success rate. Local application of drugs known for their possible suppressive effect on tinnitus can be performed either by application onto the round-window membrane or directly into the inner ear. The same principle is used for electrical stimulation by means of cochlear implants or tinnitus implants.

Local application requires a microinfusion system controlled by a micropump and adjusted to the anatomy of the inner by a specific cavity. A model developed by I. Kaugman Arenberg can be attached to the round-window membrane. So far, these application systems can be used only transiently for a period of up to 14 days. Preliminary results show the possi-

bility of tinnitus control by local drug treatment with lidocaine and glutamate.

Long-term results exist for electrical stimulation with cochlear implants for tinnitus control. More than 600 adult patients have been implanted at Medical University, Hannover, since 1984, most of them after 1993. Due to electrical stimulation and external acoustic stimuli, most patients experience tinnitus suppression, which often shows residual inhibition. Only in 5% of the cases does new tinnitus occur or is tinnitus increased by implantation or electrical stimulation (or by both).

These experiences show that local treatment of tinnitus is a potential choice that needs to be developed and evaluated further. Implantable pump systems will become one of the major goals in the near future. Electrode stimulation should also be used for tinnitus implant patients with residual hearing.

#### SHORT-ELECTRODE COCHLEAR IMPLANTS: IMPLICATIONS FOR DEAFNESS AND THE ELECTRICAL SUPPRESSION OF TINNITUS

**M. Miles Goldsmith** Georgia Ear Institute, Savannah, GA, USA

The theory and data supporting the comparable efficacy of the short-electrode cochlear implant in the rehabilitation of profound deafness are presented. Because of its comparable efficacy, cost, simplicity, and the ability to preserve residual hearing, the short-electrode device may become the implant of choice for the estimated 25 million profoundly deaf patients worldwide.

Because the short-electrode implant spares residual hearing, it affords a unique capability with respect to extended applications of such devices, including the electrical suppression of tinnitus. A feasibility trial employing the AllHear short-electrode implant for the electrical suppression of tinnitus is discussed briefly.

#### THE ALLHEAR COCHLEAR IMPLANT EFFECT ON TINNITUS

**Y. Fukuda, B.S. Zeigenboim, and P.L. Mangebeira Albernaz** Escola Paulista, Sao Paulo, Brazil

Of 13 AllHear cochlear implant users, 5 presented before surgery. One has had otosclerosis with bilateral tinnitus. After cochlear implantation, this patient's tinnitus ceased in both ears. In the second patient, the tinnitus ceased in the implanted ear and was relieved partially in the contralateral ear. In two other patients, the tinnitus was relieved but was not suppressed completely with cochlear implantation. In the last patient, the cochlear implant had no effect on tinnitus. Besides these five patients, one patient did not complain of tinnitus before surgery, and it appeared after surgery only with electrical stimulation. In conclusion, the AllHear cochlear implant in deaf patients may have beneficial effects not only in improving the patients' hearing but on their tinnitus.

#### TINNITUS IN COCHLEAR IMPLANT USERS

**A. Aschendorff, G. Pabst, T. Klenzner, and R. Laszig** Ear, Nose, and Throat Clinic, University of Freiburg, Germany

Cochlear implantation is a well-established therapy for

acoustic rehabilitation in deaf adults and children. The majority of patients suffer with additional tinnitus. Suppression of tinnitus is a known effect of electrical stimulation in cochlear implant users. We present our experience in adult and adolescent cochlear implant users. Data were obtained using a questionnaire. In the group of adult patients ( $N = 49$ ), 65% reported tinnitus preoperatively. Postoperatively, for 6 the tinnitus vanished, for 13 it was suppressed using the implant, and for 3 it was at least reduced using the device. In 10 cases, the tinnitus did not change after implantation and was not influenced by electrical stimulation. Two patients developed tinnitus after implantation but, in these cases also, tinnitus was suppressed while patients were using the implant. Nine adolescent cochlear implant users (mean age, 11.8 years) reported similar experiences. The etiology of deafness and rate of performance are discussed. Our results indicate that in 69% of patients, tinnitus is positively influenced through cochlear implantation or electrical stimulation (or both).

#### TINNITUS CONTROL IN COCHLEAR IMPLANT PATIENTS

**O. Ribari, M. Küstel, and M. Horvath** National Institute of Otorhinolaryngology, Budapest, Hungary

In the last 12 years, 86 patients were treated with cochlear implantation by the authors. Different types of implants have been used; the extracochlear and intracochlear implants significantly improved the hearing and social activity of the patients. In addition, patients suffering preoperatively from tinnitus reported substantial benefit from the implantation.

Implants using the CIS speech-coding strategy helped to improve patients' speech recognition and control of tinnitus. The authors also investigated the effects of the cochlear implantation on vestibular function. The implantation did not disturb the vestibular function of the labyrinth. In addition, in some cases significant improvement of vestibular function was noted. The authors discuss tinnitus and the cochleovestibular functions of the patients preoperatively and after cochlea implantation.

#### TINNITUS IN AUDITORY BRAINSTEM IMPLANT PATIENTS: A RETROSPECTIVE STUDY IN NINE CASES

**Johann-Friedrich Werner,<sup>1,2</sup> Stefan Müller,<sup>1</sup> and Roland Laszig<sup>1</sup>** <sup>1</sup>Ear, Nose, and Throat Clinic, University of Freiburg, Germany, and <sup>2</sup>Department of Otolaryngology, Teikyo University School of Medicine, Tokyo, Japan

To rehabilitate hearing ability, auditory brainstem implantation is recommended in patients suffering from bilateral neural hearing loss due to neurofibromatosis type 2 or other bilateral severe damage to the cochlear nerve. In a follow-up trial, it was found that in three of nine cases, tinnitus underwent a change in side, loudness, or frequency.

#### MEDICAL ASPECTS OF TINNITUS

**Cecil W. Hart** Loyola University Medical School, Chicago, IL, USA

Many individuals claiming damages for injury or seeking to augment their retirement pension (or attempting to do both)

claim they suffer from tinnitus. The nature of tinnitus is discussed, including the physiological and pathological forms, awareness of tinnitus, what causes an individual to complain of tinnitus, and comments on measurement, etiology, and treatment. The different roles of physicians, as physician and as medical expert, are discussed. The legal process, as it pertains to this subject, is reviewed. This includes definitions, validation, apportionment, permanency, and governmental regulations. Compensation may be statutory (social security and workers' compensation), by tort, and by contracts. Recommendations for further reading are made.

#### HABITUATION AND TREATMENT OF SENSORY DISORDERS: THE VESTIBULAR SYSTEM EXPERIENCE

**Marcel E. Norré** Leuven, Belgium

The classic concept of treatment for vertigo and allied disturbances consists of administration of drugs or, in some cases, of surgery. However, there is a third method: rehabilitation treatment by exercises. It is not an alternative treatment but has its proper indications and, when indicated, is the treatment of choice. Indeed, in some peripheral vestibular disturbances, only the built-in adaptive mechanisms can cure the patients, and exercise treatment is the natural way to stimulate these adaptive mechanisms. Rehabilitation is indicated in all those cases in which the adaptive mechanisms are the only means for recovery of total balance function. To understand rehabilitation, one must remember that the vestibular function is only one part of the total balance function, of which the adaptive mechanisms constitute another essential part. A patient with a peripheral disturbance has available two means by which to regain a normal total balance function, resulting in normal and adequate reflexes and absence of vertigo: One method is by disappearance of the peripheral dysfunction, which means a *restitutio ad integrum*, a complete repair. In many cases, however, some residual dysfunction persists, and only the intervention of the adaptive mechanisms (compensation, the second method) enables the patient to regain balance. This compensation is a natural process, observed experimentally and clinically after acute unilateral destruction of vestibular function.

The signs of balance dysfunction disappear progressively, notwithstanding persisting hyporeflexia and areflexia of the damaged system. This compensatory (adaptive) process has been studied experimentally and appeared to be a very complex mechanism. It can differ from one individual to the next, using different strategies per individual for reaching the same goal. The evolution can be highly different for each of the several subfunctions of balance, including vestibuloocular reflex, vestibulospinal reflex, static, and dynamic balance. It is composed of phenomena at the vestibular level (i.e., in the vestibular nuclei). Also, other central nervous system functions intervene, subserving a substitution to the defective vestibular function (e.g., the oculomotor function). It is a goal-directed process, stimulated by the presentation of error situations (i.e., an error-controlled process). Habituation is involved in this process and is a mechanism of building up the required compensation. This means that active movements, which present



the as-yet uncompensated error situation to the vestibular centers, will be the specific stimulus for developing the required compensation. Accordingly, movements eliciting vertigo and active movements eliciting instability stimulate the centers to reorganize the required reflexes in an adequate way.

#### CERVICAL TRAUMA, EAR FULLNESS, VERTIGO, AND TINNITUS

**B. Franz, P. Altidis, B. Altidis, G. Collis-Brown, and N. Cummings** Knox Private Hospital, Wantirna, Victoria, Australia

The Barré-Lieou syndrome is regarded as the clinical condition highlighting the relationship of cervical spine injury and ear symptoms, such as fluctuating hearing, vertigo, otalgia, and tinnitus. This syndrome is also called the *posterior cervical sympathetic syndrome*, pointing to involvement of the sympathetic plexus surrounding the vertebral artery. Symptoms are explained by spinal nerve root irritation or as the result of vascular insufficiency, mainly in the inner ear, from vasospasm of the vertebral or basilar arteries or from actual obstruction of these vessels. In contrast to this posterior cervical sympathetic syndrome, an alternative mechanism is presented, emphasizing the anterior cervical sympathetic plexus. During the last 3 years, we have been observing patients with C1 and C2 facet joint disorders, an activated anterior cervical sympathetic, a mild eustachian tube dysfunction, an abnormal electrocochleogram in the presence of a normal hearing level, and a Menière-like symptomatology, among which fullness in the ear, short episodes of vertigo, and tinnitus were the most prominent features. Our experiences with the management of these patients is presented, and a hypothetical explanation is given for the mechanisms of the syndrome.

#### PANEL DISCUSSION: WHIPLASH INJURY AND TINNITUS—NEUROOTOLOGICAL FINDINGS IN THE LATE WHIPLASH INJURY OF THE HEAD AND NECK

**C.-F. Claussen, G. Geiger, D. Schneider, and E. Claussen** University of Würzburg and Bad Kissingen, Germany

Injury to the head and neck is currently one of the common causes of hearing loss, tinnitus, vertigo, and dizziness. As recently as 1992, we had to deal with approximately 197,731 cases of whiplash injuries due to traffic accidents on the roads of Germany. The whiplash injury has become a disease of modern civilization. Its increasing frequency is closely related to the growing numbers of cars in our modern communities. The term *common whiplash injury* has become popularized in relation to traffic accidents owing to a 1953 publication by Gay and Abbott. The clinical syndrome of the whiplash injury was first described by Crowe in the United States in 1928.

By the use of seat belts and neck protectors, the number of direct contact wounds and fractures are reduced in modern motor vehicle accidents. However, the energy impact on the human sitting in a car that has just been struck by another car is absorbed in the head and neck through an abrupt hyperextension movement, which is called the whiplash mechanism.

Basically, we differentiate four types of posttraumatic whiplash syndromes, as there does not exist one single disease pattern. In the *cervical syndrome*, tearing of ligaments, muscles, fascia, and tendons may produce neck pain and result in such local spinal inflammatory responses as ischemia, edema, direct irritation of local tissue, free nerve endings by chemical mediators of inflammation, disruption of the posterior cervical joint complex, anterior subluxation, and cervical instability. Neck pain, neck sprain, and limited ranges of cervical motion, including various degrees of blockade of flexion, extension, and rotation, ensue. The posterior cervical syndrome also is combined with irritations of the autonomous nerve system known as the *Barré-Lieou syndrome*, including dizziness, vertigo, blurred vision, tinnitus, transitory deafness, and shoulder pain.

In the *cervicobrachial syndrome*, there is damage to brachial nerves from compression, stretch mechanisms, and peripheral entrapment by other anatomical structures. The brachial plexus may be damaged by vascular lesions or spasms, a condition known as *Root syndrome*.

In the *cervicomedullary syndrome*, herniation or extrusion of disc material may produce cord pressure. Spinal cord damage can also occur owing to shearing movements of neighboring vertebrae. There is cord damage due to ischemia or infarction of the intrinsic vessels, the extrinsic vessels, or both. Central cord syndrome, anterior spinal artery syndrome, or complete transection of the cord can occur.

The *cervicoencephalic syndrome* is a result of direct action of acceleration forces on the brain (including rotational shearing) and cranial receptors such as the inner ear and the eye. Also seen is indirect cerebral involvement (embolization due to erosion of atheromatous plaques from carotid and vertebral arteries, thrombosis of vertebral artery, compression and spasm of vertebral arteries). Among the common signs are head pain, neck pain, insomnia, irritability, mood changes, anxiety, memory loss, changes of sleep patterns, difficulties in concentrating, and intolerance to alcohol.

According to an abbreviated injury scale, we also distinguish between mild, medium, and severe stages of the aforementioned syndromes. Then the medical expert must find evidence for forming his or her opinion about the posttraumatic degree of disability. Nowadays, this is increasingly important for any cases in litigation. Cases of chronic complaints (considered also under the mantle of late whiplash injury syndrome [Balla, 1980]) play the most important role in current neurootological everyday practice. Most of these cases can be classified as cervicoencephalic syndrome.

The posttraumatic syndromes regularly are subjectively severe, even though they generally are rated by medical experts as so-called minor head injuries. Patients' complaints include headaches, dizziness, instability and vertigo, irritability, restlessness, inability to concentrate, increased sweating, depression and other personality changes, and such other sensorial disturbances as tinnitus, hearing loss, visual disturbances, double vision, and dysgeusia. The statistical occurrence of vertigo is 91.81%, of oscillopsia 64.50%, of tinnitus 83.19%, and of hearing impairment 70.80%.

In analyzing 113 of our experiences with patients suffering from a late whiplash injury syndrome, we found that the cases



had already undergone an average of 14.83 medical investigations for diagnosis and therapy (maximum, 56) and that these patients had seen, on average, 3.95 medical experts elsewhere, representing 18 different medical specialties. We observed a maximum of 23 expert opinions being sought before ours. At the time the patients presented to us, the duration of the posttraumatic complaints already was, on average, 5.48 years. At 2 years after trauma, we label such cases with the *late whiplash injury syndrome*. The jurisdiction in Germany now regularly accepts an interval of 3 years.

It has been proven, that in these long-lasting cases, neurotometry can verify most of the typical functional complaints of a cervicoencephalic syndrome. This is an important contribution of neurotology.

#### PANEL DISCUSSION: WHIPLASH INJURY AND TINNITUS

**B. Kaute** Homberg, Germany

Questions are raised by an outsider on the proprioceptive input of the posterior small cervical muscles as a source of tinnitus. After treatment of whiplash injuries and other muscular conditions with Arlen's atlas therapy, some patients reported that their tinnitus was gone along with the muscular tensions. Atlas therapy has been proven to slacken the muscles and seems to quiet afferent impulses to the brainstem to normal levels. This was proven to apply to nystagmus. Does it have the same effect on tinnitus?

#### PANEL DISCUSSION: SURGERY AND TINNITUS CONTROL—PERILYMPHATIC FISTULA AND TINNITUS

**Y. Fukuda and R.G. Testa** Escola Paulista, Sao Paulo, Brazil

From 1991 to 1997, 14 patients in whom deafness was caused by perilymphatic fistula were surgically treated. This time of onset was 1-32 days (mean, 9 days). Eleven patients had fistula of the round window. Eight patients presented profound sensorineural hearing loss (SNHL), five patients presented severe SNHL, and one patient presented moderate SNHL. After surgery, nine patients had their hearing improved, whereas in five patients, the hearing remained unchanged. Four patients complained of intense vertigo, six of moderate vertigo, and two of mild vertigo, whereas two patients had no dizziness. All these patients were highly benefited by surgery in relation to vertigo and disequilibrium. All 14 patients presented tinnitus caused by fistula. In three, tinnitus was intense, in six it was severe, and in five it was moderate. Ringing, roaring, and hissing were the most frequent descriptions of tinnitus. After surgery, five patients complained that the tinnitus was unchanged, in six patients the tinnitus was weaker, and in three it was suppressed.

#### PANEL DISCUSSION: SURGERY AND TINNITUS CONTROL

**Jun-ichi Matsushima,<sup>1</sup> Noboru Sakai,<sup>1</sup> Shigeki Miyoshi,<sup>2</sup> Norihiro Uemi,<sup>2</sup> and Tohru Ifukube<sup>2</sup>**  
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An electrical tinnitus suppressor developed at the Hokkaido University was implanted in two female and five male subjects (ages 44-77 years). The unit is located into a depression, which is drilled in the mastoid bone just behind the external ear canal. The stimulating electrode is introduced to the middle ear beneath the skin of the ear canal on the posterior bony wall. The primary coil is contained in the behind-the-ear case. A close correlation of residual inhibition existed between results found at the outpatient clinics and those at the home of patients with the implanted suppressor, except in one patient whose electrode was free from the promontory.

A self-administrated tinnitus stress test (TST), annoyance index (AI), and tinnitus intensity index (TII) showed improvement after an operation (except in one patient with electrode trouble). A positive correlation existed after the operation at the .01 level of significance among TST, AI, and TII patients, though no correlation was noted among those before the operation.

#### INSTRUMENTATION AND TINNITUS CONTROL: A TWENTY-YEAR CLINICAL EXPERIENCE

**Barbara Goldstein and Abraham Shulman** Martha Entenmann Tinnitus Research Center, Brooklyn, NY, USA

Significant advances have been made since 1977 in both the diagnosis and the treatment of tinnitus. Our clinical experience at the Tinnitus Center, State University of New York Health Science Center at Brooklyn, from 1977 to 1997, includes more than 4,500 individuals with the primary complaint of subjective idiopathic tinnitus of the severe disabling type, more than 2,000 of whom have completed a medical audiology tinnitus patient protocol (MATPP). This experience supports tinnitus as a medical audiology complaint and as a symptom of neurotological disease. Treatment is based on accuracy of diagnosis. Many options are available for relief, control, and treatment of tinnitus. Instrumentation remains in effective, safe modality of relief for 25% of the total number of patients seen. Of those who complete the MATPP and who follow through on the recommendation of instrumentation, 85% are reporting relief. Increasingly, the combined treatment protocol of instrumentation and drug therapy is being recommended and has resulted in a higher percentage of efficacy of tinnitus control. Treatment instrumentation that is commercially available includes tinnitus hearing aids, habitators, external electrical stimulation, and customized compact disc sound systems. Advanced technology incorporated into these instruments will permit optimal relief, control, and treatment for the patient suffering with tinnitus. Outcome measures and standards are being applied to make meaningful comparisons between studies reporting results and success rates using specific diagnostic and treatment protocols.

#### LINKS BETWEEN FUNCTIONAL HAIR CELL MODELS AND TINNITUS

**H.P. Zenner** University of Tübingen, Tübingen, Germany

This presentation reviews possible molecular and cellular mechanisms in the cochlea that might contribute to tinnitus.

The mechanisms constitute part of a highly integrated network in cochlear sound processing and are divided, for easier understanding, into three different models: active motor tinnitus, transduction tinnitus, and signal-transfer tinnitus. Some of the steps of the pathophysiological models can even be pharmacologically influenced (as exemplified by experimental applications of lidocaine, calcium channel blocker, benzodiazepine, glutamate, and atropine). This provides a rationale for

the efficient suppression of tinnitus by these drugs in some patients. The most evident problem of all models in tinnitus, including those proposed in this presentation, is the lack of objective verification by measurement. Thus, the well-defined clinical situation of each patient is hardly attributable to one of the models suggested. In addition, adequate therapy—perhaps one of the drugs considered—still cannot be based on a reliable clinical finding.