

# Subjective Idiopathic Tinnitus and Palliative Care: A Plan for Diagnosis and Treatment

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## KEYWORDS

- Tinnitology • Clinical types of tinnitus • Tinnitus relief
- Palliation • Tinnitogenesis • Receptor-targeted therapy
- Cognitive-based therapy

The symptom of tinnitus, an aberrant auditory sensory perception, can be a horribly annoying problem for those who are sufferers and a frustrating problem for the physicians, audiologists, and others who are challenged to help these patients find relief from the sounds they are hearing in their head or ears. To some extent, tinnitus is pervasive; reportedly, 12 million people in the United States are troubled by tinnitus.<sup>1</sup> In fact, tinnitus so commonly accompanies presbycusis, the hearing loss that occurs with aging, that many people think tinnitus is just “to be expected as part of growing older.”

In this article, the term *tinnitus* refers to subjective idiopathic tinnitus of the severe disabling type (SIT), a neurotologic disorder of the cochleovestibular system, which is acute or chronic in its clinical course, with interference in the life style of the patient.<sup>2</sup>

Despite attempts over many years to identify an underlying cause of tinnitus and its site of lesion and to elucidate the pathophysiology that would explain why tinnitus occurs, tinnitus remains a disorder that must be categorized as idiopathic. Even though the biologic substrate for tinnitus is not well defined and there is no medical or surgical treatment reliably known to eradicate the symptom completely once it has become manifest, patients who have tinnitus can be helped by those doctors and other professionals who have the empathy, inclination, and expertise to offer treatments that can in many ways ameliorate the anguish of patients who have tinnitus.

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At the Tinnitus Clinic of the Department of Otolaryngology, State University of New York, Downstate, and at the Martha Entenmann Tinnitus Research Center, Inc., since 1979, experience has been amassed with 10,000 patients who have SIT. Although the authors and their colleagues have varying levels of success in offering treatment for their patients, the basic tenet of their program is the age-old adage, “first, do no harm.” Thus, in a sense, although the authors accept the fact that eradication of the symptom of tinnitus may not be an achievable goal for many patients who come to them seeking help, they do aim to provide palliation.

Palliation has been defined as treatment given to relieve symptoms.<sup>3</sup> Palliation also implies a treatment consisting of disguising or concealing a disease. Palliative medicine is oriented to relief of the symptom rather than the underlying causal pathologic condition, with the intention of improving the quality of life (QOL) for the patient. Palliation medicine for otolaryngology has been limited and has focused primarily on symptoms associated with malignant disease of the head and neck (eg, pain control, relief and maintenance of function of the food and air passageways, hospice care).

A palliative approach for the patient who has SIT can be considered in terms of tinnitus relief achieved with combined treatment protocols, highlighted by medication and instrumentation, to achieve and maintain a QOL consistent with the goals of the individual patient (ie, maintenance of auditory function and communication abilities, physical integrity of the cochleovestibular system and normal brain function, normal behavioral psychologic responses in the presence of tinnitus, adequate sleep, participation in social activities).

Palliation for SIT combines a holistic, compassionate, symptomatic, and interdisciplinary approach to achieve at least a modicum of relief and is based on the application of varying regimens that have been developed, with information coming from advances in the understanding of auditory, brain, neural pathway, and psychodynamic functions.

## **CONCEPTS AND PROTOCOLS FOR TINNITUS DIAGNOSIS AND TREATMENT**

The following concepts of palliative medicine from the literature, when integrated with those that have evolved from the authors’ clinical experiences with SIT protocols of diagnosis and treatment, are resulting in increasing success in achieving relief for the patient who has SIT.

### **PRINCIPLES OF PALLIATIVE CARE FOR SUBJECTIVE IDIOPATHIC TINNITUS OF THE SEVERE DISABLING TYPE**

The evolution of the discipline of palliation medicine is well established in the twenty-first century and has witnessed the inclusion of nonmalignant disease, beyond quality-of-life (QOL) issues and hospice care for malignant disease, by application of clinical experiences for pain relief in nonmalignant conditions; in patients who have chronic diseases, symptoms, or injury; and in therapies directed to QOL issues.<sup>4</sup>

The statement of principles developed by the Task Force on Surgical Palliative Care and the Committee on Ethics of the American College of Surgeons (ACS) in 2005 reflects this evolution to a broad range of patients receiving surgical care.<sup>5</sup>

The following principles of palliative care for subjective SIT are recommended, reflecting modification and clinical application of the principles of palliative care proposed by the ACS:<sup>5</sup>

1. Respect the dignity and autonomy of patients who have tinnitus, patients’ surrogates, and caregivers.

2. Respect and honor the right of the competent patient or surrogate to choose among treatments, including those that may or may not provide tinnitus relief.
3. Communicate effectively and empathetically with patients, their families, and caregivers.
4. Identify the primary goals of care from the patient's perspective, and address how the professional attempting tinnitus relief can achieve the patient's objectives and present the realities and limitations of what is and is not known about tinnitus.
5. Do the best one can to achieve tinnitus relief, establish the medical significance of the tinnitus, and differentiate in treatment recommendations among the components of all sensations (ie, sensation, affect behavioral response to the sensation, psychomotor response to the sensation).
6. Recognize, assess, discuss, and offer access to services of neurology, psychology or psychiatry, social issues, tinnitus patient support groups, and national and international tinnitus organizations.
7. Provide access to therapeutic support when such support can realistically be expected to improve the QOL as perceived by the patient.
8. Recognize the physician's responsibility to discourage treatments that are unlikely to achieve the patient's goals.
9. Arrange for continuity of care by the patient's primary or specialist physician or audiologist, alleviating the sense of abandonment that patients may feel when "curative" therapies are not available. Do not tell a patient, "You have to live with it."
10. Maintain a collegial and supportive attitude toward others entrusted with the care of the patient.

### **PALLIATION MEDICINE AND TINNITUS: A BIOPHYSIOLOGIC MODEL**

The landmark neuroscience contributions of Eric Kandel<sup>6</sup> to the understanding of mind and memory are considered to provide, in part, a biophysiologic model to explain the symptomatic relief with palliative medicine, particularly with combined therapies of counseling and drug therapy for control of anxiety and medication, both of which are significant for the patient who has SIT. Specifically, it has been demonstrated that "talk" therapy and listening to the patient involve the brain pathways within the frontal lobes that are involved primarily in cognitive processing (ie, "thinking.") Neural processing is primarily "top down." Fluorodeoxyglucose (FDG) positron emission tomography (PET) brain nuclear medicine imaging has demonstrated an increase in activity in the caudate nucleus in patients who have obsessive-compulsive disorder.<sup>7</sup>

Drug therapy with selective serotonin receptor inhibitors (SSRIs) has been identified to work primarily in subcortical "nonthinking" brain regions (ie, neural processing is primarily "bottom up.") For SIT, this rationale is hypothesized to provide, in part, an explanation for the relief from SIT reported with combined therapies directed to the sensory and affect components of the SIT—specifically, the ultimate influence on the processes involved in the establishment of paradoxical auditory memory, the initial process in transformation of an aberrant auditory sensory stimulus (SIT) to an affect behavioral response (ie, the final common pathway for tinnitus).<sup>8,9</sup> The differences in relief for SIT are based on the underlying molecular genetics involved in sensory, affect, and cognitive processing, which reflect the individuality of each patient who has SIT and the heterogeneity of tinnitus in general and SIT in particular.

## QUALITY OF LIFE

QOL issues for a particular symptom or disease are individual and subjective for each patient. Reports of QOL in patients who have tinnitus should always differentiate between SIT and other clinical types of tinnitus (CTTs).<sup>10-12</sup>

QOL determinants for SIT have been individual in the authors' clinical medical audiologic neurotology experience with SIT in excess of 10,000 patients since 1979, originating in the Tinnitus Clinic of the Department of Otolaryngology, State University of New York, Downstate, and ongoing at the Martha Entenmann Tinnitus Research Center, Inc. The authors' experience has been marked by the heterogeneity and diversity of influences and end points for SIT QOL issues, including physical, psychologic, and social components. For SIT, QOL issues are highlighted by interference in sleep, concentration, communication, performance at work, and interference in social activities with family and friends, with accompanying or resultant anxiety or depression and interference in speech expression and memory. Most important in evaluating reports of QOL issues and tinnitus is the clinical diagnosis of the type of tinnitus. In this article, tinnitus refers to subjective SIT.<sup>10</sup>

In the authors' experience, a team approach of the primary physician and otology-neurotology, audiology, and neuropsychology or psychiatry specialists with a resultant stable personality increases the efficacy of modality(ies) of therapy attempting relief from SIT and the resultant QOL for the patient who has SIT.

Significant determinants have been identified to influence the clinical course of the SIT, the efficacy of therapies attempting tinnitus relief, and the resultant QOL of the patient who has SIT. Included are the following:<sup>2</sup>

- Affect/behavioral response to the presence of SIT: the antecedent or associated behavioral affect response of anxiety and depression to the presence of the SIT is the most significant determinant for the QOL in most patients who have SIT.
- Parameters of tinnitus identification of quality of tone and/or noise, intensity, location, masking effect(s), and duration: intensity is the most frequent complaint influencing the QOL (ie, the higher the intensity, the greater is the report of interference in QOL). The next most frequent complaint has been duration (ie, the longer the duration, the greater is the report of interference in QOL). Individual, occasional, and less frequent has been the report of influence of the quality of the SIT (single or multiple, tone or noise, and location) on SIT QOL. Sociodemographic factors associated with SIT include age, stress, and noise exposure; antecedent neuropsychiatric disease (eg, anxiety; depression; posttraumatic stress disorder [PTSD]; traumatic brain injury [TBI]; metabolic disease of sugar, thyroid, or hyperlipidemia; cardiovascular disease); identification, treatment, or control of hypertension or arrhythmias; and neuropsychiatric disease (eg, anxiety, depression, cerebrovascular or neurodegenerative central system [CNS] disease). Age alone has not been a significant factor for SIT except when associated with neuropsychiatric disease and neurodegenerative CNS disease.
- Neurotologic-associated conditions: Neurotologic conditions associated with SIT, as identified by the patient's history, physical examination and cochleoves-tibular testing, have been identified and are known to influence the clinical course of the SIT adversely. When not identified and controlled, such conditions have been reported to influence adversely the QOL of the patient who has SIT. Included are the presence of hyperacusis, sensorineural hearing loss, fluctuation in aeration of the middle ears, secondary endolymphatic hydrops (SEH), noise exposure, and stress.<sup>10,13</sup>

Erlandsson and Hallberg<sup>14</sup> reported on the QOL and its association with tinnitus-related factors (psychologic, psychosomatic, and audiologic) based on a sample of 122 patients who attended a hearing clinic for distress as a result of tinnitus. Six of 13 variables included in the model proved to be significant regressors and to explain 65% of the variance. The 6 predictor variables were as follows:

1. Impaired concentration
2. Feeling depressed
3. Perceived negative attitudes
4. Hypersensitivity to sounds
5. Average hearing level (best ear)
6. Tinnitus duration (the shorter the duration of tinnitus, the more negative was the impact on QOL)

The three most significant predictors were directly related to perceived psychologic distress and explained most of the variance in QOL in the patients who had tinnitus and were included in this study. An unexpected finding was that fluctuations in tinnitus, vertigo, headache, or perceived social support did not prove to belong to the significant regressors.<sup>15</sup>

A recent report highlights the significance of the impact of tinnitus on QOL in older patients who have tinnitus.<sup>15</sup> In a population-based study, in self-reported data using the Medical Outcomes Study Short Form Health Survey (SF-36) from 2800 subjects who were aged 53 to 97 years, with 669 subjects having a mild, moderate, or severe level of tinnitus, the most significant negative effects of tinnitus showed up in the domains of physical pain and stress, as opposed to the mental and emotional domains. When looking at the SF-36 data, mean scores for all eight domains (physical functioning, role-physical, bodily pain, general hearing perceptions, vitality, social functioning, role-emotional, and mental health index) worsened with the severity of the subject's tinnitus, as did mean scores for the two summary indexes (Physical Summary and Mental Component Summary). A significant ( $P < .05$ ) linear trend was observed for the role-physical, bodily pain, vitality, and Physical Component Summary index. Almost 25% of the population had tinnitus, with 9.4% reporting moderate to severe tinnitus. The researchers concluded that "quality of life is diminished in participants with tinnitus, and the effect increases with severity."<sup>15</sup>

Reports of QOL in patients who have tinnitus should always differentiate between SIT and other CTTs.<sup>10-12</sup>

## TINNITOLOGY

Tinnitology is a new distinct discipline that has been identified, defined, and developed since 1991.<sup>16</sup> It has become a multidiscipline of professionals dedicated to the study of tinnitus and to the translation and integration of clinical otology with the behavioral and basic sciences for tinnitus diagnosis and treatment. Specifically, basic scientists, clinicians, and audiologists are attempting to understand how an aberrant auditory sensation (ie, tinnitus) is transformed into an affect behavioral response. Tinnitology is evolving as an integrated multidiscipline of basic science, auditory science, neuroscience, and clinical medicine. Modalities of treatment recommended at this time are resulting in tinnitus relief (ie, palliation) in an increasing number of cases.

## DEFINITIONS AND CLASSIFICATION

Definitions of "tinnitus" are dynamic, reflecting what is and is not known of auditory science, sensory biophysiology, the cochleovestibular system (peripheral and central),

the brain (structure and function), and human behavior. Originally the definition focused on its subjective nature and was defined as the perception of an aberrant auditory stimulus unrelated to an external source of sound.<sup>17</sup>

In 1992, tinnitus was defined as a sensory disorder of auditory perception reflecting an aberrant auditory signal produced by interference in the excitatory or inhibitory process(es) involved in neurotransmission. This definition reflected the integration of clinical efforts of observation with neuroscience and nuclear medicine to identify underlying mechanisms of tinnitus and to establish the medical significance of tinnitus.

In 2006, tinnitus was defined as a clinical conscious awareness, varying in degree of consolidation, of an aberrant auditory paradoxical memory originating in response to an interference in the homeostasis between dyssynchrony and synchrony within the synaptic circuitry of the neural substrates involved, and thus interfering in the precision, specificity, and complexity involved in synaptic transmission for normal neuronal and interneuronal function.<sup>9</sup>

A tinnitus classification system has been recommended differentiating between an otologic and neurotologic clinical site of lesion.<sup>10-12</sup> The otologic classification is based on the integration of the clinical history and otologic physical examination. The neurotologic examination is based on extrapolation of correlates of electrophysiologic testing of the cochlear vestibular system, peripheral or central in location. The neurotologic or otologic classification primarily provides a basis for the diagnosis of SIT and the selection of a suitable system method for tinnitus treatment and tinnitus control. It offers a method for standardizing the reporting of SIT data for its diagnosis and treatment.

Classification based on epidemiology is further recommended to differentiate between clinical and subclinical tinnitus and auditory and nonauditory tinnitus (ie, whether the auditory system is the primary site of origin of the lesion of the tinnitus complaint [auditory tinnitus] or whether it is secondarily involved [nonauditory tinnitus]).<sup>10-12,18</sup> Other system(s) may use the auditory system to express the dysfunction. Clinically manifest tinnitus is an auditory threshold perception that the patient is experiencing. Subclinical tinnitus refers to the tinnitus as an abnormal subthreshold auditory sensation. Tinnitus may be subclinical in nature and become clinically manifest with a “trigger” event. Such an event may be that of noise exposure or inflammation, for example.

## PRINCIPLES OF CLINICAL TINNITOLGY

The following principles of tinnitology reflect the realities of the authors’ experiences for tinnitus diagnosis and treatment at this time. To be informed and to share information with the patient are principles of palliative medicine.

Principles have evolved from attempts at establishing accuracy for the clinical diagnosis of tinnitus and for attempting tinnitus relief in 2007 through 2008, which have been called “principles of tinnitology” and include the following:<sup>19</sup>

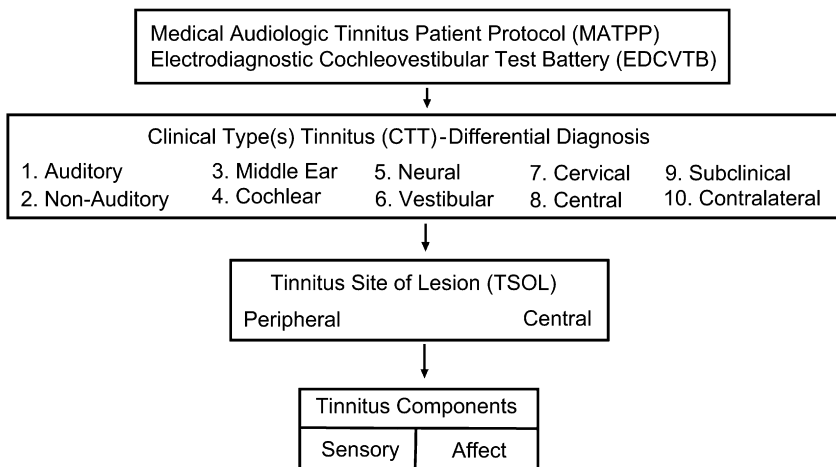
1. There is no cure for tinnitus at this time.<sup>10</sup>
2. Treatment efficacy is based on the accuracy of the tinnitus diagnosis.<sup>10</sup>
3. Not all tinnitus is the same. It is necessary to differentiate tinnitus in patients with the symptoms of SIT from tinnitus that is occasional or tinnitus that is present and not disabling.<sup>10-12</sup>
4. Tinnitus is not a unitary symptom. There are different CTTs and clinical subtypes of tinnitus.<sup>18</sup>
5. The masking of tinnitus is reflected in different types of masking.<sup>20</sup>



15. The key to efficacy for tinnitus treatment depends on the accuracy of the diagnosis for tinnitus. The completion of a medical audiologic tinnitus patient protocol (MATPP) (Fig. 2), with examination of the cochleovestibular system (ear and brain), improves the accuracy of the SIT diagnosis and efficacy of modality(ies) recommended for attempting tinnitus relief.<sup>2,28</sup>
16. A biochemical marker, the  $\gamma$ -aminobutyric acid-A receptor (GABA-AR) has been identified for a predominantly central type of tinnitus. Its clinical application is a therapy targeting the GABA-AR, which is resulting in long-term tinnitus relief.<sup>29</sup>
17. An electrophysiologic correlate has been identified for a predominantly central type of tinnitus<sup>30</sup>
18. Receptor-targeted therapy (RTT) directed to the GABA-AR called RTT-GABA has resulted in the clinical treatment application for a patient who has the predominantly central type of SIT.<sup>31</sup>
19. Tinnitus is not a phantom phenomenon. Electrodiagnostic, physiologic, and biochemical alterations in neural substrates have been identified, which are significant for different CTTs.<sup>8,29,31</sup>
20. The ultrahigh audiometric response can be used for the identification of patients who have SIT and may benefit from acoustic stimulation using ultrahigh-frequency stimulation.<sup>32,33</sup>

#### PRINCIPLES OF SENSORY PHYSIOLOGY

The basic tenet of sensory physiology that there are different clinical components for any sensation has been clinically applied for the patient who has SIT. The components are sensory, affect, and psychomotor.<sup>21</sup> For tinnitus the sensory component is the tinnitus symptom itself, the affect component is the behavioral response of the patient who has tinnitus to the presence of the tinnitus, and the psychomotor component is the somatomotor response to the behavioral component of the tinnitus.<sup>19</sup>



**Fig. 2.** MATPP: diagnosis and treatment. (From Shulman A. Medical audiologic tinnitus patient protocol. In: Shulman A, et al, editors. Tinnitus diagnosis/treatment. Forest Hills (NY): Martha Entenmann Tinnitus Research Foundation, Inc. p. 109; with permission.)

Tinnitus is an aberrant auditory sensation. Recommendations for tinnitus relief should specify and differentiate among the components of the aberrant auditory sensation (ie, tinnitus).

In general, for the SIT sensory component, a combination of instrumentation and medication is advised. For the affect component focusing predominantly on anxiety and depression, appropriate anxiolytic and antidepressant medications are recommended. Fear is a significant factor in new patients who have SIT, and appropriate psychiatric medication or psychotherapy is recommended. To be considered is that a significant number of patients, particularly in the geriatric age population, have associated complaints of interference in memory and cognition. Appropriate neurodegenerative drugs or memory enhancers are recommended.

### TINNITOGENESIS

Tinnitogenesis is a seizure type activity, cortical-subcortical in location, with a resultant aberrant auditory perception.<sup>34</sup> It is an epileptiform auditory phenomenon. It is hypothesized that a disruption in calcium homeostasis reflective of glutamate neurotoxicity results in hyperexcitability in the underlying neural substrate of epileptiform characteristics. This finding has provided a rationale for the innovative recommendation of antiepileptic agents in an attempt to achieve tinnitus relief in appropriate patients who have SIT.

### MEDICAL SIGNIFICANCE OF TINNITUS

The medical significance of tinnitus is considered to be the spectrum of clinical manifestations reflecting interference in function of the cochleovestibular system or brain, with sensory, affect, and psychomotor components.<sup>2,24</sup> The sensory component is considered to be the tinnitus sound and quality. The affect component is the patient's behavioral response to the tinnitus. The psychomotor component is a somatomotor response to the behavioral component of tinnitus.

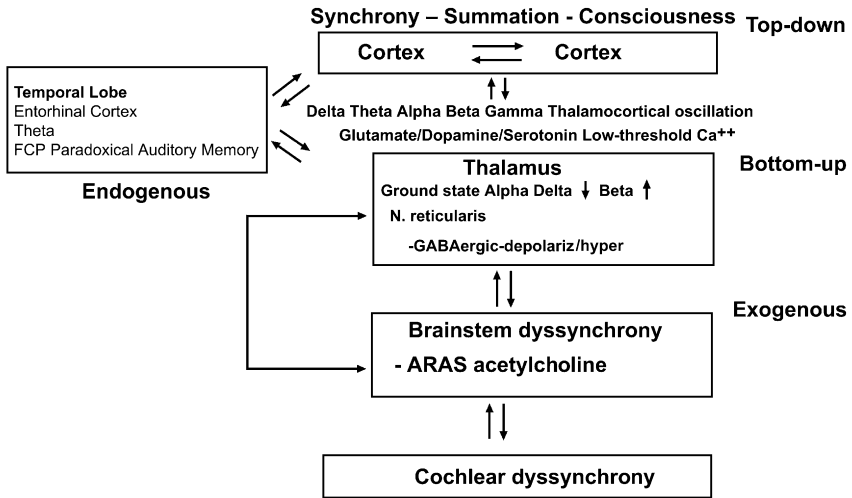
The otologic and neurotologic etiologies associated with the medical significance of tinnitus have been found to be highlighted by associations with inflammatory disease of the middle ear or mastoid, Ménière's disease, acoustic tumor, sensorineural hearing loss, and autoimmune inner ear disease.

### TINNITUS THEORIES: DIAGNOSIS AND TREATMENT APPLICATIONS

Hypotheses of mechanisms of tinnitus in the past included changes in temporal firing patterns of neuronal activity,<sup>35,36</sup> "cross-talk" among eighth nerve fibers,<sup>37</sup> analogy to pain perception,<sup>38</sup> damage to the temporal dysfunction of the inner or outer hair cells,<sup>39-42</sup> partial damage to interruption of the eighth nerve,<sup>43</sup> damage to the efferent system,<sup>44,45</sup> imbalanced activity in eighth nerve resulting in tinnitus,<sup>46</sup> and the recent tinnitus dyssynchrony/synchrony theory (Fig. 3) to differentiate between the dyssynchronous signal that is hypothesized to be tinnitus and the synchrony of neuronal activity at the brain cortex that is the function of the perception and conscious awareness of tinnitus (see Fig. 2).<sup>9</sup>

### DIAGNOSIS: CLINICAL ATTEMPT AT OBJECTIFICATION OF TINNITUS—MEDICAL AUDIOLOGIC TINNITUS PATIENT PROTOCOL

Basic principles of neurotology have been followed since 1975 for tinnitus diagnosis and treatment,<sup>28</sup> which are limited by current understanding of the cochleovestibular system and brain function. Protocols recommended for sensorineural hearing loss,



**Fig. 3.** Integrated model for the tinnitus dyssynchrony/synchrony theory: tinnitus development, propagation, brain function, final common pathway (FCP) for tinnitus. It is hypothesized that a homeostasis of neuroanatomic substrates and neurotransmitters regulates dyssynchrony and synchrony for sensory input received at the brain cortex from the peripheral nervous system or central nervous system (CNS). Rhythmic oscillations modulated by the thalamus are recorded at the cortex and reflect brain function (ie, delta, theta, alpha, beta, gamma). The sensory information ascends by way of the ascending reticular activating system (ARAS) to the thalamus, part of an exogenous system of the CNS for receipt of sensory information arising from the environment or the peripheral nervous system or central CNS. Hyperpolarization and depolarization of GABA-influenced thalamic neuron activity results in thalamocortical oscillations that displace a theoretic ground state of brain activity from the alpha-rhythm down to a theta- or delta-rhythm or up to a beta-rhythm. Input from the thalamus to the temporal lobe and the entorhinal cortex, an endogenous system of the CNS, is hypothesized to result in the establishment of a “memory” for the sensory stimulus, which has a reciprocal influence on the thalamus. The summation of synchronous neural discharges from multiple neural ensembles of neurons at the cortex results in a gamma-rhythm associated with a conscious awareness of the sensory stimulus. Synchronized neural activity in multiple neuronal ensembles is hypothesized to be the basis of perception and consciousness. (*From Shulman A, Goldstein B. Tinnitus dyssynchrony/synchrony theory: a translational concept for tinnitus diagnosis and treatment. Int Tinnitus J 2006;12:320; with permission.*)

vertigo, and ear blockage were modified initially for tinnitus. The clinical goals have been to establish the accuracy of a diagnosis of tinnitus, objectify a subjective aberrant sensory complaint, identify factors influencing the clinical course of the tinnitus, establish its medical significance, and attempt tinnitus relief. Clinicians have been impressed by the heterogeneity of the complaint; the predominance in the clinical complaint of the demonstration of the emotional and behavioral responses of the patient to the presence of the tinnitus; and the influence of noise, exposure, and stress on the clinical course of the tinnitus complaint. The dilemma presented to the basic scientist and clinician was identified as how to explain the transposition of a sensory complaint to one of affect, and how the affect and emotional states of the patient influenced the sensory complaint. Attempts to find the answer to this question are not new. Descartes attempted to answer this question in his own time.<sup>27</sup>

In general, in the authors' experience, the population that has SIT is vulnerable, highlighted by the subjective nature of the complaint and limitations of the medical audiologic professionals in what is and is not known in auditory science about an aberrant auditory sensory complaint (ie, SIT), brain function, behavior, and an understanding of the transformation of a sensory complaint to one of affect. These limitations result in frustration for patients and professionals attempting to establish an accurate diagnosis for SIT (and its relief), which is highlighted by increasing anxiety and depression for the patient and interference in that individual's QOL. Prognostication is a frequent question from the patient who has SIT, and, in the authors' experience, it cannot be predicted. Noise exposure and stress are two factors that are accompanied by the onset and increase in intensity of SIT.

The authors' approach to find answers to this complicated question has recognized the need to consider the totality of the cochleovestibular system (peripheral and central) and brain function. Initially, starting in 1975, a clinical approach for the evaluation of the patient who had tinnitus followed a protocol called the MATPP, which included testing of the totality of the cochleovestibular system (peripheral and central), central speech testing when appropriate, and auditory evoked response short-latency evoked response testing (see **Fig. 3**).<sup>28</sup>

The MATPP is recommended for all patients who have tinnitus of a severe disabling type. It includes the following:

- A. History
- B. General medical evaluation
- C. Neurotologic examination
- D. Cochlear vestibular evaluation
- E. Tinnitus evaluation: to include testing for the Feldmann masking curves and loudness discomfort levels

The MATPP is a multidisciplinary team approach advised for the medical and audiologic evaluation of SIT, which is a neurotologic complaint. Specialists include those in the areas of otology, audiology, family medicine, internal medicine, neurology, psychiatry, and psychology. The neurotologic evaluation is a team approach of audiology and medicine having as its goal the identification of CTTs; identification and treatment of factor(s) influencing the clinical course of SIT; and determination of the medical significance of tinnitus with respect to the general health of the patient and its audiologic significance, particularly with respect to hearing function and communication abilities of the patient and brain function.

The masking curves of Feldmann, which have been shown to be individual for each patient who has tinnitus, provide a basis for the identification of clinical types of SIT, the suitability of masking for the patient who has tinnitus, and the ear to be selected for a masker.<sup>20</sup> When used alone or in combination with a hearing aid, the reduction of the intensity of tinnitus is reported by the patient during its use and by residual inhibition in a postmasking stimulation (partial or total).

Since 1977, the MATPP has emphasized the ear more than the brain. The patient's clinical history has been crucial for diagnosis and has included identification of the parameters of tinnitus identification (ie, quality, location, intensity, masking, rebound). An attempt was made to associate the report of tinnitus with complaint(s) of hearing loss, vertigo, ear blockage, stress, and central nervous system (CNS) symptoms. Factors were identified that were known to contribute to the clinical course of the tinnitus. Such systemic factors were highlighted by cardiovascular (ie, hypertension, cardiac arrhythmias), metabolic (ie, sugar, hyperlipidemias), endocrine (ie, glucose, thyroid), and CNS (ie, cerebrovascular disease, mild cognitive impairment) abnormalities.

Additional factors of noise exposure, stress, anxiety, and depression have all been recognized to be associated with increasing intensity of tinnitus.

What is needed for the twenty-first century are increasing methods to objectify the tinnitus clinically and to consider the ear and brain to be equally significant for the diagnosis and treatment of tinnitus. The clinical history should include what has been described, with additional emphasis on the CNS (ie, taste, smell, memory, speech expression, cognition, consciousness) and the mind. The eliciting of the clinical history as described continues to be significant in establishing the diagnosis of tinnitus. A family history of hearing loss, stress, emotion, anxiety, and depression is equally significant. The electrodiagnostic cochleovestibular evaluation gained significance with the addition of two tests: quantitative electroencephalography (QEEG)<sup>30</sup> and cranio-corpography (CCG).<sup>47,48</sup> QEEG is a multimetric spectral analysis of the raw electroencephalography. CCG is a vestibular test system that also provides information about the psychomotor component of the tinnitus. The introduction of QEEG and CCG has provided electrophysiologic measures for tinnitus and balance diagnoses reflecting brain function in the patient who has tinnitus. Nuclear medicine imaging (MRI) of the brain for structure and single photon emission computed tomography (SPECT), positron emission tomography (PET), and CT-PET for function and the coregistration of data provide a metabolic measure of brain activity in multiple neural substrates in the patient who has SIT. Both provide electrophysiologic and metabolic measures of activity in the brain that have been translated for clinical application in the patient who has SIT for understanding underlying mechanisms of tinnitus production, increased accuracy of tinnitus diagnosis, and a monitoring technique to evaluate objectively the efficacy of modalities of treatment recommended for attempting tinnitus relief.<sup>9,28,30,34,49-54</sup>

The complaint of hyperacusis must be identified for each patient who has tinnitus.<sup>55</sup> A loudness discomfort level test is routinely performed. Different clinical types of hyperacusis have been described.

The MATPP has provided a basis for clinically attempting to objectify the subjective complaint of tinnitus. This led to the identification of different CTTs by the extrapolation of the cochleovestibular test findings as electrophysiologic correlates of cochleovestibular function and dysfunction and their integration with the clinical history and neurotologic physical examination for accurate diagnosis of tinnitus. The hypothesis that tinnitus could have its origin in the central or peripheral cochleovestibular system was clinically considered to be supported by the cochleovestibular test findings highlighted by the auditory brainstem response (ABR) results.<sup>56,57</sup>

## **SEVERE IDIOPATHIC TINNITUS CLINICAL HISTORY AND PALLIATIVE MEDICINE**

Principles of palliative medicine in general and chronic complaints highlighted by pain management specifically have found application for chronic SIT, which is persistent or recurrent in excess of 6 to 12 months. Analogies between pain and tinnitus have been proposed. Tinnitus can be considered to be pain of the auditory system (Juergen Tonndorf, MD, PhD, personal communication, 1989).

A cardinal principle of palliative medicine followed in the MATPP, in an attempt to provide relief of SIT, is the importance of listening and allowing adequate time for obtaining a complete medical neurotologic and audiologic history of the SIT complaint. Highlights include the following:

- Identify the parameters of identification of SIT at the time of consultation and time of onset.

- Establish metrics for identification of intensity and annoyance at the time of onset compared with that at consultation and follow-up visits (ie, to appreciate and identify the clinical course of SIT).
- Attempt a complete review of systems, stressing the association of SIT with the following:
  1. Cochleovestibular complaints highlighted by hearing loss, vertigo, ear blockage, and hyperacusis
  2. Ear, nose, and throat (ENT) complaints of otalgia (eg, dysfunction, hearing loss, inflammatory ear or nose sinus disease during childhood or as an adult)
  3. CNS complaint(s) reflective of the cranial nerves 1 through 12, highlighted by vision, smell, headache, cognition, speech expression, memory, motor function, and gait
  4. Metabolic disorders (eg, disorders of sugar, thyroid, and lipids)
  5. Cardiovascular disorders (eg, hypertension, atrial fibrillation, coronary atherosclerosis)
  6. Skeletal-muscular disorders (eg, cervical osteoarthritis)
  7. Menses (present or absent, replacement hormonal therapy)
  8. Pain (anatomic location, intensity, timing, medication, quality and what [if any] association with the reported SIT)
- Establish a noise and stress profile and their correlation to the clinical course of the patient who has SIT.
- Obtain a psychiatric history of patient with a focus on anxiety, depression, and medications received (with a positive or negative effect) for SIT.
- Obtain list of medications dispensed by a pharmacy to the patient for any and all complaint(s) in the year before consultation.
- Obtain prior test results (eg, audiometric or vestibular testing, brain or ear imaging).
- Obtain a list of treatment modalities attempted for relief of SIT and results (self-prescribed).
- Obtain a list of stimulants used by the patient (eg, coffee, alcohol, smoking).
- Obtain a family history focusing on disorders of the immune system, allergy, hearing loss, diabetes mellitus, epilepsy, or other illnesses in the family.

### CLINICAL TYPES OF TINNITUS

CTTs are identified by means of completion by the patient of a MATPP.<sup>10–13,28,57</sup> The consideration of CTTs is not new.<sup>58</sup>

CTTs (eg, auditory or nonauditory, clinical or subclinical) reflect the degree of ability or inability of a dyssynchronous signal to become synchronous and to establish itself as a conscious percept of memory. The establishment of and consolidation of a paradoxical auditory memory for an aberrant auditory signal reflects itself clinically in the degree of severity of tinnitus.<sup>8–13,28,29</sup>

### TINNITUS IS NOT A PHANTOM PHENOMENON

Tinnitus has been characterized as an auditory phantom disorder.<sup>59,60</sup> In the past, the term *phantom* has been applied when no neural substrate or underlying processes involved in sensory coding are known. Tinnitus is considered to reflect the basic problem in sensory physiology (ie, sensory coding). “True code” has been defined as a parameter of the signal that actually carries behaviorally useful information.<sup>61</sup>

Tinnitus is not a “phantom” but an active physical process or phenomenon occurring in multiple neural substrates in response to a peripheral or central stimulus identifiable in

electrophysiologic recordings (cortical and subcortical and metabolic activated neural substrates) reflecting a synchrony/desynchrony in homeostatic mechanisms involved in the maintenance of “normal” individual brain function. The identification of neural substrates in the brain with nuclear medicine imaging and QEEG electrophysiologic patterns of response at the cortex supports the recommendation that tinnitus is not to be considered a phantom phenomenon.<sup>8,30,49–54</sup>

## TREATMENT

### *General*

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Treatment of a symptom implies identification of its etiology and understanding of the known underlying pathophysiologic mechanisms involved, with the expectation of a cure.<sup>2,25,26</sup> Modalities of therapy attempting tinnitus relief at this time (eg, medication, surgery, instrumentation) are achieving palliation (ie, relief of the symptoms). They are based on clinical translation of theories of underlying mechanism(s) of tinnitus production, principles of the basic science of sensory physiology, identification and treatment of factor(s) influencing the clinical course of the SIT, and treatment providing neuroprotection.<sup>2,25,26,61–74</sup>

Treatment strategies attempting tinnitus relief since 1995 have been called tinnitus-targeted therapy (TTT), which has tinnitus relief (ie, palliation) as its goal. TTT is an SIT treatment protocol that includes the combination of medication or instrumentation targeting biophysiologic mechanisms hypothesized to underlie the initiation, propagation, and clinical course of the symptoms of different CTTs and the identification and medical treatment of local and systemic disease. Neuropsychiatric disease or complaints require identification and treatment.

In the authors' experience, attempts at tinnitus relief for all CTTs have increased by (1) completion of the MATPP for the identification of the CTT and identification and treatment of factor(s) influencing the clinical course of the tinnitus, (2) follow-up of the realities and guidelines for the principles of tinnitology, and (3) clinical translation of principles of basic sensory physiology for recommendations attempting tinnitus relief.

Tinnitus is a chronic complaint.<sup>10</sup> Two essential elements have been recognized for treatment: the sensory component (the tinnitus itself) and the behavioral response to the sensation.

The authors' overall results for medical tinnitus relief since 2000 are positive in approximately 85% to 90% of patients who have SIT. The recommendation for instrumentation has been reduced as the result of an increase in long-term tinnitus relief with medication. The breakdown for tinnitus relief with medication overall efficacy since 2000 has been 85% (10% with instrumentation using masking, amplification, or external electrical stimulation). The remaining 5% to 10% continue to be problem cases. These patients have been identified clinically as having a primarily central type of SIT existing alone or in combination with other CTTs.

The following is a brief summary of the protocols recommended for attempting tinnitus relief. The reader is referred to appropriate references cited in this article for additional information and details of the recommendations.

## MEDICAL TREATMENT

### *Treatment Sensory Component*

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#### ***Factors that influence the clinical course of tinnitus***

Factors influencing the clinical course of the tinnitus, when identified and treated, have been found to result in tinnitus relief.<sup>10,13,19,25</sup> Failure for such identification has been

found to interfere in the efficacy of recommendations of medication or instrumentation attempting tinnitus relief.<sup>2,10</sup>

### ***Secondary endolymphatic hydrops***

SEH has been found in patients who have SIT with or without vertigo.<sup>2,10,13,18</sup> Treatment is recommended with diuretic therapy, antihistamines, and diet-elimination stimulants. The incidence of occurrence of SEH is approximately 35% in the authors' series overall. The control of SEH indirectly contributes to tinnitus relief by increasing the efficacy of the recommendation of instrumentation attempting tinnitus relief and stabilization of the sensorineural hearing loss.

### ***Fluctuation in aeration of the middle ear***

Fluctuation in aeration of the middle ear may influence tinnitus intensity.<sup>2,10,19</sup> Its identification is attributable to inflammatory or allergic conditions of the nose, paranasal sinuses, and throat in addition to secondary Eustachian tube dysfunction. Treatment with systemic antihistamine or decongestant medication and local treatment, including pneumatotomy, have resulted in tinnitus relief in approximately 10% to 15% of the authors' patients who have SIT.

### ***Noise control***

Adequate noise protection with ear defenders and avoidance of noise are recommended.<sup>2,10</sup> Compliance is critical for any recommendations attempting tinnitus relief.

Metabolic factors of abnormalities in sugar, cholesterol, triglyceride, and thyroid function, alone or in combination, may influence the clinical course of sensorineural hearing loss and SIT. Treatment involves identification and follow-up with an internist to ensure satisfactory control.<sup>2,10,19</sup> Synergy has been questioned between hypertension, hyperlipidemias, and noise exposure, resulting in gradual progressive sensorineural hearing loss.<sup>66</sup>

Patients who have SIT with hypercholesterolemia and triglyceride elevation have also reported tinnitus relief with treatment attempting to improve the oxygen-carrying capacity of blood. Trental, 40 mg, titrated to once a day or a maximum of three times a day is recommended if there are no medical contraindications.<sup>2,10,19</sup>

### ***Cardiovascular factors***

Fluctuation in hypertension is, in the authors' experience, the most frequent significant cardiovascular factor involved in the clinical course of SIT. Its identification and control are considered fundamental for any attempt at tinnitus relief. Cardiac arrhythmias, particularly auricular fibrillation with potential consequences for emboli formation, are significant. It is recommended that treatment be directed by an internist.<sup>2,10,19</sup>

### ***Cerebrovascular factors***

Cerebrovascular disease, epilepsy, and memory and cognitive disorders, when identified and treated in appropriate patients who have SIT, have been found to be accompanied by relief of SIT. Effective drugs include the vasodilator papaverine for cerebrovascular insufficiency, Plavix in patients who have had a transient ischemic attack(s) or stroke, and antiseizure drugs for epilepsy. For memory and cognition, the neuroprotective drugs Aricept, tacrine, memantine, gabapentin, and Klonopin are recommended. These drugs attempt to improve the status of the underlying neuronal substrate that may be contributing to SIT.<sup>19</sup>

### ***Otosclerosis***

Otosclerosis, when identified by integration of the clinical history and tomographic examination of the temporal bones, is considered to be a factor influencing the clinical

course of tinnitus. Treatment is recommended starting with a Didronate, 400 mg, once a day for 2 weeks, followed by calcium carbonate with vitamin D for 4 weeks, to be repeated every 3 months<sup>19,67</sup>

### ***Treatment Affect Component-Affective Disorders, Anxiety, and Depression***

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Affective disorders highlighted by anxiety and depression are significant complaints associated with SIT.<sup>10,19,25,31</sup> Appropriate medication for anxiety or depression may secondarily influence SIT in a positive or negative manner.

Anxiety or depression is frequently associated with SIT. The stress diathesis model for depression has been translated to understand the anxiety and depression associated with tinnitus (SIT).<sup>8,22,23</sup> Specifically, increasing stress results in the clinical manifestation of anxiety and, over time, depression. The chronic nature of SIT suggests long-term treatment. Psychiatric consultation is advised to take advantage of the experience of the professional involved for anxiety and depression. Drug selection is at the discretion of the psychiatrist or psychologist. Anxiolytic and antidepressive medications, when recommended, may result in tinnitus. Medications involving neurotransmitter systems other than that of the involved drug in question are then to be used in drug selection. Significant in the literature are reports that when anxiolytic or antidepressant medication is reported to be associated with tinnitus production or to increase the intensity of tinnitus, withdrawal of the drug has resulted in elimination of the tinnitus. Treatment of the anxiety or depression is considered to be critical for the success of any and all attempts to treat the sensory component.

### ***Instrumentation and Tinnitus Control***

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The authors' first-line recommendation is medication, followed by instrumentation.<sup>10,26</sup> Specifically, control of factors influencing the clinical course of the SIT must be achieved.

Instrumentation available consists of hearing aids; tinnitus masks or tinnitus instruments; and tinnitus retraining therapy (TRT), including low-level noise generators, tapes or compact disks of the masking or relaxation external electrical stimulation, and ultrahigh-frequency stimulation.<sup>26,33,39,40</sup>

There are many devices to choose from, and there is a rationale for choosing a specific device. Improved instrumentation provides an increased ability to fit patients who have tinnitus with near-normal hearing, mild high-frequency hearing losses, hyperacusis, and high-frequency tinnitus.

Masking, the substitution of one sound for another, was reintroduced by Vernon<sup>68,69</sup> for attempting tinnitus relief. The masking stimulus, an external noise, provides tinnitus relief by "covering up" the tinnitus. In the authors' experience, the masker continues to be an effective modality of tinnitus relief in patients who have SIT in whom the factors influencing the tinnitus (ie, aeration of the middle ear, SEH) have been identified and treated, in patients who have a predominantly cochlear type of tinnitus, and in patients who have a Feldmann type 1 masking curve. Additional increase in the masker effect can be obtained in selected patients who have SIT by its combination with a hearing aid (ie, tinnitus instrument).<sup>70,71</sup>

TRT is based on the concept that that acoustic, or acoustic-like, perceptions could be habituated to if they were not considered to be a harbinger of disease, danger, or mental stress. Habituation to many sensory experiences is an integral part of human behavior.<sup>40</sup> In the authors' experience, TRT is recommended when medication approaches are ineffective for tinnitus relief. TRT has been most effective for hyperacusis control.

Ultrahigh-frequency acoustic stimulation provides tinnitus relief in a selected group of patients who have SIT and have residual hearing in the ultrahigh-frequency range.<sup>32,33,54</sup>

### ***Surgery and Transcortical Magnetic Stimulation***

In general, the results of surgery for tinnitus relief are conflicting, and there is no specific surgical procedure for the control of any CTT at this time. Results have been more satisfactory for objective tinnitus than for SIT.

Significant tinnitus relief with intratympanic steroid therapy has been reported for a predominantly cochlear type of tinnitus.<sup>72,73</sup> Investigational human cortical electrical stimulation has reported tinnitus relief.<sup>74,75</sup> Transcortical magnetic stimulation in humans has been reported to provide transient tinnitus relief.<sup>74,76</sup> Another surgical approach, deep brain stimulation, involving direct electrical stimulation of structures deep in the brain, has been reported to provide tinnitus relief.<sup>77</sup>

### ***Psychologic Issues of Tinnitus: Cognitive-Based Therapy***

The significance of personality dynamics and coping mechanisms to patients' perception of sensations; their significance for tinnitus; and their clinical application for control of the factors of stress, anxiety, and depression have been recognized and reported since 1984.<sup>78–80</sup>

Clinically, the efficacy of treatment and control for SIT has been increased since 1979 by inclusion in the MATPP of the need to treat the sensory and affect behavioral components of the SIT complaint. The MATPP recognizes the significant role played by counseling in the overall result of tinnitus relief. Specifically, methods of treatment include support groups, crisis intervention, cognitive- or insight-oriented therapies, and psychiatric consultations. Such approaches are considered to be primarily supportive and adjunctive in nature.<sup>80–89</sup> Resistance on the part of the patient who has SIT to such care has delayed the efficacy of treatment directed primarily to the sensory component. A stable personality for the patient who has SIT is considered to be essential for any or all therapies targeting the sensory component of the SIT. When reporting the results of tinnitus relief with supportive therapies, it is necessary to specify the results for SIT. In the authors' experience, the efficacy of cognitive-based therapy (CBT) depends on the readiness of the patient to change his or her behavior and thinking process(es) for the tinnitus and for himself or herself.

CBT refers to the analysis and modification of patterns of behavior, points of view, and outlooks of patients developed as a result or in response to their environment. It is based on the cognitive theory of emotions that was first developed by Beck<sup>81</sup> in the late 1960s.

CBT strategies for tinnitus treatment are not a single form of treatment and include the following:

- A. Behavioral modification
- B. Environmental or situation modification
- C. Modification of negative results on behavior secondary to environmental influences. Techniques include relaxation, hypnosis, and thought stopping, for example.

The following CBT techniques reported for tinnitus relief have been found to be of significance in the authors' approach to relief of SIT:

1. Anxiety and depression: Sweetow<sup>82–85</sup> introduced and adapted, specifically for SIT, the experiences reported by neuropsychiatrists or psychologists of CBT for

complaints of anxiety and depression. The methods are adjunctive to approaches for SIT management methods rather than a substitute for other recommended treatments. Emphasis is placed on management of the patient who has tinnitus rather than on tinnitus management or treatment. Such adjunctive approaches are geared toward an attitudinal adjustment regarding one's reaction to the tinnitus rather than toward alleviating the tinnitus itself.

2. Relaxation techniques<sup>86</sup>
3. Stress, fear, anxiety, and depression control<sup>87,88</sup>
4. Anxiety and pain control<sup>89,90</sup>
5. Incorporation of audiologic techniques for CBT, including sound enrichment<sup>91</sup>
6. Focus on education alone and a cognitive rationale<sup>92,93</sup>
7. Learning theory based on the habituation model<sup>94</sup>
8. Behavior and cognitive restructuring

The effects have been reported of an Internet-based CBT self-help treatment for tinnitus, similar to those described by Sweetow in 1995 in a traditional clinical setting "to identify and modify maladaptive behaviors and beliefs by means of behavioral change and cognitive restructuring."<sup>79</sup>

"Significant reductions in distress" were reported. A 3-month follow-up assessment reported the improvement to be maintained. In this study, 27.3% of patients were reported to have "reached the conservative criteria of clinically significant improvement;" this rate increased to 38.9% when "only those who completed treatment were considered." Significant is the lack of data in this report of the results specifically for SIT.

## ALTERNATIVE METHODS

Alternative methods of therapy in the literature include acupuncture; psychotherapy; hypnotherapy; and the use of herbal, vitamin, Gingko biloba extract 761, and antioxidant drugs. In general, such methods have reported conflicting tinnitus relief results.<sup>10,95-99</sup>

## FUTURE

Future treatment for SIT is awaiting translation of advances in auditory and neuroscience for tinnitus diagnosis and treatment. This should include pharmacology for tinnitus, identified as tinnitopharmacoproteogenomics, instrumentation, and surgery.<sup>19,69-76,100</sup>

The goal is to identify the neurobiology of tinnitus, to identify the kinetics of gene expression in the brain of patients who have SIT, to "personalize" drug therapy for a particular CTT, and to identify not only the kinetics of the genome but the specific function of the protein(s) involved in the patients who have SIT with different CTTs (ie, tinnitoproteogenomics).

The development of drugs focusing on tinnitus control is identified as tinnitopharmacogenomics, which is defined as pharmacology for tinnitus based on what is known of the genetic diversity and protein function(s) demonstrated by patients diagnosed with different CTTs.

Future identification of epilepsy genes is hypothesized to provide insight into the molecular basis of neuronal excitability and brain function, which should have application for a particular central type of tinnitus.

## SUMMARY

Those who evaluate and attempt to help patients who have SIT are advised to learn about and keep abreast of developments in the field of palliative medicine. Palliation medicine is not an alternative to other ways of managing patients who have SIT but is an approach that includes compassion, understanding, and the use of a broad range of expertise in ways that help to alleviate the anguish of patients who are constantly or intermittently exposed to the annoyance of hearing sounds they do not want to hear.

Tinnitus relief (ie, palliation) is available for the patient who has SIT based on an accurate diagnosis of tinnitus and followed by combined therapy of instrumentation and medication. Although no cure is available at this time for tinnitus of any clinical type, protocols of diagnosis and treatment are available that, when completed, provide a basis for treatment selection.

As we professionals strive to reach the goal of a cure for all CTTs, the integration of principles of palliative care into existing protocols for tinnitus diagnosis and treatment, by providing a holistic, compassionate, symptomatic, and interdisciplinary approach for tinnitus relief, should result in respect, understanding, and compassion for the patient who has SIT and a significant degree of tinnitus relief. No longer should a patient who has tinnitus be told "to live with it."

## ACKNOWLEDGMENTS

The authors gratefully acknowledge the support of the Martha Entenmann Tinnitus Research Center, Inc., Forest Hills, New York, for this educational effort.

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