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Alexander Galazyuk and Thomas J. Brozoski	
<p>Animal models have significantly contributed to understanding the pathophysiology of chronic subjective tinnitus. They are useful because they control etiology, which in humans is heterogeneous; employ random group assignment; and often use methods not permissible in human studies. Animal models can be broadly categorized as either operant or reflexive, based on methodology. Operant methods use variants of established psychophysical procedures to reveal what an animal hears. Reflexive methods do the same using elicited behavior, for example, the acoustic startle reflex. All methods contrast the absence of sound and presence of sound, because tinnitus cannot by definition be perceived as silence.</p>	
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<p>Tinnitus is commonly referred to as “ringing in the ears.” Epidemiologic studies highlight challenges associated with clinical determination of tinnitus and ascertainment of its etiology, functional effects, temporal characteristics, psychoacoustic parameters, and risk factors. Because no standards exist for capturing these factors as measures, direct comparison of data between studies is not possible. This report suggests terminology and definitions to promote standardization, with a brief overview of findings from selected population-based epidemiologic studies. Tinnitus-specific data are presented from the Noise Outcomes in Servicemembers Epidemiology study. Further epidemiologic studies are needed to develop tinnitus treatment and a cure for this chronic condition.</p>	
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<p>Tinnitus is the perception of sound in the absence of an external source. Genetic studies on families, twins, and adoptees cohorts have been conducted supporting tinnitus heritability, with higher heritability in men with bilateral tinnitus at any age, and young women with bilateral tinnitus, but not in unilateral tinnitus. The condition is associated with several comorbidities such as hearing loss, Meniere disease, sleep disorders, depression, and migraine and may lead toward suicidal attempts in extreme</p>	

cases. Several studies have reported few regulatory allelic variants in candidate genes and pathways associated with tinnitus development, but replication studies are needed to validate them.

Classification of Tinnitus: Multiple Causes with the Same Name

515

Claudia Barros Coelho, Roberto Santos, Kadja Ferraz Campara, and Richard Tyler

Tinnitus is spoken of as if it were a single thing, but there are many different causes, likely many different mechanisms, and many different subtypes. This article reviews a broad range of approaches to understand and demarcate different tinnitus subtypes, which will be critical for exploring and finding cures for different subtypes.

Noise: Acoustic Trauma to the Inner Ear

531

Ronna Hertzano, Erika L. Lipford, and Didier Depireux

Cochlear damage is often thought to result in hearing thresholds shift, whether permanent or temporary. The report of tinnitus in the absence of any clear deficit in cochlear function was believed to indicate that hearing loss and tinnitus, while comorbid, could arise independently from each other. In all likelihood, tinnitus that is not of central nervous system origin is associated with hearing loss. As a correlate, although a treatment of most forms of tinnitus will likely emerge in the years to come, curing tinnitus will first require curing hearing loss.

Noise: Acoustic Trauma and Tinnitus, the US Military Experience

543

Sarah M. Theodoroff and Dawn Konrad-Martin

Tinnitus is commonly experienced by military Service Members and Veterans, especially by the newest generation who served in Iraq and Afghanistan. When patients seek health care for tinnitus, it is important to determine its type, check for comorbid conditions that might be triggering or exacerbating the condition, and to address its functional and psychosocial effects. Otolaryngologists are usually the first health care professional to evaluate a patient with tinnitus, and it is essential to provide appropriate referrals for this high-burden condition. Noise-induced tinnitus is multifaceted; by performing a thorough assessment, appropriate action can be taken to best meet the needs of patients.

Perception of, and Reaction to, Tinnitus: The Depression Factor

555

Fatima T. Husain

Tinnitus is the perception of a self-generated sound and an individual's psychological reaction to it. This article discusses one element of the reaction: depression. Epidemiologic studies have noted high comorbidity of tinnitus and depression. Findings from recent brain imaging studies have noted shared neural networks in depression and severe tinnitus. As further evidence of this overlaps, antidepressants, counseling, and psychology-based approaches have been used to treat tinnitus. Multifaceted treatment strategies, using both sound-based therapies (not discussed in this paper) and psychology-based approaches, are a necessary part of the

treatment options, with the aim of enhancing self-efficacy in patients with tinnitus.

Does Tinnitus Fill in the Gap Using Electrophysiology? A Scoping Review 563

Victoria Duda, Olivia Scully, Marie-Sarah Baillargeon, and Sylvie Hébert

The results showed a trend of increased post-gap amplitudes and reduced gap salience; however, the small number of articles yield and limited consensus prohibit any conclusions for clinical use. Nevertheless, gap-induced EPs may be further explored as a potential tool for tinnitus detection.

Tinnitus Neuroimaging 583

Meredith E. Adams, Tina C. Huang, Srikantan Nagarajan, and Steven W. Cheung

This article reviews the use of human neuroimaging for chronic subjective tinnitus. Evidence-based guidance on the clinical use of imaging to identify relevant auditory lesions when evaluating tinnitus patients is given. After introducing the anatomy and imaging modalities most pertinent to the neuroscience of tinnitus, the article reviews tinnitus-associated alterations in key auditory and nonauditory networks in the central nervous system. Emphasis is placed on how these findings support proposed models of tinnitus and how this line of investigation is relevant to practicing clinicians.

Current Validated Medical Treatments for Tinnitus: Cognitive Behavioral Therapy 605

Laurence McKenna, Florian Vogt, and Elizabeth Marks

Tinnitus distress results from a weave of physical and psychological processes. Reducing the power of the psychological processes will therefore reduce the degree of suffering. The main psychological therapy in this context is cognitive behavioral therapy (CBT). This seeks to understand and change the influence of thinking processes, including information processing biases, and the behaviors that these motivate, on the experience of tinnitus. The results of systematic reviews and meta-analyses indicate that CBT is the tinnitus management approach for which there is the most robust evidence. In spite of this, it remains difficult to access for people with tinnitus.

Current Validated Medical Treatments: Pharmacologic Interventions 617

Carol A. Bauer

The search for an effective medication that will eliminate tinnitus has a long history. Currently, no drugs exist that universally cure tinnitus. Pharmacologic interventions that have been investigated can be divided into those that attempt to eliminate the perception of tinnitus, and those that are designed to treat the negative comorbidities associated with tinnitus, thereby mitigating tinnitus' negative impact on quality of life. A third category of drugs can also be considered that addresses an identified pathologic condition that has tinnitus as an associated symptom (for example, Meniere's disease, otosclerosis, migraine-associated vertigo). This third category is not addressed.

Current Device-based Clinical Treatments for Tinnitus

627

LaGuinn P. Sherlock and David J. Eisenman

Device-based clinical treatments for tinnitus are predominantly sound based and include ear-level sound generators, hearing aids, cochlear implants, and tinnitus treatment devices. They are intended for patients with bothersome tinnitus. Bothersome tinnitus is characterized by problems with sleep, concentration, and mood. Most people with bothersome tinnitus have hearing loss and would benefit from amplification; however, not all patients are willing to use hearing aids. Tinnitus treatment devices are available to assist those who are not good candidates for amplification, and include devices used while sleeping and devices used for specified periods during the day.

Alternative Treatments of Tinnitus: Alternative Medicine

637

Friederike S. Luetzenberg, Seilesh Babu, and Michael D. Seidman

Because Western medicine has remained largely unsuccessful at treating tinnitus symptoms, many physicians as well as patients have turned to alternative treatment options to decrease patients' suffering and improve their quality of life. Although research in complementary/integrative medicine continues to be scarce and inconclusive, studies are pointing toward the positive effects of acupuncture, herbal remedies, dietary supplements, antioxidants, melatonin, and hypnosis on tinnitus. Although the efficacies of these treatments are inconsistent and may depend on a patient's unique circumstances, studies acknowledge that each treatment is worth trying in light of the potential benefits while being both noninvasive and well tolerated.

Current Clinical Trials for Tinnitus: Drugs and Biologics

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Jonas Dyhrfjeld-Johnsen and Christopher R. Cederroth

Despite recent, major steps forward in our understanding of tinnitus pathophysiology and improved research methodology, tinnitus remains a clear unmet clinical need. Here, the authors identify current active clinical and preclinical development programs of tinnitus drug candidates using publications, databases, and company communications. The current drug development programs hold promise for new therapeutic options for tinnitus patients, but further fundamental research is needed to validate additional targets for treating tinnitus.

Avenue for Future Tinnitus Treatments

667

Tobias Kleinjung and Berthold Langguth

Tinnitus is a common symptom. Standard therapies aim at improving the quality of life and reducing the psychological stress associated with tinnitus. Most interventions have little or no effect on the main symptom. Those affected subjects, however, want such a change and prefer a specific solution, such as pharmacologic therapy to other modalities. Scientific efforts have not yet led to significant improvement in the range of therapies. This article outlines existing efforts and develops ideas on how research for improved tinnitus therapy might look in the future.

Special Article Series: Intentionally Shaping the Future of Otolaryngology

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Sujana S. Chandrasekhar

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Jennifer A. Villwock

Otolaryngologist as a Political Leader? 685

K.J. Lee and Mark E. Lee

Otolaryngologists are in a good position to advocate for our patients and our specialty. We can do it as a volunteer or as a full-time job running for political office at the state or federal level. To be taken seriously, we need to offer solutions besides citing the problems. We encourage otolaryngologists to work with our Academy and its ENT-PAC (Ear, Nose, Throat Political Action Committee). Medicine is a great profession and Otolaryngology–Head and Neck Surgery is an even better specialty.

Strengthening Our Societies with Diversity and Inclusion 701

Sujana S. Chandrasekhar

In 2018, the Joint Councils of the American Otological Society and the American Neurotology Society adopted a statement on diversity and inclusion for programs henceforth. That statement stands as a landmark touch point in our societies that heralds the engagement of all our members as we all work to advance knowledge and skills in otology and neurotology. I was asked to write this piece for Otology & Neurotology, and republication in this Clinics series establishes a baseline understanding of the historical limitations in organized otolaryngology and the willingness of societies to adapt and lead in shaping our profession's future.