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# Chemically Induced or Drug Induced Tinnitus

**Claus-Frenz Claussen, M.D.**

*Department of Neurootology - University E.N.T. Clinic, Würzburg, Germany*

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**F**or approaching the truth about the clinical phenomenon of tinnitus from more and more possible aspects, it is important in the sense of the old Aristotelean systematics of scientific thinking to choose various and alternating directions for regarding the phenomenon. Therefore, today I am also choosing a biochemical angle of view.

Our model of good and bad hearing, ear noise or tinnitus, is primarily demonstrated in the dimension of physics and modern data technology. Hearing is based on the transmission of physical sounds from the surrounding world by resonance in space to the outer ear; the physical amplifier of the middle ear; and finally by digital data transmission from the cochlea via the hearing pathways to the temporal lobe of the brain. However, the human spirit, with all its sensory capacities, does not reside in a technically isolated house nor in a computer, but in a chemically constructed and biologically functioning human body.

Many dysfunctions of the central nervous system, including the symptom of tinnitus can be elicited on a biochemical basis. For example, the toxic effect(s) of solvents or the so-called untoward side effects of various drug therapies.

From an ecological as well as as neurotologic standpoint, particularly in the past 30 years, society has become increasingly aware of the dangers to human neurosensory function(s) secondary to special industrial chemicals called solvents. A clinical syndrome has been identified, related to this danger, called CHRONIC TOXIC ENCEPHALOPATHY (CTE) (Ödkvist et al., 1988). The onset of symptoms are gradual and increase in intensity and multiplicity of central nervous system involvement following an initial and subsequent chronic exposure of the patient to the inhalation from the air of vapors of the solvent(s), e.g., Trichlorethylene, Tetrachlorethane, and Hexane (Gasoline), Cyclohexane, Toluol, Styrene, Methyl-n-butyl-ketone, Methylchloride, Dichlormethane, Trichlorethylene, Perchlor-ethylene, Lindan, etc.

The CTE syndrome has been identified in laborers, technicians, painters as well as others who work and live in a polluted environment. The predominant complaints are disturbances in concentration, memory, cognition, headache, drowsiness, malaise, and balance complaints described as unsteadiness and dizziness. Significant

accompanying complaints include hearing disorders and tinnitus. Many patients complain of reduced hearing and understanding of speech. Frequent auditory complaints include a high pitched noise and a sensation of ear blockage. Diagnosis is elusive, but is eventually established. The neurotoxic complications are increased in number and intensity when solvents are multiple in number and are released in combination into the environment. CTE is a chronic progressive disease.

Recently, a male patient, age 58, was seen in consultation for severe tinnitus. A prior diagnosis of CTE had been established 26 years ago, secondary to toxic inhalation of trichlorethylene vapors. Tinnitus was reported to have been the initial symptom. The patient discovered the beneficial effect of acoustical masking by placing the noise from a toy train close to the involved ear. It provided temporary relief from the constant and irritating tinnitus noise. Today he reports tinnitus control, i.e., relief with a tinnitus masker. The complaint of ear pressure was eliminated following removal of the patient from the toxic environment. However, the high pitch tinnitus persists. Neurotologic evaluation revealed a bilateral sensorineural hearing loss, primarily cochlear in location; and abnormalities in the early and late brain stem potentials. Vestibular testing with polygraphic electronystagmography (ENG) and cranio-corpo-graphy (CCG) recordings revealed multiple abnormalities compatible with central neurotological disturbances.

The public and professional communities should become alert to CTE. Such an awareness will result in its early diagnosis and treatment; and contribute to an increase in our understanding of environmental hazards to public health and concept of tinnitus. Specifically, the concept and diagnosis of CTE should be expanded to include both the physical and chemical worlds for the evaluation and treatment of the symptom of tinnitus.

It is well known among the lay public and medical/audiological professional communities that tinnitus may be elicited by a toxic drug overdose, e.g., Quinine and Aspirin. Many medical treatments elicit a chemically induced tinnitus, i.e., iatrogenic. From a medical perspective, the possibility of a toxic effect of a drug prescribed for its pharmacologic and beneficial effect can occur.

Classification of drug pharmaceuticals are primarily based on their principle actions. However, it is clear that

no drug has only a single or specific effect. Chemically, extremely unlikely that any drug molecule will bind to only single species of molecular receptor. The number of potential receptors is large in every patient receiving pharmacological treatment. Even if the chemical structure of the drug allows it to bind to only one kind of receptor, the process biochemically controlled by such receptors, takes place in many different cell types and is therefore linked to many biochemical functions. The result is that both the patient and the physician probably experience and report more than one drug effect.

Drugs are selective rather than specific in their actions, because they bind more tightly to one than to a few types of other receptors. Furthermore, the receptors control discrete processes that have a specific effect. It is only because of their selectivity that drugs are useful in clinical medicine. However, the beneficial effects of drugs must be routinely evaluated and correlated with their toxic effects. Such a correlation is in essence a monitoring sign, reflecting the border between the desired beneficial effect and the deleterious toxic side effect.

When studying our pharmacologic tool-box we come across a broad variety of drugs which eventually elicit tinnitus. That is an accompaniment of drug overdoses; or unusually high drug retention in the body, e.g., due to renal failure. Such drugs include the aminoglycoside antibiotics (Streptomycine, Gentamycine, Kanamycine, etc.)

Other antibiotics include Amphotericine, Chloramphenicol, Minocycline, Polymyxine B, Procain-Penicilline, Sulfonamides, Vancomycine, etc.

Antineoplastic agents like Bleomycine, Cis-Platinum, Carboplatinum, Methotrexate, Nitrogen Mustard, Vinblastin, etc. are known for their possible side effect in the field of tinnitus.

The diuretics which may elicit tinnitus as a side effect include Acetazolamide, Bumetanide, Bendrofluazide, Clorotalidon, Diapamide, Etcrynic Acid, Furosemide, Hydrochlorthiazide, etc.

Another group of drugs which possibly may induce an unwanted tinnitus contains cardiac antiarrhythmic drugs like Celiprolol, Quinidine, Flecainide, Lidocaine, Metoprolol, Propranolol, etc.

Psychopharmacological agents which may lead to tinnitus are many and include Amitryptiline, Benzodiazepine, Bupropion, Carbamazepine, Diclofensine, Doxepin, Desipramin, Fluoxetine, Imipramin, Lithium, Melitracen,

Molindon, Paroxetin, Phenelzin, Protriptilin, Trazodon, Zimelidin, etc.

Several nonsteroidal anti-rheumatic agents may lead to tinnitus as Acetyl-Salicylate, Acemetacine, Benorilate, Benoxaprofen, Carprofen, Chloroquine, Diclofenac, Diflunisal, Fenoprofen, Feprazon, Ibuprofen, Indometacine, Isoxicam, Ketoprofen, Naproxen, D-Penicillamin, Phenylbutazon, Piroxicam, Proglumetacin, Proquazon, Sulindac, Tolmetin, Zomepirac, etc.

The synthetic partially modified glucocorticoide prednisolone may elicit tinnitus. Tinnitus is a possible side effect of local anesthetics such as Bupivacain, Tetracain, Lidocaine, etc.

Antimalarial agents are potent elicitors of tinnitus, e.g., Quinine, Quinidine, Chloroquinine, Hydroxychloroquine, etc.

Other therapeutic substances with a potential risk to elicit tinnitus include Dihydroergotoxine, Doxylamine, oral contraceptives, Lidoflazine, etc.

Toxic substances long known to physicians to elicit tinnitus include alcohol, Arsenum, Lead, Caffeine, Marihuana, Nicotine, Mercury, etc.

This long and incoherent list of tinnitus eliciting drugs is so diverse that it is difficult to derive or establish one single paradigm or theory for the specific chemical interactions within the body as reflected by any and or all of these drugs. However, clinical experience in medicine has taught that tinnitus is as significant a symptom of human sickness as is pain and dizziness.

Furthermore, it is of interest that several of the above mentioned drugs are recommended for tinnitus treatment: Furosemide, Lidocaine, Amitryptiline, Carbamazepine, etc.

Scientific investigations attempting to further clarify the mechanism of tinnitus production should also consider a broad spectrum of facts provided by what is known of the specific mechanisms of action of the various chemical substances described above, and their biological effects. They are lying in front of us like the "pieces of a puzzle". Until now, the scientists have identified some of the "pieces of the puzzle", however, they are unable to draw the conclusive sketch of the mosaic. These chemical facts have not yet been placed into the definite puzzle of tinnitus. Tinnitus remains a great challenge to the community of neurotologists and also to modern biomedical sciences.