Ototoxicity in the Occupational Environment: A Neurological Problem

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Historically, hearing loss was associated with “high” noise levels, particularly over a long period of time. Difficulty in hearing is a major medical condition impacting millions of people worldwide. In the United States, noise-induced hearing loss as a result of employment (occupational exposure) is a major concern due to raising Workman’s Compensation Claims and its impact on the quality of life. However, in the 1980’s investigators [1] began to recognize that other substances could alone and in combination with noise result in hearing loss. Today, some substances (chemicals) are clearly recognized as contributors to hearing loss in people (e.g. toluene) while other substances (e.g. trimethyltin) are supported by animal investigations only [2]. This dichotomy makes protection very difficult because most substances suggested to be ototoxic are not supported with epidemiological information. What make this association even more complicated is the number of drugs (e.g. prescription and over-the-counter) that also exhibit ototoxic characteristics (e.g. loop diuretics, aspirin) [3].

Occupationally, these ototoxic agents are being expanded in the update of Noise Criteria issued by the American Conference of Industrial Hygienists (ACGIH). Although, interactions in the industrial environment of noise and substances have been clearly recognized for about three decades, there appears to be an expansion as to the degree of concern and awareness. There was some awareness of interactions with noise and hearing loss since the late 1950’s, but was not fully identified or fundamentally recognized until the publication by Bergstrom and Nystrom [1]. However, at least occupationally and more notably environmentally (Public Health concerns), ototoxic substances are a relatively new subject area that is in its infancy of understanding.

Industrial hearing loss or causation of a threshold shift can occur due to “physiological consequences” that are mechanical or metabolic [4]. For ototoxic substances, impacts can occur to cochlear hair cells or through central auditory dysfunction, a classical neuro-toxic event [5]. These agents not only impact hearing but balance as well [6]. Generally, balance is impaired before hearing and can assist in recognition that the causation is related to a “chemical” substance. Another mechanism involving ototoxicity involves hypoxia, free radical formation and loss of blood flow. These causations can be categorized as “partial” neurotoxic in nature. For an agent/substance to be ototoxic, at least by definition, it must impact the sensory/secretory cell structure (epithelia) of the osseous labyrinth or the acoustic nerves (one of the eighth pair or cranial nerves) [4]. Although not strictly part of the neurological structure, damage/impact to any part of the organ of Corti, which contains the hair cells starting the neurosensory system, can also be interrupted resulting in hearing loss. These hair cells are sensitive to mechanical changes and when stimulated produce neurotransmitters that ultimately results in an auditory message which is interpreted by the brain [7]. At least for chemicals, these agents can be categorized as neurotoxic, ototoxic, cochleotoxic or vestibulotoxic agents [7]. Some agents like Carbon Monoxide (CO), which has its impact from hypoxia, free radical formation, and inflammation, can be identified as fitting into more than one category [8]. It is also likely that this agent, CO, acts in combination with other substances that are commonly produced during its generation such as hydrocarbons. Some substances can also impact hearing with a direct effect on the actual ear structure/system through insults on the brainstem [7,9]. Most of these substances are more likely to be related to metabolism/biosynthesis of “ototoxic” agents; although, this criterion is difficult to analyze. There are other mechanisms resulting in hearing loss as noted with CO (hypoxia/asphyxiation) which are not well recognized, particularly in environmental and occupational health [4]. This raises the issue of extending these agents beyond the work environment and making an extension into “Public Health”. However, the problem
with this extrapolation is the exposure dose experienced by those in an environmental scenario is below that evaluated in industrial environments.

Johnson and Morata; Fuente and McPherson [2,5] studies have indicated those exposed to ototoxic substances “exhibit a higher prevalence of hearing loss” when compared to those not exposed to such agents. It has been reported ototoxic substances can alone induce hearing loss [6]. Interactions with noise and ototoxic agents can range from additive to synergistic in nature. The wide diversity of chemicals and drugs suggested as capable of inducing neurotoxicity related to hearing impairment makes this subject of major importance. However, issues associated with chemical exposure, most notably, in the work environment are seldom discussed. As costs for Workman’s Compensation continue to climb and efforts increase in lowering these expenses expand, a greater concern is emerging in regard to ototoxic chemical (agents) substances. Categorization of ototoxic chemicals is difficult, with some “exposures” not truly being represented as chemicals; thus, classification is generally listed as ototoxic agents/substances in attempt to broadly recognize the entire gamut of potential hazards. Substances include “components” that are commonly identified as gasses, dusts, mists and fumes. This can be illustrated in studies reporting hearing loss without “excessive” noise in professional underwater divers [9]. Although the cause for hearing loss in professional divers is not conclusive, this does suggest a physical component, other than sound pressure, could be categorized as an agent contributing to various physiological abnormalities.

The best-known agents, generally, contributing to ototoxicity are solvents (including pesticides) and heavy metals [4]. A number of solvents (e.g. toluene, styrene, xylene, ethyl benzene and trichloroethylene) and metals (e.g. copper, lead, zinc) have become well recognized through both animal and epidemiological studies as ototoxic agents [7]. Most substances identified as potentially being ototoxic have not been well described or identified. This has resulted in little concern for many substances (e.g. n-heptane) regarding their impact on hearing. These substances are generally only identified as “ototoxic” through animal investigations with little if any epidemiological studies supporting these data [7]. Some substances (e.g. n-hexane) that are supported with epidemiological information is based only on high exposure levels and as such can result in difficulty in extracting these findings to exposures commonly observed in most situations [2]. However, from a practical prospective, most industrial environment do not associate with a single type of substance, but rather combinations of exposures and from the literature many of these can be interactive in ototoxic effects [10].

Personal habits (e.g. smoking) also appears to impact hearing [7]. Increasing prevalence of drug use, notably in the United States, may also be contributing to hearing loss and likely result in various interactive effects. When factors of this nature are included with noise levels and exposure to substances in the industrial environment, a magnified concern, as illustrated by the proposed changing criteria being issued through the ACGIH, is emerging. Additional investigation is needed in regard to ototoxic substances and the hazards posed in both the environmental and occupational environment. Based on some investigations [10-12], there appears to be a debate as to whether observed/dose-response effects exits for these substances and in combination with noise. Overall, the various concerns for chemicals/agents/substances bring the neuro-sciences into greater focus with other practices areas, including environmental and occupational health and safety.

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