602 **The effect of glutathione monoethyl ester (GSHee) on hearing loss and hair cell loss in chinchillas exposed to impulse noise**

**N.G. Hight, D. Henderson, S.L. McFadden, X.-Y. Zheng, D.-L. Ding (SUNY at Buffalo)*

Recent research has shown that R-NG-phenylisopropyl-adenoisine (R-PIA), an adenosine analogue, can reduce hearing loss and hair cell loss from noise exposure. There are multiple pathways through which R-PIA could exert protective effects, including upregulation of antioxidants, promotion of blood flow, and attenuation of excitotoxicity. To begin to explore the contributions of the antioxidant pathway, approximately 15 µl of a 0.5 M solution of glutathione monoethyl ester (GSHee) was applied to the round window membrane of eight chinchillas. The other intact ear served as a control. Forty minutes later, the chinchillas were exposed to impulse noise at 150 dB pSPL. The noise consisted of 50 pairs of impulses presented 50 ms apart with 1000 ms between the onset of each pair, delivered from a speaker placed directly in front of the chinchilla at four inches from the ear midline. Thresholds at .5, 1, 2, 4, 8, and 16 kHz were assessed before and after the noise exposure by measuring evoked potentials from electrodes implanted in the inferior colliculus. Permanent threshold shifts (PTS) were measured three weeks after the noise exposure. Additionally, cochleograms of both the treated and control ears were analyzed to assess the degree of inner and outer hair cell loss. There was more PTS in the control vs. the treated ears, with mean differences ranging from 10.3 dB at 500 Hz to 34.4 dB at 4 kHz. Also, the control ears had IHC and OHC loss close to 100% in portions of the cochlea compared to nearly 0% in the treated ears. The results indicate that application of GSHee to the round window can dramatically decrease hair cell loss, and attenuate hearing loss from impulse noise.

Supported by Center for Hearing and Deafness, SUNY at Buffalo

603 **The effect of anti-intercellular adhesion molecule-1 antibody on noise-induced cochlear damage**

*W.X. Tang, *M.D. Seidman, U. Bai (Henry Ford Health System); W.S. Quirk (Wayne State University)*

The purpose of this study was to assess the effects of anti-ICAM-1 antibody on noise-induced cochlear damage. ICAM-1 has an important role in promoting ischemic-induced damage in various tissues, including the brain, heart and lung. Anti-ICAM-1 antibody has been shown to attenuate damage in these tissues. To our knowledge there have been no reports on the effects of anti-ICAM-1 antibody on noise induced cochlear damage.

Male Fischer rats (n=14) were used for this study. Subjects were exposed to 107 dB Broad-Band noise for 72 continuous hours. Control subjects were treated with the vehicle control while the experimental group received Anti-rat ICAM-1 (Discovery Research, Upjohn CO, Kalamazoo, MI) Auditory brainstem responses were performed pre- and post-noise. Immunohistochemistry was performed to assess for hair cell damage.

The control (noise alone) subjects auditory thresholds shifted by 25-40 dB while the experimental group (noise and anti-ICAM-1) had significantly smaller threshold shifts of 15-20 dB. Histologic analysis revealed less hair cell damage in the treated compared to the control subjects.

There is extensive evidence to support that noise exposure leads to reduction in cochlear microcirculation. The reduction in cochlear perfusion leads to the production of reactive oxygen metabolites (ROM) which damage cochlear tissues. Ischemia, ROM, and cytokines (TNF-alpha, IL-1, IF-r)induce endothelial cell expression of intracellular adhesion molecule-1 (ICAM-1). ICAM-1 promotes neutrophil-endothelial cell adhesion. There is a complicated chain of events that results in increases in leukotriene-B4, interleukin-1, interferon-r, platelet activating factor, and ROM, which ultimately leads to increases in vascular permeability with edema, vascular insufficiency and tissue necrosis. In the current study, noise exposure produced the expected temporary threshold shifts, which was significantly attenuated by the use of Anti-ICAM-1 antibody. The results support earlier studies which have demonstrated protective effects of ROM scavengers and blockers on noise induced cochlear damage.

Supported by NIDCD grant #DC00101-01-05 (awarded to MDS) and NIDCD grant #R29-01745 (awarded to WSQ)

604 **Protection from impulse noise with prior treatment with R-PIA**

*C.C. Liu, X.-Y. Zheng, D. Henderson, S.L. McFadden, *N.G. Hight, D.-L. Ding (SUNY at Buffalo)*

Previous research from our lab showed that application of R-N6-phenylisopropyladenoisine (R-PIA) to the round window of the cochlea reduced the effects of a 4 kHz, 95 dB SPL noise exposure in chinchillas. The effects of impulse noise, such as gunfire, have been described as being different from continuous noise because impulse noise may cause direct mechanical failure in the organ of Corti. This experiment had 6 chinchillas pre-treated with R-PIA (0.1 mM, 30 µl) 2 hours before exposure to 100 impulses at 150 dB peak SPL. These impulses mimic the waveform of an M-16 rifle fire. The ears treated with R-PIA showed less (10-20 dB) temporary and permanent hearing loss (TTS and PTS), as well as fewer missing hair cells compared to non-treated and saline-treated control ears. It is clear that R-PIA is effective in reducing the trauma associated with exposure to impulse noise. Given that R-PIA can promote blood flow and inhibit glutamate synthesis as well as promote glutathione production, it is not clear what is the specific protective pathway.

Supported by the Center for Hearing and Deafness, University of Buffalo

605 **Enhancement of noise induced permanent hearing loss by carbon monoxide (CO)**

**G.D. Chen, L.D. Fechter (University of Oklahoma, HSC)*

Intense noise could induce a series of structural and functional changes in auditory hair cells. Failure to repair the damage could lead to a permanent hearing loss. Behavioral and physiological experiments show that the permanent hearing loss caused by broadband-noise can be enhanced by carbon monoxide (CO), especially at high frequencies. In the present study, the ability of CO to enhance noise-induced hearing loss was examined in subjects exposed to one of 4 octave-band-noises (1.2-2.4, 2.4-4.8, 4.8-9.6 & 9.6-19.2 kHz) at levels of 100-115 dB SPL. The experimental subjects (pigmented rats) received CO exposure, noise exposure, or combined exposure to both the CO and the noise. Compound action potentials (CAPs) and cochlear microphonics (CM), to tones from 2 kHz to 40 kHz, were recorded from the round window following a four-week recovery from the exposure. The simultaneous exposure to both the noise and CO caused a much greater hearing loss than the sum of those to the noise alone and to the CO alone, no matter at which frequency the impairment occurred. The exposure to the CO alone did not cause any threshold shift. The high-frequency noise induced greater hearing loss than the low-frequency noise at the same intensity level. The CAP and the CM had a similar change pattern to the noise exposure, but the CM change was usually less than the CAP change. This indicates that the impairment caused by noise is not limited to the outer hair cells. We propose that the CO might reduce the hair cells' ability to repair the noise-induced damage during the recovery. Interestingly, this process seems mainly to occur in the outer hair cells, since the enhancement of the CAP-change was similar to that of the CM-change, though the noise-induced CM-change was much smaller.

Supported in part by NIOSH grant #03481 and NIH grant ES08082

606 **An acoustically augmented environment ameliorates progressive cochlear degeneration in C57BL/6J mice**

**J.F. Willott, J.G. Turner, L.S. Bross (Northern Illinois University)*

C57BL/6J mice exhibit progressive cochlear hearing loss; by age 6 mos, thresholds for high frequencies (>15 kHz) are elevated. We evaluated the effects of an augmented acoustic environment (AAE) on this process by exposing mice to 70 dB SPL noise bursts (200 msec duration, 10 msec rise-fall, 2 Hz rate; maximum spectral

Models for Assessing Risk of Occupational Hearing Loss

Laurence D. Fechter, Ph.D.
University of Oklahoma Health Science Center
College of Pharmacy
Department of Pharmacology & Toxicology
Oklahoma City, Oklahoma 73190

Hearing Loss
5 R01 OH03481-02
09/01/1997 – 08/31/2000
$179,770 ($561,752 Cum)

Publications

Chen GD, Fechter LD: Potentiation of Octave-Band Noise Induced Auditory Impairment by Carbon Monoxide. Hearing Research, in press, 1999

Fechter LD: Mechanisms of Ototoxicity by Chemical Contaminants: Prospects for Intervention. In: Cochlear Pharmacology and Noise Trauma, (eds. Prasher and Canlon), NRN Publications, pp. 129-149, Noise & Health 2:10-27, 1999

Chen GD, Fechter LD: Enhancement of Noise Induced Permanent Hearing Loss by Carbon Monoxide (CO). Association Research Otolaryngology, 1999 (Abstract)

Chen GD, McWilliams M, Fechter LD: Noise-induced Hearing Loss (NIHL) in Different Carbon Monoxide (CO) Environments. Toxicologist, 1999 (Abstract)

Tawackoli W, Fechter LD: Acute Disruption of Cochlear Potentials by Potassium Cyanide. Toxicologist, 1999 (Abstract)

Rao DB, Chen GD, Fechter LD: Effects of Exposure Duration on Potentiation of Noise Induced Hearing Loss by Carbon Monoxide. Toxicologist, 1999 (Abstract)

Unpublished Articles

Fechter LD, Chen GD, Rao DB: Characterizing Conditions that Favor Potentiation of Noise Induced Hearing Loss by Chemical Asphyxiant. Noise and Health, under editorial review, 1999

Chen GD, McWilliams M, Fechter LD: Intermittent Nosie Induced Hearing Loss and the Influence of Carbon Monoxide. Hearing Research, under editorial review, 1999