slightly higher than those induced by a 3-week-exposure at a dose of 400 mg/kg. the 12w-200 group showed less than 10% OHC loss and less than 10-dB PTS. the 24w-100 did not show significant damage, although the animals received the same amount of styrene as the other animals. the data indicate that exposure level is critical for styrene ototoxicity and that the ear fs propensity to accumulate the toxic styrene is limited. a clinical implication of this research is that short, transient, high-level styrene exposure can be ototoxic.

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156 Ototoxic Effects of Styrene Exposure During Gestation and Lactation in Rats

Manna Li [1], Guang-Di Chen[1], Chiemi Tanaka[1], Eric Bielefeld[1], Donald Henderson[1]

[1]*SUNY at Buffalo*

Styrene is extensively used in industries and many workers, including women, are exposed to styrene. Styrene ototoxicity has been well documented. However, the impact of styrene ototoxicity during gestation and lactation is still unclear. We hypothesize that styrene may induce less ototoxic effect on pregnant rats because of high estrogen levels, but may induce significant ototoxic effects on the development of the babies' auditory system. Five pregnant rats were exposed to styrene by gavage at a dose of 400 mg/kg/day starting from the fourth day of gestation for 5 days per week for 6 weeks. Six male rats were exposed at the same dosage for the same period for comparison. Two pregnant rats were unexposed and their offspring were used as controls. Three days after the last gavage of the 6-week styrene exposure, threshold shift in the mother rats and the male rats was assessed using compound action potential (CAP) recording, and their auditory hair cells were counted. the styrene exposure caused an about 15-20-dB threshold shift and 30-40% outer hair cell (OHC) loss in the mid-frequency region in both groups of the pregnant rats and the males rats. Threshold shifts of the baby rats were measured 2 months after birth by recording of both auditory brainstem response (ABR) and CAP. Significant CAP threshold shift was only observed in those rats from one mother but not the other four mothers. Interestingly, ABR threshold shift was observed in all of the 5 families. Almost all of the baby rats have normal cochlear anatomy, i.e.: no hair cells loss. the mechanism for the hearing loss in the mother rats and the pups is discussed.

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157 Functional and Structural Changes in the Chinchilla Cochlea and Vestibular System Following Round Window Application of Carboplatin

Yide Zhou[1], Dalian Ding[1], Suzanne Kraus[1], Richard Salvi[1]

[1]*University at Buffalo*

Carboplatin, a second-generation anticancer drug, has a low level of ototoxicity in most species; however, in chinchillas carboplatin preferentially destroys inner hair cells (IHC) and type I vestibular hair cells at moderate doses while at higher doses it destroys both IHC and outer hair cells (OHC) and type I and type II vestibular hair cells. to better understand the time course and mechanisms of carboplatin toxicity, carboplatin was applied to the round window membrane (5mg/ml, 50¡Ìl) of the right ear and the functional and anatomical consequences were examined at 1, 3, 7, 14 and 30 days post-treatment. Carboplatin caused a significant reduction in distortion product otoacoustic emissions (DPOAE) at all frequencies 3 d post-treatment. the threshold of the compound action potential (CAP) increased significantly from 3 to 7 d post-treatment and after 14 d the CAP was absent. Carboplatin treatment induced spontaneous nystagmus 1 d after carboplatin treatment which disappeared 2-3 d later. Cold caloric stimulation evoked a robust nystagmus response in untreated ears, but the nystagmus response disappeared approximately 3 d after carboplatin treatment. Vestibular dysfunction was associated with a significant reduction of vestibular hair cell density 3 d post-treatment. the early stages of cochlear and vestibular hair cell degeneration were associated with nuclear shrinkage and fragmentation, morphologic features of apoptosis, upregulation of initiator caspase 8 and executioner caspase 3, but absence of caspase 9 labeling. These results indicate that carboplatin rapidly penetrates the round window leading to severe functional deficits arising from programmed hair cell death initiated from the cell death receptors on the surface of cell membrane. Supported by NIH grant R01 DC06630-01

158 Effects of Cisplatin-Ethacrynic Acid Cochlear Pathology On DPOAE

Withdrawn

159 Selective Damage of Murine Cochlear Cell Types by Varying Concentrations of Ouabain

Osamu Adachi[1], Konstantina M. Stankovic[1], Arthur G. Kristiansen[1], Joe C. Adams[1], Michael J. McKenna[1]

[1]*Massachusetts Eye & Ear Infirmary*

Ouabain is a cardiac glycoside that specifically binds to Na/K-ATPase and inhibits its activity. Other authors have established that ouabain induces selective degeneration of spiral ganglion neurons when applied to the round window of gerbils. We wanted to determine whether ouabain can similarly cause selective damage in the murine cochlea. to minimize variability inherent in intratympanic application of pharmacologic agents, we used intralabyrinthine approach to delivered ouabain. a total of 10 µl of ouabain at the concentrations 1.0, 0.1 or 0.05mM was injected through a small fenestra in the posterior semicircular canal of 6 week old male CBA/CaJ mice at the volume ratio of 1µl/min after making a release fenestra in the lateral semicircular canal. Mice were sacrificed 10 days after treatment (3 mice for each concentration of ouabain) and their cochleae analyzes histologically using Azure stain, and

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19 Mantua Road, Mt. Royal, NJ 08061 USA