P1

Jones, Shamira A., L.R. Brown, III, and Sharon Chriss, Departments Of Biology and Chemistry, Southern University And A&M College, Baton Rouge, Louisiana. The Teratogenic Effects Of Arsenic And Lead On Lungs And Digestive tracts Of *Micropterus salmoides*.

Previous environmental analysis of arsenic and lead on aquatic animals revealed very interesting data. Pregnant female members of *Micropterus salmoides* were exposed to varying concentration levels of inorganic arsenic-(in the form of arsenic trioxide ranging in concentration measurements from 0.05 ppms to 0.10 ppms) and lead-(in the form of lead acetate ranging in concentrations from 0.05 ppbs to .10 ppbs) over a 2 wk to 8wk period. In our study it was shown that after a 2-wk exposure interval to inorganic arsenic at 0.05 ppms, the female members were found to have small scarlet tissue lumps developing in their lungs and stomach regions. Additionally, it was shown that after a 4-wk exposure interval to inorganic lead at 0.05 ppbs, the embryos in this group developed hardened pallets of scar tissue in the lungs and in the lower side of their fins where muscle-tissue is found. Analysis with the Inductively Coupled Plasma/ Mass Spectrometry revealed that after 8-wks of exposure to both inorganic contaminants the pregnant female members developed malformed tails and decreased eyes. Additional problems centered around the digestive tract in both contaminants induced development of lumps of tissues in the stomach and lower liver regions. This development induced severe digestive problems for the animals as well.

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P2

LYNCH*, D.W., NIOSH, DBBS, Experimental Toxicology Branch, Cincinnati, Ohio. Sodium arsenate heptahydrate - developmental toxicity in intact *Drosophila melanogaster*.

To further characterize the *Drosophila* bioassay as a screen to detect developmental toxicants, sodium arsenate heptahydrate (SAH; CAS 7631-89-2), a documented animal teratogen and developmental toxicant, was evaluated. SAH concentrations ranging from 263 - 1528 μg/vial were investigated in a series of three experiments using our published protocol (*Teratogenesis, Carcinogenesis, and Mutagenesis* 11:147-173, 1991). Each experiment utilized five SAH concentrations plus a concurrent control. In the second and third experiments, 2-3 concentrations from the preceding experiment were replicated, and 2-3 new higher concentrations were added. *Drosophila* were exposed throughout development (egg through third instar larva) in culture vials to medium containing SAH. Each vial contained 1g of powdered medium and 5ml of distilled deionized water or a solution of test chemical in water. A mated, untreated, Oregon-R wild-type female (Mid-American *Drosophila* Stock Center, Bowling Green State University, Ohio) was added to each culture vial and allowed to oviposit for 20 hours, then removed. Emerging offspring were collected over 10 days, and examined microscopically (25x) for bent humeral bristles and wing blade notches, morphological defects shown to occur with an increased incidence in flies exposed to developmental toxicants. In each experiment, the incidence of the two defects at each concentration was compared to the concurrent controls using chi-square. In cases where replicate data were available at a given concentration, incidence data were pooled and compared to the pooled controls. Using pooled data, the incidence of bent bristles was statistically increased at the following SAH concentrations - 389 (21/489, $p<0.001$), 575 (24/644, $p< 0.001$), 699 (24/520, $p<0.001$) and 850 (15/479, $p<0.001$) μg/vial. For non-replicated concentrations, the incidence of bristle defects was significantly increased at 1033 (8/241, $p<0.01$) and 1528 (11/224, $p<0.001$) μg/vial. No wing blade defects were observed at any SAH concentration. These results provide additional support for increased utilization of this test as a prescreen for developmental toxicants.

P3

Hartig, P.C. and E.S. Hunter Reproductive Toxicology Division, NHEERL, U.S. EPA, RTP, North Carolina Effects of overexpression of human p53 on arsenite-induced dysmorphology on mouse embryos in culture.

Arsenite (As3) directly affects mouse embryogenesis in vitro. As3 induces a G1 cell cycle block and produces cell death in embryos. These effects are consistent with those produced by p53 in cells in culture. To test the hypothesis that p53 mediates As3-induced dysmorphogenesis a replication deficient
ıs (AV) was used to express human wildtype p53
r mutant p53 (Mp53) in the embryo. Neurulating CD-1
ıbryos were prepared for whole embryo culture and AV was injected into the amniotic cavity. In control embryos 0% exhibited neural tube closure defects (NTDs) after 26H of culture. 3μM As3 produced 20% NTDs. Neither Mp53 nor Wp53 produced no NTDs when injected at 90 or 225 particles per nl (ppn) concentrations. In contrast to As3 alone, 225 ppn Wp53 + 3μM As3 produced 46% NTDs. 90 ppn Wp53 + 3μM As3 produced 27% NTDs in embryos. Mp53 + 3μM As3 induced 0 and 17% NTDs at 90 and 225ppn Wp53 concentrations. Lysotracker (LT) staining for cell death (in embryos after a 26H culture period) suggested that Wp53 + As3 increased the areas of LT staining compared to As3 alone. Embryonic cell cycle analysis indicated no differences after treatment with As3, 90 ppn Mp32+3μM As3, or 90 ppn Wp53+3μM As3 compared to control embryos after a 26H culture. These data suggest that overexpression of Wp53 at high concentrations increases the incidence of As3-induced malformations possibly by increasing susceptibility to apoptosis.

(This abstract of a proposed presentation does not necessarily reflect EPA policy)

P4

HUNTER, E.S. Reproductive Toxicology Division, NHEERL, U.S. EPA, RTP, North Carolina Selenite prevents the dysmorphology and early phase cell cycle changes produced by arsenite in mouse embryos in culture.

Arsenite (As3) directly affects mouse embryogenesis in vitro producing neural tube closure defects (NTDs) and other abnormalities. Previous studies indicate that the pathogenesis of As3-induced effects includes induction of cell death and cell cycle perturbation. Since concomitant exposure to superoxide dismutase (SOD) or selenite (Se3) can ameliorate As3-induced NTDs, we evaluated the cell cycle and production of cell death in order to determine if there is an association between these effects and dysmorphogenesis. 5μM As3 produced a 100% incidence of NTDs in neurulation staged CD-1 mouse embryos after a 26H culture period. 10μM Se3 + 5μMAs3 (Se+As) reduced the incidence of NTDs to 10%. 1500U SOD + 5μMAs3 (SOD+As) produced 85% NTDs. Cell cycle analysis after 6 and 9H exposures showed that Se prevents the effects of As3. However, after a 12H exposure the increase in cells in G1 and the decrease in S phase was as great as that produced by As3 alone. Embryos exposed to SOD+As exhibited cell cycle effects similar to those exposed to As3 alone at all time points. As an indication of cell death the percentage of cells with <G1 amount of DNA was compared. For embryos exposed to As, Se+As and SOD+As after 9H of exposure 10-15% of cells had <G1 amount of DNA. At both 12 and 18H embryos exposed to As3 had 30% of cells with <G1 amount of DNA. In contrast, 10-15% of cells had <G1 amount of DNA in

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THE TERATOLOGY SOCIETY
Thirty-Eighth Annual Meeting

June 20-25, 1998

Program and Abstracts

The San Diego Princess Resort
San Diego, California

Wednesday, June 24, 1998

7:00 a.m. – 8:00 a.m.	CONTINENTAL BREAKFAST — Princess Foyer
7:00 a.m. – 8:00 a.m.	**EXHIBITOR BREAKFAST** — Dockside Restaurant
7:30 a.m. – 5:00 p.m.	REGISTRATION — Princess Foyer
8:00 a.m. – 11:30 a.m.	**POSTER DISCUSSION WORKSHOPS**

Poster Discussion Workshop A

ARSENIC - Island Room
Chairpersons: *Ronald D. Hood, Department of Biological Sciences, University of Alabama, Tuscaloosa, Alabama and Richard K. Miller, Department of OB/GYN, University of Rochester School of Medicine & Dentistry, Rochester, New York*

8:00 a.m. – 8:20 a.m.	**P1**	THE TERATOGENIC EFFECTS OF ARSENIC AND LEAD ON LUNGS AND DIGESTIVE TRACTS OF MICROPTERUS SALMOIDES, S.A. Jones, L.R. Brown, III, S. Chriss, Department of Biology and Chemistry, Southern University and A&M College, Baton Rouge, Louisiana
8:20 a.m. – 8:40 a.m.	**P2**	SODIUM ARSENATE HEPTAHYDRATE–DEVELOPMENTAL TOXICITY IN INTACT DROSOPHILA MELANOGASTER, D.W. Lynch, NIOSH, DBBS, Experimental Toxicology Branch, Cincinnati, Ohio
8:40 a.m. – 9:00 a.m.	**P3**	EFFECTS OF OVEREXPRESSION OF HUMAN P53 ON ARSENITE-INDUCED DYSMORPHOLOGY ON MOUSE EMBRYOS IN CULTURE, P.C. Hartig and E.S. Hunter, Reproductive Toxicology Division, NHEERL, U.S. EPA, Research Triangle Park, North Carolina
9:00 a.m. – 9:20 a.m.	**P4**	SELENITE PREVENTS THE DYSMORPHOLOGY AND EARLY PHASE CELL CYCLE CHANGES PRODUCED BY ARSENITE IN MOUSE EMBRYOS IN CULTURE, E.S. Hunter, Reproductive Toxicology Division, NHEERL, U.S. EPA, Research Triangle Park, North Carolina
9:20 a.m. – 9:40 a.m.	**P5**	ARSENATE-INDUCED EMBRYOTOXICITY IS NOT MEDIATED THROUGH CHANGES IN WHOLE EMBRYO AP-2 DNA BINDING ACTIVITIES, L.A. Lanoue, M.A. Philips, M.S. Golub. C.L. Keen and R.H. Rice, Departments of Nutrition, Environmental Toxicology and Internal Medicine, University of California, Davis, California
9:40 a.m. – 10:10 a.m.		COFFEE BREAK — Sunset Ballroom
10:10 a.m. – 10:30 a.m.	**P6**	INORGANIC ARSENIC IS NOT LIKELY TO BE A DEVELOPMENTAL TOXICANT AT ENVIRONMENTALLY RELEVANT EXPOSURES, J.M. DeSesso, C.F. Jacobson, A.R. Scialli, C.H. Farr and J.F. Holson, Mitretek Systems, McLean, Virginia, Georgetown University Medical Center, Washington, D.C., Elf Atochem North America, Philadelphia, Pennsylvania and WIL Research Laboratories, Ashland, Ohio
10:30 a.m. – 10:50 a.m.	**P7**	AN INHALATION DEVELOPMENTAL TOXICITY STUDY OF ARSENIC TRIOXIDE IN RATS, D.G. Stump, C.E. Ulrich, J.F. Holson and C.H. Farr, WIL Research Laboratories, Inc., Philadelphia, Pennsylvania
10:50 a.m. – 11:10 a.m.	**P8**	AN ORAL DEVELOPMENTAL TOXICITY STUDY OF ARSENIC TRIOXIDE IN RATS, D.G. Stump, K.J. Clevidence, J.F. Knapp, J.F. Holson and C.H. Farr, WIL Research Laboratories, Inc. Ashland, Ohio and Elf Atochem, North America, Inc., Philadelphia, Pennsylvania