female Sprague-Dawley derived rats at concentrations of 0.2, 0.4, and 0.8 percent using a two-generation reproduction study design. Several additional endpoints were evaluated such as estrous cyclicity, sperm assessment, and developmental milestones, according to EPA Reproduction and Fertility Effects guidelines (July, 1994). There were no treatment- related differences in clinical observations, survival, reproductive organ weights or histopathology, male mating, male and female fertility, female fecundity or female gestational indices in either generation. Starting at about dosing day 42, P high-dose animals had significantly lower mean body weight compared with controls; this effect was more pronounced in F1 high-dose males. Some evidence of reduced body weight gain in the high-dose P females was also seen during the gestation and postpartum periods which correlated with reduced food consumption. There were no significant differences in clinical or gross observations for offspring in either filial generation (F1 or F2); early survival of high-dose offspring was slightly reduced because of excess offspring deaths in a limited number of litters. Statistically significant lower mean offspring body weights which were similar to the lower mean body weights observed in the P animals were seen in the F1 and F2 high-dose groups. Cross-fostering experiments showed these body weight effects to be rapidly reversible suggesting a palatability effect. The F1 generation successfully produced normal, healthy offspring after exposure to DIDP in utero, during lactation, puberty, and adulthood which indicates its lack of transgenerational effects on reproduction. In conclusion, DIDP did not produce evidence of reproductive or fertility effects under the conditions of this study. Keywords: Reproductive toxicity, di-isodecyl phthalate.

1828 ALTERATIONS OF HUMAN SPERMATOZOA PENETRATION OF HAMSTER OOCYTES AFTER EXPOSURE TO ACTINOMYCIN D (ACTD) AND DOXORUBICIN (DR).

M J Scobey[1], R S Jeyendran[2] and D P Waller[1]. [1]*Univ. of Illinois at Chicago;* [2]*Andrology Lab Services, Chicago, IL.*

Numerous reports document the ability of chemical agents to alter sperm functions such as motility, acrosomal reaction rate and ability to fertilize an oocyte. These effects are seen from exposure in vivo as well as in vitro. Some drugs are known to be present in semen and may mediate direct effects on spermatozoa function. We have evaluated the ability of ACTD and DR to inhibit human sperm function in vitro. Human spermatozoa were incubated with ACTD or DR and their ability to penetrate zona-free hamster oocytes evaluated. Washed spermatozoa suspended in protein free Tyrodes culture medium (TCM) were incubated for five minutes at ambient temperature with 20 ug/ml of DR or ACTD. These spermatozoa and untreated spermatozoa were extensively washed, re-suspended in TCM, and mixed with zona free hamster oocytes for two hours at 37° C and observed under the microscope for the number of oocytes with decondensed sperm nuclei (penetration rate-PR). The average number of decondensed sperm nuclei per oocyte was calculated (penetration index-PI). Motility was also evaluated. The PR of control, ACTD and DR treated spermatozoa were 90, 17 and 78 % respectively. The PI for these incubations were 3.5, 0.6 and 3.4 respectively. Lower concentrations of ACTD resulted in a dose related decrease in PR and PI. Motility was not altered in any preparation. These data suggest ACTD in human semen may inhibit the ability of sperm to fertilize an egg.

1829 INITIAL CHARACTERIZATION OF AN *IN VITRO* RABBIT SPERM ACTIVATION ASSAY.

D B Brown[1], D E Sawyer[1], B J Maeker[3], M J Breitenstein[4], G R Hillman[2], and S M Schrader[4]. *Depts. of* [1]*Human Biological Chemistry and Genetics &* [2]*Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX;* [3]*Diagnostic Systems Laboratories, Inc., Webster, TX;* [4]*National Institute for Occupational Safety and Health, Cincinnati, OH.* Sponsor: G A S Ansari.

Previous studies have shown that both human and rat sperm nuclei can be activated *in vitro* using a cytoplasmic extract from *Xenopus laevis* frog eggs. Activated nuclei undergo chromatin decondensation, DNA synthesis, and recondensation (human only). To complement these systems, we are developing a rabbit sperm activation assay. Lysolecithin-permeabilized rabbit sperm were incubated in ^{3}H-TTP-spiked *X. laevis* frog egg extract. Decondensation was assessed visually using phase-contrast microscopy and quantitatively using an image analysis system. DNA synthesis was assessed using autoradiography. Ejaculates from three different rabbits were used for these studies. Activated sperm nuclei from two of the rabbits decondensed to ~11 times their original size at a rate of ~175 U/min. (arbitrary units). Interestingly, multiple ejaculates from one rabbit repeatedly displayed attenuated decondensation (7.5X size increase and ~114 U/min.); the reason for this is being investigated. Greater than 95% of the activated sperm nuclei consistently replicate DNA. We plan to use the rabbit sperm activation assay to perform in vivo toxicology studies on toxic agents known to bind sperm chromatin. This assay will complement the rat sperm activation assay and allow for multispecies toxicology studies evaluating sperm nuclear activation as an endpoint.

1830 ALTERED DECONDENSATION KINETICS OF ACTIVATED RAT SPERM NUCLEI TREATED WITH A REVERSIBLE CROSSLINKING AGENT.

D E Sawyer[1], G R Hillman[2], and D B Brown[1]. *Depts. of* [1]*Human Biological Chemistry and Genetics &* [2]*Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX.* Sponsor: G A S Ansari.

Exposure of laboratory rats to chemicals that bind spermatid chromatin (e.g. cyclophosphamide, methyl methanesulfonate) increases preimplantation embryo loss. We hypothesize that the underlying mechanism of this male-mediated developmental toxicity is abnormal sperm nuclear activation, and have developed an *in vitro* rat sperm activation assay (RSAA) to test this hypothesis. The RSAA involves incubating demembranated rat sperm in a cytoplasmic extract of *Xenopus laevis* frog eggs. The activated nuclei undergo chromatin decondensation and DNA synthesis. As a first step toward validating the RSAA as a toxicology assay, we have treated rat sperm with the reversible crosslinking agent ethylene glycolbis(sulfosuccinimidylsuccinate; SEGS). Human sperm treated with this agent respond abnormally in the human sperm activation assay (Sawyer & Brown, *Reprod Tox 9*, 1995, 351–7). Decondensation kinetics were assessed using an image analysis system to measure sperm head size as they decondensed. Control sperm decondensed to 3.5 times their original size by 2 hrs at a rate of 6.7 U/min (arbitrary units) during their most rapid growth (30–60 min. after extract addition). Crosslinked sperm decondensed to 1.8 times their original size by 2 hrs at a rate of 1.0 U/min, although increased decondensation was apparent by 3 hrs (2.6 times their original size). These results indicate the RSAA is useful for detecting damaged sperm chromatin.

1831 EFFECTS OF MERCURIC CHLORIDE EXPOSURE ON REPRODUCTIVE CAPABILITY OF RATS.

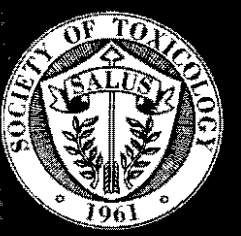
C D Shannon, A Atkinson, A T Khan, T C Graham, J E Webster, S Ali, S J Thompson, and J A Ferguson. *School of Veterinary Medicine, Tuskegee University, Tuskegee, AL.*

The effects of inorganic mercury on the reproductive performance of Sprague-Dawley rats (SDR) were evaluated. Two weeks were allowed for the animals to acclimatize before experimentation. Male rats (45–50 days old) were administered 0.00, 0.50, 1.00 and 1.50 mg/kg/day mercuric chloride via oral gavage for 60 days prior to mating. Female rats (45–50 days old) were administered 0.00, 0.75, 1.50 and 2.50 mg/kg/day for 16 days via oral gavage prior to mating. At the end of premating dosing, rats were paired 0.00:0.00, 0.50:0.75, 1.00:1.50, and 1.50:2.50 mg/kg/day males and females, respectively. Dosing was continued throughout mating. All mercury treated groups of males and their control groups were euthanized at the conclusion of mating. Females were continually dosed throughout gestation and lactation. Reproductive parameters including the mating index, fertility index, viability index, weaning index, litter size, weaning weight and sex ratios were examined. A dose-related reduction in the mean litter size per dose group was observed. The mean litter size in 0.00:0.00, 0.50:0.75, 1.00:1.50, and 1.50:2.50 mg/kg/day of paired groups were 12.05, 7.36, 6.34 and 4.00 pups, respectively. The body weight of the pups at 0, 4, 7, 14 and 21 day showed significant difference when compared to controls. Weaning index and sex ratio revealed no significant difference when compared to controls. These results provide evidence which suggests that inorganic mercury produced adverse effects on reproductive performance of SDR. (Supported by MHPF/ATSDR Cooperative Agreement # 5R51/ATR398004–05).

1832 FERTILITY AND DEVELOPMENT IN RATS EXPOSED PERINATALLY TO GENISTEIN.

C A Lamartiniere, M S Cotroneo, J X Zhang and P A Manzolillo. *Department of Pharmacology and Toxicology, University of Alabama at Birmingham, Birmingham, AL.*

Genistein, a phytoestrogen component of soy, has been associated with health



The Toxicologist

Volume 36, No. 1, Part 2,
March 97

AP

The Toxicologist

An Official Publication of the Society of Toxicology

and

Abstract Issues of

Fundamental and Applied Toxicology

An Official Journal of the Society of Toxicology

Published by Academic Press, Inc.

Abstracts of the
36th Annual Meeting
Volume 36, No. 1, Part 2,
March 97

Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster / discussion, workshops, roundtables, and poster sessions of the 36th Annual Meeting of the Society of Toxicology, held at the Cincinnati Convention Center, Cincinnati, Ohio, March 9-13, 1997.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 371.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 395.

The abstracts are reproduced as accepted by the Program Committee of the Society of Toxicology and appear in numerical sequence.

Copies of *The Toxicologist* are available at $45 each plus $5 postage and handling (U.S. funds) from:

Society of Toxicology
1767 Business Center Drive, Suite 302
Reston, VA 20190-5332

SOCIETY OF TOXICOLOGY

1767 Business Center Drive
Suite 302
Reston, VA 20190-5332

Phone: (703) 438-3115
Fax: (703) 438-3113
E-mail: sothq@toxicology.org