2102 THE CONCOMITANT *IN VIVO* EXPOSURE OF YOUNG MALE ADULT RATS TO THE PESTICIDE METHOXYCHLOR (M) AND THE ANTIESTROGEN ICI 182,780 (ICI) DOES NOT ALTER THE DECLINES IN SEMINAL VESICLE (SV) WEIGHT, SERUM TESTOSTERONE (T) LEVEL, *EX VIVO* LEYDIG CELL (LC) T FORMATION, OR *EX VIVO* LC P450 CHOLESTEROL SIDE-CHAIN CLEAVAGE (P450SCC) ACTIVITY EXERTED BY TREAMENT WITH M ALONE

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M is a pesticide used as a replacement DDT. It exhibits weak estrogenic and/or antiandrogenic activities, and its adverse reproductive effects are thought to be mediated through either the estrogen receptor (ER) or androgen receptor(AR). The current studies evaluated whether the declines in SV weight, serum T level, and ex vivo LC T formation and P450scc activity exerted by the in vivo exposure of young adult male rats to M alone are prevented by the concomitant treatment with ICI. Animals received a single injection (s.c.) of arachis oil alone or ICI (10 mg/kg b.wt.) dissolved in arachis oil 3 days prior to M exposure. At 54 days of age, animals were gavaged with corn oil alone or M dissolved in corn oil (200 mg/kg b.wt., once daily for 7 consecutive days). Animals were sacrificed 22-24 h after the last exposure. There were 12-13 animals per treatment group. Treatment with M alone decreased SV weight, serum T level, ex vivo basal LC T formation, and ex vivo LC P450scc activity to 42, 46, 39, and 53% of control, respectively. Concomitant treatment with ICI had no effect on these declines produced by M alone. In addition, animals exposed to ICI alone had values no different than control animals. These results suggest that the inhibitive effects of M on some male reproductive functions are not mediated through the ER.
The findings and conclusions in this abstract have not been formally disseminated by NIOSH and should not be construed to represent any agency determination or policy.

2103 HYPOSPERMATOGENESIS AND CHARACTERISATION OF KEY STAGES OF SPERMATOGENESIS IN THE TESTIS OF THE BEAGLE DOG – A CASE STUDY

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In a thirty nine week dog regulatory toxicology study of a novel pharmaceutical severe hypospermatogenesis was recorded in one out of four high dose and one out of four low dose group animals but not in any of the controls. The incidence and severity of the condition was outside the range of our historical data. However, subsequent evaluation of the recovery animals revealed a similar hypospermatogenesis in a control male, and examination of the breeding records for the colony revealed that all three dogs were siblings, suggesting a possible genetic aetiology for the testicular change. The ultimate conclusion was that this was not a treatment related change. This highlights the importance of both reliable historical data and breeding records for evaluation of possible toxic changes.
This poster illustrates the histomorphology of hypospermatogenesis, together with the key stages of the normal spermatogenic cycle in the Beagle dog.

2104 MALE SEXUAL MATURITY AND ADVERSE EFFECTS IN TESTES OF *MACACA FASCICULARIS*

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It can be important to include a pre-study evaluation of male sexual maturity in the criteria for inclusion of animals in a general toxicity study. In studies with *Macaca fascicularis*, the parameters indicative of male sexual maturity may include weight, age, testicular volume and testosterone concentration. Sperm analysis can also be particularly helpful because it confirms sexual maturity, and can be achieved in Macaque monkeys using electro-ejaculation techniques. We describe here a small study in which we have examined different non-invasive parameters of male sexual maturity. Selected mature animals were treated with a reference male reproductive toxicant, (s)-alpha-chlorhydrin, which was administered daily by subcutaneous injection over a 4 week-period. Treatment did not result in any alteration of the general condition of animals as shown by body weight and clinical condition. The testicular volume was measured before the start of the study and correlated with the sperm production measured on samples from electro-ejaculation. On treatment with (s)-alpha-chlorhydrin, there was a rapid diminution in testicular volume (which correlated with post-mortem histopathological findings) which was evident in the first two weeks of treatment. No changes were seen in seminology analyses on treated animals, probably because the dosing period did not cover the entire spermatogenic cycle. Histopathological examination revealed mild degeneration of the testicular germinal epithelium together with disruption of sperm maturation in some seminiferous tubules. The epididymides did not show any abnormalities either in morphology or sperm content. This study allowed us to demonstrate the toxic action of (s)-alpha-chlorhydrin to the male reproductive system. Testicular volume proved to be a simple and sensitive measure of testicular toxicity permitting in-life monitoring of harmful effects. This study shows the utility of different parameters for the evaluation of sexual maturity and adverse testicular effects.

2105 COMPARISON OF PRECISION AND ACCURACY OF PROSTATE AND TESTIS ULTRASONOGRAPHY IN THE CYNOMOLGUS MONKEY

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Cynomolgus monkeys are a well established and clinically relevant animal model for the study of male reproductive physiology. In this nonhuman primate species, prostate anatomy and the endocrine control of prostate and testicular size are very similar to that of man. Determination of testicular and prostate size by ultrasound is feasible in the cynomolgus monkey and have been reported earlier. In this work we evaluated the reproducibility and accuracy of ultrasonic volume analysis of testis and prostate as well as the relationship between age and organ volume. Prostate (transrectal) and testicular volume was measured by ultrasonography on repeated occasions and prior to necropsy for correlation with organ weight. Cross-sectional prostate size determination in 99 animals (1 – 19 yrs old) suggested that adult dimensions are attained within few years. Longitudinal data collected from 8 animals on repeated sessions yielded intra-method coefficient of variation (CV) of 3.7 – 4.1 % and inter-method CV of 5.8% for testis volumes. For prostate volumes, intra-method CV was 4.9 – 8.3% and inter-method CV was 14.8%. Testis volume and organ weight correlation (n = 28) was nearly linear (r = 0.98). Correlation for prostate volume and weight (n = 27) was very close though less pronounced (r = 0.75). Our data indicate that ultrasonography provides a reproducible and accurate method for the determination of prostate and testicular size in the cynomolgus monkeys. Importantly, method variability is higher for determination of prostate size compared to testis size.

2106 NON-INVASIVE UROFLOW ANALYSIS IN THE CYNOMOLGUS MONKEY

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Prostate diseases are highly prevalent in the aging male population and, hence, the prostate is an important target organ for pharmaceutical drug development. Uroflowmetry is being used clinically to study prostate physiology and lower urinary tract symptoms. This techniques enables quantitative analysis of uroflow parameters and micturition patterns by a non-invasive approach. In the present work, the feasibility of uroflow analysis was studied in adult male cynomolgus monkey (Macaca fascicularis). In this nonhuman primate species, prostate anatomy and endocrine control of prostate size are very similar to that of man. Animals were housed in specially fitted metabolic cages for 16 hours and the urinary patterns were recorded using the CONUS uroflow system (Andromeda Medical Systems GmbH, Germany). For this, computerized detection of single urine flows was developed and the system was adjusted to the smaller urine volume in the cynomolgus monkey. Baseline experiments proved the feasibility of this analysis and reference data were collected for 32 animals. Evaluation of uroflow comprised maximal flow rate, average flow rate, voided volume, duration of flow, duration of micturition, maximal flow onset and acceleration/delay of voiding. For the clinically most relevant parameter, maximal flow rate (Qmax), on average 4.9 ± 1.0 (SD) mL/sec (range: 3.3 – 7.4 mL/sec) were determined in these 32 animals. For man, Qmax ranges from > 13 to > 21 mL/sec depending on age. In conclusion, non-invasive uroflow analysis in the cynomolgus monkey is feasible and provides quantititative information on uroflow parameters and micturition patterns.

2107 EFFECTS OF ENVIRONMENTAL TOBACCO SMOKE ON RHESUS MONKEY SPERM FUNCTION

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Billions of people world-wide smoke cigarettes, and almost 80% of these smokers are men. Increased risk for disease also has been found in people exposed to environmental tobacco smoke (ETS). Since human studies are limited by high variability and rat studies are limited by physiological differences between the primate and

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Preface

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An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 500.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 534.

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

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