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HONORÉ, L.H., G.A. MACHIN*, and C.C. LIN*, Department of Pathology, University of Alberta, Edmonton, Alberta, Canada. Spontaneous abortion in pregnancies following ovulation induction in infertile women: A report of 21 cases.

There is no systematic study of spontaneous abortions in pregnancies following ovulation induction. From a consecutive series of 27 such cases we report 21 cases with adequate tissue for study. Of the 9/10 cases successfully karyotyped 4 were heteroploid [69XXY(2), 47X+15, 47XX+16]. These abortions, occurring mostly in the first trimester (range = 7-17 weeks menstrual), came from infertile women (mean age = 28.7 years; range = 21-35 years), treated with Clomiphene citrate (18), Clomiphene - human chorionic gonadotrophin (1), human menopausal gonadotrophin (1) or GnRH (1). Only 2 abortuses were structurally normal (one 46XX), i.e., 9% as compared with about 55% in our control population. Partial moles (5/21) were more frequent than expected, i.e., 24% compared with an estimated 6% in our control population. The other 13 cases were suggestive of "early blighting", as indicated by severe abnormalities of embryo (growth disorganization or growth retardation and severe malformations) and/or placenta (cord hypoplasia; chorial and villous hypovascularity, hypoplasia and dysmorphogenesis). This small series suggests that abortions in pregnancies following ovulation induction have a higher incidence of partial moles and "blighted ova" than abortions in spontaneous ovulators.

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HUNTER*[1],E.S., K.K SULIK[1], R.C. CEFALO*[2], and T.W. SADLER[1]. [1]Dept Cell Biol and Anatomy, [2]Dept Obstet and Gynecol, Univ North Carolina, Chapel Hill, North Carolina. Developmental effects of Cocaine.

In a recent report 14.8% of all women showed positive urine toxicology for drugs including primarily cocaine (C) at their first prenatal visit. Therefore, using ICR mice we evaluated the developmental effects of C during neurulation. In pregnant females C was administered as one IP dose (40-80mg/kg; 1%(w/v) C in saline) on day 9 of gestation (plug day = 1). The maternal LD50 was 75mg/kg, but C did not affect maternal weight gain during gestation. On day 19 pup body weights were reduced at doses ≥60mg/kg compare to controls. The number of live pups/litter was not affected and no gross malformations were observed. Renal malformations were observed in 37% of pups (29/79; 7/7 litters) at a 70mg/kg dose compared to 4% (3/70; 1/6 litters) in controls. A decreased frequency of malformations was observed at lower doses of C. At a 40mg/kg dose 13% of pups (11/82; 3/7 litters) exhibited this defect. To determine if C could directly alter morphogenesis whole embryo culture was employed. Neurulation staged (D9) mouse stage were cultured in control medium or in the presence of C (10-100ug/ml). No malformations were produced in controls or at 10ug/ml C following a 24H culture period. C induced malformations in 33% of embryos at 25ug/ml and a 70% incidence at 100ug/ml. A 25% decrease in protein content was produced by 25ug/ml and a 50% decrease at 50ug/ml compared to controls. These studies indicate that C administration during organogenesis can produce growth retardation and visceral malformations. Additionally, if sufficiently high concentrations of C were present in vivo, then cocaine itself could be involved in the embryopathic effects.

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INFURNA, R., BEYER, B., TWITTY, L.*, KOEHLER, G.*, and DAUGHTREY, W.*, Exxon Biomedical Sciences, Inc., E. Millstone, New Jersey, Evaluation of the dermal absorption and teratogenic potential of methyl salicylate in a petroleum based grease.

Methyl salicylate (MS) is used in over-the-counter preparations and in petrochemical products. MS is teratogenic in animals and can be absorbed in toxic quantities by the dermal route. Consequently, the dermal absorption and teratogenic potential of a petroleum-based grease (PBG) manufactured using MS (3%) was assessed. The test material (PBG/MS) was dermally applied at doses of either 0, 1, 3, or 6 g/kg/day to groups (N ≥ 12) of pregnant rats on gestational days 6-15. Undiluted MS was applied to the positive control group at a dose of 2 g/kg/day and was reduced to 1 g/kg/day on gestational days 10-15 due to maternal toxicity (i.e., 25% mortality and severe dermal irritation). Positive control animals evidenced a 100% incidence of total resorptions. Urinalysis revealed very high concentrations of salicylic acid in the positive controls and that a significant proportion of the available MS was absorbed from the PBG/MS test material. However, the urinary concentrations of salicylic acid in PBG treated animals were far below the toxic levels observed in MS treated animals. Despite the high doses of PBG/MS there were no signs of maternal toxicity (as measured by food consumption and body weight parameters or clinical signs) and no alterations in reproductive parameters. Fetal external and visceral examinations revealed no malformations or variations that were related to PBG/MS treatment. These findings confirm the developmental toxicity of methyl salicylate and indicate that PBG/MS was not a teratogenic hazard under these test conditions. The maternal and developmental No-Observable-Adverse-Effect-Level for PBG/MS was greater than 6 g/kg/day.

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JELOVSEK*, F.R.,MATTISON, D.R.,and YOUNG,J.F., Department of Obstetrics and Gynecology, University of Arkansas for Medical Sciences, Little Rock, Arkansas and Division of Reproductive and Developmental Toxicology, National Center for Toxicological Research, Jefferson, Arkansas. Principles of Hazard Identification: A Methodology and a Model

Developmental toxicology risk assessment can take place at a population or individual patient level.In both processes hazard identi-fication is a critical initial step, but one which must