BIRTH WEIGHTS AND MATERNAL NARCOTIC USE. Stephen R. Kandall, Lawrence M. Gartner and Beatrice B. Berle, Dept. Pediatrics and Psychiatry, Albert Einstein College of Medicine, Bronx, NY

Heroin (H) abuse during pregnancy has been associated with significantly lower birth weights (BW) in the offspring. Methadone (M) administration during pregnancy has generally resulted in more normally grown neonates. BW of babies born in 1971-2 to groups of mothers with varying histories of narcotic intake were compared. Mean BW of babies born to mothers taking H alone was 2397G±680 (N=39), and to mothers taking both H and M was 2547G±656 (N=25)(P>0.05). Mean BW of babies of mothers who had abused H in the past but were drug-free during the entire pregnancy was 2421G±430 (N=18); no neonatal withdrawal was seen in this group. Mean BW in this group was no different from the group abusing H during pregnancy (P>0.05), suggesting that H may induce physiologic changes extending beyond the period of addiction.

Mean BW of babies born to mothers taking M alone was 3017G±524 (N=35). Complete M dosage schedules during pregnancy were available for 20 of these patients. Babies born to mothers taking <70 mg/day had a mean BW of 2799G±478 (N=13) while those >70 mg/day averaged 3539G±602 (N=7)(P<0.02). A significant linear relationship between M dosage and BW was demonstrated by the calculated regression line (r=.64;P<0.01). This data suggests that M administration during pregnancy appears to correct in a dose-dependent manner heroin-associated fetal growth retardation.

INHIBITION OF FETAL PULMONARY SURFACTANT APPEARANCE AFTER MATERNAL METYRAPONE INFUSION. Robert V. Kotas, LeRoy C. Mims, and Elizabeth J. Trainor, W. K. Warren Med. Res. Ctr., Tulsa, Oklahoma. (Intr. by Mary E. Avery)

Pulmonary maturity was measured in fetal rabbits after continuous infusion of metyrapone (M)(7 mg/ml at 2 ml/hr x 24 hrs) to 24 day gestation females and compared to placebo treated controls (C). 27.5 day gestation animals (total N = 56) were compared for body weight in gm (BW), wet lung weight expressed as % of body weight (LW%), mg DNA per lung (DNA), minimal surface tension of minced lung in dynes per cm (MST), distensibility expressed as cc per gm of wet lung at peak distending P of 35 cm H_2O (cc/gm), and deflation stability expressed as % of maximal volume upon deflation to a P of 10 cm H_2O ($\%V_{max}$). All results are mean ± standard deviation; * = p < .001.

	N	BW	LW%	DNA	MST	cc/gm	%Vmax
M	41	29±7	3.0±0.2	5.1±0.9	28±1.8*	1.3±0.6	29±4*
C	15	32±5	3.5±0.3	4.9±0.9	18±1.6	1.7±0.3	44±4

Decreased $\%V_{max}$ and increased MST after M are similar to findings in 26 day gestation fetal rabbits (JAP 30:358, 1971). Two additional M litters delivered at term (31 days) and 15 out of 17 bunnies survived to one month of age. Previously reported (Amer. Rev. Resp. Dis. 107:1109, 1973) accelerated appearance of pulmonary surfactant after intermittent metyrapone (300 mg I.M. Q8HX12) may have been due to incomplete block of adrenal 11-β hydroxylation.

PLACENTAL TRANSFER AND FETAL URINARY EXCRETION OF GENTAMICIN DURING CONSTANT RATE MATERNAL INFUSION. Ralph E. Kauffman, Daniel L. Azarnoff, and John A. Morris. (Intr. V.L. Tucker). Dept's. Ped. and Pharmacology, Univ. Kansas Sch. of Med., Kansas City, Kansas and Dept. Ob-Gyn, Chas. R. Drew Post Grad. Med. Sch., Los Angeles.

Placental transfer and fetal urinary excretion of gentamicin was studied in mid-trimester goat and human previable fetuses during constant rate maternal infusion with the drug. Gentamicin was not detected in the serum of any of the goat fetuses, even when maternal serum concentrations ranged from 15.2 µg./ml. to 20.9 µg/ml. However, gentamicin was present in the amniotic fluid of four animals from which fetal urine was not collected. Gentamicin was also present in fetal urine collected from three animals. In contrast, human fetal central venous serum concentrations of gentamicin were 21% to 37% of those in maternal serum following constant rate infusion of the mother. In addition, gentamicin was present in human fetal urine in concentrations two to three times those in fetal serum. Gentamicin crosses the human placenta more readily than the goat placenta and is concentrated and excreted by the mid-trimester fetal kidney. This study illustrates the inherent danger in extrapolating information obtained from animal studies of placental transfer of drugs, and emphasizes the need to conduct carefully designed, confirmatory studies in human beings. (Supported in part by USPHS Grant 15956).

SERUM PROTEIN BINDING OF SALICYLATE DURING PREGNANCY by Joseph Krasner, John Lovecchio and Sumner J. Yaffe, State University of New York and Children's Hospital of Buffalo.

Drug-protein interaction is of major importance in modulating drug distribution and action in the intact organism. Drug binding to serum proteins in the gravid female is of special interest because of physiological changes during pregnancy which may influence drug activity in the primary host and in the developing fetus. A detailed investigation of salicylate binding to serum albumin during pregnancy was undertaken since aspirin is universally ingested by the pregnant woman and has been implicated as having adverse effects upon the fetus. Serum was obtained from 51 patients taken at their routine examinations during pregnancy and categorized into trimesters. Equilibrium dialysis was performed at 4°C utilizing varying concentrations of sodium salicylate C^{14} with 1 ml of serum. The apparent association constant (k') of the albumin-salicylate interaction was determined from the construction of Scatchard plots from the data. The mean k' values for 1st, 2nd and 3rd trimesters are 3.2, 2.8 and 2.6 x $10^5 M^{-1}$ respectively with one mole of salicylate bound at the primary site. These results indicate that there is a decrease in the binding affinity of salicylate for serum albumin as pregnancy progresses. The increased concentrations of free unbound salicylate present during pregnancy would be readily available to diffuse across the placenta and effect the fetus as well as act upon host receptors. The change in binding affinity may result from competitive or allosteric binding by endogenous compounds.

PHARMACOKINETICS OF PRIMIDONE METABOLISM AND EXCRETION IN CHILDREN. Ralph E. Kauffman, Lester Lansky, and Rolf Habersang. (Intr. by J.T. Lowman). Univ. of Kansas Sch. of Med., Depts. of Ped. and Pharmacology, Kansas City, Kansas.

The metabolism and excretion of orally administered primidone was studied in ten children, ages six to ten years, who were chronically receiving the drug for temporal lobe seizures. Plasma concentrations of primidone (Pr) peaked at 2 to 4 hours and declined exponentially from 6 to 24 hours with half-lives ranging from 6 to 12 hours. A mean of 81% of the administered dose was recovered in the urine as Pr and its metabolites. Of the total Pr excreted in the urine in 24 hours, 53.3% appeared as unchanged drug, 43.8% as phenylethylmalondiamide (PEMA), and 2.9% as phenobarbital (Pb). The rate constants for conversion of Pr to PEMA (K_1), Pr to Pb (K_2), and urinary excretion of unchanged Pr (K_3) were estimated. K_1 ranged from .013 to .072 $hrs.^{-1}$, K_2 from .0004 to .005 $hrs.^{-1}$, and K_3 from .058 to .116 $hrs.^{-1}$. Those patients with a larger K_2 tended to have a higher plasma concentration of Pb, and vice versa. Since Pb accounts for a small fraction of the total Pr excreted, a ten fold change in K_2 will have little influence on the overall rate constant for elimination of primidone, but may have an important effect on the steady state plasma concentration of Pb in patients receiving Pr. (Supported in part by PMA Foundation Research Starter Grant and USPHS Grant 15956).

EFFECT OF MATERNAL NARCOTIC ADDICTION ON SUCKING BEHAVIOR OF NEONATES. Reuben E.Kron, Mitchell Litt, and Loretta P. Finnegan (Intr. by Maria Delivoria-Papadopoulos) Phila. Gen. Hosp. and Depts. of Ped. and Psy., Univ. of Pa. Sch. of Med.

Measures of newborn sucking behavior were used to study effects on the infant's state of CNS arousal induced by maternal addiction. The sucking performance of 38 infants diagnosed and treated for narcotic withdrawal by a new symptom scoring system (Neonatal Abstinence Score) was compared with that of 50 infants whose withdrawal was regulated by acceptable clinical methods. The findings indicate the value of the scoring system in prescribing the dosage of drug therapy which resulted in better levels of CNS arousal and improved sucking performance. Also, using sucking performance as a criterion, it was found that paregoric was superior to phenobarbital in treating neonatal withdrawal. In addition,the severity of withdrawal as measured by sucking was directly related to the mother's length of time in the methadone maintenance program and her average dose of methadone. This finding may reflect the fact that patients enrolled in a maintenance program are assured of a continued supply of a long-acting narcotic drug, as compared to street addicts, whose supply is highly variable in quality and availability, and, that addicts who enter the methadone program during pregnancy tend to be given smaller doses than those who are not pregnant.