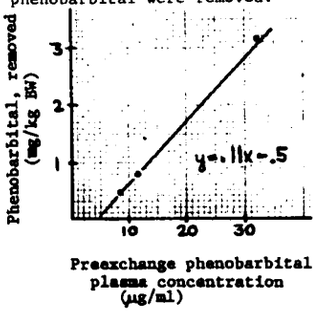
271 PHENOBARBITAL REMOVAL BY NEONATAL EXCHANGE TRANSFUSION Rolf Habersang, Warren Rosenfeld, Ralph Kauffman, and Howard Fox (Spon. by Cheng Cho). Dept. Ped., Univ. Ks. Sch. Med., Kansas City, Kansas 66103.

A significant number of sick neonates who undergo exchange transfusion to prevent bilirubin toxicity are also receiving phenobarbital for seizure control. To determine the necessity of phenobarbital reloading after an exchange transfusion, serum phenobarbital concentration was measured during the execution of an exchange transfusion and the total amount of phenobarbital removed was calculated. In three infants of 28, 30, 40 weeks gestational age weighing 1150 gm, 1340 gm and 3130 gm, 3.6 mg, 1.1 mg and 1.4 mg respectively of phenobarbital were removed. The amount removed in these three infants seems related to the preexchange plasma-phenobarbital concentration. Based on these data, the amount of phenobarbital removed by a two volume exchange is negligable. This is in accordance with an estimated volume of distribution of phenobarbital of about 1000 ml/kg in newborn infants. Exchange transfusion for the removal of sensitized red cells is efficient because the distribution volume for red cells is only 80 mg/kg.



272 PREDICTORS OF THE SEVERITY OF NEONATAL METHADONE WITHDRAWAL. R.G.Harper, G.Solish, F.Feingold, N.Gersten-Woolf & M.M.Sokal, Depts.of Ped.& Ob.-Gyn.,North Shore U.Hosp.,Manhasset, N.Y., & Depts.of Ped.& Ob.-Gyn.,Cornell U.Medical College,N.Y.,N.Y.,& Dept.of Ob.-Gyn.,SUNY-Downstate Medical Ctr.,Bklyn,N.Y. (Intr. by Fima Lifshitz).

The relationships between prenatal methadone dosage and the severity of subsequent neonatal methadone withdrawal were studied in 32 clinically well, methadone-maintained women and 19 drug-free controls. Total methadone ingestion during the last trimester, the last methadone dose prior to delivery and the absence of other drugs of abuse were known. The quantities of methadone in intrapartum maternal blood and urine, amniotic fluid, cord blood and neonatal urine were determined and the severity of neonatal withdrawal was quantitated. Severity of withdrawal was related to last maternal dose of methadone ($p < 0.01$), total amount ingested during the last trimester ($p < 0.02$), and intrapartum maternal serum methadone ($p < 0.01$). Severity was not related to levels of methadone in maternal urine, cord blood, amniotic fluid or neonatal urine. These findings indicate that careful monitoring of maternal methadone levels during the last trimester coupled with a knowledge of intrapartum serum methadone levels can predict the degree of neonatal narcotic withdrawal.

273 DRUG UTILIZATION DURING THE PERINATAL PERIOD. Reba M. Hill, Janice P. Craig, Margaret D. Chaney, Linda M. Tennyson, Lee B. McCulley. Baylor Col. of Med., Dept. of Ped., Houston, Texas.

In a progressive study, 231 gravid females and their progeny were monitored to assess drug utilization during the perinatal period. The patients came from a middle to high socioeconomic population and delivered in a university hospital. Gravid patients were found to take a mean (M) of 9.6 drug preparations (DP) during the prenatal course with a range of 1-37; 6.4 DP (R=0-28) were prescription drugs; 3.2 DP (R=0-12) were over the counter drugs; and .03 drugs (R=0-3) were not identified. Twenty-five percent of patients received a drug chronically throughout pregnancy. Ninety percent were prescribed. The mother received a M = 6.0 (R=0-14) drugs during labor and delivery. Single drugs were administered during L&D, whereas DP containing multiple agents were ingested during the prenatal course. During the post partum course the mother received a M = 8.7 drug preparations (R=1-25). Thirty-nine percent of the mothers were discharged home on medications. Fifty-nine percent of the mothers who were breast feeding were sent home on medications. During the nursery stay the progeny received a M = 3.1 drugs (R=1-15) with 23% of the infants receiving 4-15. In infants who received >6 drugs, 40% were treated because of a direct or indirect effect of maternal drugs. Within the first natal days the average newborn infant had been exposed to a M = 18.7 drugs by intrauterine or extrauterine exposure. Breast fed infants may be exposed to an additional 7.7 (R=2-15) drugs.

274 PROLONGED DETECTION OF GENTAMICIN IN NEONATES FOLLOWING CESSATION OF THERAPY. Donald M. Hilligoss, Armando E. Grassi, Jerome J. Schentag, Stanley E. Read, Stephen B. Chasko. (Sponsored by Peter A. M. Auld) The New York Hospital-Cornell Medical Center, Depts. of Pharmacy, Pediatrics (Perinatology Center and Div. of Infectious Diseases), and Pathology, New York, N.Y. and State University of New York at Buffalo, School of Pharmacy, Dept. of Pharmaceutics, Buffalo, N.Y.

Gentamicin has been detected in serum of adult patients long after the drug has been discontinued and is the result of tissue accumulation. A prospective study was designed to see if this occurs in neonates. Twelve patients were treated with gentamicin 2.5 mg/kg every twelve hours in combination with ampicillin for suspected or confirmed sepsis. Serum concentrations were measured throughout the duration of therapy and also after cessation of therapy for up to 28 days. Microbiological assay and radioimmunoassay were employed to determine serum levels. Analysis of the first four patients revealed mean serum concentrations of gentamicin at one hour after injection of 10.0, 7.5, 7.4 and 5.6 mcg/ml. At eleven hours after injection mean serum concentrations were 1.9, 2.2, 2.7 and 1.6 mcg/ml. Elimination rate constants calculated from these values do not account for the concentrations of 0.40 - 0.01 mcg/ml that were found in serum for 2 - 28 days after gentamicin was discontinued. This persistence of gentamicin for prolonged periods after cessation of therapy is due to the slow egress from a deep tissue compartment.

275 TREATMENT AND FOLLOW-UP OF NEONATAL MEPIVACAINE INTOXICATION. Laura S. Hillman, Richard E. Hillman and W. Edwin Dodson, Washington Univ. Sch. of Med., St.Louis Children's Hospital, Dept. of Pediatrics, St. Louis, Mo.

6 infants with mepivacaine intoxication secondary to accidental injection into the infant during paracervical and pudendal blocks were studied. All had depression at birth, tonic seizures with apnea in the first 6 hrs., and often unreactive dilated pupils. Two required respiratory support. Peak serum mepivacaine conc. were 9 to 25 µg/ml within the first 12 hrs. with a post-natal increase from cord and maternal conc. documented in 3 cases. CSF conc. was similar to simultaneous serum conc. Exchange transfusions in cases 3, 4, and 5 produced no significant changes in clinical status or serum conc., and the total removed by exchange was 3.5 mg in case 4 and 1.07 mg in case 5. Although gastric conc. on drainage reached 229 µg/ml in case 5 and 82 µg/ml in case 6, gastric lavage in case 6 recovered only 0.3 mg total. Urinary excretion under forced diuresis in cases 4, 5, and 6 produced 12.7 mg, 37.4 mg and 12.1 mg in the first 24 hrs. (80-96% of the total excreted in urine over 90 hrs). Thus, forced diuresis is the treatment of choice with gastric lavage and exchange transfusion used only when forced diuresis is contraindicated.

All 5 survivors were followed, 4 for 2 to 4 yrs, and are neurologically and developmentally normal. Anticonvulsants were discontinued in all, 3 at discharge. Early recognition, seizure control, and prompt resuscitation with carefully monitored respiratory support were key. If severe perinatal hypoxia can be avoided the prognosis from intoxication per se is excellent.

276 METABOLIC EFFECTS OF LEAD IN NEWBORN RATS. J.A.Kochen, U.Muller-Eberhard, M.I.Cohen, G.Dinari, Y.Greener, Albert Einstein Coll.Med.,Montefiore Hosp. Med.Ctr., Dept.Ped.,Bronx,NY;Scripps Clinic & Res.Found., LaJolla, Calif.

Lead ingestion produces profound alterations in liver morphology and enzyme levels, as well as plasma protein composition in newborn rats. Seven day old rats were given 0.5ml 1% lead acetate by gastric tube daily x 7 and sacrificed. When compared to littermate controls,lead resulted in significant weight loss (19.6 ± 3.5 vs 24.3 ± 2.0gm) (m ± SD);anemia (Hct 24.2 ± 1.9 vs 31.3 ± 4.4%); kidney enlargement (0.37 ± 0.08 vs 0.28 ± 0.07gm);and encephalopathy (cerebellar hemorrhage).Examination of liver showed no change in liver weight,protein content or DNA and RNA synthesis (^{3}H-thymidine and uridine incorporation).Hepatic UDP-glucuronyl transferase(GT) activity increased 69% in the lead treated newborn rats (1662 ± 301 vs 982 ± 207µM bilirubin/gm/40min).Lead treated adult rats showed a similar significant increase in GT activity (1864 ± 122 vs 1181 ± 172µM/gm/40min).Likewise γ-glutamyl transpeptidase activity was significantly increased in both newborn and adult rats.Analysis of plasma proteins showed a lead induced increase of 84% in albumin (2.3 ± 0.7 vs 1.3 ± 0.5gm/dl);116% increase in transferrin (12.1 ± 1.9 vs 5.6 ± 2.2mg/ml);and 74% decrease in hemopexin (0.51 ± 0.38 vs 1.96 ± 0.88mg/ml).Morphologically,lead produced ultrastructural alterations in endoplasmic reticulum and the appearance of lamellar membranous bodies.GT is a membrane-bound enzyme which is activated by sulfhydryl-blocking agents and phospholipases.Lead,by binding to sulfhydryl groups and disrupting microsomal membranes may exert similar metabolic effects by "unmasking" active enzyme sites.