396 MATERNAL DRUG USE AND THE EFFECTIVENESS OF PHARMACOTHERAPY FOR NEONATAL ABSTINENCE. Sandra L. Tunis, Donna M. Webster, Joseph K. Izes, and Loretta P. Finnegan, Thomas Jefferson University, Dept. of Peds., Phila., PA

Infants undergoing neonatal abstinence due to maternal drug use are commonly treated with paregoric, phenobarbital or diazepam. This study was designed to test the effectiveness of each of these agents as the first treatment drug in the control of abstinence symptomatology. The relationship of the type of maternal drug use to the effectiveness of treatment was also examined. Subjects were 134 infants treated for abstinence at Thomas Jefferson University Hospital between 1979 and 1983. Infants with serious medical complications were eliminated from the study. A series of least squares linear regression analyses was performed using the treatment drug, type of maternal drug use (opiates, non-opiates, or both), and the interaction of treatment and maternal drugs as predictors of whether or not a second pharmacotherapeutic agent was needed to bring the infant under control. Results revealed that if maternal drug use was limited to non-opiates, phenobarbital therapy was a significant predictor of successful treatment with one drug. Treating an infant with diazepam, however, significantly predicted the need for a second agent, regardless of maternal drug use. Paregoric was a significant predictor of successful treatment if maternal drug use included opiates or a combination of opiates and other drugs, and was a significant predictor of unsuccessful treatment if the mother abused only non-opiates. These results emphasize the ineffectiveness of diazepam for the treatment of neonatal abstinence as well as the relationship of maternal drug use to effective pharmacotherapy.

399 RELATIONSHIP BETWEEN URINE OUTPUT AND TOLAZOLINE (T) HALF-LIFE. Robert M. Ward, James W. Kendig, Catherine H. Daniel, Jeanne L. Addison (Spon. by M. Jeffrey Maisels). Penn State Univ Col of Med, M. S. Hershey Med Ctr, Dept of Peds, Hershey, PA.

The only report of neonatal T pharmacokinetics indicated half-life varied from 3.3-33 hours in 8 patients. The longest half-life occurred in an infant with a poor cardiovascular status. Adult dogs eliminate T by renal tubular base transport without detectable metabolism by a chemically non-specific assay. This transport system is saturable and immature in infants at birth thus placing infants at risk for limited T excretion. We have developed a chemically-specific microassay for T by gas chromatography-mass spectrometry and used it to study 12 T eliminations following pulse and infusion doses in 10 infants. T half-life varied from 1.5-29.6 hrs and showed a significant correlation with the logarithm of urine output from 0.40-2.35 ml/kg/hr ($R=0.77$, $p<0.01$). In 2 infants studied twice, the longer half-life occurred during lower urine output. In 2 infants who failed to void for 3-4 hrs after a T dose, concentrations measured every 30 min did not decrease until voiding resumed. This suggests that T is not significantly metabolized in infants and that decreased urine production prolongs T half-life exponentially. The variation in T half-life in these patients and those previously reported may be explained by variation in urine output. During oliguria, pulse doses of T may need to be decreased in frequency and infusion doses decreased in magnitude to avoid T accumulation and adverse effects.

● **397** THE INOTROPIC EFFECT OF PROSTAGLANDIN ($PG)_{E1}$ AND PGD_2 IN THE NEWBORN RABBIT HEART. Shigeru Uemura, Toshio Nakanishi, William F. Friedman, and Jay M. Jarmakani, UCLA Medical Center, Dept. Peds. Los Angeles, CA.

The purpose of this study was to determine the effects of PGE_1 and PGD_2 on mechanical function in the developing heart. The study was performed in the isolated, arterially perfused heart preparation of the newborn (NB) (N=34) and adult (A) (n=27) rabbits. Parameters of mechanical function [developed tension, maximal rate of contraction (+dT/dt), and relaxation (-dT/dt), and half relaxation time (1/2RT)] were recorded continuously. Positive inotropic effect was observed after PGE_1 or PGD_2 infusion in both NB and A. The effects of these drugs on +dT/dt (% of control) were:

PGE_1	10^{-8}	10^{-7}	10^{-6}	5×10^{-6}
NB	103 ± 3	109 ± 2	111 ± 3	118 ± 5
A	103 ± 2	104 ± 3	107 ± 2	102*± 1
PGD_2	10^{-17}	10^{-15}	10^{-11}	10^{-7}
NB	114 ± 4	131 ± 3	122 ± 4	120 ± 2
A	112 ± 2	104*± 3	108 ± 2	106*± 3

Mean ± SE, *$P<0.01$

In NB, the relaxation parameters (1/2 RT and the ratio of +dT/dt to -dT/dt) decreased to 80% of control after PGE_1 infusion but not after PGD_2 infusion. In A, relaxation parameters were not different from control. These data indicate that 1) the positive inotropic effects of PGE_1 and PGD_2 in NB are greater than in A, and 2) PGE_1, not PGD_2 enhances myocardial relaxation only in the NB.

● **400** EFFECT OF PDA ON GENTAMICIN PHARMACOKINETICS IN BABIES <1500 GRAMS. Kristi Watterberg, H. William Kelly, John D. Johnson. Department of Pediatrics, University of New Mexico School of Medicine, Albuquerque, NM

As part of a study of variables affecting gentamicin (G) pharmacokinetics in neonates, we examined the effect of patent ductus arteriosus (PDA) in babies <1500g. G levels were drawn at 1,4 and 8 hours. Data points were computer fitted into a one compartment, first order, open pharmacokinetic model by the method of least squares. The half life (T1/2), elimination rate constant(Ke), and distribution volume (Vd) were derived. We analyzed G pharmacokinetics in 8 babies without PDA (1161±258g) (mean±SD) and 9 babies with proven PDA (1000±255g). Six babies with PDA were treated (968±269g).

T1/2 in patients without PDA (7.4±4.4hrs), with PDA (8.1±3.3 hrs), and with PDAs requiring treatment (9.4±1.7hrs) were not significantly different. Vd, however, was .422±.078L/kg in babies without PDA, .724±.367L/kg in babies with PDA ($p=.02$), and .839±.40L/kg in babies treated for PDA ($p=.006$). Three babies had G pharmacokinetics done before and after treatment. In each case, the Vd decreased substantially (from 1.41 to .42L/kg, 1.26 to .68L/kg, and .68 to .49L/kg).

These results show that 1) babies <1500g with PDAs have larger Vds than those without PDAs, 2) babies whose PDAs require treatment have even higher Vds. In addition, Vd can drop substantially after treatment. We conclude 1) babies <1500g with PDAs may require higher G doses to achieve therapeutic peak levels, and 2) babies with PDAs who have therapeutic G levels should be reevaluated after therapy.

● **398** CORRECTION OF DEFECTIVE NEUTROPHIL CHEMOTAXIS BY SYSTEMIC VITAMIN C (VC) THERAPY IN NEWBORN INFANTS (NB). Kiran Vohra, Abdul J. Khan, Warren Rosenfeld, Vrinda Telang and Hugh E. Evans. Interfaith Medical Center/ SUNY Downstate Medical Center, Brooklyn, New York.

Vitamin C has been shown to improve defective chemotaxis in Chediak - Higashi Syndrome. We evaluated its effect on NBs whose predisposition to sepsis is partly attributable to defective chemotaxis. Ten term NBs were treated with 4 doses of 100 mgs of VC q6 hrs starting on day 2 of life. Blood was obtained for study immediately before and after VC treatment. Chemotactic index (CI) and random migration index (RM) were determined by a modified Boyden's chamber technique. PMNs were deposited on a 3μ millipore filter which divided the chamber into an upper compartment filled with Hank's solution (HS), and lower filled with a mixture containing AB serum, endotoxin and HS. Following incubation and staining a ratio of migrated cells to total cells was determined and termed CI. In a parallel run with HS on either side the ratio was termed RM. The result (table) indicates that CI and RM increased about 64% following

RESULT	PRE THERAPY	POST THERAPY	P VALUE
CI mean (±1SD)	45(17)	74(40)	< 0.02
RM mean (±1SD)	19(6)	31(15)	< 0.02

VC therapy, a difference significant at $P<0.02$. We conclude that Vitamin C by improving the PMN qualitatively may be a useful adjunct to the treatment of sepsis in NB infants in general and in leukopenic infants in particular.

401 MIDAZOLAM(M) SEDATION FOR COMPUTERIZED TOMOGRAPHY(CT) IN CHILDREN(C): PHARMACOKINETICS(PK) AND PHARMACODYNAMICS(PD). Barbara M.Weissman, Samuel J.Horwitz, Carolyn M.Myers, Michael D.Reed and Jeffrey L. Blumer, Case Western Reserve University School of Medicine, Rainbow Babies & Childrens Hospital, Department of Pediatrics, Cleveland, Ohio 44106.

Life threatening adverse reactions have occurred in C after premedication for CT scans. In an effort to find a safe and effective premedicant M, a short-acting imidazobenzodiazepine, was tested as an IV sedative for C ages 2-6 years(yr) undergoing CT scanning. A total of 14 C were studied. After an initial bolus increments of 25% of the initial dose were administered each minute until the C slept or had received a total of 50 mg M. Heart rate, respiratory rate and blood pressure were monitored continuously. Initial bolus doses were 0.1,0.15 and 0.2 mg/kg in 5,5 and 4 C respectively. Two patients at each dose did not sleep. The mean age of the responders was 4.6 yr and nonresponders 2.6 yr. In responders the serum M concentration at sleep was 6μg/ml(range 2.2-12.8μg/ml) while on awakening they averaged 1.5μg/ml(range 0.14-5μg/ml). These concentrations were ≈10 times the concentrations at awakening in adult patients receiving M as a preanesthetic medication. M metabolite accumulated more rapidly in nonresponders than in responders. In C the apparent elimination $t_{1/2}$ ranged from 10 to 120 min. compared with 2-3 hr. in adults. C exhibited no apnea or hangover and were amnestic for the experience. Drowsiness was evident with the bolus in all C. Adverse reactions included transient hypotension(1), hiccoughs(3), nystagmus(5), and agitation(1). Our findings suggest differences in both the PK and PD of M in C compared with adults.