●368 CAFFEINE AND THEOPHYLLINE METABOLISM IN OLDER PRETERM INFANTS. Carlos Duran S., Cheston M. Berlin, Stephen A. Pearlman, Mary A. Wood. The Penn St Univ Coll Med, MS Hershey Med Ctr, Dept Ped, Hershey, PA.

Because there has been a dearth of data regarding caffeine and theophylline pharmacokinetics in older preterm infants, we studied 17 premature infants with apnea at an age of 15-38 days (G.A.=29.7±1.9 wks, M±SD). They received oral or IV caffeine at a dose of 2.3 to 10.3 mg/kg/day ($\bar{x}$=4.9±1.8) once or twice daily. To 25 µl of plasma an equal amount of acetonitrile was added. After vortex and ultracentrifugation, 15 µl of supernatant were injected into a reverse phase HPLC column and monitored at 280 nm. ß-hydroxyethyl-theophylline was the internal standard. Results are as follows:

					Caffeine		Theophylline	
Frequency	GA wks	BW gm	Age d	Dose mg/kg	Cp µgm/ml	t1/2 hr	Cp µgm/ml	t1/2 hr
BID	$\bar{x}$ 29.8	1266	17.2	3.92	27.3	46.7	2.88	106.8
	± ±	±	±	±	±	±	±	±
	SE 1.24	1.97	0.37	0.58	2.87	7.08	2.18	20.2
OD	$\bar{x}$ 29.7	1274	22.2	5.33	16.7	62.4	1.22	71.2
	± ±	±	±	±	±	±	±	±
	SE 0.44	99.5	2.14	0.53	2.53	7.87	0.25	16.8

We found no correlation between gestational age, weight, age, or dose and caffeine or theophylline levels. It was significant that on similar doses, patients on a twice a day schedule had much higher peak and trough levels than on one dose/day. We now use BID doses for caffeine therapy because of the higher levels attained.

●369 MATERNAL DRUG ABUSE DURING PREGNANCY AND PHARMACOTHERAPY FOR NEONATAL ABSTINENCE SYNDROME (NAS). Loretta P. Finnegan and Saundra Ehrlich. Jefferson Medical College of Thomas Jefferson University, Department of Pediatrics, Philadelphia, PA.

Newborns exposed in-utero to opiates and/or non-opiates frequently undergo NAS. This study evaluated:1)the relationship between the type of maternal drug use and the incidence of NAS and 2)which of 3 treatment drugs was most effective--paregoric, phenobarbitol, or diazepam. NAS was assessed by a scoring system related to drug dose. Successful treatment was considered when one drug controlled the NAS. Of the 300 infants, 176(59%) were treated for NAS and 124(41%) required no treatment. Maternal drug use consisted of opiates(33%), non-opiates(14%)and varying combinations of both(53%). Infants exposed to non-opiates in-utero were less likely to undergo abstinence(36%) than those exposed to opiates(58%) or both(70%). The mean number of days to control symptoms of NAS was 7.6, and duration of treatment averaged 38,6 days, The efficacy of treatment drug for NAS depended upon the type of drug exposure in-utero. If maternal drug use included opiates alone, paregoric was the drug most successful in controlling NAS (87% of infants). In maternal non-opiate use, phenobarbital was most effective(100%). In maternal opiate and non-opiate use, paregoric was most effective(88%). Treating an infant with diazepam indicated the need for a second treatment drug in 70% of cases, regardless of maternal drug use (p=.001). These data suggest that:1)effective NAS treatment is related to the type of maternal drug use, 2)there is a higher incidence of NAS in infants prenatally exposed to opiates alone or in combination with non-opiates, and 3)diazepam is ineffective as a treatment agent for NAS.

370 CSF/SERUM THEOPHYLLINE RATIOS IN YOUNG PREMATURE INFANTS. Eugene A. Gatti, Nancy B. Robinson, Consuelo L. Saccar, Stephen J. McGeady, Herbert C. Mansmann, Jr Philadelphia, PA

Theophylline is widely used in neonatal intensive care units for respirogenesis & bronchodilation. It is important to understand the pharmacokinetics of this drug in premature infants. There are reports of fixed correlation between CSF & blood theophylline levels in premature infants beyond the neonatal period, older children & adolescents. During evaluations for sepsis simultaneous blood & CSF specimens were obtained in 12 premature infants (B.W. 785 gm - 1505 gm), including 9 neonates, who were receiving I.V. theophylline and were in steady state. One subject was studied twice. Theophylline assay was by HPLC. In contrast to earlier reports, subjects revealed no constant or predictable relationship between serum & CSF theophylline levels. CSF/serum ratios varied from 41% - 106% with a mean of 78%. The subject studied twice demonstrated ratios of 57% and 82%. Variables considered to account for these divergent observations included age, intracerebral hemorrhage, culture proven sepsis and/or meningitis, serum albumin/total proteins, & other concurrent medications. No variable or combination of variables could explain the great scatter observed. It was concluded that young premature infants exhibit unpredictable and highly variable correlation between CSF & serum theophylline levels. Considerable intersubject variability may occur without obvious cause. This agent should be used in this patient group with realization that the CSF level may be 100% of the serum level or less than 50% thereof.

371 POTENTIAL TREATMENT OF THEOPHYLLINE TOXICITY BY HIGH SURFACE AREA ACTIVATED CHARCOAL. Glenn W Ginoza, Arthur A Strauss, Melinda K Davidson, Houchang D Modanlou. Miller Children's Hospital, Univ. of Cal., Irvine, Long Beach, California.

Orally administered standard activated charcoal (surface area = 950 m2/g) has been shown to enhance clearance of theophylline in adults. The effect of SuperChar (Gulf Bio-Systems Inc., Dallas, TX), a high surface area (3376 m2/g) activated charcoal, on theophylline clearance was examined during a 48 hr study period in ten low birth weight "growing" status infants, treated with theophylline for apneic episodes, who were candidates for having the drug discontinued. Theophylline was given intravenously as aminophylline on a 12 hr schedule at normal maintenance dose. Each patient received 1g/kg/dose of SuperChar twice via orogastric tube, three hours apart between feedings. Serial theophylline levels were drawn (peak, mid-dose, trough) before and after the administration of SuperChar. Each patient tolerated the charcoal and no complications were encountered during the study. From a graph of serum levels vs. time, clearance of theophylline was calculated using the trapezoidal rule in estimating the area under the curve. There was a significant ($p<0.001$) increase in the clearance of theophylline after administration of SuperChar (Wilcoxon Signed Rank test).

			Study		Clearance (ml/kg/hr)	
	BW (g)	GA (wks)	Age (days)	Wt (g)	Baseline/SuperChar/% Change	
Mean	1151.5	31.8	26.5	1877.0	22.73	44.55	96.40
S.D.	±144.3	±1.2	±5.9	±19.1	±7.32	±14.61	±28.92

Conclusion: SuperChar enhances the clearance of theophylline in low birth weight infants and may be useful in the treatment of neonatal theophylline toxicity.

372 THE USE OF TRI-CYCLIC ANTI-DEPRESSANTS (TCA) IN METHADONE MAINTAINED (MM) PREGNANT WOMEN AND INFANT OUTCOME. Lois Green, Saundra Ehrlich and Loretta P. Finnegan. Jefferson Medical College of Thomas Jefferson University, Department of Pediatrics, Philadelphia, PA.

Little is known about TCA use in pregnancy and infant outcome. This study evaluated infants born to MM women who were concurrently prescribed TCA's for the treatment of depression. Subjects included:1)18 infants born to MM women also exposed in-utero to imipramine(N=3) or doxepin(N=15) in doses ranging from 25mg. to 100mg. and 2)18 infants born to MM women not exposed to TCA's in-utero. The women were similar with regard to age, race, gravidity, parity, methadone dose, number of prenatal visits and socioeconomic status. Although types of illicit drug use in pregnancy differed between groups, these differences were taken into account in the analysis. The infant variables compared in the 2 groups were: gestational age, birth weight, head circumference, intrauterine growth, 1 and 5 min. Apgar scores, length of hospital stay, infant complications and neonatal abstinence. Infants in the TCA group were born earlier than controls(37.1 wks. vs.38.7wks., $p<.05$), other differences between groups included lower birth weight, smaller head circumferences and lower Apgar scores, and were attributable to gestational age differences. The groups were found similar on other variables. Within the TCA group, when comparisons were made according to trimester prescribed, infants exposed during the 3rd trimester were found to be born earlier and somewhat smaller than infants with 1st and/or 2nd trimester exposure. These results suggest continued caution in prescribing TCA's in MM pregnant women. Their use can only be justified when the benefits outweigh the potential risks.

373 CHARACTERIZATION OF ALPHA-ADRENERGIC RECEPTORS IN NEONATAL PIGLET AORTAS BY RADIOLIGAND BINDING. Robert S. Green, David W. Busija, and Charles W. Leffler. (Spon. by Henrietta S. Bada) Depts. of Pediatrics and Physiology and Biophysics, Univ. of Tennessee, Memphis, TN

Vascular smooth muscle cell membranes were prepared from neonatal piglet aortas by homogenization, low speed centrifugation to remove intact cells and ultracentrifugation. Aliquots of the membrane preparation containing 100 micrograms of membrane protein (Lowry assay) were then incubated in tris buffer pH 7.45 at 25°C with varying concentrations of either tritiated prazosin (selective alpha-1 antagonist) or tritiated yohimbine (selective alpha-2 antagonist). Incubation was stopped by addition of ice cold tris; radioligand bound to the membrane preparation was separated from free radioligand by rapid filtration. Non-specific binding (other than to alpha receptors) to membrane prep or filter was quantified by identical procedure with the addition of 10 mM l-norepinephrine to the incubation medium to occupy alpha receptors. No specific binding of prazosin to membrane preparations was observed. Specific, saturable binding of yohimbine was observed and was analyzed by Scatchard plot giving a dissociation constant of 2.4 nM and a receptor content of 100 fmole/mg membrane protein. These preliminary observations suggest that the major alpha receptor subtype in the neonatal piglet aorta is the alpha-2 receptor, and there may be no alpha-1 receptors present.