330 THE EFFECTS OF MATERNAL NARCOTIC VS NON-NARCOTIC ADDICTION ON NEONATAL NEUROBEHAVIOR AND INFANT DEVELOPMENT. Ira J. Chasnoff, William J. Burns and Kayreen Burns. (Spon. by Stan Shulman). Northwestern University Medical School, Departments of Pediatrics and Psychiatry, Chicago.

In order to evaluate the effects of maternal abuse of non-narcotic drugs during pregnancy, four groups of infants born to drug-addicted mothers were evaluated and compared to a control group of normals. Group I infants (N=51) were delivered to mothers on methadone maintenance, Group II infants (N=22) to sedative/stimulant (nonnarcotic)-abusing mothers, Group III (N=13) to T's and blues-abusing mothers, Group IV (N=9) to PCP-abusing mothers and Group V (N=27) to mothers who had no evidence of drug abuse. All five groups were similar in maternal age, gravidity, socioeconomic class and neonatal gestational age. Significant decreases in weight, length and head circumference at birth were found (ANOVA) for the narcotic-exposed (Groups I and III) infants while nonnarcotic-exposed infants demonstrated normal growth parameters at birth. Using the BNBAS, Group I infants demonstrated deficits in visual and auditory orientation and motor maturity. All four groups of drug-exposed neonates demonstrated deficits in state control. Group IV infants, in addition, showed increased lability of state and poor consolability when compared to all other drug groups (Fischer's LSD). On the Bayley Scales, scores for all groups, including the control, began to fall away from the normal range at 18 months of age, a phenomenon not uncommon in infants from lower socioeconomic homes.

331 ACCUMULATION OF FUROSEMIDE FOLLOWING FREQUENT REPEATED DOSES IN NEWBORN INFANTS. Sylvain Chemtob, Apostolos Papageorgiou, Patrick du Souich, Jacob V. Aranda. Dev Pharmacol & Perinatal Res Unit, McGill Univ-Montreal Children's Hosp and Jewish General Hosp. Montreal, Quebec, CANADA

Furosemide (F) may have a reduced volume of distribution and prolonged plasma clearance following frequent repeated doses of F in newborn infants. To test whether repeated doses result in plasma accumulation of the drug, four neonates ($\bar{x}$ bt wgt 1140 g, range: 810-1645), ($\bar{x}$ gestational age 27 5/7 wks, range: 26-30 wks) with normal renal function were given F, 1 mg/kg/dose IV bolus every 12 hours for 4 doses and maintained normally hydrated during the study period. Serum F levels in mg/l (see table) were measured by HPLC 1 hr after each bolus.

PATIENT/DOSE	1st	2nd	3rd	4th
1	4.76	7.30	11.98	14.00
2	3.48	6.03	-	15.27
3	2.57	3.80	14.96	-
4	4.78	7.48	32.20	-
Mean ± S.E.	3.90 ± 5.4	69.5 ± 0.85	19.65 ± 6.2	-

Serum F concentration increased with repeated doses beyond that expected for the reported plasma $t_{\frac{1}{2}}$ of 7-19 hrs. Serum F concentration after the second dose was significantly higher than F level after the initial dose ($p<0.01$). This accumulation of F in the serum of the neonate with repeated doses may reflect delayed plasma clearance and contraction of the volume of distribution superimposed on a prolonged elimination rate. Caution should be observed when given frequent repeated doses of F to newborn infants.

332 REGIONAL CEREBRAL BLOOD FLOW (CBF) DURING BICUCULLINE INDUCED SEIZURES (S) IN THE NEWBORN PIGLET WITH OR WITHOUT PHENOBARBITAL (PB). M. CLOZEL, P. MONIN, J.L. DAVAL, P. VERT, Centre de Recherche Biologie Médecine du Dévelopement Humain, Université de NANCY I, FRANCE.

In adult animals, S induce important alterations in CBF, which have not been evaluated in the neonatal period. Thus, we measured CBF before, during and 15 min after S induced by IV bicuculline (.6 to 1.2 mg/kg) with 15 μm radioactive microspheres, in 12 urethan-anesthetized spontaneously breathing piglets (2 to 9 days). Six piglets received IP PB 10 mg/kg, 6 hrs before S, and 6 did not (controls (C)). Mean arterial blood pressure (MABP), PaO_2 and cerebral tissue pH (CtpH) were measured. The duration of S was significantly decreased by PB (mean ± SEM) (10.8 ± 1.8 vs 21.8 ± 4.1 min, $p<.05$). S induced a significant increase in MABP in both C (83.7 ± 6.3 vs 59.7 ± 7.2 mmHg, $p<.01$) and PB group (92.0 ± 8.7 vs 68.0 ± 2.4 mmHg, $p<.01$). PaO_2, $PaCO_2$ and CtpH were not significantly modified. CBF was increased during S, mostly in basal ganglia (98 and 106 % respectively for C and PB group), less in brain stem (96 and 45 %) and cerebellum (72 and 35%), least in cortex (13 and 30 %) and was unchanged in the choroid (.4 and -.8%). Fifteen min after S, CBF returned to pre S values. There was no significant difference in CBF at any time between C and PB group. CBF changes during S were independent of changes in $PaCO_2$ and PaO_2, but were positively correlated with changes in MABP ($r=.753$, $p<.01$) and CtpH ($r=.570$, $p<.05$).

Conclusions: during neonatal experimental S, 1) changes in CBF seem to be mainly due to impairment of autoregulation, 2) PB pretreatment does not modify CBF response, 3) choroid blood flow is not altered.

333 PHARMACOKINETICS AND EFFICACY OF ONCE DAILY CEFTRIAXONE. Blaise L. Congeni, Tasnee Chonmaitree, Sponsored by Katherine C. King. Children's Hospital of Akron, Akron, OH, University of Texas Medical Branch of Galveston, Galveston, TX. Dept. of Peds. Because of its spectrum and prolonged half-life ceftriaxone (RO) has been shown to be particularly useful in the treatment of pediatric infections including meningitis. In the United States it has been administered twice daily and the major side effect encountered has been diarrhea. RO 50mg/kg, administered once daily, was used to treat 18 non-meningitic infections in children aged 2.5 M to 13 yr. Etiologic agents included Staphylococcus aureus (9), Streptococcus pyogenes (8), non-enterococcal group D Streptococcus (1), Hemophilus influenzae b (3) (1 ampicillin resistant), Klebsiella pneumoniae (2), E. coli (2), Proteus vulgaris (1). Several patients had 2 organisms isolated. Infections seen included cellulitis (13)-periorbital (3), septicemia (2), urinary tract infections (4), epiglottitis (1). One patient had both a UTI and septicemia. Duration of therapy ranged from 5 to 9 days. The mean plasma RO concentrations obtained one hour after and within one hour before a dose were ± 193.8 - 10 μg/ml and 8.6 - 6 μg/ml. The mean half-life was 5.13 h - 1.05. All patients had trough RO concentrations ≥ 3.4 μg/ml exceeding the minimal inhibatory concentration of the infecting organism. All patients were cured. No patients developed diarrhea although 2 patients had eosinophilia, 2 thrombocytosis and 3 elevated transaminases. Ceftriaxone appears safe and effective when used at the lower dose of 50mg/kg administered once daily to treat infections with susceptible organisms.

334 MATERNO-FETAL TRANSFER OF THYROXINE (T_4): MATERNAL (M) AND FETAL (F) FREE T_4 (FT_4) RELATIONSHIP AND THYROMIMETIC EFFECTS IN THE FETUS U.Devaskar, S.Devaskar, P.Grim, (Spons. W.J. Keenan), Dept. of Peds., St. Louis University, St. Louis, Missouri

The role of thyroid hormones (TH) in the F development is well established. It is generally believed that TH do not cross the mammalian placenta from the M to the F in sufficient concentration to exert biological effects in the F. We administered 50μg/kg of T_4 I.M. (n=6) or saline (n=4) to the rabbit doe on alternate days starting at 21d. of pregnancy. M and F plasma glucose (G), corticosteroids (CS), FT_4 and insulin (I) and F heart (H), liver (L) and brain (B) protein and cardiac glycogen (GLY) content were quantitated on the 30d. of gestation. All data are expressed as X±SEM. (*p<0.05).

	Plasma				Protein (mg/gm)		
	FT_4 (ng/dl)	CS (ng/ml)	G (mg/dl)	I (μU/ml)	L	B	H
F(control)	.18±02	11±.03	48±5	26±4	95±3	51±2	91±2
F(study)	*.77±.11	12±.05	*66±5	20±3	*100±3	*56±7	*100±3
M(control)	.24±.05	58±10	100±6	15±3			
M(study)	*5.72±.97	53±6	98±4	12±4			

M:F plasma FT_4 concentration ratio was 8:1 and given by the equation $Y=0.1248 \times X + 0.0736$ ($r=0.86$). Fetal cardiac glycogen content was significantly lower in hyperthyroid fetuses compared to control (0.47*±0.01 vs 0.59±0.02μmoles of glucosyl units/mg homo. protein). We conclude that T_4 crosses the rabbit placenta and exerts thyromimetic effects in the fetus. A convenient animal model to study the effect of hyperthyroxinemia on fetal development in utero is proposed.

●**335** MODULATION OF CHLORAMPHENICOL(C) BIOAVAILABILITY(F) BY PANCREATIC ENZYME REPLACEMENT(PER) IN CYSTIC FIBROSIS (CF). Chris J.Dickinson, Stephen C.Aronoff, Robert C. Stern, Michael D.Reed and Jeffrey L.Blumer, Case Western Reserve University School of Medicine, Rainbow Babies & Childrens Hospital, Department of Pediatrics, Cleveland, Ohio 44106.

The effect of PER on the F of C was ascertained in 5 adolescent patients with CF. Each patient was studied on 6 occasions separated by at least 24 hours. Exocrine pancreatic function was ascertained by the urinary excretion of PABA following ingestion of N-benzoyl-L-tyrosyl PABA. C was administered as C succinate(CS) intravenously, and C palmitate(CP) or C base (CB) orally at a dose of 20mg/kg with or without PER. Multiple timed blood samples were obtained over a 12 hour period following each dose and analyzed by HPLC. Model independent pharmacokinetic analysis of CS biodisposition revealed ($\bar{x}$±SD) $t_{\frac{1}{2}}$, 3.35±1.16hr; Vd_{SS}, 1.39± 0.49 4kg; and Clp, 267.33±53.96ml/min/1.73m^2. These values were comparable to those obtained with CB and for CS in unaffected individuals. The absolute F of CB ranged from 71-154% without PER and increased by 8-17% after PER. For CP the absolute F ranged from 21-59% increasing by 2-200% following PER. In one patient CP absorption continued throughout the monitoring period after PER. The wide range of effect of PER on the F of the oral formulations of C appeared related to the level of intrinsic exocrine pancreatic function. The relative F, CP/CB, was directly related to urinary PABA excretion ($r=0.9$). These results suggest that PER may significantly enhance the F of CP through replacement of pancreatic lipase. Pancreatic enzymes may play a role in enhancing the F of CB as well.