● 349 THE EFFECT OF CHLOROTHIAZIDE (CT) ON LASIX-INDUCED HYPERCALCIURIA. Christine G. Butler and Richard A. Ehrenkranz (Spon. by I. Gross). Yale Univ. Sch. of Med., Dept. of Ped., New Haven, CT.

Infants with chronic lung disease often develop rickets secondary to prolonged lasix (L) treatment. We studied the effect of CT on the hypercalciuric response to L in 11 young adult rats (Wt 259±1.1 gm, M±SE). The rats were fed Purina rat chow and received water ad lib. At the end of a 15 day control period, urine was collected for 72 hrs. The rats were then divided into 2 groups: Group I (n=5) received 15 mg/kg/d of L IP and Group II (n=6) received 20 mg/kg/d of CT IP for 15 d, at the end of which a 72 hr urine collection was performed. Following this all rats received both drugs at the above dosage and a third 72 hr urine collection was done at the end of a 15 d treatment period. Each urine collection was analyzed for Ca concentration. Urinary Ca excretion data (mg/kg/d) are displayed below. We conclude that administration of L produces a 50% increase in urinary Ca excretion compared to control. However, the combination of L and CT caused a 24% reduction in urinary Ca excretion when compared with L alone. Urinary Ca excretion with CT alone was not significantly different than control. These data support the use of both CT and L therapy in infants with chronic lung disease when diuretic therapy is needed.

	Control	L	CT	L + CT
Group I (n=5)	2.92±0.70	4.38±0.44[a]	- -	3.29±0.38[b]
Group II (n=6)	3.01±0.78	- -	2.30±0.53	3.60±0.42

[a]Control vs L, $p<0.05$ [b]L vs L + CT, $p<0.05$ after correcting for multiple comparisons.

350 COCAINE USE IN PREGNANCY. Ira J. Chasnoff, Wm. Burns, Kayreen Burns (Spon. by James Stockman III). Northwestern University Medical School, Northwestern Memorial Hospital, Departments of Pediatrics and Psychiatry, Chicago.

With the increasing use of cocaine in the United States, there has been growing interest in its effects on the fetus and neonate of the pregnant abuser. Two groups of cocaine-using women (Group I, N=10, cocaine use only; Group II, N=10, cocaine plus methadone maintenance for narcotic addiction) enrolled in a comprehensive perinatal addiction program were studied and compared to a group of women with a history of narcotic use only, maintained during pregnancy on methadone (Group III, N=15) and a group of drug-free women (Group IV, N=15). All 4 groups were similar for maternal age, socioeconomic status and cigarette use, and the 3 drug-using groups were similar for alcohol and marijuana use. Gravidity was similar for all 4 groups, but women in each of Groups I and II had a significantly higher rate of spontaneous abortions, abruptio placentae and premature delivery than women in either Group III or Group IV. In the series of pregnancies under study, 4 pregnancies in Groups I and II had onset of labor with abruptio placentae immediately following IV self-injection of cocaine. Mean neonatal gestational age, birth weight, length and head circumference were not affected by cocaine use. Utilizing the Brazelton Neonatal Behavioral Assessment Scale, cocaine-exposed infants showed more irritability and state lability than either methadone-exposed or drug-free infants and significant depression of interactive behaviors, especially visual orientation.

351 EFFECT OF PGE_1, ON OCULAR BLOOD FLOW IN THE NEWBORN PIGLET. S. Chemtob, K. Beharry, J. Rex, N. Laudignon J.V. Aranda. Depts. of Peds. & Neonatology, McGill Univ - Montreal Child Hosp, Montreal, Canada.

Prostaglandins (PG) play a major role on cerebral blood flow (CBF) regulation of the adult and possibly newborn (NB). Ocular blood flow (OBF) appears to be subjected to similar regulatory mechanisms as CBF. The effect of PGE_1, the most commonly used PG in the NB period, on OBF was evaluated in 6 piglets, 1-3 d.o. Aorta, left ventricle, inferior vena cava, and sagittal vein were catheterized to monitor arterial, venous and sagittal blood gas, glucose, and pressure. PGE_1 was administered in the left internal carotid artery (LIC) in successive increasing doses of 10^{-7}, 10^{-6}, 10^{-5}g/kg/bolus q 20 mins, to awake piglets. OBF was measured by radiolabelled microspheres (^{141}Ce, ^{46}Sr, ^{85}Nb, ^{95}Sc)45sec post bolus.

Organ	0 dose g/kg	10^{-7}dose g/kg	10^{-6}dose g/kg	10^{-5}dose g/kg
L. eye	82.04± 72.80	48.61± 32.25	67.81± 51.96	52.73± 44.81
R. eye	135.04± 81.81	*74.19± 25.78	96.19± 40.19	103.88± 50.59

Values are $\bar{x}$ S.D. OBF (ml/min/100g); *p=0.05 compared to t = 0.

OBF decreased by 40% following PGE_1 dose of 10^{-7} g/kg. High doses of PGE_1 produced a significant effect on OBF. Blood pressure and gases did not correlate with OBF. Differences between right and left OBF may be partly explained by the LIC catheter, partially occluding flow ipsilaterally. The data suggest that therapeutic doses of PGE_1 (10^{-7}g/kg) do not significantly alter OBF. In contrast physiological concentrations of PGE_1 ($<10^{-7}$ g/kg) produced a direct vasoconstriction on ocular or cerebral vasculature, as demonstrated in adult animals. This may imply an important physiological role of PGE_1, on OBF in the NB.

● 352 CLINICAL PHARMACOLOGY OF TOLAZOLINE (Tz) IN PERSISTENT FETAL CIRCULATION (PFC). Elizabeth Chow-Tung, James H. Fischer, Rama Bhat, Dharmapuri Vidyasagar. University of Illinois at Chicago, Departments of Pharmacy Practice and Pediatrics, Chicago.

The effect of Tz in treatment of PFC was evaluated in 14 neonates (gestational age (GA) ≤ 34 weeks, n=6) receiving maximal assisted ventilation. Intravenous Tz was administered as a loading dose of 1 to 2 mg/kg followed by a continuous intravenous infusion of 1 mg/kg/hr. The dose was increased up to 4 mg/kg/hr based on the patients clinical response. Clinical status, laboratory parameters and Tz serum concentrations were monitored throughout therapy. A positive response to Tz was observed in 70% of the patients. A curvilinear relationship was noted between Tz serum concentrations and PaO_2/FiO_2 ratio. The response to tolazoline was dependent on GA, serum concentration and arterial pH. A significant difference ($p < 0.05$) in the responsiveness to tolazoline was observed between neonates > 34 weeks and ≤ 34 weeks GA. In neonates > 34 weeks, positive therapeutic response was observed with arterial pH > 7.45 and Tz serum concentrations of 2-4 µg/ml. Neonates of ≤ 34 weeks GA, a positive therapeutic response was seen at serum concentration of 4.4 - 7.7 µg/ml and an arterial pH of 7.31 - 7.44. Systemic hypotension and GI bleeding were observed in 28.6% of the patients. This was related to high serum concentrations and arterial pH < 7.30. The rational use of Tz for the treatment of PFC requires careful monitoring of respiratory status, pH, blood pressure and serum Tz concentration.

● 353 FACTORS INFLUENCING TOLAZOLINE (Tz) DISPOSITION IN NEONATES. Elizabeth Chow-Tung, James H. Fischer, Bruce Currie, Rama Bhat, Dharmapuri Vidyasagar. University of Illinois at Chicago, Departments of Pharmacy Practice and Pediatrics, Chicago.

Tz pharmacokinetics were studied in 17 neonates (gestational age (GA) 29-42 weeks; ≤ 34 weeks, n=7) with persistent fetal circulation. Therapy was initiated with 2 mg/kg I.V. loading dose followed by 1 mg/kg/hr I.V. infusion which was increased up to 4 mg/kg/hr based on clinical response. Serial blood samples were obtained post loading dose, during infusion and for 24 hours following termination of infusion. Urine for determination of Tz and creatinine clearance (CrCl) was obtained following attainment of steady-state on the Tz infusion. Tz concentrations were determined by HPLC. The mean ± SD half life ($T_{\frac{1}{2}}$), total clearance (Cl), renal clearance (Cl-Ren) and distribution volume (Vd) were 5.9 ± 2.8 hr, 155.3 ± 66.9 ml/min/1.73 m^2, 125.5 ± 69.8 ml/min/1.73 m^2 and 3.0 ± 1.0 l/kg, respectively. A significant difference ($p < 0.01$) between neonates ≤ and > 34 weeks GA was observed for Cl, Cl-Ren and $T_{\frac{1}{2}}$. Tz Cl and Cl-Ren were found to increase exponentially as a function of GA (Cl vs. GA, $Y = 0.08e^{0.14x}$, $r = 0.83$; Cl-Ren vs. GA, $Y = 0.03 e^{0.16x}$, $r = 0.81$). These parameters were also observed to be significantly correlated to CrCl (Cl vs. CrCl, $Y = 6.1X + 1.7$, $r = 0.87$; Cl-Ren vs. CrCl, $Y = 5.2X + 0.43$, $r = 0.89$). These results indicate that Tz in neonates is primarily excreted renally by tubular secretion. Tz dosage should be based on the neonate's gestational age and renal function.

354 UNALTERED EPIDERMAL GROWTH FACTOR RECEPTORS IN SENESCENT HUMAN FIBROBLAST CULTURES. Chu Chang Chua, Deborah E. Geiman and Roger L. Ladda. Penn State Univ. Coll. of Med., The M. S. Hershey Med. Ctr., Dept. of Peds., Hershey, PA.

Human fibroblast (HF) cultures have a finite proliferative potential and have been used as a model for studying the aging process. In the present study the effect of senescence on the receptor for epidermal growth factor (EGF-R) was examined. Biosynthetic labeling of young and senescent HF cells with [^{35}S]-methionine followed by immunoprecipitation with EGF-R monoclonal antibody revealed the presence of M_r 170,000 EGF-R in cells from both stages. Membranes from young and senescent membranes were isolated and included in phosphorylation reaction with [γ-^{32}P]-ATP with and without addition of epidermal growth factor (EGF). Autophosphorylation of EGF-R in response to EGF was the same in both young and senescent cells. Phosphoamino acid analysis on the autophosphorylated EGF-R indicated that tyrosine residues were phosphorylated in both cells. In addition, two-dimensional peptide mapping of [^{125}I]-EGF-R from young and senescent cells showed essentially the same pattern. Our results indicate that EGF-R does not undergo significant changes in senescent cells.