DEVELOPMENTAL PHARMACOLOGY

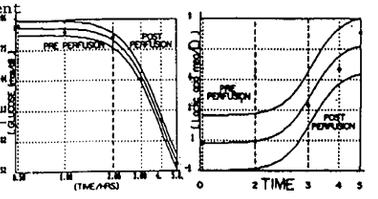
337 THE RELATIONSHIP BETWEEN ABR AND CARDIOPULMONARY FUNCTION IN PRETERM LAMBS. M.R. Wolfson, J.D. Durrant, T.H. Shaffer, N. Tran, V. Bhutani, D. Rubenstein. (Spon: Alfred M. Bongiovanni). Temple Univ. Sch. of Med., Dept. of Physiology, Pennsylvania Hospital, Philadelphia, Eye and Ear Hospital, Pittsburgh, Rolling Hill Hospital, Elkins Park, Pa.

The auditory brain-stem response (ABR) and cardiopulmonary function (as determined by the mean blood pressure [MBP], heart rate, arterial blood gases [ABG], and pH were evaluated in 9 preterm lambs ranging in age from 106-125 days gestation (70-85% term). Following epidural anesthesia of the ewe, the uterus was opened, the fetal head exposed, and a saline-filled rubber glove placed over the snout to prevent inspiration of air. Two platinum-alloy needle electrodes were inserted subdermally just posterior and inferior to the pinnae, another at vertex, and one in the snout area for ground. Click stimuli were generated and delivered by a bone conduction vibrator driven by 100 usec pulses of alternating polarity. Even the youngest group of animals revealed clearly defined 8th nerve and brain-stem response components. The latencies of waves 3,4, and 5 and the interpeak latency 1-5 decreased significantly as a function of age. Results of physiologic measures and the ABR data across subjects revealed a significant negative correlation between MBP and the latencies of waves 4 and 5 and the 1-5 interpeak latency and were suggestive of a possible inverse relationship between the wave 1 latency and pH. These findings demonstrate the presence of the ABR as early as 70% gestation as well as the sensitivity of the ABR to MBP and acid-base balance at this stage of development. (Supported by NIH Grant HL/HD 30525).

† **338** PERFUSION STUDIES OF THE HUMAN PLACENTA:Arun Yesupriya,Alex Boafo, Trisit K.Mukherjee, Ben K.Rajegowda . Martin Marcus and Asit K. Ray. (Sponsored by Lawrence Shapiro).New York Medical College, Lincoln Medical and Mental Health Center,Departments of Pediatrics, Obstetrics & Gynecology and Biochemistry, Bronx, New York.

The human placenta has long been recognized as an organ of hormogenesis. Various in-vitro and in-vivo experiments have demonstrated the biosynthesis of hormones by the placenta, e.g., HCG, HPL, estrogen, progesterone, releasing hormones, endorphins, etc. Most of these studies were done either on animal models or by perfusion of single cotyledon of a placenta.

In this study, whole term placentas were perfused immediately after delivery with packed red cells suspended in Hank's solution using the apparatus designed by Krantz and Panos. The pH, pO_2, PCO_2, glucose utilization and lactic acid production were monitored at regular intervals throughout the study period to establish the prevailing physiologic conditions. The glucose utilization and lactic acid production increased significantly during the course of perfusion indicating the viability of the placenta (fig.1) During the experiment pH,PO_2,PCO_2 were maintained within physiological limits by disc oxygenator.This model of perfusion ofwhole placenta appears to be useful for studying the regulation of hormone synthesis & metabolism of drugs by the placenta.



339 PHARMACOLOGIC MODULATION BY PGE_1 OF O_2^- PRODUCTION BY HUMAN NEUTROPHILS. Jerry J. Zimmerman (Spon. by Frank A. Oski) SUNY, Upstate Medical Center, 750 E. Adams St., Dept. of Pediatrics, Syracuse, N.Y. 13210

Prostaglandin E_1 (PGE_1), one of a series of naturally occurring prostenoic acid derivatives, has been pharmacologically exploited for its potent vasodilatory effects. However, the observation that patients with patient ductus arteriousus infused with PGE_1 may have a higher incidence of wound infection, has led to the speculation that PGE_1 might be used to modulate PMN activity to avoid neutrophil mediated host autoinjury such as occurs in adult respiratory distress syndrome and septic shock capillary leak. Suppression of human PMN NADPH oxidoreductase by PGE_1 was assessed utilizing a continuous, initial-velocity enzyme assay to quantitate lag time, linearity, rate and extent of superoxide anion production. Assays containing $\leq 10^{-9}$M PGE_1generated O_2^- at 15.8±0.8 nmoles/min/10^6 PMNs, after a lag time of 13.0±0.8 sec. Catalysis was linear for 26.7±2.4 sec after which a gradual decline in activity ensued. Progressive inhibition of O_2^- generation was noted at higher PGE_1 concentrations (10^{-9}M=0%, 10^{-8}M=16.4%, 10^{-7}M=34.8%, 10^{-6}M=58.2%, 10^{-5}M=100%). No changes in reaction lag time or linearity were noted over these PGE_1 concentrations, however, extent of reaction was severely compromised at $PGE_1 \geq 10^{-7}$M where catalysis was concluded in $\leq$1min. Calculation of plateau concentrations of continuously infused PGE_1 indicate that in vivo modulation of PMN activity is realistic. Present findings indicate the potential feasibility for pharmacologic titration of PMN activity by PGE_1 to limit or avoid inflammatory amplification host autoinjury while simultaneously avoiding nosocomial infection.

= 340 EFFECT OF PHENOBARBITAL ON REGIONAL CEREBRAL BLOOD FLOW IN THE NEWBORN BABOON. J.V. Aranda, H.Maeta , K. Beharry, R. Bhat, T. Raju, D. Vidyasagar. Depts. of Ped. McGill Univ-Montreal Child Hosp, Montreal, Canada, and Univ of Illinois, Chicago, Ill, USA.

The effect of phenobarbital (P) on regional cerebral blood flow (rCBF) was studied in 6 preterm newborn baboons (gest. age 149/184 - 168/184 d: $\bar{x}$ = 160.2 d; birth weight: 0.69 - 1.06 kg, $\bar{x}$ = 0.89 kg) to evaluate possible mechanisms underlying protective effect on intracranial hemorrhage. Polyvinyl catheters were placed in the left ventricle, abdominal aorta with umbilical or femoral artery, sagittal or internal jugular vein within 1 hr. following cesarian section birth. Arterial and venous blood gases, P, glucose, lactate, hemoglobin and rCBF, measured by radio labelled microspheres (^{141}Ce, ^{51}Cr, ^{85}Sr) before and at 30 and 60 min. following P, 20 mg/kg I.V. Using the baboons as their own control, results show that P produced a transient but variable decrease in total CBF at 30 min. (- 27.2 ± 28.2% of control values). Decreased rCBF 30 min. post P was noted in all 16 brain regions examined including superior and inferior colliculi ($\bar{x}$ ± SF: - 33.8 ± 25.6%), thalamus, (- 32.2 ± 25.7%), medulla (- 29.6 ± 25.1%), frontal lobe (- 28.9 ± 25.6%), occipital lobe (- 28.5 ± 28.8%), and parietotemporal lobe (- 26.3 ± 28.1%). rCBF values in all regions examined returned or exceeded baseline 60 min. post P; regions with the least fall in rCBF showed best recovery in rCBF. Data suggest that protective effect of P may minimally be mediated by direct effect on rCBF but largely via other mechanism (eg. sedative effect and stabilization of systemic blood pressure).

● **341** EFFECTS OF AMILORIDE ON MYOCARDIAL CONTRACTILE FUNCTION IN IMMATURE (I) VERSUS ADULT (A) RABBITS Michael Artman, David Crump, Robert C. Boerth, and Robert J. Boucek, Jr.; University of South Alabama, College of Medicine, Depts. of Pediatrics and Pharmacology; Mobile, AL

Amiloride has been shown previously to inhibit sodium-calcium (Na-Ca) exchange across the cardiac sarcolemmal membrane. We used the responses to amiloride to compare the relative contribution of transarcolemmal Na-Ca exchange to contractile function in I and A myocardium. Amiloride dose-response relationships were obtained in isometrically contracting right ventricular papillary muscles from I (14-21 days of age) and A rabbits (0.5Hz; 30°C; pH=7.4). The effects of amiloride on maximal rate of tension development (dT/dt; gm/sec/mm^2) are tabulated below (mean±SE):

	Amiloride Concentration (mM)			
	0	0.3	1.0	1.5
I(n=6)	2.6±0.4	2.2±0.6	2.4±0.8	2.2±0.7
A(n=6)	11.4±2.6	11.6±2.8	13.2±2.9*	13.7±3.0*

*different from control (0 amiloride); p<0.05.

Amiloride prolonged relaxation in both groups, but had no effect on time to peak or resting tension. An increase in contractility (+dT/dt) and prolongation of relaxation in response to inhibition of Na-Ca exchange is consistent with the concept that Na-Ca exchange is an important mechanism for lowering intracellular Ca in A. The failure of amiloride to increase dT/dt in I suggests that Na-Ca exchange contributes relatively less to the reduction of intracellular Ca in I myocardium. These results indicate that the mechanisms for myocardial relaxation may undergo postnatal maturation.

342 ZINC DEFICIENCY IN INFANTS WITH FETAL ALCOHOL SYNDROME. Farahnak K. Assadi, Mohsen Ziai (Sponsored by Ira M. Rosenthal). Departments of Pediatrics, University of Illinois Health Sciences Center at Chicago and Georgetown University, Washington, D.C.

Renal clearance of zinc was examined in 6 infants with fetal alcohol syndrome (FAS) to determine if there is a link between prenatal exposure to ethanol and zinc deficiency in the development of fetal dysmorphogenesis. Eight healthy age-matched infants served as controls. There was no significant difference in creatinine clearance, urine flow rate, or fractional water excretion values between the two groups. Plasma concentrations of zinc were significantly lower in FAS patients (62.5±2.8 µg/dL) in comparison to controls (70.3±2.3 µg/dL), (P<.00005). Urinary excretion of zinc in FAS patients averaged 646±125 µg/24 hr; significantly higher than in control subjects (330±184 µg/24 hr), (P<.00005). Fractional excretion of zinc (FE_{Zn} was significantly higher in FAS patients (2.8±1.1%) compared to control group (1.4±.07%), (P=.02), but the mean filtered zinc (FZn) was significantly lower in patients than in controls (P=.02). The changes in FE_{Zn} for FAS patients varied inversely with urine flow rate (r=-.58, P=.002) and with FZn (r=-.39, P=.0001), but varied directly with fractional water excretion (r=.20, P=.008). Thus: (1) Plasma zinc deficiency is present in infants with FAS; (2) increased fractional clearance of zinc appears to be responsible for decreased plasma zinc concentrations; (3) relative zinc deficiency in FAS patients may be responsible for some of the features associated with the syndrome.