305 CARDIOVASCULAR EFFECTS AND CLEARANCE OF EXOGENOUS ARGININE VASOPRESSIN (AVP) IN THE FETAL LAMB. Suvipa Wiriyathian, Raymond P. Naden, John C. Porter, Charles R. Rosenfeld. Univ. of Texas Southwestern Medical School, Departments of Pediatrics and OB-Gyn, Dallas.

The concentration of AVP has been shown by us to be elevated in the human and lamb fetus during perinatal stress, especially hypoxia and asphyxia, with levels being greatest in association with meconium in the amniotic fluid (AF). The role of AVP in these instances is unclear; thus, we studied in fetal lambs the cardiovascular effects and clearance of infused AVP. AVP was infused into the vena cava of fetal lambs, 129-137 days gestation, at doses of 1.94, 3.88, and 7.76 mU/min for 75 min (n=5) while monitoring fetal and maternal mean arterial pressure (MAP), heart rate (HR), and umbilical and uterine blood flows. Samples were obtained for serial determinations of fetal plasma and AF AVP in 3 studies. Fetal plasma AVP rose from 2.0 ± .02 μU/ml (Mean ± SE) to 12 to 67 μU/ml at 60 min without changes in arterial blood gases. AF AVP increased at 60 and 120 min post-infusion, but did not correlate with plasma levels. Fetal MAP at 60 min rose 16 to 24%* while HR fell 9 to 43%*; both responses were dose dependent. Umbilical and uterine blood flows and maternal MAP and HR did not change. Of note, meconium stained AF occurred in association with intermediate and high rates of AVP infusions. The $T_{1/2}$ of AVP in fetal plasma was 14 ± 2.5 min and the clearance was 51 ± 10 ml/min·kg. We conclude that AVP 1) causes a rise in MAP and fall in HR that relates to circulating levels of AVP, suggesting AVP may mediate these changes during episodes of fetal stress, and 2) may be responsible for the expulsion of meconium into the AF during such episodes. *p < .01

306 INSULIN, GLUCAGON AND GROWTH HORMONE (GH) IN RELATION TO CLINICAL CONDITIONS IN PREMATURE INFANTS. J.J. Yoon, R. Hk. Wu and A.E. Esquea, Albert Einstein Coll. of Med., Bronx-Lebanon Hosp. Ctr., Dept. of Ped., Bx, NY (Sponsored by M. Cohen).

Blood insulin, glucagon and GH were measured at 0-12, 13-24, 25-48, 49-72 and 73-96 hours of age, and were compared to birth weight above or below 1000 gm, gestational age above and below 32 weeks, size appropriate or small for gestational age, and the presence of chronic in-utero stress, perinatal asphyxia, central nervous system hemorrhage, and mortality in 31 premature infants. Plasma (P) insulin very often was undetectable (85.2%) and p. glucagon was detected in most of the samples (75.4%). P. levels of insulin and glucagon were not related to clinical conditions other than to birth weights. Infants weighing 1000 gm or less more often had measurable insulin and glucagon as compared to those weighing over 1000 gm. This finding was noted only when they were appropriate for their gestational age. Premature infants with adequate in-utero growth seemed to have adequate insulin secretion before they reached 1000 gm and were ready for the future fetal growth. When the actual growth spurt took place, these infants often did not have circulating insulin. These data suggest that circulating insulin detected may not be the biologically active form. In contrast to insulin, GH did not seem to be related to fetal growth. Infants with birth weights of 1000 gm or less and perinatal asphyxia had GH that were often 2.5 ng/ml or less. All infants with GH 2.5 ng/ml or less died. No infant with chronic in-utero stress had GH 2.5 ng/ml or less. These data support the concept that severe insult may shut off GH secretion as in hypopituitarism, and chronic stress may increase GH secretion.

DEVELOPMENTAL PHARMACOLOGY

307 MEAN ARTERIAL BLOOD PRESSURE (MAP) RESPONSE TO PANCURONIUM BROMIDE (PB) IN THE NEWBORN PIGLET. Craig W. Anderson (Spon. by Grant Morrow,III) Ohio State Univ. College of Med., OSU Hospitals, Dept. of Pediatrics, Columbus, Ohio.

Pharmacological induction of muscle paralysis with PB is frequently used in the newborn to facilitate artificial ventilation. Cardiovascular responses to this drug have not been as well documented in the neonate as in the adult. Sixteen newborn piglets (wt 800-2300 gms) were anesthetized with ketamine (IM) and placed on a Bourns LS-105 ventilator. Heart rate, systolic, diastolic and MAP were continuously monitored. PB was given IV in varying dosages (.03-.72 mg/kg)for induction of complete paralysis. Acid-base imbalance (pH 7.03-7.65) was produced by altering ventilator settings and by lactic acid infusion. Fifty-eight percent of PB injections resulted in an increased MAP ($\uparrow\bar{X}$ 12.9 mmHg),9% lowered MAP($\downarrow\bar{X}$ 16 mmHg)and in the remaining 32%,MAP continued unchanged. The following variables were also analyzed: weight, drug dosage, blood pH and change in heart rate (HR). Analysis of variance revealed that HR changes were the only statistically significant variable ($p<.05$). A significant rise in HR was noted with either an increase or decrease in MAP, while the HR remained relatively constant when MAP was unchanged. In adults, PB increases HR and MAP; however, in the newborn piglet, the response to PB is variable. Alterations in MAP have significant effects on tissue-organ blood flow. If the variable HR and MAP responses to PB seen in the newborn animal model can be extrapolated to humans, careful monitoring of cardiovascular function is advisable in neonates undergoing muscle paralysis.

308 DETERMINANTS OF DRUG EXPOSURE IN A NEWBORN INTENSIVE CARE UNIT (NICU). Jacob V. Aranda, Judith M. Collinge Patrick Seliske, Eugene W. Outerbridge. Depts of Pediatrics, Pharmacol & Ther. McGill Univ-Montreal Children's Hosp. Res. Inst. Montreal, Quebec, Canada.

Factors possibly associated with increased use of drug exposure in a NICU were evaluated prospectively in all neonates admitted to NICU since Feb 1977. Demographic, clinical and laboratory data on all babies (Bb) were recorded by a physician/nurse monitor team and stored in the computer. Analyses of data from the first 461 neonates (bt wgt range 734-4850 g, gestational age (GA) 24-43 wks) show that 128 different drugs were used. 76.1% of babies received 1 to 35 drugs (excluding routine Vit K and AgNO3) with a mean exposure of 4.6/Bb. Babies with GA <32 wks (18%) had 3X more drug exposure than those with GA >32 wks (9.7 vs 3.4 drugs/Bb). GA and bt wgt were inversely related with drug exposure (number of drugs/Bb). Drug exposure was greater in disease states more commonly associated with prematurity; 14.2 drugs/Bb in PDA, 16.8 in necrotizing enterocolitis, 14.5 in persistent fetal circulation, 12.5 in renal failure, 13.1 in liver disease. 17 different antimicrobials were used in 47.7% of Bb, diuretics in 17.4%, cardiovascular drugs in 9.8%, steroids in 4.3% and sedatives and narcotics for palliation in 13.0%. Mean bt wgts and GA were significantly lower in babies who received antimicrobials, diuretics, and methylxanthines. Data underscore the necessity of requisite pharmacologic studies in the low bt wgt infants who are at greater risk of drug exposure.

● **309** EFFECT OF CAFFEINE ON CONTROL OF BREATHING IN NEAR-MISS SUDDEN INFANT DEATH SYNDROME (SIDS) Jacob V. Aranda, Jonathan Davis, Tomris Turmen, Danielle Grondin, Raezelle Zinman. Depts of Pediatrics, Pharmacol & Ther. McGill Univ-Montreal Children's Hosp. Res. Inst. Montreal, Quebec, Canada.

Abnormalities in control of breathing have been associated with near-miss SIDS. Since caffeine (C) is a respiratory stimulant, its effect on breathing pattern was evaluated in 12 infants with near-miss SIDS. Mean birth weights (±SE), gestational and postnatal age were 3.1±3.0 kg, 37.0±1.1 wks, and 7.9±1.7 wks, respectively. Ventilatory responses were measured with a face mask attached to a pneumotachometer to measure flow and integrated to yield volume before and 1 hour after caffeine citrate (20 mg/kg IV). Analysis of data before and after caffeine shows a significant increase in ventilation (Mean ±SE = 350.1±42.7 to 444.2±39.3 ml/kg/min, $p<0.005$); tidal volume (6.8±0.6 to 8.4±0.8 ml/kg, $p<0.005$) and mean inspiratory flow (V_T/T_I = 12.2 ± 1.2 to 15.9±1.2 ml/kg/sec, $p = 0.001$). In contrast, no changes were noted in inspiratory time (T_I), expiratory time or total cycle curation. These effects were observed with plasma concentrations of (C) (measured by HPLC) ranging from 8 to 20 mg/l. Data suggest that caffeine increases ventilation mainly by increasing central inspiratory drive and not by effective timing (T_I/T_{TOT}) and suggest possible efficacy of caffeine in near-miss SIDS.

● **310** DEPRESSION OF MYOCARDIAL CONTRACTILE FUNCTION(MCF) IN ACUTE IRON POISONING: Michael Artman, Richard D.Olson and Robert C. Boerth; Vanderbilt Univ.Med.Ctr., Dept. of Pediatrics, Nashville, Tennessse 37232.

Shock produced by acute iron (Fe) poisoning is thought to be due to venous dilation with decreased ventricular filling. This study examined the effects of acute Fe^{++} on MCF. Heart rate(HR), mean blood pressure(BP), mean right atrial pressure(RAP), cardiac output(CO), strain gauge measurement of right ventricular force (RVF; % of time 0), and arterial pH were measured in open-chest rabbits. Animals were divided into 3 groups (N=7 in each group): 1)Control (no Fe); 2) Fe(200mg/kg administered into the duodenum); and 3)Fe(200mg/kg)plus $NaHCO_3$ (9 meq/hr, IV). Variables did not differ among the groups at time 0. Results (mean ± SEM) 30 minutes after Fe administration are shown below.

	HR(bpm)	BP(mmHg)	RAP(mmHg)	CO(ml/min)	RVF	pH
Control	274±7	79±3	7±2	147±12	98±3	7.52±0.03
Fe	243±16	60±6	5±1	69±12*	71±6*	7.25±0.03*
Fe+HCO_3	234±11*	72±7	7±1	93±10*	77±4*	7.46±0.04

* = different from control at $p < 0.01$.

Within 30 minutes, Fe produced a significant reduction in MCF as evidenced by decreased CO and RVF, with no reduction in filling pressure (RAP). Fe produced myocardial depression independent of acidosis. The direct depressant effect of Fe on MCF could be responsible, in part, for the shock seen in acute Fe ingestion. These findings may provide the basis for new approaches to the treatment of shock in Fe poisoning.