384 PREVENTION OF BRONCHOPULMONARY DYSPLASIA (BPD) BY ADMINISTRATION OF BOVINE SUPEROXIDE DISMUTASE (SOD). W. Rosenfeld, H. Evans, L. Concepcion, R. Jhaveri, H. Schaeffer, A. Friedman. Department of Pediatrics, Interfaith Medical Center and Downstate Medical Center, Brooklyn, New York.

The effectiveness of bovine SOD in the prevention of BPD was evaluated in a prospective double blind controlled study of 45 neonates (m GA 28.7wks; m b.wt. 1154gms) with severe IRDS. All were ventilator dependent with $FiO_2 \geq 0.7$ at 24 hours of age. Either bovine SOD (0.25mg/kg) or placebo (saline) was administered SC q12h according to random selection until patients could be maintained in room air without ventilatory or CPAP support.

Twenty-one patients (m GA 28.8wks; m b.wt. 1156gms) received SOD and 24 (m GA 28.5wks; m b.wt. 1153gms) received placebo. 14/21 SOD and 17/24 placebo patients survived (p=NS). SOD levels were detected in all treated cases. Mean peak values at 4 hrs. p dose ranged from 0.15ugm/ml (dose #1) to 0.45ugm/ml (dose #10).

Among survivors evidence of BPD on xray (hyperaeration and/or atelectasis) was significantly less in SOD patients (3/14 vs 12/17; $p < 0.02$). Clinical signs of BPD (wheezing, pneumonia) were less in SOD patients (3/14 vs 12/17; $p < 0.02$). SOD patients required fewer days of CPAP ($p < 0.03$). There were no differences in days of O_2 , IPPB, incidence and severity of PDA and IVH. SOD administration was safe and well tolerated.

SOD reduced the severity of BPD using clinical and radiologic criteria. This extends our earlier observations (SPR 407A, 1983) and suggests the need to investigate variation in dosage schedule, and combined treatment with other antioxidant agents.

385 EFFECT OF BENZYL ALCOHOL (BA) ON RAT PLASMA LACTATE DEHYDROGENASE (LDH). Philippe Samson, Robert M. Bidwell, Edwing A. Contreras, Surendra K. Varma, and Fathy S. Messiha, Texas Tech University Health Sciences Center, Departments of Pediatrics and Pathology, Lubbock, Texas.

There are increasing numbers of clinical reports on the toxicity of BA. This deserves more attention since BA is a preservative agent being used in various injectable drugs in the neonatal unit. One experimental approach may reside in studying the effect of BA on certain plasma enzymes known for their rapid changes during development and growth, which may be also implicated in some of BA toxicity on the heart, i.e., LDH. This study utilized rat blood plasma as the source for LDH and evaluated the *in vitro* effect of BA on the activity of its "H" and "M" isoenzymes in young (30 to 45 days old) and in adult male rats (90 to 110 days old). Enzymatic activity was determined spectrophotometrically and expressed as specific activity measured at 30°C. The young rats showed 1.67 and 4.5 units of plasma H and M LDH isoenzyme, respectively. The presence of 90 mMol of BA in the reaction mixture resulted in 48% inhibition of the "H" isoenzyme compared to 14% of the "M" subunit. The LDH activity assayed in plasma of adult rats was 0.8 units for the "H" isoenzyme and 2.9 units for the "M" LDH isoenzyme. There was a 51% inhibition of the former and a 19% inhibition of the latter LDH subunits by equimolar concentration of BA, i.e., 90 mMol. The results indicate that the "H" isoenzyme, which predominates in the heart, is more sensitive towards the BA-effect noted than the "M" isoenzyme of LDH. This implies that measurement of "H" LDH may be useful in monitoring some of the cardiac toxicity of BA.

386 EFFECT OF BENZYL ALCOHOL ON SUBCELLULAR LACTATE DEHYDROGENASE IN THE MALE RAT. Philippe Samson, Edwing A. Contreras, Robert M. Bidwell, and Fathy S. Messiha, (Spons. by Surendra K. Varma). Texas Tech University Health Sciences Center, Departments of Pediatrics and Pathology, Lubbock, Texas.

Benzyl alcohol (BA) can evoke cardiac toxicity on the premature newborn when given in conjunction with various injectable medications and/or I.V. flush solutions. Little is known on the underlying mechanism involved. This study evaluates the *in vitro* effect of BA on rat heart lactate dehydrogenase (LDH) isoenzymes in distinct subcellular fractions as a possible reflection of such toxicity. Both heart H and M subunits were measurable in the nuclear (NC), mitochondrial (MT) and cytoplasmic (CT) fractions of juvenile and adult rats. Presence of 90 mM BA exerted inhibitory action on MT LDH which was age-dependent, i.e., 67% and 59% inhibition of the H subunits occurred in the young and old rats, respectively. The MT M isoenzyme was not inhibited by 90 mMol BA in the young but a 29% inhibition occurred in the old animals. Changes determined in the H subunit of NC-LDH were less profound than those of the MT isoenzyme using the same concentration of BA. The latter concentration exerted only minimal action on the H subunit of the CT fraction of old but not of young rats. The results demonstrate BA toxicity on heart LDH in general and on its H subunit in particular. Also, a differential subcellular LDH sensitivity to BA toxicity was noted. The data suggest that BA adverse cardiac reaction may be associated with altered LDH activity.

387 PLASMA BETA ENDORPHIN CONCENTRATION IN INFANTS WITH APNEIC SPELLS. Koravangattu Sankaran, K. Wayne Hindmarsh and Valerie G. Watson, Perinatal Research Laboratory, Department of Pediatrics and College of Pharmacy, University of Saskatchewan, Saskatoon.

In an attempt to determine whether plasma beta endorphin (β -ED) concentrations correlate with occurrence of apnea in preterm infants, measurements were made in three groups of infants. Group 1 consisted of 11 control infants with a mean gestational age of 30.5 ± 0.8 weeks, a mean birthweight of 1650 ± 180 g, and a mean postnatal age of 1.3 ± 0.5 days. Group 2 consisted of 8 infants with a mean gestational age, birthweight and postnatal age of 30 ± 0.9 weeks, 1165 ± 90 g and 7.8 ± 1.9 days, respectively. Group 3 consisted of 8 infants with a mean gestational age, birthweight and postnatal age of 31 ± 0.8 weeks, 1380 ± 125 g and 2.6 ± 0.9 days, respectively. Group 2 and Group 3 infants suffered varying degrees of apnea. Group 2 infants suffered clinically severe apneic spells with bradycardia and hypotension whereas Group 3 did not. β -ED was measured by a method previously published (Hindmarsh) involving Sephadex G-50 column chromatography and subsequent radioimmunoassay. The plasma endorphin concentrations were 26.9 ± 2 , 68.0 ± 9.0 and 39.6 ± 2.0 pg/ml in Groups 1, 2 and 3, respectively. Significant elevation in β -ED concentration was observed in Group 2 when compared to control (Group 1) and Group 3. Elevation of plasma β -ED is observed in infants with severe apneic spells. The association of increased plasma β -ED release with severe apneic spells may suggest that these endogenous opioids play a role in the pathophysiology of apnea of prematurity.

388 DEVELOPMENT OF HEPATIC N-DEMETHYLASE ACTIVITY AS MEASURED IN VIVO BY THE AMINOPYRINE BREATH TEST. Robert J. Shulman, Charles S. Irving, Thomas W. Boutton, William W. Wong, Buford L. Nichols, and Peter D. Klein. Baylor College of Medicine, Texas Children's Hospital, USDA/ARS Children's Nutrition Research Center, Department of Pediatrics, Houston, TX.

The aminopyrine (AP) breath test (BT) has been used in adults as a measure of hepatic N-demethylase activity. In order to study maturational changes in enzyme function, ^{13}C AP (2 mg/kg) was administered orally to infants ($n=13$) between the ages of 1 and 38 wk. Breath samples for measurement of $^{13}CO_2$ enrichment were collected for six hours after administration. Nine of 10 term infants < 6 wk of age showed no detectable oxidation (peak $^{13}CO_2$ output < 0.05% dose/min). Three of 3 infants over 14 wk of age showed oxidation (0.221, 0.196, and 0.261% dose/min at 15, 18, and 38 wk, respectively). Absorption was excluded as a limiting variable since no improvement in oxidation rates was found when the AP was administered again as an IV bolus in 9 of the original 10 infants < 6 wk. Elimination of labeled $^{13}CO_2$ as a limiting variable was excluded since the 9 infants displayed normal bicarbonate kinetics measured by a 6-h ^{13}C bicarbonate BT using an IV dose of 50 μ mol/kg. Conclusions: 1) Maturational differences are seen in the metabolism of AP; 2) These differences may reflect immaturity of N-demethylase activity or diversion of the liberated formaldehyde into biosynthetic rather than oxidative pathways.

389 PHENYL-ISOPROPYL ADENOSINE (PIA) CAUSES ALTERATION IN FETAL ELECTROCARDIOGRAM (ECOG) PATTERNS AND CESSATION OF FETAL BREATHING MOVEMENTS (FBM) IN THE FETAL SHEEP. Kim G. Smith, Paul L. Toubas, Roger E. Sheldon, Thomas W. Seale, (Spon. by Owen M. Rennett) Dept. of Pediatrics, Univ. of Okla. Health Sci. Ctr., Okla. City.

In studying the control of ECOG and FBM, we equipped 4 fetal lambs with intratracheal, amniotic, vascular catheters and ECOG electrodes. 2 of these were equipped with EKG electrodes. After 48 hours recovery, at 0.9 gestation, continuous recordings of tracheal and amniotic pressures, ECOG and EKG were begun. During 1000 minute control periods, low voltage high frequency (LVHF) ECOG predominated 61.5% of the total time. FBM occurred 35.6% of the total time and only during the LVHF ECOG. PIA, a known agonist for both A1 and A2 receptors, 0.125mg (0.050mg/kg estimated fetal weight) was given intravenously to each fetus during established LVHF ECOG and FBM. LVHF ECOG converted in 45 ± 30 seconds (mean $\pm$ S.E.M.) to high voltage low frequency (HVLF) ECOG which persisted for 12 ± 2 minutes. These were followed by an intermediate ECOG pattern, neither LVHF or HVLF, that persisted for 125 ± 15 minutes. FBM ceased within 2 ± 1 minutes and did not recur over the subsequent 143 ± 22 minutes. A rebound increase in FBM (51.0% of the total time) occurred over the subsequent 500 minutes (control 35.6%) without a significant increase in the LVHF ECOG. No significant changes in blood gases were observed. By inspection, EKG tracings in 2 fetal sheep showed a several second decrease in fetal heart rate (175 ± 7 BPM to 95 ± 7 BPM) and a several minute loss of beat-to-beat variability. Similar subtle changes have been seen with doses between 0.001 and 0.01mg/kg. We conclude that fetal ECOG, FBM, HR and beat-to-beat variability are influenced by adenosine and its receptors.