1648 VENTILATORY RESPONSE TO HYPERCAPNEA AND INSPIRATORY RESISTIVE LOADING IN INFANTS RECOVERED FROM RESPIRATORY DISTRESS SYNDROME (RDS). S. Duara, S. Abbasi, D. Heaf, T.H. Shaffer, and W.W. Fox. Dept. of Peds., Univ. of Pa. Sch. of Med. and Children's Hospital of Philadelphia, and Temple University, Dept. of Physiology, Philadelphia, PA.

The effect of inspiratory resistance (R_I) on the carbon dioxide response curves was studied in 6 infants recovering from RDS. Mean ± SEM birthwt.=1.46±0.21 kg, estimated gestational age = 32±0.6 wks., wt. at study=1.76±0.1 kg, and age at study=5.9±1.4 wks. Control data consisting of lung compliance (C_L), minute ventilation (MV), tidal volume (TV), frequency (f), inspiratory time/total respiratory time (T_I/T_{Tot}) and alveolar carbon dioxide ($PACO_2$) were obtained in room air. After a control period, carbon dioxide (CO_2) response curves without loading were obtained with a CO_2 gas mixture sufficient to produce hypercapnea (mean ± SEM maximum $PACO_2$=61±1.7 mmHg) for 5 mins. R_I=250 cm H_2O/L/min was subsequently placed in line with inspiratory CO_2 gas mixture and CO_2 response curves were obtained for 5 mins. Control C_L=3.46±0.6 ml/cm H_2O, MV=869.5±116.1 ml/min, TV=18.3±2.9 ml, f=51±4.6 breaths/min, T_I/T_{Tot}=0.45±0.02, $PACO_2$=36.8±4.4 mmHg. Hypercapnea produced a significant increase ($p<0.02$) in MV. R_I significantly decreased the slopes of the CO_2 response curves from mean ± SEM 36.82±8.43 ml/min/mmHg CO_2 to 11.25+4.51 ml/min/mmHg CO_2 ($p<0.02$). These data demonstrate that preterm infants recovering from RDS significantly decrease their hypercapnea response when challenged with an inspiratory resistive load over time. This may be important in neonatal obstructive apnea.

1649 HOME APNEA MONITORING IN THE SIBLINGS OF SIDS VICTIMS Paul Duffty, M. Heather Bryan. Hospital for Sick Children, Toronto, Ontario, Canada.

Prolonged sleep apnea (> 20 seconds) has been postulated as the final pathway in SIDS. To evaluate this we managed a high-risk group of 50 siblings of SIDS victims, including 11 survivors of 9 multiple pregnancies, on apnea monitors at home.

The mean birth weight and gestational age was 3.2±0.6 kg. and 38.4±2.7 weeks respectively. Monitoring started at 3.5±3.6 weeks in the singleton siblings and 16.4±6.6 weeks in the multiple pregnancy survivors. Twelve infants (24%) had at least one definite apneic spell with 8 having >5 episodes. The mean age of the first and last spells were 2.8 and 6.6 months respectively. Clustering in time was noted in 8, and precipitating factors, especially "colds", were associated with apnea in 9 babies. No deaths occurred, but 9 babies needed vigorous stimulation on at least one occasion. Monitoring ended at an age of 10.2±2.4 months in babies with apnea and 7.1±2.3 months in those without apnea.

The apneic babies were no different in respect to sex (χ^2= 0.01) and prematurity rate (χ^2=1.46). The incidence of apnea was the same in the survivors of multiple pregnancies as in the singleton siblings (χ^2=0.08). There was no relationship between the timing of the apnea and the age at death of the sibling.

Prolonged apnea in the first 9 months of life is commoner than expected in the siblings of SIDS victims and we speculate that it may be inherited as an autosomal recessive condition.

1650 THE EFFECT OF BETAMETHASONE (B) AND THYROTROPIN RELEASING HORMONE (T) ON LUNG (L) ANTI-OXIDANT ENZYME LEVELS IN THE FETAL (F) RABBIT. Allen Erenberg, Robert J. Roberts, and Robert D. Shaw, U. of Iowa Coll. Med., Dept. Ped., Iowa City.

In the adult, administration of exogenous thyroxine or corticosteriods is associated with enhanced development of L oxygen toxicity. To determine if pharmacologic acceleration of F L maturation influences the L anti-oxidant enzyme levels, superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GP) were measured in F rabbit pups at 28 days gestation following 48 hour maternal treatment with saline (S), B (0.1-0.2 mg/kg/day) or T (40 ug/kg/day). In the B and T groups, mean F body weight and lung weights were significantly lower compared to the S group; the mean F lung weight/body weight were similar in all three groups. Mean (± SEM) L DNA (ug/gram lung) and SOD, CAT and GP (units/mg DNA) are shown below. SOD was significantly decreased in B and T groups. L CAT and GP were similar in S and B groups but significantly decreased in T group. Conclusion: 1) Exposure of the F rabbit to B from 26 to 28 days gestation decreases L SOD levels. 2) Exposure of the F rabbit to T from 26 to 28 days gestation results in decreased L SOD, CAT and GP levels.

	DNA	SOD	CAT	GP
S (N = 11)	252 ± 25	81 ± 13	752 ± 195	2.7 ± 0.7
B (N = 11)	307 ± 42	40 ± 5*	674 ± 107	2.0 ± 0.3
T (N = 15)	543 ± 39	18 ± 1.3@	305 ± 44x	1.4 ± 0.2

* $p<0.005$ @ $p<0.001$ x $p<0.01$

1651 THE PRETERM BABOON WITH HYALINE MEMBRANE DISEASE (HMD) AS A MODEL FOR BRONCHOPULMONARY DYSPLASIA (BPD). Marilyn B.Escobedo, James L. Robotham, James L. Hilliard, Franklin R.Smith, Keith Meredith, David Johnson, Jacqueline J. Coalson,William Walsh, Thomas J.Kuehl,(Spon. by Robert C. Franks). Univ of Tex Health Sci Center, Depts Pediatr, Anesth, Pathol; SW Found for Research & Education, San Antonio, Texas.

BPD could be produced clinically and confirmed pathologically in preterm neonatal baboons (Papio cynocephalus) with HMD who were supported with mechanical ventilation (IPPV) and treated with 100% O_2 for >1 week. Ten dated pregnancies were delivered at 74-100% of term, weighing 495-988 gms. They were managed with techniques and equipment used for human neonates. Of 9 preterm animals 6 had HMD by clinical and X-ray criteria and 3 survived to develop pathologically confirmed BPD. HMD was pathologically confirmed in 2 animals who died <1 week.

ANIMAL	A	B	C	D	E	F	G	H	I	J
PRETERM	✓	✓	✓	✓	✓	✓		✓	✓	✓
HMD		✓	✓	✓	✓	✓				✓
100% O_2>24hrs			✓	✓	✓	✓	✓	✓	✓	✓
IPPV		✓	✓	✓	✓	✓		✓	✓	✓
SURVIVAL >1 wk	✓	✓			✓	✓	✓			✓
BPD					✓	✓				✓

It appears that the major factors thought to contribute to the development of BPD in human neonates may also produce BPD in neonatal baboons: prematurity, HMD, high FIO_2, IPPV and time. With the development of an animal model for BPD, the etiologic variables should be amenable to future investigation. (Supported by the Ladies Forum of the SWFRE)

1652 CRITERIA FOR EXOGENOUS SURFACTANTS: E.E. Farrell, M. A. Cox, J. Torday, K. Keough, M. Anton, H.W. Taeusch, Harvard Medical School, Boston, MA and Memorial University of Newfoundland, St. John's, Newfoundland.

Exogenously administered surfactant (SAM) should achieve the same surface activity (SA) as natural surfactants and meet additional criteria for rate of surface dispersion and bulk phase thermal properties. We used three methods for isolating SAM from tracheal lavage of adult rabbits: (1) simple centrifugation, (2) a single sucrose density gradient, and (3) multiple continuous/discontinuous density gradients (King/Clements). Standard amounts of SAM (30nM lipid phosphorous) were studied for surface activity and surface dispersion rates. SA criteria are minimum γ (dynes/cm); compressibility (cm/dyne); and surface areas at 12 dynes, and at first film collapse. SAM dispersion rates were defined as $\Delta\gamma$/sec. when SAM was applied to a 30cm^2 surface area at 24^{0}C. Scanning calorimetry defined the temperature of maximal melting (Tm,C^0). No differences were found for the 3 methods in SA or disaturated phosphatidylcholine (DSPC)(µg/mg dry SAM). Protein content is greater in the least pure extract ($p<.001$). Crude (1) and pure (3) SAM were instilled in immature rabbits (27 days' gestation) with significant improvement in pulmonary deflation pressure volume relationships.

SAM	DSPC±SD	PROT	YMIN	COMPRESS	DISPERS	Tm
1	594±54	17±2	1.7±.6	.02±.003	1.5±.4	34
2	556±42	14±4	1.0±.6	.01±.004	1.4±.4	-
3	495±17	9±1	1.1±.3	.01±.002	1.4±.3	34

These criteria should be useful in predicting in vivo behaviour of synthetic surfactants.

1653 PHARMACOKINETICS OF SALIVARY THEOPHYLLINE IN ASTHMATIC CHILDREN. Charles Feldman, Charles Pippenger, Irwin Mandel, William Davis. Columbia University College of Physicians and Surgeons, Department of Pediatrics. New York, New York (Spon. by Michael Katz).

Although salivary theophylline concentrations have been used to monitor therapy and compliance, considerable variation has been noted. To determine whether the factor of time-dependency can account for this variability, we have measured simultaneous saliva (S) and plasma (P) samples between 2 and 6 hours post oral drug administration in a group of 7 asthmatic children aged 10-14 years. Comparison of the S/P ratios of theophylline revealed higher values during the absorption phase (mean 0.72) and lower values during the elimination phase (mean 0.49) ($p<0.01$). A comparison of free drug fractions in S and P indicated consistently higher levels in S compartment (mean Free S/Free P ratio of 1.79 with range of 1.0 - 2.85),indicating an active transport mechanism. Our data demonstrate a clear time-dependent relationship for theophylline in S corresponding with drug absorption and elimination. We conclude that: 1) salivary levels of theophylline may in part depend on an active transport mechanism; 2) salivary levels should be obtained at fixed time intervals when evaluating their usefulness in monitoring theophylline therapy.