1870 CHARACTERISTICS OF AN EXOGENOUS SURFACTANT FOR HUMAN USE (TA SURFACTANT). W. Taeusch, K. Keough, R. Slavin, E. Steele, A. Lee, N. Kariel, M. Williams. Harvard Medical School, Boston; Memorial Univ. of Newfoundland, Canada; Univ. of Calif. at San Francisco

TA Surfactant is a bovine surfactant that has been developed, tested, and used in over 30 infants with Respiratory Distress Syndrome in Japan by Drs. T. Fujiwara, Y. Tanaka, and colleagues. It is manufactured on a pilot basis by Tokyo Tanabe Co. in Tokyo. In preparation for further clinical trials, we have measured several characteristics of the surfactant. The material contains 83-90% (by weight) phospholipid, of which 69% is phosphatidylcholine (PC), 10% sphingomyelin, 7% phosphatidylethanolamine, and lesser amounts of other phospholipids. Approximately 85% of esterified fatty acids in PC are saturated. Qualitative analysis indicates the presence of free fatty acids, triglycerides, and a trace of cholesterol. Protein represents 1-3% of dry weight. Surface adsorption rates and measures of minimal surface tension equal values obtained for mammalian lung surfactants. Surfactant, sonicated in 0.9% sodium chloride (33 mg/ml), was instilled into adult rats (100 mg/Kg), that had been lavaged to remove endogenous surfactant. In all treated rats (n=6) prompt increases in serial PaO_2 were noted. Static pressure volume characteristics indicated increased compliance in the treated group vs controls. Electron microscopic studies of pelleted TA Surfactant show vesicles, stacked membranes, and amorphous material. These studies indicate this substance should be an efficacious exogenous surfactant.

1871 IN VITRO STUDIES OF SURFACTANT SYNTHESIS ARE SIGNIFICANTLY AFFECTED BY THE PO_2 OF THE CULTURE SYSTEM. Keith Tanswell, Fred Possmayer and Madan Joneja (Spon. by Graham Chance) Univ. Western Ontario, Depts. Paediatrics, Obstetrics and Gynaecology and Biochemistry, London, Ontario and Queen's Univ., Dept. of Anatomy, Kingston, Ontario.

Immature rat fetal lung (d19:term=d22)monolayer cell cultures have an increased rate of precursor incorporation into phospholipids when studied at a PO_2 of 30mm Hg (to approximate fetal PO_2) compared with a conventional 95% air; 5% CO_2 system with a PO_2 of 148mm Hg.

	PC	SPC	LPC	SM	PE	PG	PS
choline (30mm Hg)	459±90	182±37	24±8	24±9	-	-	-
(148mm Hg)	337±47	141±27	3±3	21±8	-	-	-
glycerol (30mm Hg)	286±99	106±17	4±3	-	57±39	9±6	5±3
(148mm Hg)	59± 9	32± 6	0	-	3± 2	3±1	0

pmol/10^6cells/24h All values M±SEM

Cultures from d22 fetal lungs had similar rates of incorporation in either PO_2 and were similar to d19 cultures at a PO_2 of 30mm Hg. Dexamethasone and triiodothyronine(0·055-5·5nM) increased choline incorporation into SPC at a PO_2 of 148mm Hg, but not at a PO_2 of 30mm Hg. These O_2-dependent differences could not be explained on the basis of enhanced cell differentiation at a lower PO_2 since lamellar body-containing cells did not increase in number to d22 culture values. Nor could they be explained by cell toxicity since a PO_2 of 30mm Hg improved plating efficiency and growth.

In vitro studies of surfactant synthesis can be significantly affected by the PO_2 at which they are conducted.

1872 EFFECT OF POSITIVE END-EXPIRATORY PRESSURE ON PULSE RESPIRATORY COMPLIANCE IN VENTILATED INFANTS. William G. Teague, Robert A. Darnall, and Paul M. Suratt (Sponsored by J. Kattwinkel). University of Virginia Hospital, Department of Pediatrics, Charlottesville, VA.

Positive end-expiratory pressure (PEEP) decreases dynamic respiratory system compliance (Crs) in ventilated infants. As dynamic Crs measurements reflect airway resistance, we utilized a pulse method (J. Appl Physiol. 49:1116) to test the effect of PEEP on static Crs. We measured Crs in 11 infants (gestational age 33±4{mean±S.D.}weeks, weight 2052±704 gms, and study age 29±35 days) with respiratory failure supported with a constant flow ventilator. Flow, transrespiratory pressure, and tidal volume were recorded. We calculated pulse Crs by dividing flow by the slope of the linear portion of the pressure tracing. Static and dynamic Crs were measured by standard methods. Values of Crs were compared from PEEPs of 2.5 to 10.0 cms H_2O. At the baseline ventilator settings, pulse and static Crs were similar (b=0.94, r^2=90%), and both exceeded dynamic Crs (p<0.005). The effect of PEEP is shown below:

Crs Method	PEEP Increments (cm H_2O)				P Value
(ml/cm/kg)	2.5	5.0	7.5	10.0	(Anal. of Variance)
Pulse	1.75±0.24	2.47±0.29	1.77±0.28	1.29±0.07	0.02
Dynamic	0.84 0.09	0.77 0.88	0.89 0.08	0.81 0.08	NS

Comparing individual regression slopes, pulse Crs decreased uniformly among the infants (F=1.80) from PEEPs of 5.0 to 10.0 cms. PEEPs exceeding 5.0 cms may overdistend the lungs and chest wall of ventilated infants as demonstrated by a decrease in pulse Crs.

●1873 SURFACTANT TA (FUJIWARA) AND DRY SURFACTANT (MORLEY): EFFECTS ON LUNG MECHANICS AND ALVEOLAR SIZE DISTRIBUTION IN PREMATURE RABBITS. Haruo Maeta, Tetsuro Fujiwara, Mineo Konishi, Shinichi Asakura, Masao Saito (Spon. by D. Vidyasagar). Department of Pediatrics, University of Iwate, Morioka, Japan.

We compared the efficacy of surfactant TA (Fujiwara) and the dry DPL+PG surfactant (DS, Morley) on pulmonary compliance (Cl), P-V curves and alveolar size distribution by texture analyzing systems (Leitz) in 4 groups of rabbits; 21 received 800 µg of TA suspended in saline (Gr.TA), 15 received DS surfactant (Gr.DS), 16 were premature controls (Gr.PC). All three groups were preterm delivered at 27 days gestation. Fourth group was mature controls (Gr.MC n=26).(Table: Mean ± S.E., *p <0.001).

(n)	TA (21)	DS (15)	PC (16)	MC (26)
P5 (ml/kg)	46.8±4.1	9.3±2.1	1.5±0.3	52.9±2.8
P30 (ml/kg)	75.0±4.1	33.1±6.7	9.7±2.0	72.7±2.8
CLP10 ml/cmH_2O/kg	1.69±0.08	0.63±0.15	0.09±0.02	1.52±0.04

Premature controls had low volumes at P5 and P30 as compared to matures. Lung volumes reached mature levels in Gr.TA; in Gr.DS, improvement was less than in Gr.TA. Alveolar size distribution in Gr.TA was identical to mature controls, but marked non-homogeneous distribution of alveolar size was noted in Gr.DS. P-V curves and compliance differences were: Gr.TA showing mature pattern superior to Gr.DS. These results suggest that saline suspended S-TA improves pulmonary mechanics and alveolar histology to mature patterns to a greater extent than the dry surfactant of Morley et.al. (Abbr. in Table: P5 and P30=Pressure at 5 and 30 cm. H_2O).

1874 THE EFFECT OF HYPEROXIA AND CALORIC RESTRICTION ON PULMONARY DISATURATED PHOSPHATIDYL CHOLINE (DSPC). Feizal Waffarn, Theodore Glatz, Univ of Calif, Irvine Calif College of Med, Dept of Peds, Orange CA (Spon. by I. Lott)

To study the individual and combined effects of hyperoxia and caloric restriction on pulmonary DSPC, 100 one day old newborn rabbits were randomly grouped into Grp 1 (n=23), FiO_2 .21, fed full calories; Grp 2 (n=31), FiO_2 .21 fed 1/3 cals; Grp 3 (n=19), FiO_2 .95, fed full cals and Grp 4 (n=27), FiO_2 .95, fed 1/3 cals. Rabbits were weighed daily and gavage fed equal volumes of full or 1/3 cal veterinary formula and housed in heated incubators through which humidified FiO_2 .21 or .95 was circulated. After 84 hours exposure to the above conditions the DSPC content of the alveolar wash (AW) and lung homogenate (H), as well as the lung protein (P) and DNA were estimated.

	Grp 1	Grp 2	Grp 3	Grp 4
Wt. gain (gm)	+7.6 3.7	-0.3 2.3*	+5.1 2.8	-1.4 2.7*
Protein (mg)	75.39 10.1	72.6 12.8	64.7 .16	77.5 16.6
DNA (mg)	3.58 1.1	2.91 6.2	2.59 .88	2.19 1.2*
AW-DSPC/P(mmols/mg)	.031 .009	.023 .009	.029 .018	.018 .007*
H-DSPC/P(mmols/mg)	.059 .016	.068 .024	.051 .014	.046 .015

(*p .005 compared to Group 1 by one way ANOVA)

The data suggest that restricted cals alone inhibit weight gain while neither hyperoxia nor restricted cals individually affects lung P, DNA, AW, or H-DSPC content. However, together they have an additive and inhibitory effect on the number of lung cells and alveolar surfactant content. Similar exposure to hyperoxia and caloric restriction in the human neonate may adversely affect recovery from pulmonary disease.

1875 NASAL RESISTANCE AND NASAL HISTAMINE CHALLENGE IN ALLERGIC SUBJECTS STUDIED BY POSTERIOR RHINOMETRY. Sue B. Walker, Gail G. Shapiro, Susan G. Marshall, William E. Pierson, Clifton T. Furukawa, C. Warren Bierman.

Posterior rhinometry allows quantitative measurement of nasal airway resistance and nasal power. We used this research tool in two separate studies.

Initially 10 atopic and 6 nonatopic adults had nasal resistance and nasal power measured at 2 hour intervals for 6 hours on two separate days. A computer digital program was used to collect and analyze the data. Statistical analysis showed considerable intra subject and inter subject variability as well as significantly higher mean measurements of nasal resistance in the allergic population. Nonatopic subjects showed very constant lower values for nasal resistance.

We then evaluated whether intranasal insufflation of histamine would cause eustachian tube dysfunction (ETD) in atopic adults. These subjects had normal baseline nasal power measurements by posterior rhinometry and normal eustachian tube function by swallow test. All had quantifyable changes in nasal power after a single dose of 0.55 mgm histamine delivered into each nares for 6 seconds. Four of the five atopic subjects had eustachian tube obstruction documented by 9-step tympanometry within 5 to 20 minutes after peak nasal power was recorded.

In both studies, posterior rhinometry was a useful tool to objectively quantify measurement of nasal resistance so that we could document the higher and more variable measurements found in atopic patients and correlate nasal resistance changes caused by histamine with ETD in these patients.