†1771 ENHANCED PMN LOCOMOTION (AGGREGATION,CHEMOTAXIS) BUT NORMAL ADHERENCE BACTERIAL KILLING AND SUPEROXIDE PRODUCTION IN CHILDREN WITH CYSTIC FIBROSIS (CF).J.Griffith,D.Hicks,C.Wong,C.VandeVen,M.Cairo. (Spon. by D.Sperling)Univ.Calif.Irvine,Child.Hosp.Orange Co. Orange, CA. 92668

CF is a genetically linked multisystem disease which demonstrates alterations in humoral and cellular immune function.Defective PMN locomotion was recently described (NEJM 306:486,1982) and may be implicated as a cause for increased pulmonare infections and complications.Other PMN function in children with CF during normal and active pulmonary exacerbations has not yet been examined.PMN functions of ten previously diagnosed CF patients (8-23 yrs; 6 M & 4F) were studied at a time of acute exacerbation of pulmonary disease and after recovery.Cells were tested for FMLP (N-Formyl-l-methionyl-l-leucyl-l-phenylalanine) stimulated aggregation and superoxide (O_2^-)production bacterial killing of S.aureus and adherence to nylon wool fiber.E.Coli endotoxin induced chemotaxis was also examined in the presence and absence of CF serum.In contrast to other investigators we found enhanced aggregation and chemotaxis ($p<.01$ and $<.02$) in CF patients (sick).No significant difference was found in PMN adherence,bacterial killing and O_2^- production. In addition, significance was not observed in CF PMN functions between the control and well phases.

	AGG.(cm^2)	%CHEMO	%ADH	%BK	C_2^-Prod. (nmoles/10^7C)
CONTROL	30.0±3.2	16.0±3.1	65.0±5.9	53.9±14.3	173.8±20.7
CF(sick)	36.0±7.7	23.7±4.8	70.7±9.2	60.9±11.8	193.3±63.8
P-Value	p<0.01	p<0.02	NS	NS	NS

Further studies are presently being conducted to elucidate additional differences involving peripheral PMN function as a marker for intrapulmonary complications and immunologic alterations in children with CF.In contrast to previous reports we identified enhanced PMN locomotion during acute exacerbations of pulmonary disease in children with CF.

1772 PULMONARY FUNCTION IN HYPOGAMMAGLOBULINEMIA, M.P. Grodofsky, K.K. Belani, N. Scarpa, M.E. Conley, R.W. Wilmott, Children's Hosp. of Phila., Dept. of Peds., U. of Pa. Sch. of Med., Phila., Pa.

Pulmonary function tests (PFT) were performed on 18 patients with hypogammaglobulinemia in the period 1975-84 (7 with X-linked agammaglobulinemia, and 11 with common variable hypogammaglobulinemia, of which 4 were adult when diagnosed). Mean age at most recent study was 18.12 years (range: 9.5-30). 16 of 18 patients had small airway obstruction with diminished MEF 75%, and FEF 25-75% being the most frequent and most severe abnormalities (mean % predicted 42.8% and 57.9% respectively). Decreased VC occurred in 11 patients with airway obstruction, and an increased RV/TLC ratio was seen in 8 patients. One patient had restrictive changes. 13 of 16 patients tested improved after bronchodilators. Seven patients have been followed in our clinic since early childhood and treated with IM gammaglobulin replacement and frequent or prophylactic antibiotics. Serial PFTs done in this group were unchanged or improved with time. A comparison of the mean % predicted values for this subgroup with the other seven patients who have had their disease since early childhood but who were initially treated with IM gammaglobulin replacement alone indicated greater obstructive disease in the second group. VC was 92.0% vs. 66.2% ($p<0.005$); RV/TLC ratio was 27.9 vs 41.2. ($p<0.05$); FEF 25-75% was 65.8% vs 38.0% ($p<0.05$); and MEF 75% was 51.5% vs 17.8% ($p<0.05$). These findings suggest that early and vigorous intervention with both IM gammaglobulin and frequent antibiotic use limits the progression of obstructive lung disease in patients with hypogammaglobulinemia.

1773 EVALUATION OF A HIGH FREQUENCY JET NEBULIZER M.P. Grodofsky, D.Jakobowski, N.Scarpa, R.W.Wilmott,

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A new "jet nebulizer" (JN) system adapted from high frequency jet ventilation was evaluated as a delivery system for bronchodilators. Pulmonary function tests were compared in 15 patients with stable chronic asthma at zero, 15, 30, 60, 120 and 180 minutes after receiving 0.2 ml of metaproterenol sulfate in 2.8 ml of saline by JN and conventional nebulization (CN). One patient developed severe bronchospasm following JN and could not complete the study. In the remaining 14 patients there was no significant difference between CN and JN for the percentage improvement in FVC, FEV1, Peak Flow Rates, and FEF25-75 at any of the time points. Significantly more metaproterenol was delivered by CN (Mean 2.1 ± 0.3 (SD) gm of solution versus 1.9 ± 0.5 (SD) gm by JN). This may have been due to greater loss of aerosolized medication with CN. Several patients reported that the JN treatment led to increased sputum clearance, although this finding was not objectively quantified. Thus, JN does not appear to offer an advantage over CN in the treatment of patients with asthma, although the similar improvement with less medication delivery may reflect improved aerosol deposition. Further research with JN is indicated; first to clarify whether there is improved aerosol particle deposition and secondly, in light of the subjective findings, to investigate whether use of JN in patients with chronic sputum production is advantageous.

1774 FETAL LUNG EPITHELIAL CELLS CULTURED ON FIBROBLAST FEEDER LAYER. D. Guzowski and R. Bienkowski (Spon. by E.M. Scarpelli). Pulmonary Division and Research Center, Schneider Children's Hospital, LIJ-HMC, New Hyde Pk., NY.

Mouse embryo fibroblasts (line 3T3) elaborate an extracellular matrix comprising macromolecules essential for attachment and growth of various types of differentiated cells. We investigated whether a feeder layer of these fibroblasts would promote growth of lung epithelial cells. Epithelial cells were isolated from lungs of mature fetal rabbits (28-29 d gestation) by either explant culture or exposure to 0.25% trypsin followed by differential adherence. The cells were cultured in Dulbecco's Modified Eagle's medium + 10% fetal bovine serum on either plastic or a feeder layer of 3T3 fibroblasts rendered mitotically inactive by treatment with mitomycin C. Epithelial cells cultured on plastic degenerated and died within 7 d. In contrast, cells cultured on a feeder layer could be passaged weekly for 10 wk and underwent 6 population doublings. Light microscopy showed that spindle-shaped 3T3 fibroblasts surrounded colonies of cuboidal lung cells. The latter were judged to be type 2 epithelial cells on the basis of the following ultrastructural criteria: cuboidal shape, presence of microvilli, tonafilaments, and characteristic lamellar bodies (during first wk). The cells contained organelles indicative of a high level of biosynthesis (rough endoplasmic reticulum, Golgi apparatus) and numerous mitochondria, and they formed junctions. Multivesicular lamellar bodies were present in late cultures (4-8 wk). These results demonstrate that a feeder layer of 3T3 fibroblasts can support extended culture of fetal lung epithelial cells.

=1775 REVERSIBLE AGGREGATION OF LUNG SURFACTANT LIPIDS BY AN APOPROTEIN AND CALCIUM IS ASSOCIATED WITH RAPID SURFACE FILM FORMATION. Samuel Hawgood, Bradley J. Benson, Robert L. Hamilton, Hava Efrati. (Spon. by R.H. Phibbs), Univ. of Calif. SF, San Francisco, CA 94143.

The apoprotein complex of canine pulmonary surfactant has components of Mr of 36,000, 32,000 and 28,000 daltons. Each protein was isolated by electro-elution from SDS-PAGE gels. The amino-acid composition of each protein was similar containing 17% glycine and 5% hydroxyproline. The partial amino acid sequence was identical in each case with an N-terminus of isoleucine. Endoglycosidase F digestion reduced the apoprotein complex to a single unglycosylated protein (Mr 28,000 daltons) suggesting that the complex is a variably glycosylated single polypeptide. The purified apoprotein complex was reconstituted with unilamellar liposomes of canine surfactant lipids. The extent and rate of aggregation was followed by changes in turbidity and was confirmed by electron microscopic study of negatively stained samples. Ca^{2+}, Sr^{2+}, and Ba^{2+} but not Mg^{2+} or Mn^{2+} caused massive aggregation of the proteoliposomes at a threshold concentration of 0.5mM. Aggregation of protein-free liposomes occurred only at divalent cation concentrations >10mM. Aggregation was reversed by EDTA, trypsin or collagenase. Similarly, Ca^{2+}, Sr^{2+}, and Ba^{2+} but not Mg^{2+} or Mn^{2+} facilitated the ability of the proteoliposomes to form surface films at 37°C compared to the protein-free lipids. Extensive aggregation of protein-free surfactant lipids by 20mM Ca^{2+} or 20 mM Mg^{2+}did not promote rapid surface film formation. These results are consistent with the hypothesis that a specific glycoprotein and Ca^{2+} influence the structure and function of extracellular surfactant.

†1776 HIGH FREQUENCY EXTERNAL OSCILLATION WITHOUT INTUBATION. Zamir Hayek, C. Anthony Ryan, Abraham Peliowski, Richard Jones, Cheryl Merkel, Neil Finer, University of Alberta, Royal Alexandra Hospital, Departments of Pediatrics and Medicine, Edmonton, Alberta, CANADA

High frequency ventilation with a jet or oscillator requires either a tracheotomy or intubation. A method of external oscillation in a cat model was developed which does not require either tracheotomy or intubation. Twelve mongrel, mature cats, (2.0 - 3.80 kg) were placed in a specially made thoracoabdominal plexiglass chamber connected to a high frequency oscillator (Metrex) and a vacuum source to create different levels of negative pressure, the mouth being held open with a retractor. The chamber was then oscillated at an initial frequency of 3 Hz with mean pressure excursions of 6.3 cm H_2O (range 2-14 cm) while varying the mean chamber pressure (MCP) with the vacuum source. Following an initial blood gas after commencing oscillation the animals were given pancuronium bromide 200 mcg/kg PRN throughout the remainder of the experiment while being maintained in the oscillated chamber for a minimum of 4 hours. Oscillation was associated with a significant fall in PCO_2 ($p=.006$) and pH ($p=.006$) and increase in pO_2 ($p=.03$). PCO_2 and $A\text{-}aDO_2$ were minimal between 1 & 3 Hz and increased with higher frequencies ($p<.01$). Increasing negative MCP resulted in decreased $A\text{-}aDO_2$ and increased FRC ($p<.001$). Tidal volume fell with increasing frequency from 1-9 Hz ($p<.01$). Blood pressure was well maintained throughout the experiment. External negative pressure oscillation without intubation is an effective form of ventilation in paralyzed normal cats and may be applicable to apneic infants.