MINOR PHYSICAL ANOMALIES AND PLASMA DOPAMINE-β-HYDROXYLASE ACTIVITY IN HYPERACTIVE BOYS. Patricia Quinn and Judith Rapoport, Georgetown Univ. Sch. of Med., Washington, D.C. (Intr. by J.A.Bellanti).

As part of a study comparing imipramine and methylphenidate treatments of 76 hyperactive boys, minor physical anomalies (stigmata) and plasma dopamine-β-hydroxylase (DBH) were measured during the predrug evaluation of behavioral, neurological, and cognitive status.

Stigmata scores were positively correlated with severity of hyperactivity and aggressivity, and with paternal childhood hyperactivity ($p<.05$) or reported obstetrical complications in early pregnancy ($p<.001$). In addition, children with high stigmata scores had higher mean plasma DBH activity than did low stigmata children ($p<.01$).

DBH was not related to behavioral activity ratings, but specifically to stigmata score. Both drugs significantly increased plasma DBH activity; however clinical improvement did not parallel this change.

These children with multiple minor physical anomalies are suggested as an important subgroup within the behaviorally defined heterogeneous population of hyperactive children, and provide evidence for congenital contributors to behavior disorders.

PERINATAL BRAIN METABOLISM: EFFECTS OF ANOXIA AND ISCHEMIA. R.C. Vannucci* and T.E. Duffy*, Dept. of Neurology, Cornell Med. Col., New York, N.Y. 10021 (Intr. by W.W. McCrory)

Resistance to anoxia is characteristic of developing nervous tissue, and is most pronounced in the fetus. Whether this tolerance resides in differences in structural-functional maturity or in metabolic factors i.e. "resting" levels of cerebral energy reserves, rates of energy utilization, or glycolytic capacity is unresolved. Fetal rats at term, delivered by maternal decapitation and hysterotomy, survive in N_2 at 37°C (LD_{85}=50 min) twice as long as 1-day (1D) and 5 times as long as 7-day (7D) postnatal rats. Total energy reserves in quick-frozen forebrains [~P=2(ATP)+ADP+P-creatine+2(glucose)+2.9 (glycogen)] of fetuses (27.0 mM/Kg) were 11% and 13% higher than in 1D and 7D rats, owing chiefly to differences in glycogen. Following decapitation, lactate accumulated in fetal and 1D brain in linear fashion up to 5 min (maximal glycolytic flux), but at a greater rate in fetuses (0.97 vs 0.69 mM/Kg/min). In 7D rats maximal lactate production (1.94 mM/Kg/min) occurred from 1-2 min, following a lag. From the changes in preformed and potential cerebral energy stores during ischemia initial rates of energy consumption (metabolic rate) were obtained (Lowry et al, 1964). In fetal and 1D rats, energy consumption was linear for 5 min with slopes of 1.57 and 1.33 mM ~P/Kg/min, respectively. In 7D rats energy use was linear for only 2 min and about twice as fast (2.58). Thus, in postnatal (1D and 7D) rats anoxic survival and cerebral energy consumption were inversely related; no such correlation was observed for fetal animals. (Supported by NIH #NS-03346)

PULMONOLOGY

CHRONIC PULMONARY INSUFFICIENCY OF PREMATURITY (CPIP). P.A.M. Auld, A.N. Krauss, D.B. Klain, Dept. Peds., Cornell Univ.Med. College, 1300 York Ave., New York, N.Y., 10021

The purpose of this report is to describe a syndrome of delayed respiratory distress occurring in premature infants, usually under 1250 gms. at birth. Unlike hyaline membrane disease (HMD), this syndrome occurs after 5-10 days of life in a previously healthy infant; unlike HMD it persists for 2-4 weeks. Chronic pulmonary insufficiency of prematurity (CPIP) carries a 10-20% mortality. The infants are frequently apneic and require supplemental oxygen, but lack the characteristic radiologic findings of HMD, bronchopulmonary dysplasia, Wilson-Mikity syndrome, or oxygen toxicity. Compared to healthy infants under 1250 gm. at birth (nl) infants with CPIP demonstrate the following abnormalities:

Age	FRC		PaO_2		$PaCO_2$		pH_a	
days	nl	CPIP	nl	CPIP	nl	CPIP	nl	CPIP
0-3	30±3	27±8	48±4	36±10	40±1	42±9	7.40±.03	7.37±.08
4-10	28±3	22±3	48±4	28±16	50±3	53±7	7.35±.01	7.33±.01
11-17	36±5	15±5	58±2	24±8	48±3	71±6	7.33±.01	7.37±.03
18-24	33±8	----	60±5	40±10	45±3	64±4	7.38±.04	7.35±.01
25-31	44±6	30±7	55±6	58±7	42±2	48±5	7.41±.01	7.38±.05

Recovery is usually complete in 60 days. An awareness of CPIP can eliminate a false sense of security, often communicated to anxious parents, during the 5-10 day period before the onset of CPIP. The physiologic similarity between CPIP and HMD suggests lack of surfactant as the etiology of CPIP.

REDUCED SENSITIVITY TO CO2 IN PREMATURE INFANTS. P.A.M. Auld, A.N.Krauss, D.B.Klain, Dept. Peds.,Cornell Univ. Med. Coll., 1300 York Ave., New York, N. Y. 10021. Reduced ventilatory response to CO2 (less than a 50cc/min/mmHg P_{CO_2} increase in minute ventilation has been demonstrated in premature infants of 28-32 weeks post-conceptional age. Diminished ventilatory response to CO2 may be due to either mechanical limits on ventilatory work or true loss of CO2 sensitivity. Though premature infants are neurologically immature,they have been shown to possess chemoreceptor tone for oxygen. They also have small,stiff lungs and high total pulmonary resistance. The present study was undertaken to determine if mechanical or neurological factors limit the CO2 response of these infants. Adult patients with pulmonary disease have been shown to increase respiratory work during CO2 stimulation even though their minute volume fails to increase. Pulmonary work was therefore calculated from tracings of tidal volume and intraesophageal pressure during rebreathing of 5%CO2-40%O2 (Read, Austral.Ann.Med. 16:20 '67) on 13 occasions in 12 premature infants. Evidence of CO2 sensitivity,as demonstrated by increased respiratory work, was found in 5 of 7 infants whose ventilatory response to CO2 was less than 50cc/min/mmHg P_{CO_2}. Two infants showed no evidence of CO2 sensitivity by failing to increase either work or ventilation,suggesting true absence of chemoreceptor tone. Both neurological and mechanical factors may limit the CO2 response in premature infants, and may influence the course of hyaline membrane disease and the occurrence of "crib death" (SIDS).

CYSTIC FIBROSIS (CF) AND RESPIRATORY ENERGY PRODUCTION. Gerald J. Barqman and Lucy Weisz (Intr. by J.A.Mangos) Department of Pediatrics, University of Wisconsin Medical School, Madison.

Serum, saliva and fibroblast culture media from homozygotes (HM) and heterozygotes (HZ) with CF induce inhibition of ciliary activity or ion transport in a number of biological systems. The possibility that this inhibition may result from respiratory energy alterations was investigated in the nauplii of brine shrimp Artemia Salina (N-BS). "Spent" culture media from HM and HZ fibroblast cultures reduced respiratory energy production by isolated mitochondria from N-BS. This was determined by the micromoles phosphorus esterified/microatoms oxygen consumed (P/O). P/O ratios were: normal controls (NC) 1.6±.3 (10)*; HZ, 1.3±.3 (6); and HM, 1.2±.3 (8). The probability is high that NC and HM are different ($P=0.01$) but not NC and HZ ($P>0.05$). When intact N-BS were exposed to mixed saliva from NC, HM and HZ, the O_2 consumptions (ul O_2/hour · nauplius) were: HM, 0.017±0.012 (10), HZ, 0.049±0.010 (10) and NC, 0.087±0.003 (10). HM and HZ values were statistically different from NC and from each other with $P<.001$. The results suggest that fibroblast culture media and mixed saliva from HM and HZ decrease respiration and mitochondrial energy production of N-BS and may provide a common effect that quantitatively detects previously described CF factors. This effect on oxidative energy production may provide further insight into the pathogenesis of CF. Furthermore, it appears that N-BS could be used to develop a bioassay for detection of HZ for CF. *Numbers in parentheses indicate number of experiments.

LUNG FLUID AND PROTEIN DYNAMICS IN UNANESTHETIZED SHEEP DURING ALVEOLAR HYPOXIA. Richard D. Bland, Robert H. Demling, Samuel L. Selinger, and Norman C. Staub (Intr. by Roderic H. Phibbs). Univ. of California, San Francisco, Cardiovascular Research Institute, Dept. of Physiology and Dept. of Pediatrics, San Francisco.

To determine if hypoxia has a direct effect on pulmonary microvascular fluid and protein transfer, we measured steady-state lung lymph flow ($\dot{Q}$lym) and protein transport ($\dot{Q}$prot) in 7 unanesthetized sheep breathing 10% O_2 in N_2 for 4 hr and in 2 sheep breathing the same gas for 48 hr. We surgically prepared the animals to isolate and collect lung lymph and to measure mean pulmonary artery (Ppa) and left atrial (Pla) pressures. After recovery, the sheep breathed air through a tracheostomy for 2-4 hr, followed by 4 or 48 hr of hypoxia. In 12 4-hr studies, mean PaO_2 fell from 97 to 38 torr; Ppa rose from 20 to 33 cmH_2O; $\dot{Q}$lym and $\dot{Q}$prot were unchanged. During 48 hr hypoxia, with a sustained elevation in Ppa and a decline in Pla, $\dot{Q}$lym and $\dot{Q}$prot diminished progressively, with a decrease in the lymph-plasma protein ratio (L/P) from 0.70 to 0.60. We conclude that 4 hr of severe hypoxia did not increase lung fluid filtration or protein permeability, a finding supported by normal post-mortem histology and a mean extravascular lung water content of 4.27 ml/g dry bloodless lung. The decreased $\dot{Q}$lym, $\dot{Q}$prot and L/P during prolonged hypoxia are unexplained, but indicate that no increase in vascular permeability to plasma proteins occurred. [Supported in part by HL14201 (SCOR).]