

## 1225 AN ASSOCIATION BETWEEN BRACHYCEPHALY & EUSTACHIAN TUBE (ET) DYSFUNCTION, Gordon Worley, Raymond A. Sturmer, James Green, Thomas E. Frothingham, Duke University

School of Medicine, Department of Pediatrics, Durham. We evaluated 203 healthy pre-school children between the ages of 4½ and 5½ during 1 week in March. Using anthropologists' calipers, maximum head lengths (glabella to opisthocranium) and the maximum head breadth (euryon to euryon) were measured. A second investigator performed tympanometry. Neither investigator knew the other's results when assessing a subject. Cephalic index (CI) =  $\frac{\text{Maximum head breadth} \times 100}{\text{head length}}$  Mean = 76.1 SD ± 3.7

Children were considered brachycephalic whose CI > 79.8 (+1 SD), those with a CI between 72.4 and 79.8 were mesocephalic; and those with a CI < 72.4 (-1 SD) were considered dolichocephalic. A tympanometry failure was defined as a Jerger's Type B tympanogram in one or both ears.

Tympanogram:	Dolichocephalic	Mesocephalic	Brachycephalic
Type B	8	27	12
Types A & C	28	117	19

$\chi^2 = 6.2 \quad p < .05$

Brachycephalic children were also found to have significantly more effusions than meso- and dolichocephalic children considered together ( $p < 0.05$ ). Apache Indians are brachycephalic people (CI = 90) and have poor ET function, as is the case with those having Down's syndrome. It is possible that brachycephaly reflects an anatomical variation in the cranial base which, in turn, predisposes to poor ET function and middle ear pathology.

## 1226 DEPRESSED CELLULAR ZINC UPTAKE IN ANENCEPHALY AND SPINA BIFIDA. Andrew W. Zimmerman, David W. Rowe, Mary L. Stever (Spon. by A. J. Altman).

Univ. of Connecticut School of Medicine, Deps. of Neurology and Pediatrics, Farmington, CT. Zinc is essential for normal embryonic growth and differentiation. A high rate of fetal neural tube defects occurs in pregnancies of women with untreated acrodermatitis enteropathica and in experimental gestational zinc deficiency in rats; however, serum zinc is normal in children with spina bifida and in mothers of anencephalics during gestation. Confluent cultures of skin fibroblasts from two term newborns with anencephaly and lumbar meningocele and three age-matched controls were studied in triplicate in six experiments.  $^{65}\text{ZnCl}_2$  (2  $\mu\text{Ci}$ , 55 nM  $\text{Zn}^{++}$ ,  $2 \times 10^5$  cells) was added in fresh media (10% horse serum) and counted in whole washed cell suspensions at 24 hours.  $^{65}\text{Zn}$  uptake was significantly ( $p < .001$ ) lower in the infants with neural tube defects (281 ± 9.5 cpm/ $\mu\text{g}$  DNA) compared to controls (382 ± 50.7). The rate of zinc uptake was repeatable in each cell line. These results may reflect an abnormality of cellular zinc metabolism in infants with neural tube defects. We postulate that depressed embryonic uptake of zinc, perhaps due to heritable regulatory mechanisms, limits cellular differentiation during critical periods and thereby contributes to defective CNS formation.

## 1228 EFFECTS OF INSPIRATORY LOADING ON VENTILATION IN INFANTS RECOVERING FROM RESPIRATORY DISTRESS SYNDROME (RDS). S. Abbasi, S. Duara, T.H. Shaffer, and W.W. Fox.

Dept. of Peds., Univ. of Pa. Sch. of Med. and Children's Hosp. of Phila., and Temple Univ., Dept. of Physiol., Phila., PA. To evaluate the effects of inspiratory flow resistance ( $R_I$ ) on ventilatory response, 7 infants recovering from RDS were studied: Mean wt. 1.6 kg, age 21 days, gest. age 32 wks. Control tidal vol. (TV), min. vent. (MV), peak insp. flow ( $\dot{V}_I$ ), insp. time/tot. resp. time ( $T_I/T_{\text{Tot}}$ ), resp. freq. (f), dynamic compliance ( $C_D$ ) and  $\text{PACO}_2$  were obtained before applying a 250 or 450 cm H<sub>2</sub>O/L/sec.  $R_I$ . Studies were repeated immediately, 5 and 10 minutes following application of  $R_I$ . Infants were breathing room air throughout the study. Mean ± SEM control values were: TV=14.4 ± 6.5 ml, MV=804.8 ± 313.8 ml/min,  $\dot{V}_I$ =2.13 ± 1.08 L/min,  $T_I/T_{\text{Tot}}$ =.44 ± .03, f=53.66 ± 10.91,  $C_D$ =3.46 ± 1.48 (n=5),  $\text{PACO}_2$ =41.1 ± 4.5 mmHg. Following application of a  $R_I$  of 450 cm H<sub>2</sub>O/L/sec there was a decrease immediately and at 5 and 10 minutes for: TV(ml)=7.0 ± 3.8 ( $p < .002$ ), 7.5 ± 4.9 ( $p < .0001$ ), 8.0 ± 5.4 ( $p < .001$ ). MV(ml/min)=329.6 ± 145.3 ( $p < .001$ ), 385.2 ± 227.2 ( $p < .0001$ ), 377.9 ± 254.4 ( $p < .0001$ ).  $\dot{V}_I$ (L/min)=.50 ± .34 ( $p < .002$ ), .53 ± .34 ( $p < .002$ ), .58 ± .45 ( $p < .002$ ) respectively. There were no sig. changes in f,  $T_I/T_{\text{Tot}}$ ,  $\text{PACO}_2$  after loading, nor sig. diff. between the 250 and 450 insp. loads. These demonstrate a progressive decrease in resp. response in infants recovering from RDS after insp. loading of 250 and 450 cm H<sub>2</sub>O/L/sec. It appears that infants recovering from RDS do not compensate for insp. loading and this lack of compensation may be responsible for some forms of neonatal obstructive apnea.

## 1229 LONG TERM GASTROINTESTINAL AND NUTRITIONAL ASSESSMENT OF INFANTS WITH NECROTIZING ENTEROCOLITIS (NEC). S. Abbasi, S. Duara, S. Moskowitz, J. Watkins, G.R. Pereira.

Dept. of Peds., Univ. of Pa. Sch. of Med. and Children's Hospital of Philadelphia, Philadelphia, PA. The influence of NEC on growth and gastrointestinal (GI) function, was determined at 1 year of age in 9 premature infants (Mean ± SD birthweight=1.45 ± .33 kg and gestational age=31.4 ± 3 wks.) who had radiologically confirmed NEC. Seven of these infants were treated medically and 2 required surgery, (1 for prox. jejunal resection; 1 for post NEC colonic stenosis). Nine infants of similar weight and gestation were used as controls. Mean ± SD discharge age for controls=23.4 ± 32 days and for study group 59 ± 40 days. Both groups had comparable dietary history since discharge. Followup at mean ± SD 13 ± 2 months showed that both groups had similar weight, height and head circumference (50-85%ile) and similar mid-arm circumference and skinfold thickness (50-85%ile). Serum iron, albumin, pre-albumin, retinol binding protein, liver function studies and hematocrit were normal in both groups. Mean increment in serum vit. E levels 4 hrs. after an oral dose of 25 mg/kg vit. E was comparable for both groups (mean 0.3 vs. 0.34 mg/dl). Lactose malabsorption load (2 mg/kg) determined by hydrogen excretion was present in 2/9 control infants and 1/9 post NEC infants. This preliminary report suggests that in the absence of significant small bowel resection there is no detectable long term effect on nutritional status and GI function in infants who have recovered from NEC in the neonatal period.

## NEONATOLOGY

### 1227 ENDOCRINE STUDIES IN OFFSPRING OF TERBUTALINE-TREATED MOTHERS. Carmela Green-Abate, Edward O. Reiter, Bhavesh Shah, Baystate Medical Ctr., Univ. of Mass.

Med. School, Dept. of Peds., Springfield, MA. Terbutaline (T) a  $\beta_2$ -sympathomimetic, has been extensively used as a tocolytic agent in premature labor. To assess the influence of fetal  $\beta_2$ -sympathomimetic stimulation upon glycemic (G) and calcemic (Ca) status, we compared the offspring of 12 women who had received T with 12 age and weight-matched infants of untreated mothers. Umbilical cord serum cortisol (F), insulin (I), growth hormone (GH), parathyroid hormone (PTH), calcitonin (CT) and glucagon (GLC) were measured by RIA. Mean GA at onset of T was 30.7 wks; 69% were treated for less than 48 hrs. Mean time from last dose of T was 6.7 hours. Age, weight and hormone data are listed below; means (±SE) do not differ.

T-Rx	GA(wk)	Wt(kg)	G	Ca	PTH	CT	I	GLC	GH	F
(n=12)	33.6	1.83	188	10.4	20	71	10.3	99	24.2	3.1
controls	+0.6	+0.2	+25	+0.4	+11	+9.6	+1.8	+24.6	+5.6	+0.8
(n=12)	34.3	2.20	161	10.3	27	76	12.7	109	26.5	3.0
	+0.4	+0.1	+15	+0.3	+14	+11	+3.1	+22	+6.6	+0.2

At 24 hours, serum Ca was lower ( $p < 0.02$ ) in T-treated (7.4 ± 0.3) than in control babies (8.5 ± 0.3). Previously reported  $\beta_2$ -agonist-induced neonatal hypoglycemia was not demonstrated, presumably prevented by glucose infusions. In conclusion: 1) Differences did not exist in cord glucose, calcium and hormone levels. 2) T-treated offspring showed significant lowering of postnatal Ca, possibly due to exaggerated neonatal hypoparathyroidism secondary to adrenergic stimulation of maternal parathyroid glands.

### 1230 The Pharmacokinetics of Phenobarb and Phenytoin in Neonates. I.F. Abrams, M.D., F.J. Bednarek, M.D., D.P. Hays, Pharm.D., L.J. Lesko, Ph.D., B.F. Johnson, M.D. (Sponsored by James B. Hanshaw, M.D.)

The pharmacokinetics of Phenobarb and Phenytoin were evaluated in 14 neonatal patients. The average gestational age at birth was 32 (±5) weeks range, 26-41 weeks. The average post-conceptual age was 33 (±6) weeks, range 26-44. The average weight was 1.67 (±1.05) Kg, range 0.72-4.48. The patients were randomized as to which drug they would receive first. The drug was administered as a 20mg/Kg IV loading dose. If the first drug administered did not control the seizures, the second drug was given. Maintenance therapy was not begun, and serum levels were obtained at 2 hours, 12 hours, then every 12 hours after the dose until the phenytoin concentration was <10ug/ml and the phenobarbital concentration was <17ug/ml. At this point maintenance therapy was begun.

The average phenobarbital  $t_{1/2}$  was 173.0 (±169.3) hours, range 28.2-607.8. The volume of distribution for phenobarbital was 0.84 (±0.26) l/Kg, range 0.24-1.20. The average phenytoin  $t_{1/2}$  was 100.1 (±112.1) hours, range 24.2-370.8. The volume of distribution for phenytoin was 1.58 (±0.54) l/Kg, range 1.03-3.24.

From this data, it would appear that a 25-30mg/Kg loading dose of either drug would produce serum levels in the middle to upper part of the therapeutic range. The calculated values are 30-36ug/ml for phenobarbital, and 16-19ug/ml for phenytoin.