223

NONNUTRITIVE SUCKING(NNS) ENHANCES MATURATION OF THE SUCKING REFLEX IN PREMATURE INFANTS. Judy Bernbaum, Gilberto R. Pereira, John B. Watkins. Univ. of Pa.

Sch. of Med., Dept. of Peds. & Child. Hosp. of Phila., Phila., PA. Coordinated sucking during feeding is rarely achieved until 33-34 wks. gestation. To define sucking patterns after birth & to determine the influence of pacifier stimulation (NNS) during gavage(NG) feeding, 20 medically stable, NG fed AGA infants (mean gest. age(GA) 32 wks. (range 28-34) were studied. Infants matched for birthwt. & GA were randomized into 2 groups. NNS received a pacifier prior to and during every NG feeding, the control received no pacifier. Intraoral negative(suction) pressure and sucking patterns were recorded weekly during NG feedings. Both groups at 30-33 wks. gest. had low suction pressure(35-65mmHg); after 33 wks., intraoral pressure increased and sucks were organized into repetitive bursts(>3 rapidly consecutive sucks) with fewer sporadic sucks. However, the NNS group showed greater suction pressures($p<.05$) from 34 wks. (89vs.62mmHg) to 39 wks. (120vs.73mmHg). In both groups, burst frequency increased from 7 to 12/2min; however, sucks/burst were greater in NNS($p<.05$) from 34wk (8vs5/burst through 39wk(12vs7/burst) with fewer sporadic sucks (avg. 2.5vs. 7.5/2 min, $p<.05$). Finally, the NNS completed their first bottle feeding more rapidly(6.4±2.1 vs10.4±4.3min/oz avg±SD, $p<.05$) and made an earlier transition to total PO feeding(10±2.7 vs. 16±6.8 days, $p<.02$). Conclusion: Following birth, the sucking pattern in prematures is characterized by an increase in intraoral negative pressure and a transition from sporadic sucking to organized bursts; NNS opportunities significantly enhance this pattern and also facilitate an easier transition to bottle feedings.

224

REMODELING OF THE EPITHELIAL BASAL LAMINA (BL) BY THE MESENCHYME DURING MORPHOGENETIC TISSUE INTERACTION. Merton Bernfield and Shib Banerjee, Stanford Univ.

School of Medicine, Department of Pediatrics, Stanford, CA. The multilobular morphology of the 13 day mouse embryonic submandibular epithelium (Ep) is maintained by its BL. Although the Ep alone produces a BL with identical characteristics as the BL in intact glands, it requires mesenchyme for morphogenesis. To assess mesenchyme function, the turnover of BL-glycosaminoglycan (GAG) was measured during in vitro morphogenesis. After labeling with ³H-glucosamine, the mesenchyme was removed and the isolated Ep were divided into stalk, lobules (the sites of new growth and branching) and the base (which contains the morphogenetically quiescent interlobular clefts). Incorporation kinetics and precursor pool specific activities showed that the stalk is in the steady state regarding GAG metabolism, that the base accumulates GAG at a 5-fold greater initial rate than the lobules, and that the rate of GAG loss in the lobules is greater than in the base and, during morphogenesis, becomes greater than its rate of replacement. Autoradiography showed that the bulk of the GAG is in the BL and that during a chase BL-GAG is lost more rapidly from the lobules than from the clefts. However, this rapid loss occurs only in the presence of mesenchyme. Thus, BL-GAG turns over more rapidly on the lobules than on the clefts and the GAG degradation is due to the mesenchyme. The rapid remodeling of the BL on the lobules may allow more Ep growth and branching than the more stable BL on the clefts. One mechanism of morphogenetic tissue interaction may be mesenchymal degradation of the epithelial BL. (Supported by NIH grant HD 06763.)

225

RESERVE BILIRUBIN BINDING CAPACITY (RBBC) MEASURED BY ABSORBANCE DEVIATION (AD) AT SATURATION OF PRIMARY ALBUMIN-BINDING SITES (PABS). Larry H. Bernstein,

Raul C. Banagale, David Kingsley (Spon. by A. P. Erenberg), Depts. of Path. and Ped., Iowa Methodist Medical Center, Des Moines, IA and Dept. of Ped., Univ. of Iowa Hospitals and Clinics, Iowa City, IA.

This method requires the sequential addition of 5 µl increments of bilirubin solution (BS) of 25 mg/dl to 50 µl of neonatal serum (NS) in 2 ml of 200 mM phosphate buffer, pH 7.4. With each addition of BS to the NS, there is a constant increase in absorbance at 484 nm until all PABS are exceeded. The table shows the expected absorbance change ($\Delta A_{484 \text{ nm}}$) per addition of BS which results in a linear relationship between added BS and $\Delta A_{484 \text{ nm}}$ until saturation of PABS.

µl BS added	2.5000	5.00000	10.00000
Mean $\Delta A_{484 \text{ nm}}$	0.0204	0.04023	0.07609
Coeff. var.	7.8%	4.8%	5.5%

Deviation from linearity occurs when the saturation of PABS is exceeded. The volume of BS that can be added to a NS before this point is reached provides an index of how far a patient is from the point at which bilirubin (BR) concentration will exceed primary capacity and unbound BR will rapidly rise. The proposed method is less cumbersome than the methods currently being used, other than the less available BR hematofluorometer (Pediatrics 65:767, 1980).

Uniform lots of stable BS were provided by A. Louderback of Clinical Chemistry Consultants, Temple City, California.

226

DEVELOPMENT OF BILIRUBIN CONJUGATION IN HUMAN NEWBORNS. Norbert Blanckaert, Philip Rosenthal, and Michael M. Thaler. Univ. of California, Department of Pediatrics and Liver Center, San Francisco.

The gestational age at which conjugation of bilirubin (BR) begins is unknown, and the BR conjugates initially formed have not been identified. Using alkaline methanolysis-HPLC and TLC, chemical, and enzymic tests on ethyl anthranilate azoderivatives, we determined and characterized the BR fractions in duodenal bile (DB) from 8 fullterm jaundiced infants (age 4-9 days) and in plasma from (1) cord blood (C) obtained at 46 unselected deliveries and from (2) 54 premature (P) and fullterm (F) newborns. In DB, BRs (50-317 µM) consisted of 1-12% unconjugated BR, 32-50% mono- and 43-67% di-ester conjugates; the conjugating sugars corresponded with xylosyl (up to 5%), glucosyl (3-12%), and glucuronyl (83-96%) groups. Total plasma BR (TB) in C averaged 20±7.9 µM and consisted entirely of unconjugated BR. In P and F, TB increased from 29 to 116 µM during the 1st week, peaking at 5 days. In contrast with C, BRs in P and F comprised 2-5% BR glucuronides; monoconjugates appeared during the 1st day, and diconjugates were detectable only 48 hrs. after birth. Conclusions: development in F of conjugation with glucose and xylose seems to parallel that of glucuronidation, and the proportions of the 3 sugar conjugates formed in newborns and adults are comparable. However, the proportion of diconjugates in bile of F is smaller than in bile of adults. Also, our findings suggest that initiation of BR conjugation in P and F occurs at birth and is independent of gestational age.

227

DISTRIBUTION OF HEPATIC VENOUS BLOOD IN FETAL LAMBS. James Bristow, Abraham Rudolph, Joseph Itskovitz, Richard Barnes. Univ. Calif., C.V.R.I., San Francisco

We have shown that 50% of umbilical venous (UV) blood passes through the liver; the liver contributes ±30% of total venous return to the heart. Also, more UV blood traversing the ductus venosus (DV) is shunted across the foramen ovale (FO) than distal inferior vena caval (DIVC) blood. Because O₂ sats of fetal left (LHV) and right (RHV) hepatic veins differ, their patterns of distribution are important. In 7 fetal lambs (116-122d) we placed catheters in descending aorta (AO), DIVC, UV, and R or L, or both HV. Calculated upper to lower body ratios (U/L) of radioactivity of microspheres injected into DIVC, UV, RHV, or LHV indicated relative shunting across the FO of venous blood into which the microspheres were injected. Studies were done during control (C) (AOP₀₂ 21, pH 7.38) and fetal hypoxia (H) (AOP₀₂ 11, pH 7.37) produced by maternal hypoxemia. U/L were (m±SD):

Right HV C:	.33(IVC).35(HV)	.43(UV)	H: .34(IVC).48(HV).59(UV)
	±.08 ±.08 ±.09	±.13 ±.17 ±.13	
Left HV	.41 .64 .60	.51 .70 .71	
	±.19 ±.24 ±.23	±.04 ±.25 ±.12	

Thus, RHV blood, which has a lower O₂ sat than LHV blood, is distributed like DIVC blood during C, but FO shunting increases with H. LHV blood, with high O₂ sat, streams like DV blood preferentially across the FO; this did not change with H. The selective streaming of LHV and RHV blood is probably due to valve-like membranes covering the orifices in IVC. Shunting of HV blood to the upper body may be important in O₂ delivery, as well as in providing glucose during stress.

227A

DILANTIN AND NEUROBLASTOMA GROWTH. Bruce A. Buehler, Shannon E. Smith, and Leslie Jerominski. University of Utah College of Medicine, Department of Pediatrics Salt Lake City, Utah.

Recently, a link between Fetal Dilantin Syndrome and the occurrence of neuroblastoma in the affected fetus has been suggested by four cases. Our laboratory has previously presented data on the suppression of normal fibroblast polyamine biosynthesis by Dilantin in vitro. Because polyamine production has been implicated in the pathogenesis of neoplasia, the activity of the key polyamine biosynthetic enzyme, Ornithine Decarboxylase (ODC), was investigated in human neuroblastoma cells.

The levels of Ornithine Decarboxylase in human neuroblastoma cells in vitro is 5-10 times greater than in normal fibroblasts. Acute exposure of neuroblastoma cells to Dilantin showed significant enhancement of ODC activity at concentrations of 1-3 µg/ml, while higher concentrations caused suppression of ODC activity. This enhancement effect could not be demonstrated in normal fibroblasts. Dilantin exposure of growing neuroblastoma cells showed enhancement of cell number at the 1-3 µg/ml concentration range, whereas cell growth was inhibited by higher concentrations of Dilantin.

The stimulation of neuroblastoma cell ODC activity and growth in vitro by low therapeutic doses of Dilantin may be important in the pathogenesis of neuroblastoma cell tumors in fetuses exposed to Dilantin in utero.