1618 CYTOSKELETAL STRUCTURES MAY LINK CHOLESTEROL SYNTHESIS TO GLIAL DIFFERENTIATION.

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Cholesterol synthesis is a highly critical process in developing brain, particularly in glia, because cholesterol is a major constituent of all cellular membranes, including myelin. We have shown recently that the rate limiting enzyme in cholesterol biosynthesis, HMG-CoA reductase (HMG-R), is actively regulated in cultured C-6 glial cells, a model of the differentiating glial cell, and that this regulation involves microtubules. This study elucidates further the role of cytoskeletal structures.

Microfilaments were disrupted by exposure of the cells to cytochalasin D (cD). Within 1 h of the addition of 1 μ M cD, there resulted a 50% reduction in HMG-R activity, and after 3 h an 80% reduction. A decrease of 50% occurred with just 0.2 μ M cD (3 h). The effects were fully reversible. The specificity of the effect was indicated by the findings of no change in the activities of five other critical glial enzymes or in the rate of total protein synthesis. That the decrease in HMG-R activity caused by cD is related to a decrease in enzyme content was suggested by the observation that cycloheximide blocked the recovery of activity after removal of cD. A relation of the effect of cD on reductase to disruption of microfilaments was suggested by striking concomitant morphological changes caused by the drug.

Coupled with our previous findings, the observations suggest a link between a microfilament-microtubular system and both glial differentiation and cholesterol biosynthesis. Such a link would be of major neurobiological importance because it would provide a mechanism for coupling membrane biogenesis to cellular differentiation. (Supported by NIH grant R01 HD-07464).

1619 PERIVENTRICULAR LUCENCY: THE MOST COMMON CT LESION IN FULL-TERM NEONATES WITH CNS DISEASE.

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In 1979 74 CT head scans were obtained on 57 AGA (31 male, 26 female), >2500-gm, 28 days-of-age newborns with suspected CNS disease in the NSUH NICU. Indications for CT scan included: CNS bleed - 2; cyanotic episode - 3; myelomeningocele - 3; seizure - 34; macro/microcephalus - 10; miscellaneous - 6. Eight scans were normal; 4 showed CNS bleed; 4 showed congenital malformations; 6 showed hydrocephalus; and 37 showed periventricular lucencies: 8 mild, 12 moderate, and 17 severe. Of the infants with periventricular lucencies, respirator support was required for 27% (10/37); Apgar scores were ≤ 6 in 27% (10/37); abnormal EEG's occurred in 49% (18/37); and seizures occurred in 68% (26/37). Hospitalization stay averaged 27 days. In our experience, periventricular lucency is the most common CT head scan abnormality found in full-term infants with neurologic disease and correlates with other parameters of negative neurologic outcome.

1620 COMPARATIVE ONTOGENY OF NERVE GROWTH FACTOR (NGF) IN MALE MOUSE BRAIN AND SUBMAXILLARY GLAND (SMG).

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NGF is a protein found in highest concentration in the adult male mouse SMG and essential for maturation and maintenance of adrenergic neurons in the peripheral nervous system. We have previously detected NGF in adult and neonatal mouse brain. Using a specific and sensitive radioimmunoassay for NGF, we compared the postnatal patterns of ontogenesis of NGF concentration in SMG and brain of male Swiss-Webster mice. Mean SMG NGF concentration was 0.19 ± 0.02 ng/mg protein at age 11 days and increased to 103, 2678, and 20,353 ng/mg protein at ages 21, 32 and 60 days of age respectively. Cerebellar NGF increased from 681 to 2241 pg/mg protein between ages 2 and 15 days, and subsequently fell to a plateau level of 1484 pg/mg protein by age 17 days. Cerebral NGF increased steadily from 251 to 1383 pg/mg protein between ages 2 and 32 days, whereas brain stem NGF maintained a plateau averaging 1100 pg/mg protein.

Conclusions: 1) The developmental patterns of NGF concentration in brain and salivary gland are clearly different. 2) SMG NGF levels increase exponentially after 11 days of age. 3) Brain NGF levels increase during the first 2-4 weeks seeming to parallel known patterns of cell differentiation in each brain region. 4) The results support the possibility of intrinsic brain NGF synthesis.

1621 NONINVASIVE NEONATAL REGIONAL CEREBRAL BLOOD FLOW.

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Alterations in CBF are believed to be causally related to hypoxic-ischemic encephalopathy and intracranial hemorrhage in newborn infants. Using a modification of the standard 133-Xenon inhalation technique, rCBF was measured in 10 neurologically normal low birth weight (LBW) infants of mean birth weight 1322 g, gestational age 31.2 wks. The infants were studied at mean postnatal age 4.4 wks and had mean systolic BP 70, hgb 12.2g. 133-Xenon was administered as a small bolus (0.5 mCi/kg). Arterial Xenon concentration was measured with an external chest probe and used to correct for recirculation. Fifteen min. desaturation curves were obtained from 4 homologous cerebral regions and analyzed with Obrist's program. Compared to normal adults, mean grey matter flow (89.8 ml/100 gm/min) was significantly higher ($p < .01$) and mean grey matter weight (28.6%) significantly lower ($p < .001$). The interregional variation showed a trend towards low frontal and high occipital flows which is the opposite of adult regional flow patterns. There was a highly significant ($p < .001$) inverse correlation between CBF and hgb concentration. Unlike previous reports in the literature, the correlation between CBF and systolic BP was not significant, and the slope of the least squares regression line was not significantly different from zero. Our results demonstrate that noninvasive neonatal rCBF studies are possible and suggest that normal LBW babies have intact CBF autoregulation and physiologic responses to alterations in hgb concentration.

PULMONARY

1622 BROVIAC CATHETERS FOR PROLONGED ANTIBIOTIC ADMINISTRATION IN CYSTIC FIBROSIS PATIENTS.

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An efficient and safe program for continuous home administration of parenteral antibiotics was developed for chronically ill cystic fibrosis children. Six patients, ages 9 to 20 yrs, who required frequent hospitalizations for pseudomonas bronchitis had Broviac or Hickman catheters placed under general anesthesia. Catheters were utilized over intervals of one month to two years. A combination of tobramycin (5-7.5 mg/kg/day) and carbenicillin or ticarcillin (300 mg/kg/day) was given every six to eight hours by patients or their parents. Peak tobramycin levels between 5 - 10 μ g/ml were achieved. Compared to a control period prior to beginning the program, a decreased frequency of hospitalizations for pulmonary symptoms was noted in 4 of 6 patients. All patients benefited by their ability to maintain normal activities at home and at school. No objective improvement in pulmonary function tests utilizing peak flow measurements was observed in this patient group. No catheter-related complications were observed. Two catheters required repair because of leakage of the external segment. Prolonged administration of antibiotics utilizing the Broviac catheter may benefit some patients with cystic fibrosis. However, the long term effects of this therapy on the progression of their pulmonary disease are unknown.

1623 EVALUATION OF GASTROESOPHAGEAL REFLUX AND APNEA IN NEAR MISS FOR SIDS INFANTS.

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Continuous endoesophageal pH monitoring is an accepted technique to evaluate gastroesophageal reflux (GER). Although several studies have reported GER in infants who have apnea, few studies have recorded endoesophageal pH and respiration simultaneously to examine for a chronological relationship between these 2 events. We have examined 43 full-term near miss for SIDS infants (1-34 wk old; mean 10 wk) who were referred after medical evaluation, where a parent witnessed the infant to be pale or cyanotic, flaccid or stiff and vigorous stimulation or mouth-to-mouth resuscitation was needed. Endoesophageal pH, respiration (using an abdominal strain gauge) and electrocardiogram were recorded. A flexible glass pH electrode (Microelectrodes, Inc.) 1.2 mm in diameter was passed nasally into the stomach to confirm a pH < 4 then the tip was positioned with fluoroscopy at the mid-left atrial position. The pH probe was calibrated before insertion with standard buffer solutions of pH 7.0 & 4.0. Infants were monitored for a period of 18-20 hrs; they were fed and handled in the usual manner. There was a mean of 8 events (range 0-29) of pH < 4.0 of which 53% were < 1 min and 47% > 1 min. No events were longer than 30 min. 85% of recorded reflux events occurred with body movement. The majority (71%) of the GER reflux occurred when the infant was very active or awake. Apnea was not seen concurrent with a fall in pH < 4.0 . In this study we were unable to document an association between GER reflux and apnea.