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EVOLUTION OF HEPATIC CIRRHOSIS IN PEROXISOMAL DYSFUNCTION DISORDERS: THE SPECTRUM OF HISTOPATHOLOGIC ABNORMALITIES. Ronald D. Holmes, Golder N. Wilson, Amiya K. Hajra, James W. Hanson, Holly H. Ardinger and Mendel Tuchman, William Beaumont Hospital, Divisions of Gastroenterology and Genetics, Royal Oak, MI, University of Michigan, Dept. of Biochemistry, Ann Arbor, MI, University of Iowa, Division of Medical Genetics, Iowa City, IA, and University of Minnesota, Dept. of Pediatrics, Minneapolis, MN.

Patients with peroxisomal dysfunction disorders lack peroxisomes or certain peroxisomal enzymes. Assay of activity of the peroxisomal membrane enzyme dihydroxyacetone phosphate acyl transferase (DHAP-AT) provides a biochemical test for identifying patients with peroxisomal disorders.

We report 8 patients with a spectrum of peroxisomal disorders. All patients have dysmorphism, failure to thrive and hepatomegaly. Serum transaminase levels are elevated and activity of DHAP-AT is reduced. All patients have other chemical abnormalities associated with peroxisomal dysfunction. One infant had Zellweger's cerebro-hepato-renal syndrome (CHRS) and died at age 10 months. The other patients presented with either a variant of Zellweger's CHRS or neonatal adrenoleukodystrophy (4), dicarboxylic aciduria (1), infantile Refsums' disease (1) or chondrodysplasia punctata (1).

Histopathologic changes in the liver include micronodular cirrhosis (2), fibrosis (4), and paucity of intrahepatic ducts (2). In addition, there was accumulation of hepatocyte hemosiderin in 1 patient and abundant deposition of glycogen in 3 patients.

Peroxisomal disorders present with a variety of clinical problems. Infants with failure to thrive, hepatomegaly and suggestive dysmorphism should be screened by assaying DHAP-AT.

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CLINICALLY SIGNIFICANT ESOPHAGITIS IN TUBE FED HIGH RISK NEONATES: A PREVIOUSLY UNRECOGNIZED PROBLEM. VF Hupertz, SJ Czinn, D Gregory, RM Kliegman. Case Western Reserve Univ., Dept. Peds., Cleve, OH
Esophagitis (E) is being recognized more frequently in the pediatric population; however, the diagnosis appears to be rare during the neonatal period. Over the last 2 years, 8 seriously ill neonates were evaluated for the possibility of E. Indications for esophagogastrosomy (EGS) included irritability or arching with feeds (3/8), refusal of oral feeds (4/8), frequent gastric aspirates or emeses (6/8), and the presence of blood in aspirates (6/8). Gestational age ranged from 25-32wks. 7/8 had nasogastric (NG) tubes for 3-7 1/2 mo. and the 8th had a gastrostomy tube (GT) s/p NEC. 5/8 patients were on long term theophylline therapy and 3 were on ventilators. At EGS, wt ranged from 1590-5390gms. All 8 had evidence of erosive E with severe mucosal edema, erythema, exudation and ulceration. 4/9 had pseudopolyps. 2 had gastric outlet obstruction secondary to a pancreatic rest or a pyloric web subsequently documented at surgery. Of the remaining 6, 4 improved after removal of the NG tube and treatment with cimetidine and/or antacids. 1 died due to the underlying disease and 1 required a GT because of poor oral intake. 7/8 had no complications during the EGS; only 1 patient had a transient bradycardia during intubation of the esophagus. In conclusion, EGS is a useful and safe test to evaluate neonates with irritability, refusal of feeds and repeated or bloody gastric aspirates. Our findings suggest that NG tube trauma, as well as rare causes of gastric outlet obstruction, may be responsible for these symptoms which are often seen in premature infants.

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DEMONSTRATION IN AN ANIMAL MODEL OF A HEAT LABILE TOXIN PRODUCED BY C. PYLORIDIS (CP). Vera F. Hupertz and Steven J. Czinn (Spon. by Jeffrey L. Blumer) Case Western Reserve University School of Medicine, Rainbow Babies and Children's Hospital, Department of Pediatrics, Cleveland, Ohio.
The production of enterotoxins by various bacterial cell lines has been widely studied in a variety of models including both animal and tissue culture cells. A report of a mouse model for measurement of virulence has been published recently (McCardell, et al., J. Infect. Immun.; 153:177, 1986). Similar results with CP, a gram negative, curved bacterium associated with chronic gastritis, have been obtained in our laboratory. Using a modification of this animal model to identify the presence of toxins, sterilely filtered cell lysates of CP obtained from a pediatric patient were injected ip into 6-8 week old CF-1 outbred female mice. CP was grown on Columbia agar with 5% sheep blood and incubated at 37°C, microaerophilically for 4 days. Harvested cells were lysed and the particulate matter was removed by centrifugation. The supernatant was sterilely filtered. One ml of sterile filtrates at various protein concentrations were injected ip into mice. The mice were observed for 4 days for death. Control mice were injected with PBS that was used to wash uninoculated Columbia agar plates. Protein concentrations ranging from 1 to 5 mg were evaluated. Concentrations greater than 1.3 mg were uniformly toxic (90% mortality within 48 hours). No deaths were noted during the 4 day study period with protein concentrations below 1.3 mg/ml. Additional work has shown that the toxic factor was inactivated by trypsin, heat (100°C for 15 min), and acidification to pH 4.0. The toxic factor was precipitated with 80% NH₄SO₄ and is nondialyzable. Postmortem examination of the mice shows edema and distention of the duodenum with the remainder of the bowel appearing normal. The above work demonstrates that there is a toxic factor that is present in certain strains of CP. This factor is lethal to mice when given ip and is probably protein in nature. Whether this factor is responsible for the epithelial damage seen in patients with active CP associated gastritis remains to be determined. Further work will also determine if this toxic factor can be demonstrated on the various tissue culture models used for toxin assays.

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NEUTROPHIL (PMN) MIGRATION IN RESPONSE TO CHEMOTACTIC FACTORS GENERATED BY THE INVADING PATHOGENS IN ACUTE BACTERIAL ENTERITIS (ABE) Abdul J. Khan, Mathew Varghese, and Hugh E. Evans. SUNY/Health Science Center And Interfaith Medical Center, Brooklyn, NY

The role of chemotactic and random migration (RM) in ABE is not known. They were determined in 9 pts with ABE due to shigella or salmonella between days 3&5 of admission and 9 controls. One day prior to study each isolate was grown in medium 199 to generate specific chemotactic factors (SCF). Leukocytes were harvested from heparinized blood and 1.0x10⁶ PMNs were deposited on to 3 u millipore filter which was placed in the Boyden's chamber. The upper compartment of the chamber was filled with Hank's solution (HS) and the lower with SCF 100uL/mL of HS. Three simultaneous chambers were also set up with endotoxin activated serum (EAS), E. coli generated factors (ECF) and HS alone in the lower compartments. After 3hr's incubation filters were stained and cells which migrated to lower surface were counted. A ratio of migrated to total cells with SCE, EAS & ECF was termed as chemotactic index (CI) and RM with HS alone. In 4 pts studies were repeated after therapy. Mean (+1SD) values are presented (table): Mean CIs of patients with all the 3 factors were significantly lower than those of controls and significantly increased after therapy. RM was similar. Suppression PMN chemotaxis may be one step in the pathogenesis of ABE. Counteracting it with drug/agents may improve the outcome.

GROUP(N)	SCF	EAS	ECF	RM
Patients(9)	27(4)	32(10)	30(10)	27(15)
Controls(9)	49(10)	56(12)	52(11)	20(7)
P-Value	<0.005	<0.005	<0.005	>0.1
Pts(Post Rx)	52(7)	62(13)	58(9)	19(7)

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VITAMIN K₁ AND VITAMIN K₂ STATUS OF FULL TERM AND PRE-TERM INFANTS. S Khayata, F Greer, R Heimler, J Suttie. Departments of Pediatrics and Biochemistry, Medical College of WI-Milwaukee, and Univ of WI-Madison, WI.
There is little definitive information about vitamin (vit) K₁ (phyloquinone) and K₂ (menaquinone) in newborns. We measured serum concentrations of K₁ and fecal K₁ and K₂ in 25 full term (FT) infant/maternal pairs and 11 preterm (PT) infants (29-36 wks gestation) during the first week of life. In FT infants, mean maternal K₁ (1.69±1.04 ng/ml) was higher (p<0.02) than cord blood (1.10±0.58) without significant correlation (r=0.17). There was a difference in cord K₁ between FT (1.10±0.58 ng/ml) and PT (2.95±1.8 ng/ml) infants, (p < 0.001). All infants received vit K at birth. In FT infants at 5 days of life there was no difference in K₁ between breast fed (n=13) and formula fed (n=10) infants (21.0±12.4 vs 27.5±9.7 ng/ml). In PT infants (NPO) at 48 hrs post K₁ IM injection, mean serum K₁ varied greatly (n=113, range 2.3 to 429 ng/ml) but was positively correlated with weight (r=0.74). In the first week of life, FT formula fed infants compared to breast fed infants had higher fecal K₁ (2.35±2.34 vs 0.55±0.88 µg/g dry wt, p < 0.01). Significant levels of K₂ (> 200 pg/g dry wt) were detected in 8/9 formula fed infants and 2/9 breast fed infants (p<0.025, chi square). In NPO PT infants, fecal K₁ and K₂ were undetectable. We conclude: 1) Maternal K₁ is higher but does not correlate with FT infant K₁ at birth 2) There is a significant difference in cord blood vit K₁ levels between FT and PT infants. 3) There is a marked difference in K₁ and K₂ in the stools of breast fed, formula fed, and NPO infants during the first week of life.

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INTESTINAL GLUCOSE ABSORPTION IS DISTINCTLY DIFFERENT IN CHRONICALLY CATHETERIZED RATS COMPARED TO ACUTELY CATHETERIZED. Robert E. Kimura, Jasminka Ilich, and Jillian Clerk. (Spons. by G. Chan). U of Utah, Salt Lake City, UT.
Studies of rat intestinal glucose absorption have been performed shortly after anesthesia and abdominal surgery. In order to determine if these factors affect intestinal glucose absorption, we compared portal venous (PV) and aortic (A) blood glucose ([gluc]) concentrations from acutely (AC) and chronically catheterized (CC) rats. PV, A and gastrostomy catheters were surgically placed in adult rats. Ten ml of 5% dextrose was infused into the gastrostomy within 1 hr of catheter placement in the AC rats. In the CC rats, the dextrose was infused after the rats had regained preoperative wt (6-10 days). PV and A blood was drawn at 0, 5, 15, 30, 45 and 60 min after the dextrose infusion. The values are µmol substrate / g blood (mean±SD, n=4-5). In CC rats A-[gluc] increased from a baseline of 7.6±0.3 to a maximum of 14.3±2.4, 15 min following the dextrose infusion and decreased linearly to baseline concentrations (7.4±0.3) 60 minutes after infusion. In contrast, the A-[gluc] in AC rats continued to increase linearly after the dextrose infusion from a baseline of 7.3±0.2 to 9.6±2.0 (15 min), 12.1±2.3 (45) and 13.5±1.7 (60). The A-[gluc] of CC rats were significantly different from AC at 15 and 60 min (p<0.05). The glucose concentration gradients between portal venous and aortic blood ([gluc(PV-A)]) in AC rats were significantly greater than 0 at 5, 15, 30 and 45 min after the dextrose infusion with an average of 1.78 µmol/g blood. In the CC rats, there was no significant [gluc(PV-A)] at any sampling time. There was no significant difference between AC and CC rats in [gluc(PV-A)] 60 min after the dextrose infusion. These studies indicate that glucose absorption was delayed in the AC rats compared to the CC rats. Since the rate of glucose absorption = [gluc(PV-A)] X mesenteric blood flow (MBF), the presence of a significant [gluc(PV-A)] in the AC rats during a time of decreased glucose absorption indicates a decrease in mesenteric blood flow compared to CC. This study suggests that physiologic PV and A blood substrate concentrations following feedings should be obtained under chronically catheterized conditions.