685 SIGNIFICANCE OF OROTIC ACID(OA) EXCRETION IN REYE's SYNDROME.

Ingeborg Krieger, Era Bawle, Ashok Sarniak. Wayne State U., Children's Hosp.of Mich. Detroit. MI

The hyperammonemia of early RS stages is thought to be caused by mitochondrial damage, affecting the first two enzymes of the urea cycle, mainly ornithine transcarbamylase(OTC). However, the degree of OTC deficiency, demonstrated by enzyme assays, is - by published reports - not sufficient to cause hyperammonemia, as judged by comparison with genetic OTC deficiency. OA-uria is a marker of OTC deficiency. By contrast, deficiency of the first & limiting enzyme of the urea cycle, CPS, is not associated with OA-uria. Hyperammonemia without OA-uria and amino acid elevation signifies a defect of the first step: CPS or it's substrates. We have measured in 20 RS cases on admission OA and NH_4, and determined the correlations between, #1: OA and NH_4; #2: OA and RS stage; #3: NH_4 and RS stage; #4: NH_4 and outcome; #5: OA and outcome. Mean admission NH_4/OA (normal: <0.6/<36.7) was in stage I: 1.5/29.5 (n:4); in stage II: 1.6/18.6 (n:9); in stage III: 2.4/68.1 (n:3); in stage IV: 3.3/48.0 (n:4). Mean admission NH_4/OA was 1.7/20.3 in 16 patients who recovered, and 3.5/88.6 in 4 who died. Althoug mean OA and NH_4 values were higher in patients admitted and tested in stages III and IV, correlations #1-4 were not significant; correlation #5 was highly significant. We conclude that hyperammonemia was in the majority due to limitation of the first step of the urea cycle, probably substrate deficiency causing insufficient activation of CPS. Significant OA-uria, which occurred only in stages III and above, is predictive of a poor outcome, attributable to mitochondrial damage, causing increasing OTC deficiency relative to CPS activity and OA-uria , despite decreased flow through the urea cycle.

686 INTESTINAL LIPID PEROXIDATION: INFLUENCE OF ISCHEMIA AND VITAMIN E DEFICIENCY

John S. Latimer and Merrily A. Poth Department of Pediatrics, USUHS, Bethesda, MD (Spon. by Gerald W. Fischer).

Free radical mechanisms are important mediators of ischemic injury in many tissues. Unscavenged free radicals can react with cellular fatty acids leading to fatty acid peroxidation (FAP) and loss of membrane function and integrity. Vitamin E (vit E) is an important defense against free radical injury. We have developed a model to explore the susceptibility of small intestinal mucosa to FAP in response to ischemia and vit E deficiency. Vit E deficient and replete Sprague-Dawley rats were subjected to mesenteric artery occlusion of 45 min followed by a 15 min reperfusion period. Nonoccluded control animals, vit E deficient and replete, were subjected to sham, time matched laparotomy and exposure. Following ischemia and reperfusion or sham operation, intestinal mucosal scrapings from separate portions of the gut (duodenum, jejunum, and ileum) were homogenized and assayed for in vitro FAP based on thiobarbituric acid assay of malondialdehyde. With n=4 for each of the four groups (vit E deficient and replete, with and without arterial occlusion) the following observations have been made: 1) there is no difference in FAP between control and vit E deficient rats in the duodenum and no changes in FAP are observed in this proximal gut segment with ischemia; 2) significantly greater ($p<0.05$) FAP occurs in the jejunum and ileum of nonoccluded vit E deficient compared to replete animals; 3) ischemia causes no change in FAP in any gut segment of replete animals, but causes a significant ($p<0.05$) further increase in FAP in the ileum of vit E deficient animals.

● 687 ELEVATED LEVELS OF PROTEASE INHIBITORS AND OF INHIBITOR PROTEASE COMPLEXES IN THE PLASMA OF NEWBORNS.

Jeremiah J. Levine, Kurt J. Bloch, Barbara Everndon, Michael F. Epstein, John N. Udall, Depts of Pediatrics and Medicine, Harvard Medical School, Boston, MA.

We have previously demonstrated that the intestine of newborn animals absorbs increased amounts of intact proteases compared to that of weaned animals (AJP 247:G183, 1984). The absorbed proteases circulate in combination with α1-antitrypsin (α1-AT) and α2-macroglobulin (α2-MG). In this study we measured α1-AT and α2-MG in the plasma of healthy three-day old newborns and adults using radial immunodiffusion. In addition, plasma α2-MG-protease complexes (α2-MG-PC) were analyzed before and after reduction with dithiothreitol using gradient (2.5-15%) polyacrylamide gel electrophoresis and scanning densitometry. (This approach depends upon the resistance of α2-MG-PC to reduction.) The presence of reduced and nonreduced bands was confirmed by immunofixation.

	Newborn* (n=8)	Adult* (n=8)	p value
α1-AT	256 ± 14 mg/dl	203 ± 12 mg/dl	< 0.02
α2-MG	413 ± 24 mg/dl	262 ± 27 mg/dl	< 0.001
α2-MG-PC	41 ± 6%**	1 ± 1%**	< 0.001

* X̄ ± S.E.M. ** Percentage of α2-MG resistant to reduction

These results indicate that both protease inhibitors (α1-AT and α2-MG) and α2-MG-PC are significantly increased in newborn compared to adult plasma. The elevated level of antiproteases in newborn plasma may reflect a response to the need for neutralizing proteases absorbed from the intestine, as well as a decreased clearance of α2-MG-PC.

688 NONINVASIVE SCREENING TESTS FOR ENTEROPATHY IN CHILDHOOD.

Jerry Levine, Ernest Seidman, W. Allan Walker. Department of Pediatric GI/Nutrition, HMS, Children's Hospital, Boston, MA

No study has compared the 3 most commonly used screening tests for enteropathy and jejunal biopsy results. A retrospective survey of all jejunal biopsies at CHMC (7/83-7/84) was undertaken to evaluate which test best predicted a normal biopsy. Screening tests: Lactose breath hydrogen test (LBHT, 2gm/kg, max 50gm; abnormal≥10ppm rise after 60min); serum D-xylose (Xyl, 0.5 gm/kg, max 25gm; abnormal<20mg% at 60min); and fecal fat (FF, abnormal> 10% of intake over 72 hours). Histology was reviewed and scored blindly as N (normal-minimal villous blunting) or Abn. (moderate-severe villous atrophy, crypt hyperplasia). Results: Jejunal biopsies were obtained from 117 children. 49 patients had no prior screening test and were excluded.

TEST	(N)	Sens. (%)	Spec. (%)	Correl. Coeff. (φ)	Signif. Pred. Value (X^2)	Neg. (%)
LBHT	(45)	54	47	0.007	N.S.	72
Xyl.	(26)	80	75	0.54	0.002 p<0.01 (7.5)	86
FF	(39)	50	96	0.56	p<0.01 (12.4)	85

Conclusions: None of the screening tests analyzed were ideal. Xyl and FF were significantly correlated with biopsy results. A normal result in either was highly predictive of a normal biopsy. The xylose test is preferable on the basis of greater sensitivity and ease of patient compliance.

689 PROGNOSTIC FACTORS ASSOCIATED WITH SURVIVAL DURING REFEEDING IN MALNOURISHED CYSTIC FIBROSIS PATIENTS.

L. Levy, P. Pencharz, P. Durie, M. Corey. Dept Paed and Res Inst, The Hospital for Sick Children, Toronto, Canada.

Malnutrition in CF patients is associated with a decrease in survival. Therefore we began intensive enteral and parenteral feeding support in 20 non-selected CF patients with malnutrition. As 10 of 20 died within a mean time of 0.20y, we conducted a retrospective analysis to determine if there were factors predictive of outcome. Pre-intervention factors studied included those shown in the table as well as serum albumin, hemoglobin,heart and respiratory rates(5 day averages),arterialized blood gases, and the type of Pseudemonas present in the sputum culture (cepacia or aerginosa).

	X̄ Age(y)		X̄ Wt/Ht%ideal		X̄FVC%predicted	
ALIVE 6M/4F	16.8±6.1(SD)	NS	82±11	NS	58±23	p<0.025
DIED 6F/4M	17.8±1.0		77±10		38±10	

Living patients had survived 1.5±1.0y at the time of this analysis. Patients who died lived only 0.2±0.2y after intervention. A multivariate analysis of the data yielded a linear function(D=116 .42-0.53(HR)-12.98(0=absence,1=presence of Ps.cepacia in sputum) $-0.95(PaCO_2)-1.01$(Age).$r^2=0.86$)which classified these patients as to outcome. Ten additional patients were assessed. Outcome was again correctly forecast with 8 of 10 surviving the refeeding period. Where D>0, survival of the refeeding process is probable. Where D<0, survival is not likely. The magnitude of D does not reflect a scale indicative of length of survival. We propose this function as an aid in determining if aggressive nutritional intervention is warranted in a particular malnourished CF patient with advanced lung disease.

† 690 LONGTERM GASTROSTOMY FEEDING IN MALNOURISHED C.F. PATIENTS.

L.Levy, P.Pencharz, P.Durie, M.Corey. Dept Paed,Res Inst,Hosp for Sick Children, Toronto, Canada.

Progressive malnutrition associated with a fall in lung function is a major clinical problem in CF patients. As we failed to restore energy balance by oral supplemental feeding, a feeding gastrostomy was inserted (incisionless method) in 14 CF patients (5M/9F), mean age 13y(5-22y) with growth failure (X̄ Ht.velocity= 74%standard,X̄ Wt.vel.=28%std.)malnutrition(X̄ Wt/Ht%std.=82)marked lung disease (X̄FEV_1=41%predicted)and steatorhoea. Overnight feeding with a semi-elemental formula (1000 Kcal) was done for up to 3.0y. Diet and medications were unchanged. Response was assessed with respect to changes in growth, body composition, and pulmonary function. Subjects were pair matched from the HSC CF data bank. There were marked changes in body comp.(total body potassium, nitrogen, fat, fat free mass) and growth rate as shown after a mean time of 1.2y (range 0.40-2.80y).

Δ%Fat	ΔFFM(kg)	ΔTBK(g)	ΔTBN(kg)	Δ% Ht Vel	Δ% WtVel
+2.9	+3.4	+18.0	+0.10	+332	+700
p<0.005	<0.005	<0.005	<0.05	<0.005	<0.005

Mean Wt/Ht%std.±SD increased 2.0±2.0 in the treated group and declined 3.0±2.0 in controls($p<0.05$). Mean change FEV_1%pred.was -5.4 in treated patients (NS) and -13.0 in controls ($p<0.01$).Two of three patients who died during this study outlived their controls by 1.3 and 1.8y. We conclude that timely introduction of nutritional support in selected malnourished CF patients may delay the rate of decline in lung function seen in this group of patients. The mechanism by which nutritional rehabilitation affects pulmonary function remains to be determined.