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SERUM 25-HYDROXYCHOLECALCIFEROL(25-OHD) LEVELS IN PATIENTS WITH CYSTIC FIBROSIS(CF). Van S.Hubbard, Philip M. Farrell and Paul A. diSant'Agnese, NIH, Bethesda.

Our previous study attempting to explain the paucity of reports of rickets in CF patients revealed elevated serum total vitamin D activity determined by bioassay(Pediat.Res.11:443, 1977). A more precise evaluation was sought by determining serum 25-OHD levels, the major circulating vitamin D metabolite, by a specific protein binding assay. Fasting blood was obtained from 17 patients with proved pancreatic insufficiency (PI) and 2 patients without PI aged 6-47 years. All patients with PI had received pancreatic enzyme and multivitamin supplements. All patients had normal serum Ca and P levels and none had radiographic evidence of rickets or osteomalacia.

CF Patients	With PI(n=17)	Without PI(n=2)	Normal
Carotene(μg/dl)	33 ± 7($\bar{x}$ ± SE)	119; 85	50-300
Vitamin A(IU/dl)	130 ± 15	103; 207	65-275
25-ODH(ng/ml)	33.6± 60	59.3; 112.0	15-80

The mean 25-OHD level in the lower range of normal in CF patients with PI with vitamin D supplementation is similar to findings for other fat soluble vitamins. 4 patients had levels below the normal range, with 1 being undetectable. CF patients without PI had high levels of 25-OHD. The observed difference between the results in our studies assessing vitamin D status is at least partially attributable to the assay for 25-OHD being specific, whereas the bioassay is non-specific and measures the sum of the activities due to vitamin D_2 and D_3 and their metabolites.

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RADIOLOGICAL AND ULTRASOUND EVALUATION OF THE GALLBLADDER (GB) IN PATIENTS WITH CYSTIC FIBROSIS (CF) Van S. Hubbard, Gordon L. Head, Thomas H. Shawker and Paul A. di Sant'Agnese. NIH, Bethesda, Maryland.

A 40% incidence of abnormal GB studies is reported in patients with CF and it is thought that the incidence increases markedly with age. Also, evaluation of the GB sometimes indicates the cause of abdominal pain in CF patients. Accordingly, we studied all CF patients over 14 years of age in our clinic. Results of oral cholecystograms in 31 CF patients are summarized.

	Patient Age (yr)			
X-ray Evaluation	14-17	18-20	21-47	Total
Normal	5(83%)	6(75%)	11(65%)	22(71%)
Abnormal	1(17%)	2(25%)	6(35%)	9(29%)
Nonvisualization	1	1	5	7(23%)
Calculi	0	1	1	2(6%)

6 out of the 7 patients with nonvisualization of the GB underwent ultrasonography. The GB remained undetectable in 4 and was smaller than normal (3 x 1cm) in 2. No calculi were seen on ultrasound in patients with nonvisualization on oral cholecystography, however calculi were identifiable by ultrasonography in patients known to have cholelithiasis. Our results indicate that although the incidence of abnormal GB studies increases slightly with age, the older CF patient does not have as significantly increased risk of GB disease as previously suspected (Am.J.Roentgenol.128: 953,1977). Also, ultrasonography may be a useful tool in the evaluation of the CF patient who presents with abdominal pain of unknown etiology, especially in the right upper quadrant.

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LIVER ULTRASTRUCTURE: DISSIMILARITY BETWEEN REYE'S SYNDROME AND HERITABLE DEFECT OF CARBAMYL PHOSPHATE SYNTHETASE OR ORNITHINE TRANSCARBAMYLASE. George Hug, Jeff Kline and William Schubert. Dept. of Pediatrics, Cincinnati, OH and Columbia, MO.

Liver in Reye's syndrome (RS) indicates marked fatty infiltration and by electronmicroscopy (EM) in mitochondria: ameboid disfiguration, variation in size, matrix rarefaction, absent granules. Biochemically in RS, the two mitochondrial urea cycle enzymes (carbamyl phosphate synthetase(CPS), ornithine transcarbamylase(OTC)) are transiently reduced to 28 and 32% of normal. Whether CPS or OTC reduction is responsible for the altered mitochondrial appearance was studied by EM of liver in: (A) heritable CPS deficiency (CPS < 5%); and in: (B) heritable OTC deficiency (OTC < 5%). EM-A indicated plethora of Golgi apparatus; unusual lipofuscin bodies; loss of microvili in dilated bile canaliculi; normal deposits of lipid and glycogen and no mitochondrial changes. EM-B indicated normal Golgi apparatus; minimal lipid and plentiful glycogen deposits; few residual bodies; autophagic vacuoles; microbodies varying widely in size (some ballooning) with floccular matrix and disintegrating membranes; in mitochondria: no enlargement; no ameboid disfiguration or matrix rarefaction; no granules. In summary: EM-A or EM-B (though showing abnormalities) was unlike EM-RS. Thus in RS, CPS or OTC reduction is not likely to cause the altered mitochondrial appearance; rather the biochemical and EM changes may both be the consequence of a primary mitochondrial injury.

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URINARY 3-METHYLHISTIDINE EXCRETION IN NORMAL AND STRESSED INFANTS.

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The unusual amino acid 3-methylhistidine (3MH) is present only in muscle (the major protein mass in the body). Urinary 3MH is an ideal indicator of protein catabolism because the one mole of 3MH released upon breakdown of each mole of actin and myosin heavy chain is excreted from the body without reutilization. We are presently investigating the effects of parenteral nutrition on the protein metabolic state of neonates whose oral nutrient intake for various clinical conditions is inadequate. In a preliminary study 17 3MH/creatinine ratio measurements were performed on spot urines in 6 premature and 5 term infants. The newborns who were healthy and growing were found to have a ratio of 0.222± 0.016 (mean and S.D.) which value is about two times higher than that of normal adults in our population. The 3MH/creatinine ratio was significantly elevated (range 0.270 - 0.690; mean 0.377 ± 143 S.D.) in infants who were losing weight and had low nutrient intake because of prematurity, sepsis or postoperative condition. The relatively high 3MH/creatinine ratio in normal growing infants is consistent with the elevated metabolic rate and protein turnover in neonates. The rise in the ratios of stressed infants reflects increased muscle protein catabolism which is apparently secondary to malnutrition. (Supported by HD-10235)

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CONCENTRATION OF CHOLESTEROL IN DIFFERENT BODY POOLS OF MINI-PIGS FED ATHEROGENIC AND CONTROL DIETS.

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Relationships of dietary cholesterol to its distribution and deposition in various tissues were studied in male mini-pigs fed isocaloric a high cholesterol-high fat (HC-HF) and control (C) diet from 30 through 55 weeks (wks) of age. Cholesterol was measured in serum at alternate wks throughout the study; in lipoprotein fractions, liver, muscle, and adipose tissue at the end of the experiment. Although cholesterol levels were higher in all tissues of HC-HF group, a statistically significant difference from the C group was observed only in case of cholesterol content of liver, serum and lipoprotein fractions. LDL and HDLc carried the highest amounts of cholesterol in the HC-HF group than the controls which had no HDLc. Cholesterol content of VLDL and HDL was also significantly greater in the HC-HF animals than the C group. A 4-fold increase in serum cholesterol was observed within 5 wks after feeding the HC-HF diet and a peak was reached within 15 wks followed by a significant decline to more or less a constant level after 40 wks of age despite a uniform daily intake of dietary cholesterol. It seems that the pig after 40 wks of age acquires some mechanism(s) to either metabolize dietary cholesterol more effectively or the endogenous synthesis of this steroid is decreased. (Supported from NIH grant (NS 06779-08) and Frank G. Bressler Research Fund.)

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EFFICACY OF PANCREATIN PREPARATIONS ON FAT AND NITROGEN ABSORPTIONS IN CYSTIC FIBROSIS PATIENTS.

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The efficacy of Viokase, Cotazym and Pancrease on fat and nitrogen absorptions were assessed in 12 cystic fibrosis patients, ages 8 to 14 years in a metabolic unit. Dietary intake was fixed for the entire study period for each patient. Mean intake of calories was 81 Kcal/Kg/d, fat 2.7 Gm/Kg/d and protein 3.0 Gm/Kg/d. 3 dosage levels of each preparation were used; Viokase 4,8 or 12 tablets, Cotazym 2,4 or 6 capsules and Pancrease 1,2 or 3 capsules per meal per metabolic period. Patients were randomly assigned to 1 of 2 study groups; Viokase or Cotazym verus Pancrease. Fat and nitrogen absorptions were significantly increased on each preparation over the placebo. But no significant difference in absorption was noted between the 3 preparations at each dosage level. The results of this study indicate that Pancrease, a pH sensitive enteric coated microspherules pancreatin preparation is as effective as Viokase and Cotazym, but at significantly lower enzyme doses.

	Mean % Absorp. ± S.E.		Ratio Total Enzyme Given	
	Fat	Nitrogen	Lipase	Proteases
Pancrease	79.1 ± 5.1	83.4 ± 2.9	1.0	1.0
Viokase	83.7 ± 3.5	88.2 ± 1.4	5.8	4.8
Cotazym	76.3 ± 7.9	86.8 ± 4.2	3.6	2.2
Placebo	67.9 ± 7.6	67.6 ± 8.2	0	0

Pancrease; Johnson & Johnson. Viokase; Viobin Corp. Cotazym; Organon, Inc.