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HYPERLIPOPROTEINEMIA ASSOCIATED WITH APO C-II VARIANTS AND APO E DEFICIENCY. R. Rebourcet, W.C. Breckenridge*, J.L. Bresson, R. Benbrahem, F.Rey AND J.Rey. INSERM U12, Hôpital des Enfants Malades, Paris, France. *Dept of Biochemistry, Dalhousie University, Halifax, Canada.

Lipoprotein lipase (LPL) deficiency and anomalies of LDL catabolism are both responsible for hypertriglyceridaemia and hypercholesterolaemia. Genes coding for apolipoprotein (apo)CII, the obligate LPL activator, and apo E, the signal part of LDL for its receptor captation, are closely linked on chromosome 19. We report here an unique case of a patient in whom a defect affecting both proteins has been demonstrated.

Plasma triglycerides (5000-7000 mg/dl) and cholesterol (500-700 mg/dl) were transported primarily by a small chylomicron remnant particle which contained apo B-48, B-100, apo AI and AIV but no detectable apo E by immunoassay or by Western blot of isoelectric focussing gels. Activation of LPL was reduced to 20 % of normal while plasma apo CII concentration were elevated 3-5 fold over normal values. Two dimensional electrophoresis with immunoblotting for apolipoproteins revealed apo CII with approximately the same molecular weight but with a different net electric charge than normal apo CII. The proband's parents who were first cousins, had slight elevations of triglycerides but no obvious abnormalities of apo CII. The subject was placed on fish oil diet. Despite a rapid increase in the content of eicosapentanoic acid (from 0,5% to 6,8 %) and docosahexaenoic acid (from 1,0 to 7,2 %) in plasma triglycerides there essentially was no change in plasma triglyceride concentration.

These data are consistent with the hypothesis that the patient is homozygote for a deletion affecting a segment of DNA coding for both a small part of apo CII and an important part of apo E. They suggest also that apo CII and apo E have coordinate regulation and may be processed together.

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PLASMA FATTY ACIDS IN PARENTERALLY FED PREMATURE AND TERM BORN INFANTS: CHANGES INDUCED BY INTRALIPID AND SUNFLOWER-SEED OIL. Yvan Vandenplas, Luc Leyssens, Adel Bougatef, Liliane Sacre, Baudouin François.

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Premature infants receiving PN free of fat soon develop essential fatty acid (EFA) deficiency, whereas they often have less than 1% of their body weight as fatdeposit. Experience has shown that Intralipid (IL) is a good source of calories and EFA. However, infants who are hypoxic, acidotic or septic present intolerance for IV administered fat-solutions, even at rates of infusion that have been tolerated before (Pediatr58:787,1976). Because these conditions are frequently encountered in premature babies and neonates, articles on cutaneous application of sunflower-oil (SO) appeared very attractive (Pediatr58:650,1976). 19 premature and term born babies on PN were studied during 14 days. IL 20% was administerd to 10; SO was rubbed 6times daily on the skin of 9. Plasma fatty acids were determined at birth, day 7 and 14. Levels of C16:0, C18:1, C18:2 and C20:4 did not change in the IL-group. In the SO-group a deficiency in C18:2 developed, that could be corrected by the administration of IL. We conclude that despites IL administration, is often controversal in prematures (displacement of albumin-bound bilirubin, altered synthesis of prostaglandins, cholestasis, impairment of pulmonary function and vasculitis, fat-overloading syndrome,...), the latter is necessary to prevent EFA deficiency. A deficiency in C18:2 can not be prevented by topical application of SO, even not in very-low-birth-weight infants.

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TOTAL PARENTERAL NUTRITION ASSOCIATED PHOSPHOLIPIDOSIS OF THE LIVER IN INFANTS.
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A variety of histologic aspects have been reported to occur during the course of parenteral nutrition(PN)in pediatrics as well as in adults patients.Phospholipidosis has been described with drugs administration.After a month of TPN we studied liver histology in 7 infants ranged from 2 to 8 months.All were without any previous liver disease and presented protracted diarrhea requiring bowel rest. PN Provided daily nitrogen(602±37mg/kg)and no protein energy(369±51KJ/kg) intakes,without intravenous fat emulsion during the first month. In addition to repeated liver function tests,we performed percutaneous liver biopsy after 30 PN days,using Hepafix® needle(1,4mm).Liver specimens were fixed in buffered formalin and stained using lipids histochemistry:oil red O,Nils blue,Holczinger,Adams and Baker OTAN.

Results indicated hepatocytes and macrophages phospholipidis deposits in 5 patients.Other abnormalities were observed including:portal and periportal fibrosis(5/7)bile ductular proliferation(6/7),severe portal and periportal inflammation(6/7)with mild necrosis in 2 patients;steatosis affecting less than 20% of hepatic parenchyma(2/7). Histologic cholestasis was not observed.

Beside well known liver abnormalities,hepatic phospholipidosis is first described during TPN in infants.The mechanism of this phospholipids accumulation is unknown.It could be due to the alteration of phospholipids metabolism and/or to the interaction with TPN solution components even in the absence of fat emulsion administration.

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SERUM GLYCINE (G) AND TAURINE (T) CONJUGATED BILE ACIDS (BA) IN PREMATURE FORMULA-FED INFANTS BEFORE AND AFTER TAURINE SUPPLEMENTATION.
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Tauro-conjugated BA,which are predominant during development,are more polar and more resistant to passive intestinal absorption than G-conjugated.To further elucidate the possible impact of postnatal BA conjugation pattern on the dynamic of enterohepatic circulation,we have studied 16 premature formula-fed infants (29-36 gw): at the age of 2 weeks,they were randomly assigned to receive an adapted formula(F)with or without T (25 µmol/dl).Before and after 4 weeks of this diet,fasting serum levels of cholic (CA) and chenodeoxycholic (CDCA) acids were determined by competitive solid phase enzyme immunoassay,after TLC separation of the G and T conjugated forms.

$\bar{X}$ + SEM	Formula n=8		Formula+T n=8		Adults n=10
CA (µMol/L)	9.0 ± 3.0	⟶ 8.4 ± 2.2	9.7 ± 3.1	⟶ 5.4 ± 1.5	0.4 ± 0.1
tauro-CA %	33.6 ± 2.8	31.3 ± 1.9	26.4 ± 4.8	42.7 ± 7.6	51.0 ± 5.0
CDCA (µMol/L)	13.2 ± 3.2	12.5 ± 3.0	9.4 ± 2.7	8.9 ± 1.9	1.0 ± 0.3
tauro-CDCA %	51.7 ± 5.3	42.1 ± 3.1	48.6 ± 6.0	55.0 ± 3.4	44.0 ± 4.7

The predominance of G-conjugates(mainly of CA)in serum of prematures,contrasts with the reported excess of T-conjugated BA in their duodenal fluid and may be due to later appearance of the active ileal transport system,for which T-conjugates are almost exclusively dependent to be absorbed.T-feeding produced a slight change in the relative proportion of G and T conjugates in serum,which seems limited to CA,in agreement with the "in vitro" observation of higher synthesis of conjugates for CA than CDCA.The sensible decrease of serum CA levels after T supplementation may be related to the inability of prematures to absorb increased amounts of tauro-CA,while extensive passive absorption would permit conservation of the more hydrophobic CDCA.

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FECAL BILE ACID (BA) EXCRETION IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE (IBD).
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Fecal BA composition was studied in children with IBD and healthy controls, using capillary column gas chromatography. The feces were collected during 72 hrs. 16 children with ulcerative colitis and 2 with Crohn's disease and colitis (age range 10-17 yrs) were compared to 5 healthy children (age range 10-17 yrs). All patients were on sulphasalazine and all except one had normal stools. The patients excreted significantly more BA than the controls, 8.43 ±0.8 (S.E.M.) mg/g dry wt feces and 3.06 ± 0.6 (S.E.M.) mg/g dry wt feces, respectively, p<0.001. The patients had significantly more primary and conjugated BA compared to controls.

BA	IBD a)	Controls a)	p
Cholic acid	1.80 ± 0.6 (21)	0.07 ± 0.02 (1.5)	p<0.005
Chenodeoxycholic acid	0.91 ± 0.3 (11)	0.05 ± 0.01 (2.5)	p<0.01
Glycin-conjugates	0.12 ± 0.02 (1.5)	0.02 ± 0.01 (0.5)	p<0.05
Taurine-conjugates	1.22 ± 0.2 (14.5)	0.05 ± 0.02 (1.5)	p<0.001
Sulphated	0.07 ± 0.02 (1.0)	0.05 ± 0.04 (1.5)	NS

a) Mean value ± S.E.M. mg/g dry wt feces. Values in brackets are % of total BA.

BA in fecal water (FW) were also studied. The FW was prepared by centrifugation of feces at 15000 rpm for 2 hrs. The total concentration of BA in FW was significantly higher in patients than controls, 0.08 ± 0.02 (S.E.M.) mg/g feces and 0.02 ± 0.005 (S.E.M.) mg/g feces respectively, p<0.001. The BA composition in FW was almost the same as in total feces, with more primary (48% vs 11%) and conjugated (8.5% vs 4%) BA in patients compared to controls. The study shows markedly changed BA pattern in juvenile IBD without diarrhea.

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DO IGF-1/SMC SERUM LEVELS REFLECT IMPAIRED GROWTH IN CROHN'S DISEASE ?
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Growth retardation in juvenile patients with Crohn's disease is only diagnosed retrospectively by growth rate measurements, however treatment requires early detection. In order to evaluate parameters useful to predict growth retardation we prospectively followed 26 juvenile patients and estimated standard deviation score of growth velocity (SDS-G), of weight gain (SDS-W), Best activity index (AI), and serum levels of α-1-glycoprotein (GP) and RIA-IGF-1/SmC.

Age corrected IGF-1/SmC levels were correlated to growth velocity (r=0.51). There was no relation to AI, GP and weight changes in these and a group of 17 adult patients (r-values:0.05 to 0.3). Specificity and sensitivity of these parameters possibly indicating growth retardation (<-0.3 SDS-G corrected to bone age) were calculated at the beginning (b) and the end (e) of the observation periods of 6-12 months:

	IGF-1 (<0.1 SD)	AI (>100)	GP (>90 mg/dl)	SDS-W (<-0.3)
(b) spec.	0.63	0.63	0.72	
(b) sens.	0.51	0.27	0.36	
(e) spec.	0.81	0.9	1.0	0.75
(e) sens.	0.63	0.25	0.25	0.25

IGF-1/SmC levels appear to be a superior index of growth retardation compared to the other parameters tested. Sensitivity and specificity could be increase to >0.9 and >0.8 respectively by selecting a SDS-G cutoff <-0.1, however calculation was limited by the small number of patients (n=5).