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EXAMINATION OF THE SEVERITY OF LIVER DISEASE, IN CHILDREN WITH THE NON-INVASIVE SALIVARY CAFFEINE CLEARANCE TEST

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Salivary caffeine clearance (SCC) can be considered a measure of hepatic microsomal enzyme activity. It may thus provide a quantitative assessment of hepatic function . To assess this we have studied 20 children with a variety of liver disorders; 8 had cirrhosis with serum albumin (ALB) < 35g/l . Caffeine (3mg/kg) was administered orally following an overnight fast. Salivary caffeine concentration was measured by HPLC at 0,1,4,6,12,24 hr. Caffeine saliva half life ($t_{\frac{1}{2}}$) was calculated from SCC. $t_{\frac{1}{2}}$ in normal controls ranged from 2.2 to 5.4 hr. $t_{\frac{1}{2}}$ in liver disease from 4.4 to 56 hr ; a significant correlation was obtained between $t_{\frac{1}{2}}$ and ALB (r=-0.65). There were also significant correlations with prothrombin time (PT) and total serum bilirubin (r= 0.65 and 0.84 respectively) ; there was no relationship between $t_{\frac{1}{2}}$ and any other liver function test. However, the mean PT and $t_{\frac{1}{2}}$ were significantly higher in the 8 cirrhotic children when compared to the other children. In two children, one with biliary cirrhosis and the other with alpha-1-antitrypsin, SCC improved dramatically following orthoptic liver transplantation, $t_{\frac{1}{2}}$ before /after;41 to 5.5 hr ,9.6 to 5.4 hr, respectively. In one child with Wilson's disease $t_{\frac{1}{2}}$ changed from 56 to 7.0 hr following treatment . We conclude that the SCC may permit quantification of liver function in a fashion not possible with standard biochemical tests

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CONGENITAL ANOMALIES IN EXTRAHEPATIC BILIARY ATRESIA (BA):AN ADDITIONAL REASON FOR EARLY RECOGNITION AND REFERRAL.

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With appropriate surgery prior to 8 wks of age, over 70% of patients with BA become jaundice-free & 90% survive beyond 10yrs.of age[1]. To assess the frequency of significant congenital anomalies butside the hepatobiliary system & their effect on management, we have retrospectively analysed the case records of 237 cases seen between June '70 & June '85. Major anomalies occurred in 47 (20%) 27 having more than one, 16 had one or more cardiac anomalies (Pulmonary stenosis 7, VSD 5, ASD 3, PDA3, others 7) requiring specific investigation which sometimes delayed biliary surgery.Operative management was complicated in 3 with intestinal atresia requiring prior surgery & a further 16 had intestinal malrotation. 17 (7%) had polysplenia & 2 asplenia. In 10 of these the portal vein was pre-duodenal. 9 had abdominal situs inversus making dissection & identification of structures in the portahepatis difficult. In the 171 cases operated on by one surgeon, age @ surgery rather than the presence or absence of anomalies was crucial in obtaining a jaundice-free state. This was achieved in 73% of those operated on by 8weeks of age, as opposed to 27% with later surgery. 8 of 31 (26%) with anomalies & 50 of 140 (33%) without are jaundice free. With more than 70% having surgery after the optimum age, earlier recognition & referral of suspected cases is essential.

1. Ohi R et al. World J.Surg. 9, 285-293 (1985)

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INCREASED ABSORPTION OF A FATTY MEAL TEST (FMT) IN CYSTIC FIBROSIS (CF) PATIENTS ON TAURINE (T).

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The aim of this study was to test the possibility that T supplementation could increase the absorption of a FMT in CF. In a cross-over design study four CF patients (12.1±2.6 yrs) and 3 controls received placebo (P) or T (30 mg/kg/j) for two 1-week periods a month apart, followed by a FMT (51 g/1.73 m^2 of triglycerides (TG) containing 60% of 18:2). Blood samples were drawn at 0,1,2,3,5,8 hrs. Tabulated results are expressed as the change in total TG (Δ % = peak increase), as TG area under the curve (AUC = mg•h/dl) and as the total amount of C 18:2 (mg %).

	P		T	P	T
TG peak	23.2±6.5	p<.05	62.6±11.9	74.7±27.1	95.2±48.4
TG (AUC)	130±86	p<.05	310±50	296±84	332±115
18:2 OH	38.9±3.0	NS	41.4± 2.9	93.2± 1.4	91.9± 4.9
18:2 peak	51.0±6.6	p<.05	70.0± 7.5	137.3± 5.7	147.3± 9.4

The difference of TG-AUC on and off T in CF was significantly (p<.05) correlated with the degree of steatorrhea, the Shwachman score and the weight percentiles. Two facts ruled out an endogenous origin of the above mentioned data: chylomicrons had a fatty acid pattern similar to that of FMT and their peak occurred simultaneously with TG and 18:2 peaks. These results suggest that T supplementation could be used as an adjuvant form of therapy in CF, particularly in patients with a severe steatorrhea.

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DEFECTIVE EXPRESSION OF HLA-DR ANTIGENS (DR-Ag) : ANOTHER CAUSE OF CHRONIC DIARRHEA.

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Defective expression of DR-Ag on mononuclear cells has been recently described as a new cause of combined immuno-deficiency, with chronic diarrhea and failure to thrive as main features. We were interested in relating these symptoms with an eventual defect of DR-Ag expression on enterocyte membranes, in 17 patients. 15 had diarrhea, starting between 1 and 6 months in 8, later on in 7, becoming chronic afterwards in all cases. Documented malabsorption was demonstrated in only 4. Candidiosis was noted in 16 and cryptosporidiosis in 3. Intestinal biopsies were performed in 10 patients : villous atrophy was partial in 8, subtotal in 2 ; intestinal IgA plasmocytes were absent in 4, strongly decreased in 3 out of 7. In 5 patients cryostat sections were incubated with various monoclonal antibodies directed against DR-Ag and lymphocyte subpopulations. In contrast to controls and coeliac patients, no enterocyte staining was visible either in the crypts or the villi. In 4 patients a strong epithelium and lamina propria infiltration of cytotoxic/suppressor lymphocytes was noted. In conclusion, chronic diarrhea, nearly constant in this disease, might be related more often to the near complete lack of immunological reactivity towards exogenous antigens than to the intestinal lesions observed. It is remarkable that the latter occured even though enterocytes did not express DR-Ag.

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INCREASED JEJUNAL PROSTAGLANDIN PGE2 CONCENTRATIONS IN CHILDREN WITH COELIAC DISEASE

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The purpose of the present study was to evaluate PGE2 levels in chronic enteropathy. 98 children (3 months-19 years) were studied: untreated coeliac disease (UCD) with total villous atrophy (TVA) (n=12), treated coeliac disease (TCD) with normal mucosae (n=3) ; untreated cow's milk protein intolerance (CMPI) with partial villous atrophy (PVA)(n=10) ; giardiasis (n=19) ; idiopathic chronic enteropathy (ICE) with PVA (n=22). 32 normal biopsies were used as controls. PGE2 concentrations (ng/g tissue) in jejunal samples (per-oral suction biopsies) were measured by radio immunological assay.

	RESULTS					
	UCD	TCD	CMPI	ICE	GIARDIASIS	CONTROLS
x	161	71	56	85	68	54
SEM	26	49	15	9,5	7,3	6,5
n	12	3	10	22	19	32

A significant difference was observed between UCD and all the other groups $p < 0,01$ but not between the latter. PGE2 concentration was significantly different in TVA versus PVA ($p<0,001$) or controls ($p<0,001$) and significantly correlated to the number of IEL ($p<0,001$). These data showed that the increase of intestinal PGE2 seems to be related to VA and to the number of intra epithelial lymphocytes (IEL).

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NON PARRALEL LEVELS OF SERUM IMMUNOREACTIVE PANCREATIC LIPASE AND PROTEOLYTIC ENZYMES AT BIRTH. ADAPTATION PROCESS IN NEONATAL LIFE ?

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Serum immunoreactive pancreatic lipase (Lip), trypsin(ogen)1(Tg) and chymotrypsinogen (ChTg) concentrations were determined in newborns (NB) and adults (Ad) sera, using specific and sensitive non-competitive enzyme immunoassays. The levels of proteolytic enzymes are either higher (Tg) or similar (ChTg) at birth than in adulthood whereas the levels of lipase are lower.(Mean (ug/l + sd) = Tg NB : 36±15 , Tg Ad :21±8 ; ChTg NB : 21±9 , ChTg Ad: 25 ±8 ; Lip NB : 4 ±3, Lip Ad : 12 ±7). The measurement of the 3 immunoreactive pancreatic enzymes in amniotic fluids (17-18 weeks of pregnancy) confirm the values observed in newborn sera . Tg and ChTg are present but with scattered values (from 5 to 100 ug/l), and lipase is nearly undetectable. The difference observed between proteolytic and lipase serum levels at birth could reflect an adaptative like process, due to the late appearance of enterokinase in the intra-uterine life (from the 26th week of pregnancy).A defect in the full conversion of proteolytic zymogens into active enzymes could lead to an increased synthesis of proteolytic enzymes as observed in adaptative studies when proteases inhibitors are added to the diet.