53 HANDLING OF MEDIUM CHAIN TRIGLYCERIDES (MCT) IN THE HUMAN STOMACH.

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We have shown previously that MCT are hydrolysed and absorbed from the stomach of suckling rats. We now report evidence that MCT are absorbed from the stomach of infants. Three groups of infants were chosen: 5 suffering from pyloric stenosis (P.S.), 7 from prematurity and 5 from miscellaneous problems. Infants with P.S. were chosen because of the delayed gastric emptying inherent to this condition so that the more rapid disappearance of MCT as compared to LCT must be due to absorption rather than to possibly more rapid gastric emptying of MCT. To each infant 10 ml/kg of formula were administered by gastric tube. Prematures received Enfalac (50% of fat as MCT) while the other groups received Pregestimil (40% MCT) (Mead-Johnson Co, Evansville, III). Aliquots of 3 ml. were removed at 0,20,40 and 60 minutes. We found that in the P.S. group 35% of Total MCT were absorbed in the first hour. Corresponding figures for the prematures and the miscellaneous groups were 22.8% and 58.5% respecticely. C_8 was absorbed more rapidly than C_{10}. These results show that MCT are absorbed from the gastric mucosa of infants. In view of the presence of MCT in breast milk and in infant formulas, this may be of physiological importance.

54 CHARACTERISATION OF ANTI-LIVER KIDNEY MICROSOMAL (LKM) ANTIBODY IN CHILDREN WITH AUTOIMMUNE CHRONIC ACTIVE HEPATITIS (aCAH)

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LKM antibody defines a subgroup of aCAH in childhood, characterised by a severe prognosis. To define the nature of this antibody we have determined, by indirect immunofluorescence technique, isotype and complement fixing ability of this antibody in 10 patients. Using anti-total immunoglobulin (Ig), anti LKM titres ranged between 1:40 and 1:160. When tested for the immunoglobulin classes IgG, IgM and IgA, LKM antibody proved to be IgG in all cases. When IgG subclasses were investigated, 9 of 10 patients had IgG1 titres similar to those obtained with anti-total Ig (1:80-1:640). IgG2 LKM antibody was present in low titre in 3 patients (1:20, 1:20, 1:40), including the one negative for IgG1. IgG4 LKM antibody was positive in two cases (1:40, 1:160), while no patient had IgG3 LKM antibody. In all instances anti-LKM proved to be able to fix complement (1:40-1:640). The restriction to the IgG1 isotype of anti-LKM antibody suggests a strong genetic influence on its production. Since LKM antibody has been shown to cross-react with liver plasma membrane (1) it is conceivable that this autoantibody contributes to liver damage by activating complement

(1) Lenzi M, et al., Clin.Exp.Immunol.1984,55,36-40

55 EVIDENCE OF IMPAIRED ANTIGEN NON-SPECIFIC BUT NORMAL ANTIGEN SPECIFIC SUPPRESSOR FUNCTION IN CHILDREN WITH AUTOIMMUNE CHRONIC ACTIVE HEPATITIS (aCAH)

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Children with aCAH have impaired Concanavalin A(Con A) induced suppression of Pokeweed stimulated immunoglobulin synthesis.Since this system tests non-specific immunoglobulin production, we investigated suppression of in vitro production of antibody to Tetanus toxoid (TT), a T-dependent antigen, by lymphocytes from 11 children with aCAH and 14 age-matched healthy controls, all previously immunized. Both patients and controls had similar serum anti-TT levels (mean ± SEM 1.8 ± 0.85 IU/ml, 2.0 ± 0.86 IU/ml) and in vitro production of anti-TT in response to optimal dose of TT (0.005 IU/ml)($5.3 \pm 0.88 \times 10^{-3}$ IU/ml, $6.7 \pm 0.94 \times 10^{-3}$ IU/ml) as measured by ELISA. Suppressor function was induced by 24 hour incubation of lymphocytes with high dose TT (5 IU/ml) or with 20μg/ml Con A. Washed cells were then added to stimulated autologous lymphocytes. TT-induced suppression of anti-TT production was similar in patients (69.8 ± 4.2) and controls (72 ± 3.8%). In contrast, Con A-induced suppression of anti-TT was significantly lower in patients (15.7 ± 2.5%) than controls (46.7 ± 4.9% $p<0.01$ Rank Test). Our data indicate that antibody production to a T-cell-dependent antigen is under the control of at least two regulatory mechanisms, one antigen specific and one antigen non-specific, only the latter being defective in aCAH.

56 ACTIVATION OF CYTOTOXIC-SUPPRESSOR HLA-DR POSITIVE T LYMPHOCYTES IN CHRONIC HEPATITIS B VIRUS (HBV) INFECTION IN CHILDHOOD

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Children with autoimmune chronic active hepatitis (aCAH) have preferential activation of T Lymphocytes expressing Interleukin-2 receptor (IL2r) and helper/inducer (H/I) phenotype. To assess whether a similar pattern of activation is present in HBV related chronic liver disease (CLD) we studied 19 children with chronic HBV infection, 13 having biochemical and/or histological evidence of CLD. HLA-DR and IL2r expression on purified T lymphocytes was assessed by immunofluorescence with phycoerythrin conjugated monoclonal antibodies. Functional subsets of activated T-cells were studied by double-staining with fluorescein conjugated anti-cytotoxic/suppressor (C/S)(Leu2) or H/I (Leu3) monoclonal antibodies. HLA-DR positive T-cells were significantly increased both in patients with (mean±SD 13.9±7%: $p<0.01$ Rank Test), and without evidence of CLD (8.9±1.8%, $p<0.01$) when compared to 18 healthy children (2.8±2%). 59% of the HLA-DR positive cells were C/S and 37% H/I. Percentage of IL2r positive T cells was similar in patients with chronic HBV infection (1.3±1.5%) and controls(0.14± 0.09%). In Chronic HBV infection there is preferential activation of T lymphocytes expressing HLA-DR and C/S phenotype. These may be the effectors of the in vitro cell cytotoxicity to autologous hepatocytes found in HBV related but not in autoimmune CLD (1).

(1) Mondelli M. et al. J.Ped 1985, 106, 899-907.

57 SERUM LAMININ - A NON-INVASIVE INDICATOR OF SINUSOIDAL CAPILLARIZATION IN HEPATOBILIARY DISORDERS OF INFANCY?

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In chronic liver disease, the development of a continuous basement membrane along the liver sinusoids (sinusoidal capillarization) results in impaired hepatic circulation and furthur liver damage. Using immunohistochemistry, we have shown laminin, a major component of basement membranes, to be present along the liver sinusioids in diagnostic biopsies from pre-cirrhotic infants (6 biliary atresia [BA] and 5 idiopathic hepatitis of infancy [IHI]) but absent in 4 with no histological abnormality. To determine whether this is reflected in serum, we have measured serum laminin at presentation in 32 patients with BA, 23 with IHI and 9 with α1-antitrypsin deficiency [α1ATD] and at follow up in 10 with BA, 9 with IHI and 6 with α1ATD.

At presentation, all patients had raised serum laminin (3.28±0.97 U/l in BA, 3.46±1.37 in IHI and 2.59±0.47 in α1ATD) compared to age-matched controls (1.67±0.41). At 40-60 week follow-up, serum laminin remained elevated in all 10 patients with BA; all had cirrhosis and laminin was similar in the 4 who were jaundiced and the 6 who were jaundice-free. In IHI, serum laminin became normal at follow-up in all patients, although 3 had cirrhosis (1 with jaundice) and 2 others had abnormal LFTS. Similarly, serum laminin became normal at follow up in all patients with α1ATD, although 4 had cirrhosis (none with jaundice) and the other 2 had abnormal LFTs.

We conclude that there is no clear cut association either at presentation or follow up between serum laminin and cirrhosis. Persistently elevated laminin in serum in surgically treated BA may reflect on-going sinusoidal capillarization.

58 BACTERIAL INFECTIONS: THE MAIN CAUSE OF NEONATAL CHOLESTASIS

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Different factors like parenteral nutrition, infusion of fat emulsions, short gestational age, low apgar scores, late enteral feeding, and infections are discussed in the genesis of "idiopathic" neonatal cholestasis. To test the **hypothesis** that bacterial infections are the main cause of cholestasis in intravenously fed infants two groups were studied retrospectively. Group I: 152 newborn infants who were born from 1973 till 1981 were fed intravenously for at least 7 days and developed severe bacterial infections. Group II: 92 newborn infants who were matched to the group I cases with respect to the year of birth, birth weight and gestational age, apgar scores and duration of parenteral nutrition but did not develop infections. Bacterial infections were diagnosed on the basis of impaired microcirculation with prolonged capillary filling time, shift to the left in the white differential and positive blood culture. Diagnosis of cholestasis was made at total bilirubin of ≥4 mg/dl with a portion of ≥40 % conjugated bilirubin. **Results:** All 40 cases of cholestasis were found in group I. All other above mentioned factors were distributed equally to both groups and could not be attributed as a major factor in the etiology of idiopathic neonatal cholestasis. **Conclusion:** Bacterial infections were the main cause of neonatal cholestasis.