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Abstracts selected for presentation at the XXI Annual Meeting of ESPGAN, Copenhagen, Denmark 19–21 May, 1988

1 CHANGES IN MUCOSAL MORPHOLOGY AND THE RATE OF CRYPT CELL RENEWAL INDUCED BY A CELL MEDIATED IMMUNE RESPONSE IN HUMAN SMALL INTESTINE

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T-cells in explants of human foetal small intestine (17–22 wk old) in organ culture were activated in situ with a T-cell mitogen (PWM) or monoclonal anti-CD3(T-cell)-antibody to directly test the hypothesis that activated T-cells play a role in the development of enteropathy in human small intestine. On days 1,3 and 5 post-activation, crypt cell production rate was measured by colchicine induced metaphase arrest, and villous height and crypt depth were directly measured after microdissection. T-cell activation in intestinal explants occured only in the lamina propria and was associated with crypt hypertrophy, short villi, and an increased rate of extrusion of enterocytes from the villous tips. The rate of crypt epithelial cell production was increased 10 - 20 fold compared with control cultures. These effects were not seen at day 1, peaked at day 3, and were still present at day 5. In younger fetal intestine which contains few T-cells, addition of PWM or anti-CD3-antibody only elicited minor changes in mucosal morphology. These experiments show that activated T-cells can cause changes in epithelial cell renewal in the human small intestine similar to those seen in a number of clinical enteropathies. This human model is easily manipulable in organ culture and should enable the dissection of the mechanisms underlying such changes.

2 ANTIBODY DEPENDENT CELL-MEDIATED CYTOTOXIC ACTIVITY IN INFANTS WITH COW'S MILK PROTEIN INTOLERANCE

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In the present study antibody dependent cell-mediated cytotoxicity (ADCC) against betalactoglobulin (BLG) was evaluated in infants with cow's milk protein intolerance (CMPI) as compared to infants with coeliac disease (CD) and healthy controls.

Methods: Sera from patients were tested in an ADCC assay with lymphocytes from healthy adults as effector cells, and as target cells autologous papainized erythrocytes coated with (BLG) using $CrCl_3$. A standard ^{51}Cr release technique was used in the assay. The ADCC-titres were related to the ELISA-titres for IgG- and IgA-antibodies against BLG.

Patients: CMPI; Late reactions, failure to thrive and villous atrophy n=8(A); Acute reactions, skin- and gastrointestinal symptoms n=6(B); Acute reactions, skin symptoms only, n=8(C) CD; untreated n=9(D); treated n=9(E). Healthy controls n=10(F).

Results	CMPI A	B	C	CD D	E	Controls F
(mean) ADCC	6.58±3.31	5.86±1.14	2.06±1.33	2.88±0.99	1.13±0.33	0.91±0.29
BLG-IgG	211	162	63	262	226	126
BLG-IgA	242	57	32	1738	318	193

The CMPI-group with gastrointestinal symptoms, irrespective of late or acute type, showed increased ADCC-titres compared with controls and the CMPI-group with skin symptoms only. The ADCC-titres in CMPI patients with gastrointestinal symptoms were found to correlate significantly with ELISA-titres against BLG for IgG ($p<0.001$). In contrast CD have low ADCC-activity, despite high antibody levels against BLG. According to the results, ADCC may be a immunopathologic mechanism in gastrointestinal CMPI.

3 RELATIONSHIP BETWEEN E. coli COLONISATION FACTOR I SPECIFIC SECRETORY IgA IN HUMAN MILK AND SALIVA

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The concept of a "common mucosal immune system" explains the presence of specific secretory IgA antibodies at sites distal to the gastrointestinal tract following antigenic stimulation of the human gut. The aim of this study was to determine the relationship between human milk and salivary secretory IgA (SIgA) specific to colonisation factor I (CFA/I) of Enterotoxigenic E. coli.

Enzyme linked immunosorbant assays were developed a) for the quantitation of SIgA and b) for the detection of CFA/I specific SIgA in human milk and saliva. Paired specimens of milk and saliva obtained from Sri Lankan (40), Asian immigrants to UK (12) and caucasian UK (45) women were analysed using the above methodology.

The percentage positivity of CFA/I specific milk SIgA in Sri Lankan and Asian immigrant women were 40% and 33% respectively. CFA/I specific salivary SIgA in these two groups were 45% and 42% respectively. No CFA/I specific SIgA was detected in milk and saliva from caucasian UK women. There was good correlation ($r = 0.56$, $p<0.01$) between CFA/I specific SIgA in breast milk and saliva from Sri Lankan and Asian immigrant women.

These findings, in addition to supporting the existence of an entero-mammary link in SIgA production, also provide evidence for the concept of a "common mucosal immune system".

4 NEONATAL AND ADULT MICE DIFFER IN THEIR IMMUNE RESPONSES TO GUT PROCESSED ANTIGEN

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We have previously shown that oral tolerance (OT) cannot be induced in newborn mice fed with ovalbumin (OA) at a dosage (1mg/g weight) known to induce systemic immune hyporesponsiveness in adult animals (1). We have also demonstrated that adoptive transfer of serum collected 1 hr after feeding OA induces antigen-specific suppression of systemic DTH responses in adult mice (2). The absence of neonatal OT induction could be responsible for clinical food hypersensitivity since this is most common in infancy. The underlying mechanisms may be due to immaturity of the immune system and/or the failure of the antigen processing by the gut. In our studies groups (n=6-10) of adult and neonatal BALB/C mice, including appropriate age-matched controls, were used. Serum collected 1 hr after feeding OA to adult mice was transferred (50ul/g weight) to mice aged 1, 3 and 42 days. Recipients were immunised with OA/CFA 4 weeks later. Systemic immune responses were measured 3 weeks after immunisation. The results show that systemic DTH responses were significantly suppressed (60%) in adult mice ($p<0.01$). In contrast, neonatal mice did not show suppression of DTH responses ($p>0.5$).

Conclusions: These findings suggest that immaturity of the antigen processing capacity of the gut is not the sole factor underlying the prevention of OT induction in neonates. The immaturity of the gut associated and/or systemic immune system is probably more important.

1. S Strobel et al. Paediatr Res (1984); 18:588.
2. S Strobel et al. Immunology (1983); 49:451.