41 ADENOVIRUS ANTIBODIES IN CHILDHOOD COELIAC DISEASE, ANTI-GLIADIN ANTIBODIES IN ADENOVIRUS DISEASED CHILDREN - WHAT IS THE CHAIN OF EVENTS?

Lähdeaho M-L, Lehtinen M, Mäki M, Parkkonen P, Rissa H-R, Hällström O, Visakorpi JK.

Medical Faculty, University of Tampere, Tampere, Finland.

We have analysed serum antibodies by ELISA to evaluate the possible relationship between adenovirus infections and coeliac disease (CD). Sera were collected from 24 children with CD (mean age 9.6 yrs, range 2-16.5 yrs) and 24 age- and sex-matched healthy controls. The sera were taken at the time of the initial diagnosis of CD. During autumn -88 an outbreak of adenovirus epidemic took place in our community. Paired sera from 62 children hospitalized for adenovirus infection were available.
The ELISA analysis revealed an excess of adenovirus IgA-antibodies in the children with CD. When antibodies to other viral antigens (rubella, mumps, herpes simplex virus) were measured increased IgA-antibody levels to rubella and mumps viruses were also found. Anti-gliadin antibodies were determined in the 62 adenovirus diseased children. In 9 cases the anti-gliadin antibody levels were found to be increased. When anti-reticulin antibodies were analysed 3 out of the 9 cases showed increased antibody levels.
Our results indicate that children with CD show enhanced IgA responses to viral infections, adenovirus included. CD may also predispose to adenovirus infections. We conclude that both the phenomena are most likely due to the genetic constitution and phenotype of the children with CD. The role of adenoviruses in the pathogenesis of CD remains open.

42 RESTRICTION FRAGMENT LENGHT POLYMORPHISM OF HLA CLASS II GENES IN COELIAC PATIENTS, THEIR FAMILY MEMBERS AND CONTROLS.

Saija Koskimies*, Virpi Lipsanen*, Markku Mäki**, Jarmo Visakorpi**

*Finnish Red Cross Blood Transfusion Service, Helsinki,**Department of Pediatrics, University Central Hospital of Tampere, Finland

We have analysed HLA class II polymorphism at the DNA level in coeliac patients. 25 patients and 35 controls were studied on Southern blot using restriction enzymes TaqI, MspI, PstI and BglII together with gene specific probes for DRα, DQα, DQß, DPα,DOß and DZα genes. Twelve families of 12 patients; a total of 35 healthy family members, were used to analyse class II haplotypes.

TaqI enzyme generated a fragment of 4.8 kb in size which could be visualized with DQα probe. This fragment was present in all patients but only in 27% of the controls. In 12 families studied, the fragment was present in 83% of the parents and 70% of the healthy siblings. The haplotype analysis revealed the frequency of the fragment to be 70% of the patients' haplotypes, 47% of the parents' and 30% of the healthy siblings' haplotypes. The fragment was present in 11 DR3 positive haplotypes which all differed in class I alleles from each other and it was absent in one DR3 positive haplotype. The fragment was also present in two DR5 positive haplotypes. A detailed RFLP analysis will be given on class II genes on haplotypes.
This fragment shows the strongest association to the coeliac disease shown thus far.

43 THE KINETICS OF ORAL HYPOSENSITISATION TO A PROTEIN ANTIGEN IN PREVIOUSLY IMMUNISED MICE

S. Strobel, H.-J. Peng and M. W. Turner

Department of Immunology, Institute of Child Health, University of London, 30 Guilford Street, London WC1N 1EH, U.K.

We have investigated the immunological consequences of feeding a protein antigen to previously immunised animals. BALB/c mice were systemically primed with ovalbumin (OVA) in complete Freund's adjuvant (CFA) and fed with high (10mg/g body weight), medium (1mg/g body weight) or low (1µg/g body weight) doses of OVA once (day 1, 7 or 14) or sequentially for 5 days (days 1-5, 7-11, 14-18). The specific IgG antibody response was suppressed only by early feeds of high-dose OVA (days 1-5). Medium-dose OVA fed on day 14 or low-dose OVA fed at any stage after immunisation enhanced the IgG antibody response. In contradistinction, systemic delayed-type hypersensitivity responses (DTH) were usually suppressed by early feeds of high or medium doses of OVA but never after feeding low-dose OVA. The results suggest that systemic DTH and IgG antibody responses to oral antigen are subject to different control mechanisms which depend on the immune status of the animal and are controlled by antigen dose, time and frequency of feeding. The immunologic effects observed are also demonstrable following adoptive transfer of spleen cells collected 14 days after multiple feeds of high-dose OVA to immunised mice. Our findings suggest that oral hyposensitisation after systemic immunisation is regulated by (suppressor) spleen cells which are activated by gut-processed antigen.

44 A RAT MODEL OF INTESTINAL HYPERSENSITIVITY: MUCOSAL MAST CELL ACTIVATION FOLLOWING REPEATED FEEDING OF ANTIGEN

M. W. Turner, Gabrielle E. Barnett & S. Strobel

Department of Immunology, Institute of Child Health, University of London, 30 Guilford Street, London, WC1N 1EH, U.K.

To study the effects of chronic enteral antigen administration to anaphylactically sensitised individuals and to study the involvement of the mucosal mast cell (MMC), we developed a rat model to monitor MMC activation by repeated blood measurements of the rat mast cell protease II (RMCPII). Groups of rats previously sensitised systemically with a low dose of ovalbumin were gavaged with buffer, ovalbumin, bovine serum albumin or a mixture of the two proteins over different time periods commencing 14 days after priming. Blood samples were obtained 1, 3 and 6 hours after the challenges and serum levels of the RMCPII determined by immunoassay. Release of this specific mucosal mast cell mediator was only observed in animals challenged with ovalbumin and the initial challenge released levels of RMCPII fifteen-fold higher than normal resting levels. Subsequent daily challenges evoked the release of progressively lower levels of mediator (four, three and two-fold higher than resting levels). After a ten-day rest period before further challenges the levels of RMCPII released were still within the lower range, whereas animals not previously challenged were still capable of releasing high levels of the mediator at the time of first mucosal contact with the antigen. This animal model will be useful in investigating the effects of chronic antigen administration on gastrointestinal and mucosal mast cell physiology.

45 YEAST OPSONISATION IN CHILDREN WITH CHRONIC DIARRHOEA

I.R. Sanderson, P. Hindocha, J.A. Walker-Smith

Queen Elizabeth Hospital for Children, London.

Children with defective yeast opsonisation are more likely to have chronic diarrhoea and this can be halted by infusion of fresh plasma[1]. It is not known whether these children have diarrhoea because of persistence of known stool pathogens, development of an enteropathy or some other mechanism. This study seeks to explore the association of stool pathogens and small intestinal enteropathy with defects in opsonisation. Thirty-two children (10F;22M, aged 3 mo to 7 yr) with chronic diarrhoea were investigated for yeast opsonisation, stool pathogens and an enteropathy. Thirteen (3F:10M) had severe opsonisation defects, of whom two had stool pathogens and six had an enteropathy, which appeared to account for the idarrhoea; however in six stool bacteriology an small bowel biopsy were normal and no other diagnosis was reached. Conversely, in those with normal opsonisation who had a normal small bowel biopsy and were free of stool pathogens a diagnosis was reached in all but one case. This included toddler's diarrhoea, response to food elimination. Severe atopy, IgE subclass deficiency and small intestinal bacterial overgrowth. The chronic diarrhoea found in children with defective yeast opsonisation often occurs independently of the presence of stool pathogens or an enteropathy.

1. Candy DCA et al. ARch Dis Chil 1980; 55 : 189.

46 INTRACTABLE ULCERATING ENTEROCOLITIS OF INFANCY

I.R.Sanderson, A.Risdon, J.A.Walker-Smith
Queen Elizabeth Hospital for Children, London

Five children (3M:2F) presenting in the first year of life with intractable diarrhoea had a number of distinctive features in common. All had ulcerating stomatitis; all had partial villous atrophy on proximal small intestinal biopsy; all had severe colitis, characterised by large ulcers with overhanging edges. (The intervening mucosa was inflamed and infiltrated by acute and chronic inflammatory cells. There were crypt abscesses, but in areas crypt architecture and goblet cell populatins were maintained); four had severe perianal ulcerations; no stool pathogens were detected. One child later developed ulceration of the distal small intestine.Therapy with steroids, sulphasalzine and azathioprine was unsuccessful. (Cyclosporin was tried in one without benefit). All five required subtotal colectomy and ileotomy.

Four are chidren of consanguinous marriages; two are siblings of Pakistani origin; two are cousins of arabic origin, the fifth is Portuguese.

A diagnosis of incomplete Behcet's syndrome has been suggested in two children because of the presence of flasked shaped ulceration, although a visculitis was not evident. In addition, none have abnormalities outside the gastro-intestinal tract. It is therefore possible that this is a distinct recessively inherited condition affecting the whole gastrointestinal tract, particularly the colon.