

41

AMINES PREVENT THE *IN VITRO* TOXICITY OF GLIADIN PEPTIDES (gp) ON CULTURES OF FETAL RAT INTESTINE AND INHIBIT THE AGGLUTINATING ACTIVITY ON K 562 (S) CELLS.

G. de Ritis*, L. Maiuri*, V. Raia*, M. De Vincenzi**, E. Mancini**, R. Porta*, V. Gentile*, S. Auricchio*.

*Dept of Pediatrics, II Medical School, and**Institutes of Chemistry and Biological Chemistry, I Medical School, University of Naples, Naples, Italy. °°Dept of Comparative Toxicology and Ecotoxicology, Istituto Superiore di Sanità, Rome, Italy.

All proteins and peptides which *in vitro* and/or *in vivo* are toxic for the celiac small intestine are able to damage the *in vitro* developing fetal rat intestine and to agglutinate K 562 (S) cells (S. Auricchio et al., J. Ped. Gastroenterol. and Nutr., 9, 23, 1985). The minimal concentration of peptic-tryptic gp agglutinating all the cells (MAC) was found to be 73 mg/l. Various amines were able to inhibit the agglutinating activity of gp. The minimal concentration (mM) of the amines completely preventing cell agglutination induced by a gp concentration four fold the MAC was: 1.3 for putrescine, 0.8 for spermidine, 1.2 for spermine, 3 for glycineethyl ester, 2.3 for histamine, 1.6 for serotonin and 2.5 for monodansylcadaverine. 10 mM spermine or spermidine were unable to protect the cells from the agglutinating activity of Wheat Germ Agglutinin and Concanavalin A. Spermidine 0.35 mM significantly protected the *in vitro* developing fetal rat intestine from the toxic activity of gp tested at a concentration of 0.1 mg/ml culture medium in 11 experiments. Spermidine and other amines are therefore able to prevent the activity of gp in these *in vitro* systems; this effect might be related to a possible regulatory role of amines in endocytosis and/or in brush border membrane functions (A. Elgavish et al., Biochim. Biophys. Acta 777, 1, 1984).

42

ABNORMAL INTESTINAL PERMEABILITY IN CHILDREN WITH IGA NEPHROPATHY (IgAN).

C. Pecoraro, R. Troncone, G. Parrilli*, V. Di Crosta, M. Mascagna, M. T. Saravou, G. Budillon*. Dept of Pediatrics and *Center of Hepatology, II Medical School, University of Naples, Naples, Italy.

Circulating immune complexes containing IgA have a pathogenetic role in IgAN. Dietary antigens are thought to represent a major component of immune complexes (1). Aim of this paper was to investigate the integrity of the gut mucosal barrier in children with IgAN.

Intestinal absorption and permeability were measured in 14 children with IgAN (mean age: 10.5±4.5 years), 12 celiac patients on normal diet and 15 age-matched controls. After an oral load of 2.5 g lactulose (Lac), 0.5 g rhamnose (Rh), 2.5 g D-xylose (Xy) and 1.25 g 3-O-methylglucose (3-O-MG), plasma levels and urinary recovery were assessed by thin layer chromatography (2).

Patients	n	Plasma ratio Xy/3-O-MG (2)	Urine ratio Lac/Rh (2)
Normals	15	1.13 ± 0.13	0.026 ± 0.013
IgAN	14	0.96 ± 0.26*	0.044 ± 0.020*
Celiac	12	0.49 ± 0.18**	0.140 ± 0.080**

Difference from normals: *p(0.05); **p(0.001)

The results indicate that abnormal gut permeability may play a role in IgAN. It remains to be established if it represents a primary defect or the result of a deranged mucosal immunity.

1) Sancho J. et al., Clin. Exp. Immunol., 1983, 54:194-202.

2) Menzies I.S. et al., Lancet 1979, ii, 1107-1109.

43

COLITIS AND COW'S MILK PROTEIN SENSITIVE ENTEROPATHY
JP. Olives, C. Le Tallec, E. Bloom, P. Agnese, J. Familiades, J. Ghisolfi. Médecine Infantile D et Laboratoire d'Anatomie Pathologique. CHU Purpan 31059 Toulouse Cédex FRANCE.

Cow's milk proteins induce noxious effects on the mucosae of the upper gastrointestinal tract. The purpose of this study is to appreciate the incidence of colonic involvement in cow's milk protein intolerance (CMPI) with confirmed villous atrophy.

29 children were investigated (17 boys-12 girls), aged 1 to 10 months. All received cow's milk protein for at least 20 consecutive days. Clinical symptoms and specifications of the diarrhea were collected. Jejunal biopsies were obtained with Watson's probe beyond Treitz flexure; all cases presented villous atrophy: partial: n=9, subtotal: n=13 and total: n=7. Colonoscopies and biopsies were performed with fiberoptic allowing rectosigmoid examination in all cases, exploration of the left colon in 12 cases and right colon in 3 cases. The degree of inflammation was quoted: normal moderate or severe according to endoscopic and pathological data.

Results: only nine children presented mucus and blood in their stools evoking colitis. Correlation between endoscopic and clinical features were as follow: both examinations were normal in 2 patients -19 apparently normal endoscopies displayed indisputable pathological signs of inflammation -8 patients showed both abnormal examinations and most particularly 2 children with severe ulcerative and hemorrhagic colitis.

Colonic mucosal inflammation was found in 93% of our cases. These microscopic lesions were moderate in 86%, but in 7% severe acute colitis was observed. These data seem to give evidence of the lesions throughout all the gastro intestinal tract during CMPI.

44

DRUG MODULATION OF INTESTINAL HYPERSENSITIVITY REACTIONS IN THE RAT

Turner MW, Boulton P, Levinsky RJ, Shields JG & Strobel S

Dept Immunology, Inst of Child Health, London WC1N 1EH, UK.

Bloch and Walker (1) showed that there was enhanced uptake of an unrelated bystander protein (bovine serum albumin) from the gut when rats pre-sensitized to ovalbumin were challenged intraduodenally with that antigen. We have recently confirmed and extended these observations (2) which may help to explain the development of multiple food protein hypersensitivities in man. In the present study we have used this animal model to investigate the modulatory action of various anti-allergic drugs on the uptake of bystander protein and release of the mediator serine protease RMCP II which is specific to the mucosal mast cell. Four drugs were tested at a single high dose by simultaneous administration with the BSA. Of these, beclomethasone dipropionate was the most effective in reducing BSA uptake (p<0.002). Nedocromil was also active (p<0.02) but disodium cromoglycate was only marginally active. Doxantrazole, a drug known to inhibit histamine release from mucosal mast cells *in vitro*, was, however, inactive. In contrast, at the doses used, none of these drugs had any effect on the release of the RMCP II enzyme. This suggests that the reduction in protein uptake from the gut observed with some drugs is not paralleled by any inhibition of RMCP II release.

(1) Bloch KJ & Walker WA (1981). J Allergy Clin Immunol 67:312.

(2) Turner MW et al (1988). Immunology (in press)

45

ANTIBODY RESPONSE TO YERSINIA ENTEROCOLITICA IN SERUM AND SALIVA OF THALASSAEMIC CHILDREN.

J M Hadjiminias, J A Walker-Smith, M G Hadjiminias and T T Macdonald

Department of Paediatric Gastroenterology, St Bartholomews Hospital, London and Thalassaemia Centre, Nicosia, Cyprus.

Y. enterocolitica requires iron for growth making thalassaemic children susceptible to infections with this organism. In order to investigate the hypothesis that a common mucosal immune system exists in man, serum and salivary antibodies to *Y. enterocolitica* O3 and serum antibodies to *E. coli* and *B. vulgatus* were measured by ELISA in Greek Cypriot thalassaemics and controls. Serum IgG antibody levels to *Y. enterocolitica* O3 were raised in 17/47 thalassaemics compared to 3/37 controls [p=0.006]. Serum IgA antibody levels were raised in 13/47 thalassaemics compared to 2/37 controls [p=0.018]. Serum IgM antibody levels were not significantly different in patients and controls. However serum IgG, IgA and IgM antibody levels to *E. coli* and *B. vulgatus* were not significantly different in thalassaemic patients compared to controls. Several thalassaemic patients also had raised salivary antibody to *Y. enterocolitica* indicating either transfer of IgA from serum to secretions or local salivary IgA production by B cells which have migrated there from the gut. It is concluded that a subset of Greek Cypriot thalassaemic patients have high antibody levels to *Y. enterocolitica* O3 indicating prior infection and that the presence of salivary antibodies to *Y. enterocolitica* provides preliminary evidence to support the hypothesis that a common mucosal immune system exists in man.

46

DOES BREAST FEEDING PROTECT AGAINST INFECTIOUS DISEASE IN THE FIRST 6 MONTHS OF LIFE IN DEVELOPED COUNTRIES? DH Rubin, JM Leventhal, PA Krasilnikoff, JF Jekel, B Weile, A Levee, M Kurzon, S Kuo, and

A Berget. Gentofte Univ. Hosp., Denmark, Albert Einstein Col. of Med., Bronx, NY and Yale Univ. Sch. of Med., New Haven, CT.

Prior studies investigating the relationship between infant feeding and infectious illnesses in developed countries have concluded that there is a protective effect of breast feeding against gastrointestinal illness during the first 6 months of life. However methodological shortcomings such as the failure: (1) to include illnesses managed at home, (2) to define carefully "illness" and "breast feeding," and (3) to consider the effect of confounding variables, have weakened the conclusions of these studies.

We prospectively studied 500 infants born consecutively in a university affiliated community hospital in Copenhagen, Denmark over the first 6 months of life using a detailed monthly mailed questionnaire (return rate at 6 months=77% (385/500)) which focused on feeding practices and illnesses. All or mostly breast feeding decreased from 88% (407/461) at 1 month to 7.5% (29/385) at 6 months of life. Using strict criteria for breast feeding and illnesses, gastrointestinal (GI) illnesses averaged 17.4%/month and upper respiratory (UR) illnesses averaged 27.8%/month. There was no relationship between the type of infant feeding and the incidence of these (GI and UR) or other infectious illnesses during the study period.

These data suggest there may be minimal protective effect of breast milk against infectious illnesses early in life in well fed urban populations in developed countries.