35 EFFECT OF NALOXONE ON THE MITOGENIC ACTIVITY OF PURE GLIADIN DERIVED PEPTIDES. A. Ashkenazi, D. Idar, R. Simantov. Inst. of Pediatric Research, The Unit of Pediatric Gastroenterology and Nutrition, Kaplan Hospital, Rehovot.

Gliadin peptides (GP) stimulate the incorporation of 3H thymidine in peripheral blood lymphocytes (FBL) in vitro. GP have opiate like activity in different in vitro systems. This activity was inhibited by naloxone and for this reason these endorphin-like compounds were named exorphins. In the present study we examined the mitogenic effect of two purified gliadin peptides: peptide 3142 and - 3146 in four groups of subjects. 1)-normal controls (NC), n= 23; 2) - Gastrointestinal investigation (GII), n=19; 3) - CD patients consuming normal gluten containing diet (CD ND), n=25; 4) -CD patients consuming gluten free diet (CD GFD), n=35. These peptides induced 3H thymidine uptake in PBL in a dose dependent way in a proportion of the samples tested. The effect of the active (-) stereoisomer of the opiate antagonist naloxone was tested in a selected group of PBL responding to the peptides 3142 and 3146. (-) Naloxone had a dose response inhibitory effect on the mitogenic activity of the gliadin peptides, whereas (+)naloxone had no effect. The conclusion of these results is that GP in susceptible subjects behave as opiates being in line with the recent finding that the amino acid sequence of the peptides used herein is similar to amino acids 12-17 of beta endorphin. The interaction between gliadin peptides and opioids may therefore play an important role in CD.

36 INTESTINAL MACROMOLECULAR TRANSMISSION: PEG 1000 AS A MARKER IN PRE- AND POSTCLOSURE PIGLETS. Weström, B.R., Tagesson, C., Karlsson, B.W.

We have shown that polyethyleneglycols in the 414-942 Da range (PEG 600) cross the intestinal mucosa of the pig regardless of whether the mucosa is permeable or not to protein (Gut 25:520, 1984). The results indicate that PEG 600 and other low Mw markers commonly used as permeability probes (mono- or disaccharides, e.g. mannitol and lactulose, and $^{51}$Cr-EDTA) are not suitable for studying macromolecular permeability. To find a more suitable marker for testing macromolecular intestinal transmission, PEG 1000 (766-1382 Da) was gavage-fed to newborn, unsuckled (preclosure) and 36 h old suckled (post-closure) pigs together with BSA and colostrum. The blood serum levels and the urinary recovery of BSA and the PEG polymers after 2 and 4 h were determined by reversed-phase HPLC.

The serum levels of the PEG:s were higher in preclosure than in postclosure piglets. An increased uptake of PEG:s greater than 1100 Da into the blood was also found in the preclosure pigs. The results indicate that PEG:s with a Mw > 1100 Da behave as macromolecules before and after intestinal closure, since they probable follow the same route of transmission as the macromolecules. Therefore these PEG:s may be useful as markers of macromolecular permeability.

37 INTESTINAL MACROMOLECULAR TRANSMISSION: THE USE OF THE NONAPEPTIDE DDAVP AS A MARKER IN GROWING RATS AND PIGS. Weström, B.R., Lundin, S., Karlsson, B.W.

Intestinal transmission of macromolecules occurs during the neonatal period for many species, but ceases (intestinal closure) in the rat at weaning, while already within 24-36 h after birth in the suckled pig. After closure, a small residual transmission of macromolecules to the blood is seen, which increases with decreasing Mw. The nonapeptide (Deamino-cysteine D-arginine) vasopressin, DDAVP (Mw = 1007 Da) was gavage-fed to pre- and postclosure and pre- and post-weaning rats and piglets. The blood serum concentration of DDAVP was used as a measure of the intestinal transmission and was determined with RIA after 0.5, 1, 2 and 4 h.

Significantly higher serum levels were found both in preclosure pigs (newborn, unsuckled) and rats (14 days old) as compared to postclosure pigs (36 h old) and rats (30 d old and weaned). In the piglet, the postclosure serum level was constant until weaning (32 days), when a marked decrease in the DDAVP level occurred after 4 days. However, the DDAVP concentration returned to the preweaning levels at 60 days of age. The results indicate that DDAVP might be a useful marker, since it behaves as a macromolecule around closure. In addition, DDAVP can be used to monitor intestinal permeability changes at weaning, where traditional macromolecules like BSA are of limited usefulness.

38 INTESTINAL UPTAKE AND TRANSMISSION OF FITC-DEXTRAN AND BSA IN THE NEONATAL PIG AND RAT. Ekström, G; Weström, B; Telemo, E; Karlsson, B.

Macromolecular transmission from the intestinal lumen into the circulation, and its cessation - intestinal closure, were investigated in young pigs and rats and compared to the capability of the enterocytes to internalize macromolecules. Pre- and postclosure pigs and rats were fed FITC-labelled dextran 70.000 and BSA by stomach tube. The intestinal transmission was assessed as the serum concentration of the markers after 4 or 6 hours, when the uptake of FITC-dextran into the enterocytes was also examined by fluorescence microscopy.

In both preclosure piglets (newborn, unsuckled) and rats (14 days old) high serum concentrations of the markers were correlated with highly fluorescent enterocytes, indicating a high uptake into the intestinal cells. Although the enterocytes in the postclosure pig (36 h old) showed high fluorescence similar to that in the preclosure pig, no marker transmission into blood occurred. In the postclosure rat (30 days old) fluorescence in the enterocytes was lacking and no transmission of markers was found. The results indicate that in the rat, intestinal closure is a consequence of a decline in the macromolecular uptake into the enterocytes, while in the pig, closure seems to be related to a cessation of further passage of internalized material through the cells into blood.

39 THE EFFECT OF COMPOSITION OF MILK FEEDS ON INTESTINAL MUCOSAL PERMEABILITY, MORPHOLOGY AND KINETICS IN THE NEWBORN LT Weaver & A Lucas
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Marked differences in intestinal mucosal permeability follow enteral feeding in the naturally and artificially fed human newborn. A guinea pig model has been used to study whether such changes are associated with morphological and kinetic changes.

17 newborn litters were fed either naturally (Nat) or a cow's milk formula (CMF) from days 1 to 5. Intestinal permeability was measured with lactulose and mannitol given as oral loads followed by five hr. urine collections. Jejunal crypt and villus morphology was studied by microdissection after bulk Feulgen staining. Mucosal proliferation was measured by a metaphase arrest technique.

Comparable growth was achieved between the two groups. Intestinal permeability to lactulose fell slightly in the Nat group, but rose rapidly and remained high in the CMF ($P<0.01$). There were no differences in the crypt depths or villus heights in the two groups. Crypt cell production rates were higher in the CMF group on all days ($P<0.01$).

The newborn guinea pig may be successfully reared on a CMF. Comparable changes in intestinal lactulose permeability occur in the newborn human and guinea pig. Cow's milk may damage the mucosa causing an elevation in passive permeability and a compensatory crypt cell proliferative response.

40 PROSTANOID CONTENT OF SMALL INTESTINAL MUCOSA IN RAT MODEL OF PROTEIN HYPERSENSITIVITY. D. Branski, P. Sharon, M. Eran, E. Gross-Kieselstein, S. Freier. Bikur Cholim Hospital and Shaare Zedek Hospital, Jerusalem, Israel.

The purpose of this investigation was to establish whether there is an elevated prostanoid content in the intestinal mucosa in rats suffering from an immediate type gastrointestinal allergic reaction. Ten rats of the Hooded-Lister strain were sensitized with 250 $\mu$g/0.5 ml ovalbumin(OA) intraperitoneally (i.p.) together with B. Pertussis adjuvant. On the 14th day a booster of 2.5 $\mu$g OA/0.5 ml was given i.p. This procedure has previously been shown by us to produce local intestinal hypersensitivity. Control rats were given adjuvant only. The challenge procedure was identical in test and controls. Five days after the booster the rats were challenged with OA. Twenty-five mg. OA was introduced intragastrically and 45 minutes later the rats were sacrificed and 5 cm. of proximal small intestine removed. Prostanoid content of scraped mucosa was determined by radioimmunoassay. It was found that the $PGE_2$ content in the sensitized intestine was $691 \pm 310$ pg/mg protein as compared to a level of $424 \pm 155$ pg/mg protein in controls This difference was significant ($p < 0.05$). There was no significant rise of 6-Keto $PGF_{1\alpha}$ or $TXB_2$ in the sensitized rats. These results show that $PGE_2$ participates in intestinal immediate type responses and may explain some of the clinical manifestations of food protein allergy.