29 THE ROLE OF CHOLECYSTOKININ (CCK), FOOD AND SUBSTANCE P (SP) IN THE RELEASE OF INTESTINAL IMMUNOGLOBULIN A (IgA).

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The ingestion of food augments the release of IgA in rat intestine. This study is intended to show that this phenomenon is mediated by CCK, and furthermore, that SP another of the gut-brain peptides also promotes a rise in intestinal IgA. Hooded Lister rats weighing 160-180 gm. were immunized with ovalbumin and Freund's complete adjuvant. On day 14 a booster dose was given. On day 21, a 10 cm. long segment of intestine was isolated 10 cm. distal to the pylorus and perfused with saline at a rate of 0.5 ml/2.5 mins. After a 10 mins. equilibration period, the CCK antagonist Proglumide(Milid Laboratories, Milano) 20 mg was injected i.v. to the "food" group. Ten mins. later 1 ml. of the protein hydrolysate Pregestimil (Mead Johnson Co. Evansville) was administered intragastrically. In the SP group, 25 μ m SP were administered i.v. Results: 1. In the "food" group, there was a significant rise of IgA after the administration of food ($P < 0.05$) and this was inhibited by the prior administration of the CCK antagonist. 2. In the SP group there was a significant rise of IgA at 2.5 mins. ($P < 0.001$) and this became significant again from 10-20 mins. Conclusion: 1. Food induced rise of IgA in the intestine is probably mediated by CCK as it is inhibited by a CCK antagonist, and 2. SP is another neuropeptide promoting IgA release in the intestine . The effect of SP is much more prolonged than that of CCK.

30 ORGAN CULTURE OF FETAL RAT PANCREAS : EFFECT OF CCK AND INSULIN ON AMYLASE ACTIVITY.

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In fetal rats, just before birth, there is a dramatic increase in pancreatic amylase activity. Besides the well demonstrated role of corticosteroids in this process, in vivo studies have suggested that CCK, a trophic hormone for the pancreas in adult rats, might also be involved (Werlin, Biol Neonate 1983 ; 44 : 287-94). Since in vivo studies cannot rule out an indirect maternal effect through corticosteroid secretion, we studied the direct effect of CCK on fetal rat pancreas in organ culture. Furthermore, the role of insulin, another important hormone for the exocrine pancreas in adult rats, was checked by using streptozotocin (STZ).

Pancreata from 20 day-old rat fetuses were cultured in a serum-free medium (SFM) for 6 days, with or without dexamethasone 3.10^{-6}M (DXM) and/ or CCK8 2.10^{-11}M. In the presence of these two hormones, and with or without insulin (0.1 U/ml),cultures were exposed to STZ 10^{-7}M for the first day of culture.Pancreatic explants were assayed for proteins and amylase on days 0, 2, 4, 6. Amylase specific activity (ASA) was expressed as percentage of day 0.

With SFM alone, almost all the ASA disappeared by day 2 (17.7 % ± 12.5), but was partially but significantly maintained when CCK (48.6% ± 8.8) or DXM (47.9% ±14.4) was added. The DXM effect was significantly maintained for 6 days but not the CCK effect which lasted only 2 days. On day 2 of culture the latter was dose-dependent with a maximum occuring between 10^{-12} and 10^{-10}M and was inhibited by aspertlcin 10 µM . A combination of CCK and DXM gave the best results in maintenance of ASA (87.4 % ± 21.8 on day 2 ; 81.9% ± 15.9 on day 4 ; 62.2% ± 10.3 on day 6).When cultures in this optimal medium (CCK + DXM) were exposed to streptozotozin for the first day of culture, a significant decrease of the ASA was found on days 4 (63.2% ± 21)and 6 (47.6% ± 12.8). This difference was corrected when, in the same protocol, insulin was added for the complete time of culture.

Conclusions : CCK, like DXM, is important in the prenatal development of the pancreas in the rat. Its action on ASA is different from and additive, but not synergistic, to that of DXM. The effect of STZ, corrected by insulin, suggests also a role for this hormone. The paracrine effect of insulin on exocrine pancreas, well demonstrated in the adult rat, might be already efficient in the fetus.

31 THE EFFECT OF DIETARY LACTOFERRIN AND IRON ON THE FAECAL FLORA OF THE NEWBORN

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The development of the faecal microflora in the gut of the breast fed infant could be attributed to the presence of lactoferrin and the absence of iron in breast milk. In vitro studies suggest that lactoferrin could inhibit colonisation of the gut by E. coli in the breast fed baby. Lactobacillus sp do not require iron as a growth factor which could contribute to their overgrowth in the gut of the breast fed baby.

The effects of bovine lactoferrin and iron (separately and in combination) in an infant formula on the aerobic and anaerobic faecal flora of 84 babies at 4 and 14 days were studied. 28 breast fed babies were also studied.

At 4 days there was no difference in the faecal microflora in the babies fed the 4 different diets, but more breast fed babies were colonised with Staphylococcus sp ($p<0.05$) and had an increased dominance of Bifidobacterium and Lactobacillus sp ($p<0.05$).

At 14 days lactoferrin had no effect on the composition of the faeces, but faeces from babies fed formulas lacking iron showed an overgrowth of Bifidobacterium and Lactobacillus sp ($p<0.05$) and a reduced dominance of Streptococcus sp ($p=0.07$).

A species difference (bovine not human lactoferrin was used) could be responsible for the apparent inactivity of the lactoferrin, but other factors (lysozyme and antibody) necessary for its in vitro bacteriostatic activity were not present in the formulas. A lack of iron in the formula tends to make the faeces similar to those of a breast fed infant. Perhaps this fact should be considered when adding iron to infant formulas to be consumed by the newborn.

32 CESIUM 134 + 137 IN BREAST MILK,COW'S MILK AND INFANT FORMULAS IN AUSTRIA AFTER THE CHERNOBYL ACCIDENT.

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Austria was among the countries with the highest deposition of 134 Cs and 137 Cs after the accident on April 26,1986. Therefore, we carefully monitored these radioisotopes through January ,1988. Using a sodium iodide scintillation detector, we analyzed 2131 samples of cow's milk from Austrian dairies, 221 pooled and individual breast milk samples and 242 samples of powdered infant formula. The detection limit for both 137 Cs and 134 Cs in 100 ml of milk was 3 Bq. Concentrations of 134 + 137 Cs combined (median; 95th percentile) in cow's milk were highest in May (48;491 Bq) and June (89; 213 Bq) 1986 and decreased until October 1986 (9; 38 Bq). A second increase was observed during the winter months 1986/87 with concentrations reaching their peak in April 1987 (69; 196 Bq). This was caused by the feeding of silage or hay that had been contaminated during the summer 1986. Since June 1987, the 95th percentile has not exceeded 37 Bq, the upper limit for infant food set by the EEC. The 95th percentile in breast milk and in infant formulas (imported from non-contaminated areas) never exceeded 21 Bq. Mothers were advised to continue breast-feeding as long as possible or to use infant formulas and until June 1987, mothers were advised to avoid feeding of cow's milk.

33 DEFECTIVE BILE SECRETION OF BILE ACID GLUCURONIDES IN RATS WITH HEREDITARY CONJUGATED HYPERBILIRUBINEMIA: IMPLICATIONS FOR THE MECHANISM OF CHOLESTASIS.

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Bile acids glucuronides have been identified in human bile, plasma and urine. We investigated the biliary secretion of lithocholate-3-O-glucuronide (LCG) and of cholate-3-O-glucuronide (CG), as well as the cholestatic potency of LCG in normal Wistar rats and in Wistar rats with hereditary conjugated hyperbilirubinemia. These rats show an impaired biliary secretion of bilirubin conjugates and other organic anions, but have a normal bile acid secretion. Bile secretion of an i.v. administered dose of (3H)LCG was strongly reduced in the mutant rats; 24% recovery in bile at 1h after injection vs. 96% in control rats. Corresponding values for biliary recovery of (3H)CG at 1h were 71% and 98% resp. Bile secretion of (3H)LCG was delayed by i.v. infusion of dibromosulphthalein (DBSP, 1.1 umol/min/kg) in control rats, whereas that of a simultaneously administered tracer dose of (14C)taurocholic acid was slightly accelerated. Low doses of LCG (0.5-2.0 mg) caused a transient reduction of bile flow in control rats, followed by a choleresis. A dose of 4 mg caused an almost complete cessation of the bile flow within 30 min. In contrast, LCG at the same dosages did not affect bile production in the mutants. It is concluded that bile acid-3-O-glucuronides share transport systems for biliary secretion with bilirubin and DBSP. Our data indicate that transport across the canalicular membrane is of importance for the development of LCG-induced cholestasis.

34 LACTULOSE AND AMMONIA METABOLISM

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It is commonly believed that lactulose lowers the blood NH_4 by acidification of the colonic contents and by its laxative effects. We have reason to believe that the major effect of lactulose on blood NH_4 is due to bacterial absorption of NH_4. To differentiate between the effects of pH and the presence of an energy source, 4 suspensions were prepared from single stool specimens of 19 healthy volunteers. 2 suspensions were kept at pH 7.0 and two at pH 5.0. After 6 and 18 h of incubation lactulose (62mg/g) was added to 1 suspension of each pH. NH_4 was measured after 1,6,12,18 and 24 h.

Ammonia mmol/l, mean, (SD), n=19

Hour	Contr pH7	Contr pH5	Lact pH7	Lact pH5
1	2.7 (1.3)	2.2 (1.2)	2.6 (1.1)	2.2 (1.1)
6	5.9 (1.7)	3.3 (1.4)	5.7 (1.7)	3.2 (1.4)
12	7.9 (1.4)	4.4 (1.8)	1.2 (1.7)	2.3 (1.3)
18	9.9 (2.3)	5.3 (2.0)	4.0 (2.8)	1.6 (1.1)
24	10.1 (2.5)	5.7 (2.0)	0.5 (1.0)	0.5 (0.8)

Mean NH_4 conc. in Contr pH5 compared to Contr pH7 was 56.4% after 24 h. Addition of lactulose invariably caused a large decrease in NH_4,resulting in mean conc. of 4.4% (pH7) and 7.9% (pH5) compared to control incubations. We conclude that lactulose reduces already formed NH_4. This is pH independent. The NH_4 reduction is caused by bacterial utilization and exerts a more important effect on lowering NH_4 than the slower production rate caused by acidification.