CCK stimulation on rat acini (Korc et al. Am. J. Physiol. 241 (1981) G116–G121; Matozaki et al., Am. J. Physiol. 257 (1989) G594–G600).

In conclusion, these data clearly demonstrate that in transgenic mouse acini the activation of pancreatic CCK_B/gastrin receptors with gastrin stimulates crucial biological functions of the pancreas.

Communication no. 5

Histological changes in the upper gut by CCK-A receptor antagonist administration in neonatal calves. M. Biernat[a], P. Sysa[a], B. Sosak-Swiderska[b], I. Le Huërou-Luron[c], R. Zabielski[d], P. Guilloteau[c] ([a] Department of Histology and Embryology, Warsaw Agricultural University, Warsaw, Poland; [b] Department of Analitical Research, Institute of Ecology, Polish Academy of Sciences, Dziekanow L., Poland; [c] Laboratoire du Jeune Ruminant, Inra, 65, rue de St Brieuc, 35042 Rennes, France; [d] Department of Animal Physiology, Warsaw Agricultural University, Warsaw, Poland)

Little is known on the role of CCK in the development of the upper gut in mammalian species. The aim of the present study was to investigate the role of CCK in exocrine pancreatic secretion and in the upper gut micro structure in neonatal calves assessed by a repetitive intraduodenal administration of a selective CCK-A receptor antagonist (FK-480, Fujisawa Pharmaceuticals, Osaka, Japan). The experiment was performed on ten neonatal calves (six control and four treated with CCK-A receptor antagonist) surgically prepared with an accessory pancreatic duct catheter as well as duodenal and duodenal bulb cannulas. Surgery was performed under halothane + rompun general anaesthesia soon after birth. The secretion of pancreatic juice was measured everyday before and after the morning and evening meals and the juice was analysed for volume and trypsin output. The perfusions with FK480 were made during the first 6 days of life before morning and evening colostrum (days 1 and 2) and milk (days 3–6) feeding. CCK-A receptor antagonist was administered for 1.5 h into the duodenal bulb cannula with a peristaltic pump (0.5 mg/kg/h). On day 7, 3-cm-long whole thickness segments of the small intestine (duodenal bulb, mid-duodenum, proximal jejunum and terminal ileum) were fixed in Bouin's solution. After hematoxylin and eosine staining, the depth of crypts, length and width of villi and thickness of tunica mucosa and muscularis mucosa were measured (mean + SEM).

The periprandial pancreatic juice secretion was significantly reduced in FK480-treated calves. This reduction in juice volume and trypsin activity mostly concerned preprandial secretion and the secretion during feeding (i.e. cephalic phase). The depth of the crypt in the duodenal bulb in FK480-treated calves was significantly greater than that in control calves (257 ± 4 versus 232 ± 4 μm, $P < 0.0001$). In contrast, the depth of crypt in the mid-duodenum, jejunum and ileum of FK480-treated calves was significantly smaller than that in control calves. The length of villi in FK480-treated calves did not differ from control calves besides in the jejunum (848 ± 12 versus 568 ± 22 μm, $P < 0.0001$). The width of villi was increased in the duodenal bulb and reduced in the other parts of the intestine. The mucosa thickness was reduced in the mid-duodenum (1005 ± 17 versus 916 ± 14 μm, $P = 0.0012$), and increased in the jejunum (883 ± 20 versus 1115 ± 13 μm, $P < 0.0001$) in FK480-treated calves. The thickness of the tunica muscularis was not significantly different in the duodenum, whereas it was increased in the jejunum (264 ± 8 versus 284 ± 7 μm, $P = 0.0012$), and reduced in the ileum (322 ± 9 versus 295 ± 10 μm, $P = 0.036$).

The present results suggest that the blockade of CCK-A receptors by FK480 during the first 6 days of life reduced the pancreatic

exocrine secretion and induced several modifications of the microstructure of the upper gut. The structural changes in the proximal part of the small intestine are not surprising, since the expression of CCK-A receptors has been demonstrated in several animal species. In contrast, no CCK-A receptor mRNA has been found in the ileum. In conclusion, in neonatal calves the influence of CCK on upper gut development has been shown. It could act both directly via CCK-A receptors expressed on the upper part of the small intestine and indirectly by the modulation of pancreatic secretion.

Communication no. 6

Effect of nitrite on electrical activity of rat gastric fundus and duodenum in vivo. M. Ceregrzyn, M. Wiechetek (Department of Pharmacology and Toxicology, Faculty of Veterinary Medicine, Warsaw Agricultural University, Nowoursynowska 166, 02-787 Warsaw, Poland)

In addition to methemoglobin formation and vasodilatation, nitrites influence the motility of the gastrointestinal tract. Our recent observations show that nitrite markedly decreases gastrointestinal motility in vitro and it should be pointed out that the in vitro effects of nitrite are elicited by doses that do not cause classic toxic signs. Thus, the aim of the present study was to determine if doses considered non-toxic might induce changes in gastrointestinal electrical activity in rats in vivo.

The experiment was performed on four female Wistar rats. Two bipolar electrodes were surgically implanted, one in the stomach (the border between fundus and corpus, along the greater curvature) and the second in the duodenum. The intragastric cannula was placed into the stomach near the oesophagus on the lesser curvature. The experiment was performed 10 days after surgery on freely moving animals, which had free access to water and food until the experiment began. The electrical activity of the gastrointestinal tract was recorded 30 min before and 90 min after the 0.9 % NaCl or sodium nitrite (SN) administration (single dosage of 0.5 mL of $NaNO_2$ solution through an intragastric cannula reaching doses of 20, 30 or 65 $mg \cdot kg^{-1}$). The recording of the electrical activity was performed using an analogue digital recording system (MacLab, ADInstrments). The frequency of sampling was 100 samples/s, the signal was filtered at 50 Hz (high frequency cut) and 0.3 Hz (low frequency cut).

SN caused a change in the spiking activity of the gastrointestinal tract, whereas the administration of the same volume of 0.9 % NaCl did not cause any changes in the electrical activity of rat stomach and duodenum. The frequency of spikes during the control period of observation was 48.35 ± 13 and 27.2 ± 5 spikes/min (± SEM) in the stomach and in the duodenum, respectively. Twenty $mg \cdot kg^{-1}$ of SN was the lowest effective dose decreasing the frequency of spikes in the stomach and in the duodenum. The decrease in the frequency was observed for 10 min after the SN administration and the inhibition of electrical activity lasted about 60 min. The frequency of spikes recorded 10 min after the administration of 20 $mg \cdot kg^{-1}$ SN reached 26.6 ± 1 and 22.1 ± 1 spikes/min in the stomach and in the duodenum, respectively. The amplitude of spikes remained unchanged except during the short interval of the lowest frequency observed after the administration of the highest dose of SN (65 $mg \cdot kg^{-1}$). Clinical signs of methemoglobinemia (cyanosis and increased breath rate/min from 40 ± 5 in the control period to 65 ± 4) appeared 80 min after nitrite administration only in the case of the highest dose of SN.

The results obtained indicate that nitrites in doses not producing clinical signs of methemoglobinemia induce changes in the electrical activity of the stomach and the duodenum of rats.