

the gallbladder is enhanced also by prostaglandins which are released from the distended wall. The distension and increased intraluminal pressure simultaneously result in ischaemia of the gallbladder mucosa and wall. These chemical and mechanical influences cause inflammation even prior to the bacterial contamination which usually takes place later. The gallbladder at the culmen of inflammation is thickened, oedematous and hyperaemic, filled with turbid bile containing a large amount of fibrin and pus. The state of the gallbladder containing only pus is referred to as gallbladder **empyema**. The gallbladder in severe cases changes into a greenish black necrotic sack with larger or smaller perforations – **gangrenous cholecystitis**.

Approximately 5–10% of cases of acute cholecystitis develop without the presence of bile stones (**acalculous cholecystitis**). The causes of the inflammation include serious trauma and burns, difficult parturitions, simultaneous failure of several organs, sepsis, etc. The gallbladder is usually large and tense, with evident weakness and slowness of evacuation. The main cause is considered to be the ischaemic impairment of the gallbladder as the cystic artery is the terminal artery without collateral circulation.

Acute cholecystitis usually begins as an attack of biliary colic which does not withdraw and is accompanied by fever and further signs of inflammation (leukocytosis, high rate of erythrocyte sedimentation). Anorexia associated with vomiting can lead even to extracellular volume depletion. The appearance of jaundice signifies either obstruction of the biliary pathways by a stone, or a state when the oedematous inflammation involves the bile ducts and surrounding lymph nodes. Acute cholecystitis can be the cause of severe complications. The bile stasis is inclined to become complicated by e.g. bacterial superinfection which spreads via lymphogenic and ascendent pathways and causes an inflammation of intrahepatic biliary ducts (cholangitis), perforation with the development of abscess, rupture with generalized peritonitis, fistula with bile or stone drainage into the adjacent organs etc.

Chronic cholecystitis develops in 90% of cases in consequence of repeated acute cholecystitis or due to permanent mechanical irritation of the wall of the gallbladder. The gallbladder is shrunk, its wall is thickened, fibrotically changed and physiologically unfunctional. The disease often has a latent course

with dyspeptic difficulties after dietary faults, with infrequent acute exacerbations. A prolonged total obstruction of the cystic duct causes that the lumen of the obstructed gallbladder fills and progressively distends with mucus (**mucocoele**) or clear transudate (**hydrops**) produced by mucosal epithelial cells.

7.22 Gastrointestinal hormones

The contacts of the human organism with the surrounding environment are intermediated by complicated neurohumoral pathways. The neurohumoral connection with the gastrointestinal tract represents an extensive labyrinth, the junctions of which are only partially known.

The major contact of the gastrointestinal tract with the external environment represents the food intake. Almost all gastrointestinal hormones are secreted as a response to the accepted food.

Gastrin is produced by G cells of the antral glands of the duodenum and small intestine. Coffein and wine (not destilates) stimulate its release similarly as proteins and amino acids (especially fenylalanine and tryptophane). GRP (gastrin-releasing peptide) and its equivalent in apmhibians – bombesin, have a stimulating effect whereas somatostatin (SMS) suppresses its release. Gastrin belongs to the strongest secretogogues of the gastric juice. It affects the motility and trophics of the gastric and intestinal mucosae. The antagonist of gastrin – proglumid – inhibits the growth of the cellular line of colorectal carcinoma in tissue cultures.

Cholecystokinin (CCK) is produced by I cells of the duodenum and upper jejunum. As most important function is considered to be the stimulation of the secretion of pancreatic juice, induction of the contractions of the gallbladder and relaxation of Oddi's sphincter, as well as the lower oesophageal sphincter. CCK stimulates the peristalsis of gastric antrum, small and large intestines, causes hypertrophy and hyperplasia of the pancreatic cells, improves the lymphatic flow and moderately stimulates the gastric secretion. It belongs to the so-called hor-

mones of satiety and carefreeness. The neurons containing CCK affect the myenteric and Meissner's submucosal plexi, thus inducing motility. CCK increases the release of insulin and somatostatin from the pancreas, pancreatic polypeptide, gastric inhibitory peptide and calcitonin.

Secretin is produced by S cells of the duodenum and jejunum. It stimulates the secretion of fluid and bicarbonates in pancreas, large intestine, and secretion of pepsin in the stomach. It inhibits the secretion of HCl, motility of the stomach and the tonus of the lower oesophageal sphincter. It supports the chemically induced carcinogenesis in the pancreas. Its level decreases in coincidence with peptic ulcers.

Motilin is produced in M cells of the duodenum. It induces the contractile activity of the stomach and intestines. Its effect is cancelled by atropin and antimotilin serum. Erythromycin and its analogues stimulate the interdigestive myoelectric complex by the fact that they bind with the receptor in the small intestine. The erythromycin derivate EM 5231 increases the release of motilin and is 18-fold more effective than erythromycin. Assumedly, it could be used as remedy (antidepressants, anticholinergics, diuretics) and for hypomotility of bowels induced by surgery.

Gastrin-releasing peptide (GRP) or bombesin occurs in nerves, stomach and intestines. It is a strong stimulator of gastrointestinal peptides i.e. of gastrin, PP, CCK, motilin, neurotensin, enteroglucagon, glucagon, insulin and somatostatin. Both, central and peripheral administrations induce the sensation of satiety. It is also produced by small cellular carcinoma of the lungs where it acts as an autocrine growth factor. The central administration cancels thermoregulation and leads to hypoglycaemia. Assumedly it also plays a role in carcinogenesis. It was revealed that its receptor antagonist RC-3095 might have a role in the therapy of pancreatic carcinoma.

Neurotensin is produced by N cells and nerves in the ileum and large intestine. It decreases the tonus of oesophageal and intestinal sphincters, peristalsis, the gastric, intestinal and pancreatic secretions and blood perfusion. It stimulates the smooth muscles of the large intestine. By its means, the so-called ileal brake takes place, which is a delayed peristalsis in the small intestine in the instance when the chyme enters the duodenum. It is assumedly responsible for the gastrocolic reflex.

Pancreatic polypeptide is released from PP cells in the neighbourhood of Langerhans islets which occur between A and B cells. Only 10% of pancreatic polypeptides come from the duodenal mucosa. Plasmatic concentration of the pancreatic polypeptide is increased in endocrine active tumours of the pancreas, after vagus stimulation and in stress. It might serve as a tumour marker and a marker of stress.

YY polypeptide is released from L cells of the duodenum, jejunum, ileocolic mucosa and pancreas. The term YY is given by the fact that at each end of the peptide is a molecule of tyrosine. It inhibits the secretion and motility of pancreas and stomach, increases the resorption of fat and other nutrients by delaying the transition of chyme via intestines. It delays the evacuation of the stomach. It is co-responsible for the so-called ileal brake which serves for the improvement of the resorption of nutrients. Unabsorbed nutrients in the ileum decrease the evacuation of the stomach, pancreatic secretion and intestinal motility so that time is acquired for an additional resorption of nutrients.

Substance P (SP, tachykinin) occurs in the nervous and muscular sheaths, but also in endocrine cells of the duodenum. It stimulates the secretion of saliva, pancreatic and intestinal exocrine secretion. It inhibits the release of somatostatin (SMS). It releases acetylcholine, dopamine and serotonin. It inhibits the absorption of sodium and increases the secretion of chlorine in the small intestine. It causes vasodilation and hypotension in the splanchnic region. The substance P is secreted by some carcinoids. A deficit of the fibers producing SP was observed in the intestine in Hirschsprung's disease. SP has an impact in the projection of pain.

Glucagon is a hormone of alpha cells of the Langerhans islets. It stimulates glycogenolysis, gluconeogenesis and lipolysis. It inhibits gastric and intestinal motility and absorption and decreases the tonus of the oesophageal sphincter.

Enteroglucagon is a hormone of extrapancreatic origin. It is produced by L cells of the ileum and large intestine. The trophic effect of enteroglucagon on the mucosa of the small intestine might have an impact on the malabsorption syndrome. Antispastic effect and inhibition of the secretion in the small and large intestine is already now exploited in diagnostics.

Galanine is a neuropeptide of the submucosal and

myenteric plexus and nerves of the pancreas. It stimulates ravenous appetite, inhibits insulin and SMS secretion. At the same time it stimulates the release of glucagon.

Gastric inhibitory polypeptide (GIP) is produced by endocrine K cells of the duodenum and jejunum. The original term (GIP) which referred to its ability to inhibit the secretion of HCl was due to its function – stimulation of insulin secretion changed into the term the glucoso-dependent insulinotropic peptide. It is released especially after oral administration of glucose. In coincidence with inadequate GIP secretion, the organism is procured by the fact that its secretion does not increase after the intake of polysaccharides, but only after the increase of glycaemia.

Neuropeptide Y is produced by the nervous endings in the brain, medulla and enteric nervous system. Intravenous administration causes vasoconstriction, stimulates the intake of food and changes the circadian rhythms. Vasoconstriction is of long-term character. The effect of neuropeptide Y is 124-fold stronger than that of noradrenaline. It decreases the motility and perfusion. Central administration leads to a reverse situation, i.e. hypotension, reduction in pulse and number of breaths per minute.

Opioid peptides. Two substances with the properties of opiates – the met- (methionine) and leu- (leucine) enkephalins were isolated in 1975. These substances represent sequences of the large original molecule of proopiomelanocortin which contains also ACTH and MSH (melanocytes-stimulating hormone). Opioid peptides increase K^+ -conduction in nerves, inhibit the release of acetylcholine, substance P and noradrenaline. They delay the intestinal transition and as exogenous morphine they increase the tonus of Oddi's sphincter and inhibit the blood flow through the mucosa. They regulate the glucose homeostasis. Enkephalin is a neuromediator of GIT. It increases the acidity of the gastric juice which is inhibited by naloxone and atropin. It inhibits the secretion of the exocrine pancreas, stimulated by cholecystokinin. It delays the evacuation of the stomach and leads to the triggering of the contractile activity of the central and peripheral origin.

Somatostatin (SMS) – is produced by endocrine and paracrine D cells in the entire intestine. It inhibits the motility in GIT and exocrine and endocrine secretions.

SMS decreases the contraction of smooth muscles of the intestine, gallbladder and decreases the blood perfusion through internal organs. It controls the release of gastrin by a feedback.

The effects of SMS on the gastrointestinal tract:
Endocrine secretion: inhibition of gastrin, secretin, cholecystokinin, VIP, glucagon, insulin, motilin, neurotensin, pancreatic polypeptide, GIP.

Exocrine secretion: inhibition of HCl and pepsin, pancreatic bicarbonate and enzymes, intestinal fluid and bile.

Absorption: reduction in carbohydrates, fat, and amino acids.

Circulation: decreased perfusion via the coeliac vein and mesenteric artery.

Motility: inhibition of gastric evacuation, gallbladder contractions and the delay in the passage via the small intestine.

Growth: decreased proliferation of the gastrointestinal mucosa and tissues of organs.

Epidermal growth factor is produced by cells of the duodenum. It inhibits the gastric secretion. It occurs in submandibular salivary glands, thyroid gland, pancreas, jejunum, duodenum and in the kidneys.

It inhibits pentagastrin- and histamin-stimulated secretion of gastric acid. It has a trophic effect on the intestinal mucosa and causes an increase in weight. It accelerates the growth of malign tumours – including the tumours of the breasts.

Pancreostatin is produced by nerves and endocrine cells in the entire intestines. It inhibits the glucoso-stimulated secretion of insulin and cholecystokinin-stimulated exocrine pancreatic secretion.

Thyrotropin-releasing hormone (TRH) occurs also in the gastrointestinal tract. The local function of the hormone is however unclear.

Calcitonin gene-related peptide (CGRP) occurs also in the enteric nervous system. CGRP stimulates the release of SMS.

Vasoactive intestinal polypeptide (VIP) is secreted from the nerve endings of the entire GIT.

Biologic effect: control of blood supply and sphincters. The histidine-nethionine (PHM) peptide yields a similar effect. It relaxes the lower oesophageal sphincter and causes vasodilatation in the intestine and brain. It inhibits the secretion of HCl, pepsin, gastrin, bicarbonates in the pancreatic juice and re-

sorption of sodium. It stimulates the secretion of chlorine in the intestine and releases insulin, glucagon and SMS. A decrease in the number of nervous fiber producing VIP brings about an increased tonus of sphincters and motility impairments.

Some of the presented hormones have become a significant aid in diagnostics (pentagastrine stimula-

tion of the stomach; cholecystokinetic effect after administration of CCK at radiologic and ultrasonographic examinations of the gallbladder; secretin and CCK at the examination of the pancreatic functions or as a provoking test at the examination of Zollinger-Ellison's syndrome; glucagon at the endoscopy of papilla and intestines).