7.7 Impairment of the exocrine function of pancreas

Pancreatic juice is a clear colourless alkaline fluid. It is discharged into the duodenum in volume of 1–1.5 l per day. The secretion of pancreatic juice is relatively frequently decreased (the evaluation is performed after stimulation by certain substances, e.g. by dietary burden). A severe damage of pancreas is associated with so-called pancreatic achylia, i.e. minimal secretion. Various stages of pancreatic insufficiency can be caused by acute or chronic pancreatitis, kwashiorkor, fatty degeneration of pancreas, toxic impairment (e.g. alcoholism), or tumours (most frequently carcinoma). The pancreas reacts very sensitively to an impairment of the protein metabolism. A decreased supply of proteins leads to an impairment of the endogenous stimulation of pancreas. This condition can be manifest by atrophy of acinous cells and fibrosis of pancreas (e.g. long-term fasting). The changes in the amount of pancreatic juice are often associated with a decreased contents of pancreatic enzymes. This can be evoked either by a decreased secretion of their proenzymes, their insufficient intraluminal activation, or inactivation of enzymes which have been already activated. E.g. in patients with coeliac sprue, the secretions of lipase and trypsinogen are decreased. Trypsin deficiency is automatically associated with the deficiency of chymotrypsin and other enzymes which are activated from proenzymes by trypsin. An increased intraluminal inactivation of enzymes (especially those of amylase and lipase) takes place in cases of gastrinoma. In such cases a small amount of acid gastric juice gets into the duodenum and its pH drops to 1–1.5 for a long period. This state externally manifests itself as a malabsorption syndrome with weight loss (further symptoms include macrocytic anaemia, metabolic osteoporosis, hypoalbuminaemia).

7.7.1 Pancreatitis

Acute pancreatitis constitutes approximately 1–2% of patients hospitalised in surgical wards with the diagnosis of acute abdomen. The incidence of the disease in men equals that in women. The disease occurs especially in the fifth decade of life. The occurrence of pancreatitis coincides with further factors, such as alcoholism, cholelithiasis, obstruction of biliary ducts, peptic ulcer, hyperlipidaemia and the impact of some drugs (Tab. 7.1).

<table>
<thead>
<tr>
<th>disease of gallbladder and bile ducts</th>
</tr>
</thead>
<tbody>
<tr>
<td>alcoholism</td>
</tr>
<tr>
<td>obstruction of draining ducts and Vater’s papilla</td>
</tr>
<tr>
<td>duodenal diseases (ulcer, diverticulum, obstruction)</td>
</tr>
<tr>
<td>injuries, surgeries</td>
</tr>
<tr>
<td>infections (viral, bacterial and parasitic)</td>
</tr>
<tr>
<td>endocrine metabolic impairments (diabetes mellitus, hyperlipaemia, hypercalcaemia)</td>
</tr>
<tr>
<td>toxic substances (alcohol, drugs – thiazides, glucocorticoids, etc.)</td>
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<tr>
<td>immunologic factors</td>
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<tr>
<td>hereditary factors</td>
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<tr>
<td>idiopathic pancreatitis</td>
</tr>
</tbody>
</table>

7.7.1.1 Acute pancreatitis (acute haemorrhagic pancreatitis)

Acute pancreatitis is an inflammatory impairment of pancreas associated with oedema, various stages of autodigestion, necrosis and haemorrhage in its parts. The cause of this impairment is ascribed to the intrapancreatic activation of proteases. It is not exactly known as to why intrapancreatic activation of proteases takes place. The course of acute pancreatitis allows us to construct the development of its etiopathogenesis from its origin to the fatal end. Its etiopathogenesis can be depicted as a cascade of causes and consequences:
7.7 Impairment of the exocrine function of pancreas (M. Bernadić)

- at the beginning, the cell impairment of the ducts and acini is either evident (biliary reflux, choleliths, ethanol, trauma) or hidden (increased pressure in the system of pancreatic ducts),
- which brings about the release of digestive pancreatic enzymes,
- hydrolases trigger the activation of proteolytic, lipolytic and other pancreatic enzymes by an impairment of acinar cells,
- the activation of these enzymes causes an impairment of blood vessels and lymphatic pathways,
- the impairment of capillaries and lymphatic ducts ends up by their obstruction or overall destruction,
- consequently, an impairment or even autodigestion of the acinar cells release and activate enzymes and cellular proteins,
- the pancreatic kallikrein system is activated,
- further progression brings about an overall vasodilatation, increased capillary permeability, shock with acute renal failure,
- the subsequent change resides in the occurrence of ARDS (adult respiratory distress syndrome),
- and finally the chain of events leads to irreversible shock.

The entire process is often associated with the reflux of bile into the efferent pancreatic ducts. This situation enables also the activation of pancreatic enzymes. The biliary reflux most frequently takes place due to obstruction of pancreatic pathways in the area of its junction with the bile duct, i.e. in papilla of Vater. Activated enzymes (trypsin, elastase, lipases) impair the cells of pancreas. Oedema appears, impairment of vessels results in haemorrhage, and necrosis intervenes (local effect). Enzymes enter the circulation, impair vascular walls and other organs (lungs, kidneys) by their toxic effect. This systemic effect developing in coincidence with acute pancreatitis causes high morbidity and mortality. The mortality rate in severe haemorrhagic necrotic pancreatitis currently reaches even 70%.

The most important phenomenon of the pancreatitis is pain. The pain projects from the epigastric area as far as into the back. It varies from moderate discomfort to a severe debilitating pain badly tolerated by the patient. The pain is evoked by oedema, distension of pancreatic ducts and acini, chemical irritation and peritonitis, or by obstruction of biliary pathways.

Manifestation of pancreatitis includes nausea and vomiting with intestinal hypermotility, or even paralytic ileus in consequence of peritoneal irritation. Peritoneal exudation appears in the abdominal cavity (ascites). Obstructive jaundice develops either owing to the pressure caused by the oedematous enlargement of the pancreatic head, or owing to an overgrowth of pancreatic tumor. The release of enzymes into circulation is severely complicated by hypovolaemia, hypotension, or even circulatory shock together with heart failure in consequence of vascular bed dilatation. The impact of pancreatic proteolytic enzymes in circulation leads to defibrination and disseminated intravascular coagulation. A part of patients (10%) develops tachypnoe and secondary hypoxaemia in consequence of pulmonary oedema and the appearance of atelectases (destruction of pulmonary surfactant).

The decrease in perfusion pressure leads to an impairment of renal functions. The necrotic tissue takes up calcium more intensively, possibly leading to the development of tetany (however, a decreased response to parathormone is present as well). The overall state is complicated also by transient hyperglycaemia which is associated with the release of glucagon from the impaired alpha cells of pancreatic islets. Frequent impairments include those of CNS, the condition of which is referred to as pancreatic encephalopathy.

The basic therapeutic rule is to discontinue autodigestion and avoid the systemic impairments developing in consequence of the release of enzymes into circulation. Surgical intervention may reside in resection of necrotic part of pancreas and removal of ascitic fluid.

7.7.1.2 Chronic pancreatitis

Chronic pancreatitis is characterized by progressive destruction of glandular parenchyma with gradual extinguishment of acinar cells, fibrosis and tissue atrophy. The clinical picture includes impairments of the pancreatic exocrine function; impairment of endocrine function occurs later. The main criterion of
morphological classification is the stage of impairment of the pancreatic ducts.

Pathophysiological mechanisms of chronic pancreatitis are similar to those present in acute pancreatitis. Furthermore, it is held that chronic pancreatitis can appear in consequence of autoimmune diseases. It is possible to prove antibodies against pancreatic cells in patients with chronic pancreatitis (these antibodies are present also in patients with pancreatic cancer).

### 7.7.2 Cystic fibrosis of the pancreas (mucoviscidosis)

Cystic fibrosis is an autosomal recessive hereditary systemic disease characterized by a severe impairment of metabolism. The disease is manifestant already in childhood (the incidence in live birth is 1:2000) as a dysfunction of exocrine glands producing mucus in the bronchi, pancreas, liver and intestine. The secretions in gastrointestinal, bronchial, salivary, lacrimal and sweat glands are extremely viscous. The viscosity of secretions causes obstruction of glandular ducts. The pancreatic ducts dilate, cysts are formed and fibrosis develops. Acinar tissue becomes atrophic, but islets of Langerhans remain intact. The lungs develop obstructive bronchitis. Bronchiectasis and pulmonary fibrosis supervene. The disease becomes manifestant also in the liver, namely by accumulation of bile and fibrosis. The clinical picture varies. Primary manifestation includes pulmonary infections which occur in consequence of bronchiectasis and bronchial obstruction by mucous plugs. Obstruction of the pancreatic ducts leads to the diffuse form of interstitial chronic pancreatitis. As many as 85% of children with cystic fibrosis suffer from manifestant malabsorption which is determined by impairment of the pancreatic exocrine function (even pancreatic achylia). The intestinal mucus is coated by a thick layer of mucus which inhibits normal resorption of nutrients. The sera of patients yield an increased level of alpha-glucosidase (its level correlates with the severeness of the disease). Abnormal intestinal secretion of viscous mucus in newborns can lead to the formation of so-called meconium ileus. Steatorrhea represents the consequence of insufficiency of lipases in pancreatic juice, a majority of patients yields bile acid losses by stool. The diagnosis becomes obvious already from perspiration and saliva examinations by detecting abnormal concentrations of NaCl. The therapy is antiinfectious (antibiotics), supportive and substitutional.

### 7.8 Small intestine

The small intestine is a tube reaching 3.5 m in length. It comprises 3 segments: duodenum, jejunum and ileum. The duodenum is a part which extends from the pylorus to the ligament of Treitz. The jejunum has a wider lumen and anatomically it is not too distinct from ileum. The ileum terminates in the ileocoecal valve or sphincter, the function of which is to control the transition of chyme into the large intestine and to prevent its reflux from the colon into the small intestine.

The vascular supply of the duodenum arises from the gastroduodenal artery. Both jejunum and ileum are supplied by the branches of the superior mesenteric artery. The superior mesenteric vein joins the splenic vein and their blood drains into the portal circulation. The lymphatic drainage leads to the thoracic duct. The secretion, motility, pain and intestinal reflexes are regulated by parasympathetic nerves. The sympathetic activity inhibits the motility and induces vasoconstriction. Motor innervation is procured by the myenteric and submucous plexi. The mucous plicae present in the small intestine slow down the passage of food and enlarge the surface of resorption. They are more pronounced in the jejunum and the upper part of ileum. The absorption of substances per se is performed by intestinal villi which cover the mucosa. Each villus represents a functional unit. It produces enzymes necessary for digestion. The villi comprise absorbent cylindrical cells and mucus-producing cells. Despite the fact that the tightness of mutual adhesion of the cylindrical cells increases toward the intestinal lumen, water and electrolytes are absorbed through the intercellular space. The surface of each cylindrical cell is covered by thin projections – microvilli. In this way, the overall mucosal surface is enlarged seven-fold, thus enabling the absorption of substances to take place