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 mucosa 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 spleenic 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

on a larger surface. Lamina propria below the epithelial cells contains macrophages, lymphocytes and plasma cells producing immunoglobulins. Each villus is supplied by a central artery which branches into two capillaries. Each villus comprises also a central lymphatic canal which is important for absorption and transport of fat molecules.

Among the villi, Lieberkühn's crypts are located. They extend as far as into the submucosa. The crypts comprise **non-differentiated secretory cells**. These cells represent precursors of cylindric epithelial cells. Non-differentiated cells leave the crypt's base and move toward the peak of the villi. During this process they mature regarding their morphology and function. When they reach the peak of the villi, they fulfil their function for several days and thereafter they exfoliate into the intestinal lumen where they are destructed and digested. The exfoliated epithelial cells are a significant source of endogenous proteins. In 4–7 days the population of all epithelial cells regenerates. Many factors – e.g. fasting, vitamin $B_{12}$ deficiency, cytostatic drugs and radiation – suppress the substitution of these cells and thereby decrease the height of the villi. A decreased cellular overturn results in atrophy, decreased absorption, diarrhea and impairment in nutrition. A reverse effect is induced by food intake and also by intestinal resection.

## 7.8.1 Digestion and absorption in the small intestine

The process of digestion is initiated in the stomach by the breakdown of proteins and destruction of fibrous components of food by hydrochloric acid and pepsin. During the passage via the duodenum, the chyme is exposed to the impact of further secretions and only some food components are resorbed herein. The digestion continues in the proximal part of the small intestine where the chyme is exposed to the effect of pancreatic enzymes, intestinal enzymes and bile salts. Saccharides are split into monosaccharides and disaccharides. Proteins are degraded to amino acids and peptides. Fat is emulsified and degraded to fatty acids and monoglycerides. These compounds together with water, vitamins, and electrolytes are absorbed through the intestinal mucosa by active transport, diffusion or enhanced diffusion. The constituents of saccharides and proteins reach the capillaries in the intestinal villi and afterwards the liver via the portal circulation. The components of lipids get into the lymphatic circulation, or by the blood into the liver. Intestinal movements procure the contact of chyme with the large mucosal surface. Various constituents of the gastrointestinal contents are absorbed in various intestinal areas.

### 7.8.1.1 Absorption of water and electrolytes

Cellular epithelial membranes are constituted by lipid layers. Therefore these cells behave in a hydrophobic manner. The transition of water in both directions (from lumen into capillaries and vice versa), as well as the transition of a particular amount of electrolytes is performed through intercellular space, hence not through the membranes of epithelial cells. Water diffuses passively depending on the hydrostatic pressure and osmotic gradient. In addition to other substances, the greatest share in the exertion of osmotic pressure is carried out by sodium. Sodium transgresses not only the intercellular space, it is also actively transported through cellular membranes in order to be exchanged for hydrogen ions. The sodium pump is localised on cellular basolateral membranes. Sodium and glucose are transported by common transport mechanisms, while sodium absorption increases the transport of glucose. Chlorides actively enter the cells in order to substitute bicarbonates and thus to maintain the electroneutrality. Potassium transgresses passively through intercellular space depending on the electrochemical gradient.

### 7.8.1.2 Saccharides

Saccharides are absorbed in the duodenum and in the upper part of jejunum. The salivary and pancreatic amylases split polysaccharides into oligosaccharides which are hydrolysed as far as on the intestinal surface. The intestine is able to absorb solely monosaccharides (galactose, glucose, fructose). Absorption of sugar is carried out on the principle of diffusion. Glucose and galactose are actively transported through the membrane by means of the sodium carrier and therefore they are absorbed more rapidly than fructose. Insulin is not necessary for the absorption of saccharides in the intestines.

#### 7.8.1.3 Proteins

Adults should accept 44–56 g of protein by food. Out of this protein intake, under physiological conditions, 5–10 % is discharged by stool. Digestion of protein is initiated in the stomach by the impact of pepsin, but the essence of digestion is carried out in the small intestine. Pancreatic enzymes, namely trypsin and chymotrypsin hydrolyse large protein molecules, and carboxypeptidases split off amino acids. The hydrolysis of proteins is performed also on the surface of epithelial cells. The superficial enzymes of epithelial cells hydrolyse large oligopeptides into smaller peptides which transgress cellular membranes. Amino acids are actively transported through the basal membrane. According to the type of transport, amino acids can be divided into three groups:

1. methionine, glycine, phenylalanine, tryptophane
2. arginine, ornithine, lysine, cystine
3. proline and hydroxyproline

Each of the above presented groups of proteins enter the circulation by specific transport mechanisms. Protein absorption is directly associated with active sodium transport. Only a small proportion of proteins enters the cells by means of pinocytosis. Proteins are absorbed, similar to saccharides, in the proximal part of the small intestine.

#### 7.8.1.4 Fat

People accept 90–100 g of fat in average per day. Fats are a significant source of calories, as well as primary components of cellular membranes and organelles. The main compounds of fats in food are triglycerides. Cholesterol, phospholipids and fat-soluble vitamins are important regarding the nutrition. Digestion and absorption of fat is carried out in four phases:

1. emulsification and lipolysis
2. formation of micelles
3. fat absorption
4. resynthesis of triglycerides and phospholipids

Mechanical activities of the stomach and small intestine disperse the triglycerides into small droplets. **Emulsification** assisted by fatty acids, monoglycerides, lecithin, cholesterol, proteins and bile acids produces small particles; a reverse aggregation of droplets to larger drops is impossible. Emulsified fats are in this way prepared for **lipolysis by pancreatic lipase**. The lipase splits triglycerides into diglycerides, monoglycerides, free fatty acids and glycerol. The impact of lipase comes to the effect merely in the presence of the pancreatic ezyme – colipase which enables lipase to penetrate the molecules of triglycerides. The products of hydrolysis of lipids must be soluble in water in order to be effectively absorbed in the intestinal lumen. This can be achieved by formation of molecules which are soluble in water and referred to as **micelles**. Micelles are composed of bile salts, products of fat hydrolysis, fat-soluble vitamins and cholesterol. Fat constitutes the nucleus of micelles and polar bile salts form the coating layer with the hydrophobic part directed towards the molecular centre and the hydrophilic part directed outwards. Owing to this fact the micelles get into intermediate contact with the intestinal epithelium, whereas the bile salts remain in the lumen and are moved as far as into the ileum. Inside the ileum, they are absorbed, and returned to the liver.

When individual components of fat get inside the epithelial cells, they repeatedly resynthesize to triglycerides and phospholipids. The triglycerides are coated by phospholipids, lipoproteins and cholesterol. They constitute particles which are referred to as **chylomicrons**. Chylomicrons are shifted to the basolateral membrane of cylindric epithelial cells where they are eliminated into the intercellular space. From here they get into lymphatics or blood circulation.

#### 7.8.1.5 Minerals and vitamins

The optimal **intake of calcium** ranges from 1000 to 1500 mg per day. The amount of 500–600 mg of calcium basically re-circulates, as it originates from the exfoliated enterocytes. High concentration of calcium in the lumen brings about its absorption by passive diffusion. However, if the concentration of calcium in the intestinal lumen is low, it is transported actively through cellular membranes by means of a protein carrier. The participation of the carrier requires the presence of the active form of vitamin D (1,25–dihydroxyvitamin D). The

calcium-protein complex enters the epithelial cell where calcium binds with proteins or other substances. Thereafter, by means of diffusion or active transport via the basolateral membrane, enters the interstitial fluid. Calcium is absorbed in the small intestine, dominantly in the ileum. It is absorbed faster in children, in pregnancy and lactation. The overall turnover of calcium is greater in these groups of the population. Bile acids indirectly increase the absorption of calcium by increasing the absorption of vitamin D and free fatty acids.

Elderly people daily accept 300–350 mg of magnesium. Magnesium is absorbed by active transport or passive diffusion in the jejunum and ileum. Absorption of phosphates is carried out in a similar manner. Their level in body is regulated to a substantial extent by intestinal absorption and secretion.

A daily **intake of iron** is 15–30 mg. A general principle is held that absorption of iron is carried out merely in an amount which is necessary. Iron insufficiency enhances its absorption. The primary sources of iron in animal proteins are represented by haemoglobin and myoglobin. This iron is quickly absorbed by epithelial cells of the duodenum and jejunum. The absorption of anorganic iron from fruit, eggs, and vegetables is also relatively fast.

Iron absorption is assisted by the presence of vitamin C. Adversely, calciumphosphate and phosphoproteins (milk, antacids) and tea bind iron in bowel and in this way they reduce its absorption.

Iron in cytosole is primarily bound with protein – ferritin, as well as non-protein low-molecular components of cytosole. Iron transport through the basolateral membrane is determined by the amount of iron present in circulation.

At a sufficiently high concentration in the plasma the absorbed iron remains in the epithelial cells. Iron gets back into the intestinal lumen together with epithelial cells after their exfoliation. Adversely, during bleeding, in pregnancy, or during growth, iron is actively transported from epithelial cells into plasma. In coincidence with sudden iron losses caused by bleeding, the intestinal absorption of iron increases appropriately in 3 days. This period is necessary for the precursor cells in Lieberkühn's crypts to become functionally formed, and to migrate to the surface of the villi. This process is stimulated by the iron deficiency. The transfer of iron into the plasma is carried out by transferrin (the component of globulins).

**Water-soluble vitamins** are absorbed by the sodium-dependent active transport. Vitamin $B_{12}$ is released from food by means of peptic digestion. Each change in the gastric mucosa which results in an insufficiency of the intrinsic factor leads to insufficient absorption of the $B_{12}$ vitamin. Vitamin $B_{12}$ deficiency impairs the maturation of erythrocytes.

## 7.8.2 Motility of the small intestine

Movements of the small intestine are a significant component of natural digestion and absorption of substances. The presence of chyme entering the small intestine from the stomach stimulates the intestinal movements which procure the mixing of chyme with enzymes, and currently the contact with the large intestinal surface. Intestinal motility is composed of two types of intestinal movements. Firstly, the intestinal motility is carried out by **rhythmic contractions of the circular musculature**. They appear in various parts of the small intestine and with various velocity. The upper part of the small intestine yields 12 contractions per minute. The lower part yields 8 contractions. The sites of their origin comprehensively alternate. This contraction assists in the mixing of chyme and procures the contact with the surface of villi. The contraction of intestinal smooth musculature is triggered by stimuli originating in the myenteric plexus. The contractions can be intensified by the impact of the vagus nerve.

In addition to the above presented segmental movements, the small-intestinal motility is also carried out by longitudinal muscular fibers. Their contraction brings about a peristaltic movement in a short section of 10 cm. The velocity of the contraction proceeding in this section reaches 1–2 cm per second. Peristaltic movements procure the movement of chyme in aboral direction. Their significance does not reside solely in the movement of chyme. Owing to the peristaltic movements, the position and altitude of the villi alter optimising thus their contact with chyme. Very important changes involving the absorption of substances are brought about by the fact that the increased pressure procures evacuation of the plicae and movement in the lymphatic vessels.

The **optimal intestinal motility** is procured by neuroreflexive mechanisms. The ileogastric reflex inhibits the gastric motility in coincidence with intestinal distension. Hence, the transition of subse-

quent bulks of chyme from the stomach into the distended small intestine is inhibited. The intestinointestinal reflex procures the hindrance of intestinal motility in cases when some part of the intestine is extremely distended. The gastroileal reflex arises in coincidence with increased gastric motility and secretion. It causes an increase in the motility of ileum. In this way, a more rapid evacuation of the ileum is procured, in order to continue the acceptance of more chyme. The gastroileal reflex is probably regulated by neurotensin. During long-term fasting, or sleep, a slow contraction proceeds from the stomach to the terminal ileum. In this way this reflex procures the evacuation of gastric and intestinal contents into the large intestine. The gastrocolic reflex (urgency to defecate after meal) is pronounced especially in childhood.

The ileocoecal junction is procured by a valve (sphincter) which is enclosed at rest. Its opening is stimulated by peristaltic waves. After the transition of a small part of chyme it encloses again. This mechanism inhibits both regurgitation of chyme and extreme distension of the large intestine.

## 7.9 The large intestine

The large intestine is approximately 1.5 m in length. It is constituted by the coecum, appendix, colon (ascendent, transverse, descendent, sigmoid), rectum and the anal canal. The coecum accepts the chyme from the ileum. The vermiform appendix might have its significance in elimination of unusual components of food present in the bowel. The sphincter in the distal part of the sigmoid colon controlling the transport of chyme into the rectum is in comparison with the ileocoecal sphincter less demarcated. It is an intestinal part which fulfils the task of a sphincter of a longer section. The anal canal encloses the internal sphincter constituted by smooth musculature and the external sphincter which is constituted by striated muscles.

The longitudinal musculature of the large intestine constitutes three stripes referred to as colic taeniae (taeniae coli). The fact that they are shorter than the bowel thus determines its typical shape. The circular musculature is separated into sections which are referred to as haustra. Muscular contractions reduce and enlarge the haustra.

The large-intestinal mucosa contains cylindric cells which absorb water and electrolytes. Mucus-producing cells create a protective layer on the mucosal surface.

The **motor and secretory acitivities** of the large intestine are regulated from the myenteric plexus which is to a great extent independent from other systems. The parasympathetic innervation of the coecum, ascendent colon and the first part of the transverse colon originates from the vagus nerve which in this area of the large intestine stimulates rhythmic contractions. The distal colon is parasympathetically innervated from the pelvic nerves. The internal anal sphincter is innervated by the sympathetic nervous system (the sympathetic system enhances contractions) and parasympathetic system (the parasympathetic system supports relaxation). It is permanently in state of contraction. It relaxes only for a short time in coincidence with the distension of the rectum and at defecation. The external sphincter is innervated by sacral branches of spinal nerves. The sympathetic innervation originates in the coeliac and superior mesenteric ganglia. Destruction of the lower part of medulla spinalis paralyses the external sphincter whereas the internal sphincter does not respond. The sympathetic activity in the area of the large intestine modulates intestinal reflexes, somatic sensations and pain.

Basic movements of the large intestine are represented by **segmental contractions** which always involve an entire haustrum. **Peristaltic movements** involve several haustra. They procure the transition of the faecal mass aborally to the rectum. The gastrocolic reflex enhances peristaltic movements of the large intestine after the stomach filling, which stimulates defecation. It is probable that gastrin participates in this reflex.

Fluid is absorbed in the large intestine by diffusion or by active transport. Under the influence of aldosteron, the diffusion of sodium into the cells and its active transport through the basolateral membrane into the interstitial fluid increase. Together with sodium, also chlorides – as complementary anions – are absorbed. They enter the cells on the basis of exchange for bicarbonates. The active transport