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Учреждение образования
«Гомельский государственный медицинский университет»

Кафедра патологической физиологии
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МЕТОДИЧЕСКАЯ РАЗРАБОТКА

Для проведения занятия со студентами
3 курса ФПСЗС, обучающихся на английском языке
по патологической физиологии

Тема: **Патофизиология системы пищеварения**

Theme: **Pathophysiology of digestive system**

Время 3 ак. часа

1.Actuality of the theme. The diseases of digestive organs take considerable place in general morbidity of the population. Chronic gastritis and peptic ulcer meet in all agegroups and don't the tendencies to decrease. The most of them course chronically and is characterized by bend to relapses and acute. It lead to loss of working ability and disability. It should account, that not only organic, but also the functional disorders of alimentary system seriously influence on state of the whole organism, on it metabolism. The leading etiological factors of disturbance of digestion are the errors in digestion, infectious agents, toxic substances and medicines drugs abusing by alcohol and nicotine, psychic, traumas, negative emotions. Pathogenetical the grounded methods of prevention and treatments of illnesses of gastrointestinal tract is based on knowledge of the nature of these pathogenic factors and mechanisms of those disorders, which arise under their action.

Learning goals of the lesson: to study etiology and pathogenesis of digestive system disorders.

Educational goals of the lesson: formation of scientific outlook and theoretical basis of future specialists on the basis of fundamental knowledge and the latest achievements of pathological physiology.

Objectives of the lesson:

1. To know main causes and mechanisms of development of typical forms of digestive disorders.
2. To learn causes and mechanisms of ulceration.
3. To be able to recognize, based on the history, characteristic symptoms and results of laboratory tests, the development of the patient's gastrointestinal tract disease (by the example of situational tasks).
4. To be able to explain mechanisms of formation of compensatory-regenerative processes in digestive system.

To repeat the following questions from related disciplines to ensure absolute mastery of the material:

1. Structure of gastrointestinal tract. (histology, cytology, embryology disciplines).
2. Digestion in stomach, and intestine (normal physiology discipline).

Control questions of the lesson:

1. General etiology and pathogenesis of digestive system disorders.
2. Disorders of appetite, taste, salivation, chewing, swallowing, esophagus functions: causes and consequences.
3. Disorders of secretory stomach function: causes and mechanisms. Types of pathological secretion.
4. Disorders of motor and evacuation stomach functions: types, causes and mechanisms. Interrelation of secretory and motor disorders.
5. Stomach and duodenum ulcers.
6. Violation of intestine secretory function. Disturbance of digestion and absorption. Disturbance of intestinal motility: types, causes, mechanisms, consequences.
7. Violation of intestine barrier function: types, causes, mechanisms, consequences.
8. Disorders of pancreas secretory function: acute and chronic pancreatitis.

Calculation of study time

Total study time 3 ac.hours

№ п/п	Contents	Calculation of study time
1.	Introduction. Motivational characteristic of the theme	3 minutes
2.	Written control of students on the topic of the lesson	15 minutes
3.	Interviews with students about the topic of the lesson	60 minutes
4.	Self-managed student work	15 minutes
5.	Summing up the results of the lesson	5 minutes
6.	Decision of situational tasks	20 minutes
7.	Task for the next lesson	2 minutes

Additional material:

The alimentary tract provides the body with a continual supply of water, electrolytes and nutrients:

- 1) movement of food through the alimentary tract,
- 2) secretion of digestive juices and digestion of the food,
- 3) absorption of water, various electrolytes and digestive products,
- 4) circulation of blood through the gastrointestinal organs to carry away the absorbed substances,
- 5) control of these functions by local nervous and hormonal system.

Typical forms of gastrointestinal system pathology

Impairment of taste, appetite,
oral cavity digestion,
swallowing and esophagus
digestion in stomach,
digestion in intestines

Taste impairments

The main causes are CNS impairments

- hypogeusia is taste analyzer impairment (receptor, nerve trunks, neurons)
- hypergeusia is cortex neuron impairments, receptor hypersensitization
- parageusia is a false taste
- dysgeusia is a perversion of taste (use of out-of-date or toxic products)

Impairment of taste adequacy to real irritant: parageusia, dysgeusia

Appetite impairments

- hyperrexia is a pathologic increase in appetite. it is associated with polyphagia and acoria
- hyporexia is a high decrease in appetite. it is presented in severe diseases, oncologic diseases, neuron- and psychogenic impairments.
- anorexia is a absence of appetite
- pararexia is a pathologic change in appetite (use of inedible products)

The main cause: impairment of central control (trauma, tumor, psychogenic disease).

Impairment of salivation

- Hyposalivation (inflammation, neuron-humoral control impairments)
- Hypersalivation (intoxication, acute gingivitis, acute stomatitis, helminths, oral cavity infections, activation of parasympathetic system)

Impairments of chewing

Impairments of chewing (stomatitis, gingivitis), impairment of muscular joint apparatus of lower jaw, absent of teeth and others.

Dysphagy

Stages of swallowing: 1) oral (voluntary); 2) pharyngeal (quick voluntary); 3) esophageal (slow voluntary).

Damage of the 5th, 9th and 10th cerebral nerve can cause paralysis of swallowing mechanism. Such diseases as poliomyelitis or encephalitis can impair normal swallowing by damaging the swallowing center. Paralysis of the swallowing muscles occurs in muscle dystrophy and failure of neuromuscular transmission in myasthenia gravis or botulism.

The abnormalities that occur include: 1) complete arrest of the swallowing act; 2) failure of the glottis close (so that food passes into the lungs instead of the esophagus); 3) failure of the soft palate and uvula to close the posterior nares so that food refluxes into the nose during swallowing.

Impairments of food passage through the esophagus

Achalasia is a condition in which the lower esophageal sphincter fails to relax during the swallowing. So food swallowed into the esophagus fails to pass from the esophagus into stomach.

Causes: damage in the neural network of the myenteric plexus in the lower two thirds of the esophagus. So the myenteric plexus has lost its ability to transmit a signal to cause «receptive relaxation» of the gastroesophageal sphincter as food approaches this sphincter during the swallowing.

Treatment: stretching the lower end of the esophagus by means of the balloon inflated on the end of a swallowed esophageal tube, use of antispasmodic drugs. Also impairments of food passage through esophagus is presented in diffuse esophageal spasm, systemic scleroderma.

Impairment of the stomach

Impairment of the stomach motor function: hyper tone — increase in muscular tone, hypo tone — high decrease in muscular tone, atony — absence of muscular tone

Stimulants of gastric secretion

- Acetylcholine
- Gastrin, histamine
- Prostaglandins (PgF2a)
- Enkephalin
- Bombesin
- Insulin
- GC, growth hormone, TSH
- Prolactin

Inhibitors of gastric secretion

- Secretin
- Cholecystokinin-pancreozymin
- GIP, VIP
- Calcitonin, neurotensin
- Substance P
- Somatostatin
- Prostaglandins-PgA1, E2
- Estrogens
- Mineralocorticoids

Duodenogastric reflux disease

The condition of duodenogastric reflux disease is caused by the reflux of duodenum contents into the stomach. It results from the decrease in HCl and gastrin secretion, the increase in cholecystokinin level. The increase in alkaline contents causes the impairment of mucous barrier, microcirculation impairments, dystrophy and necrosis of epithelium.

Impairments of peristalsis

Hyperkinesis is an increase in peristalsis and gastric tone. It occurs in acute pain, heartburn, sometimes in case of vomiting. It is stimulated by histamine, serotonin, substance P.

Hypokinesis is a decrease in peristalsis and gastric tone. It occurs in myocardial infarction, infectious diseases. Stomach motor function is inhibited by somatostatin, secretin, neuropeptide Y, peptide YY.

Motor function impairments

Pyrosis is a technical term for what is popularly called heartburn, a burning sensation in the upper abdomen.

Belching is a normal process to relieve distention from the air that accumulates in the stomach. The upper abdominal discomfort associated with excessive swallowed air may extend into the lower chest, producing symptoms suggesting heart or lung disease.

Hiccough is an extraordinary type of breathing movement involving a sudden intake of air (inspiration) due to an involuntary contraction of the diaphragm accompanied by closure of the vocal apparatus (glottis) of the larynx.

- **Heartburn**
- **Eructation**
- **Hiccups**
- **Nausea**
- **Vomiting**

Heartburn (pyrosis) warmth or burning sensation in the lower esophagus, in the chest, in the upper part of the epigastrium

Eructation hit in the mouth of the esophagus or stomach contents

Hiccups (singultus) is reflex spasms of the diaphragm, stomach twitching and sudden severe inspiratory narrowing of the glottis

Nausea is a subjective, unpleasant sensation that often precedes vomiting. Nausea is caused by distention or irritation anywhere in the GI tract, but it can also be stimulated by higher brain centers. Interpretation of nausea occurs in the medulla, which is either adjacent to or part of the vomiting center.

Vomiting is a complex reflex mediated through the vomiting center in the medulla oblongata of the brain. Afferent impulses travel to the vomiting center as both vagal and sympathetic afferents. Afferent impulses originate in the stomach or duodenum in response to excessive distention or irritation, or sometimes they originate in response to chemical stimulation by emetics (agents that cause vomiting), such as syrup of ipecac. Hypoxia and pain can also stimulate vomiting by means of activation of the vomiting center. Vomiting can also occur through direct stimulation of an area of the brain adjacent to the vomiting center in the brain. Certain drugs initiate vomiting by activating this center, called the chemoreceptor trigger zone, which lies in the floor of the fourth ventricle. Vomiting as a result of rapid motion change is believed to work through stimulation of this trigger zone. Activation of the chemoreceptor trigger zone can cause vomiting either directly or indirectly by its subsequent activation of the vomiting center. Input from higher brain centers in the cortex and increased intracranial pressure (ICP) can also stimulate vomiting, probably by directly stimulating the vomiting center. Projectile vomiting occurs when the vomiting center is directly stimulated, frequently by increased ICP.

When the vomiting reflex is initiated in the vomiting center, it is carried out by activation of several cranial nerves to the face and throat, and spinal motor neurons to the diaphragm and abdominal muscles. Excitation of these pathways results in the coordinated response of vomiting. Certain symptoms generally precede vomiting, including nausea, tachycardia, and sweating.

Dumping syndrome

Dumping syndrome is a pathologic condition results from quick evacuation of gastric contents into duodenum. It develops after the stomach resection.

Pathogenesis: 1) hyperosmolarity of duodenum contents results from concentrated food hitting from the stomach, 2) intensive transport of fluids from the vessels into the intestines according to osmotic pressure gradient, 3) hypovolemia, 4) intensive absorption of glucose → hyperglycemia, 5) stimulation of insulin secretion, 6) hyperglycemia, ionic imbalance, acidosis.

Clinical manifestations: wasting after the food intake, tachycardia, arrhythmia, acute arterial hypotension, drowse, wasting, sweating, dizziness, nausea, muscular tremor, loss of consciousness

Impairment of secretion

Typical impairments of stomach secretion

- change in gastric juice volume: increase, decrease, absence
- impairment of mucosa secretion: increase, decrease, absence
- impairment of HCl secretion and change in gastric juice acidity: hyperchlorhydria, hypochlorhydria, achlorhydria
- impairment of pepsin secretion: increase, decrease, absence

Gastrointestinal peptides

Many GI hormones, including gastrin, secretin, cholecystokinin (CCK), glucagon-like peptide-1 (GLP-1), and glucose-dependent insulintropic polypeptide (GIP), play important roles in the digestive function of the GI tract. Other hormones released from the stomach or intestine, including ghrelin and peptide YY (PYY), are involved in controlling appetite. These hormones and their roles are discussed in the text that follows.

Gastrin is secreted from the stomach antrum in response to distention of the stomach after a meal and the presence of protein in the food. In addition, gastrin secretion is stimulated by the release of gastrin-releasing peptide from the nerves of the submucosal plexus as a result of parasympathetic stimulation. Gastrin acts to stimulate the secretion of histamine and gastric juices from the gut lining and hydrochloric acid (HCl) from the parietal cells of the stomach.

Histamine also stimulates HCl secretion. HCl in turn activates pepsin, the most important digestive enzyme in the stomach.

Pepsin and the gastric juices begin the digestion of protein in the stomach, removing the stimulation for further gastrin secretion. Thus, gastrin release is inhibited by excess acid, which is an excellent example of negative feedback. Gastrin also stimulates intestinal motility.

Secretin is secreted from the small intestine primarily in response to HCl present in the chyme entering the small intestine from the stomach. Secretin stimulates intestinal secretions of base as well as the pancreatic release of bicarbonate to neutralize the acid. Neutralization of acid is essential because the enzymes required for digestion in the small intestine cannot work in an acidic environment. Secretin also slows the further passage of food from the stomach into the small intestine, allowing adequate time for digestion of food already in the small intestine.

Cholecystokinin (CCK) is secreted from the small intestine primarily in response to fat and other food particles entering the intestine in the chyme. CCK causes gallbladder contraction; it also causes the release of pancreatic and intestinal digestive enzymes and of bile. The digestive enzymes and bile serve to promote the digestion and absorption of the food particles.

Glucagon-like peptide-1 (GLP-1) and **glucose-dependent insulinotropic polypeptide (GIP)** is secreted from the upper small intestine in response to fatty acids, amino acids, and glucose in the chyme. These hormones function to slow further stomach emptying, thereby allowing the effective digestion of the food already present in the small intestine. They also increase the release of insulin from the pancreas; GLP-1 and GIP account for approximately 50 to 60% of the insulin released during a meal. Evidence suggests that a deficiency in GLP-1 and/or GIP may contribute to glucose intolerance and reduced insulin secretion characteristic of type 2 diabetes mellitus.

Ghrelin and **peptide YY (PYY)** are both appetite-modulating hormones. First identified in 1999, ghrelin is secreted from the stomach and functions to regulate energy balance by stimulating food intake and decreasing fat metabolism. It appears to act with other signals to inform the central nervous system (CNS) regarding food intake and body fat mass. Ghrelin also stimulates growth releasing hormone from the hypothalamus. It also appears to affect the hypothalamic-pituitary-gonadal axis. PYY is co-secreted with GLP-1 from the small intestine in response to food entering from the stomach. PYY levels are proportional to meal energy content, and plasma levels peak postprandially after 1 hour. PYY acts as a satiety hormone in that it inhibits further food intake. It appears to function at the level of the CNS

Vasoactive intestinal peptide (VIP) is a 28-amino acid polypeptide. VIP is produced in many tissues of vertebrates including the gut, pancreas, and suprachiasmatic nuclei of the hypothalamus in the brain. VIP was first classified as an intestinal hormone because it was isolated from the digestive tract and plays a role in electrolyte secretion (bicarbonate secretion) in the intestinal tract, but it was subsequently found to be extensively distributed as a neurotransmitter in tissues. VIP exerts neural modulating activity on secretion, gastrointestinal motility, and blood flow in the pancreas and intestine, and the peptide shows similar activities in the cardiovascular, respiratory, and urological systems

APUD-system

Amine precursor uptake and decarboxylation regulate: water secretion, secretion of electrolytes, mucus, enzymes, trophics, hydrocarbonate acid, moves, absorbtion, hormone excretion, neurotransmission.

- EC-cells (in all parts of GIT, mainly in pyloric glands of stomach and intestinal crypts) — produce serotonin, melatonin, motilin
- D-cell (mainly in duodenum and jejunum) — somatostatin
- D1-cells (mainly in duodenum) —VIP
- K-cells (mainly in duodenum) — GIP
- ECL-cells (fundal part of stomach) — histamine and catecholamines.
- R-cells (pyloric part of stomach, duodenum, jejunum) — bombesin
- N-cells (stomach and ileum) —neurotensin, which stimulates the secretion of HCl and other glandular cells.
- G-cells (mainly in pyloric part of stomach) — gastrin and morphine-enkephalin peptide.
- S-cells (mainly in duodenum) — secretin,
- I-cells (duodenal) — cholecystokinin-pancreozymin
- EG-cells (small intestine) — enteroglucagon

Effects of GI hormones and transmitters

- Duokrinin stimulates duodenal secretion.
- Endogenous (enkephalins) and exogenous opiates inhibit ganglionic transmission.
- Enterokrinin stimulates secretion in the small intestine.
- Gastrin releasing peptide (GRP) and bombesin release gastrin from G-cells.
- Motilin stimulates gastrointestinal motility.
- Neuropeptide Y and neurotensin stimulate neurotransmission.
- Pancreatic Polypeptide (PP) from the PP-cells inhibits pancreatic and biliary secretion, which delay the absorption of nutrients. PP is released by meals.
- Pancreatin inhibits the pancreatic exocrine secretion.
- Somatostatin strong, universal inhibitor - both blood-born and paracrine.
- Substance P stimulates smooth muscle contraction and thus the GI motility.

- Glicentin (intestinal glucagon) stimulates insulin secretion as other incretins.
- Villikrinin stimulates the rhythmic movement of villi in the intestine.

Non-peptic ulceration

Non-peptic ulceration in stress: impairment of microcirculation → spasm of arterioles of stomach muscular layer → stasis → stasis → bleedings

Etiology

- burns (Curling's ulcer)
- cerebral trauma, myocardial infarction, sepsis
- hemorrhages
- neurological surgery (Cushing's ulcer)
- drugs: a decrease in mucosa production — aspirin, indometacin, glucocorticoids and prednisolone
- endocrine pathology: Zollinger-Ellison's syndrome — A-cell-insulinoma, hyperacidosis, ulceration of stomach and duodenum
- others: chronic adrenal failure, arterial hypertension, atherosclerosis

Parasympathetic innervations stimulate the production of HCl, proteolytic enzymes and mucosa, gastrin. Also it increases sensitivity of secretion cells to gastrin and histamine. It activates gastric blood circulation, and decreases concentration of somatostatin. Somatostatin inhibits gastrin secretion.

Sympathetic innervations stimulate alpha and beta-adrenoreceptors → decrease in HCl and pepsinogen secretion, decrease in stomach blood circulation.

Peptic ulceration

Cause: imbalance between the rate of secretion 1) the gastroduodenal mucosal barrier and 2) the neutralization of the gastric acid by duodenal juices

Pathogenesis of peptic ulceration

Factors of aggression:

1. Endogenous

- acid-peptic (HCl and pepsin)
- bile acids and lysolecithin, pancreatic enzymes (in duodenogastric reflux)
- ischemia (caused by PAF-factor of thrombocyte activation, LTC₄ –leukotriene C₄)
- motor function impairment

2. Exogenous:

- *Helicobacter pylori*
- Alcohol
- NSAID (nonsteroidal anti-inflammatory drugs)

H. pylori is a nonsporing curvilinear gram-negative rod measuring approximately 3,5–5,0 μm. *H. pylori* is a part of genus of bacteria that have adapted to ecologic niche provided by gastric mucosa, which is lethal to most bacteria. The specialized traits that allow it to flourish include:

- Motility (via flagella), allowing it to swim through viscous mucus
- Elaboration of a urease, which produces ammonia and carbon dioxide from endogenous urea, thereby buffering gastric acid in the immediate vicinity of the organism
- Expression of bacterial adhesins, such as BabA, which binds to the fucosylated Lewis B blood-group antigens, enhances binding to blood group O antigen bearing cells.
- Expression of bacterial toxins, such as cytotoxin association gene A (CagA) and vacuolating cytotoxin gene A (VacA).

The *H. pylori* genome is 1.65 million base pairs and encodes approximately 1500 proteins. Extensive molecular studies suggest that the bacteria cause gastritis by stimulating production of pro-inflammatory cytokines and by directly injuring epithelial cells (discussed later).

After initial exposure to *H. pylori*, gastritis occurs in two patterns: a predominantly antral-type gastritis with high acid production and elevated risk for duodenal ulcer, and a pangastritis that is followed by multifocal atrophy (multifocal atrophic gastritis) with lower gastric acid secretion and higher risk for adenocarcinoma. The underlying mechanisms contributing to this difference are not completely clear, but host-microorganism interplay appears to be critical. IL-1β₂ is a potent pro-inflammatory cytokine and a

powerful gastric acid inhibitor. Patients who have higher IL-1 β 2 production in response to *H. pylori* infection tend to develop pangastritis, while patients who have lower IL-1 β 2 production exhibit antral-type gastritis.

A number of diagnostic tests have been developed for the detection of *H. pylori*. Noninvasive tests include a serologic test for antibodies, fecal bacterial detection, and a urea breath test.

The breath test is based on the generation of ammonia by bacterial urease. Invasive tests are based on the identification of *H. pylori* in gastric biopsy tissue. Detection methods in gastric tissue include visualization of the bacteria in histologic sections, bacterial culture, a rapid urease test, and bacterial DNA detection by the polymerase chain reaction.

Patients with chronic gastritis and *H. pylori* usually improve when treated with antibiotics. Relapses are associated with reappearance of the organism. The current treatment regimens include antibiotics and hydrogen pump inhibitors. Prophylactic and therapeutic vaccine development is still in the early research stage, but it holds the promise to eradicate or at least greatly reduce the worldwide prevalence of *H. pylori* infection.

Pathogenesis of *H. pylori* infection: 1) colonization of gastric mucosa (it is possible because of motility, adhesion, urease, resistance to acids), 2) persistence (it is possible because of the metabolic products, enzymes and meal-binding proteins), 3) injury (it is possible because of pro-inflammatory factors: Cag, neutrophil activating protein, lipopolysaccharide), tissue injury (cytotoxin, ammonium genesis, hyperactivation of immune system, impairment of HCl synthesis control \rightarrow ulcer).

Diagnostics of *Helicobacter pylori* infection

- 1) bacteriological tests: finding out in imprint smears, culture isolation
- 2) serologic tests: Bordet-Gengou test (complement-fixing reaction), red cell-linked-antigen test, immune-enzyme analysis, *H. pylori* finding out in feces, saliva and oral cavity
- 3) morphologic test: cytotoxic — finding out in biopsy material (Romanovsky's stain), histologic
- 4) biochemical tests: urease test with biopsy material, urease respiratory test (13C and 14C is found out in expired air after the radiolabeled urea intake)
- 5) molecular genetic test: PCR (polymerase chain reaction)

Comparison of Gastric Ulcers and Duodenal Ulcers

Feature	Gastric Ulcers	Duodenal Ulcers
Percentage of ulcer cases	25%	75%
Epidemiology	Male-female ratio 1:1 Smoking does <i>not</i> cause PUD but delays healing	Male-female ratio 2:1 Increased risk in cirrhosis, COPD, renal failure, hyperparathyroidism
<i>Helicobacter pylori</i>	~80% of cases	90-95% of cases
Pathogenesis	Defective mucosal barrier due to <i>H. pylori</i> Mucosal ischemia (reduced PGE), bile reflux, delayed gastric emptying BAO and MAO normal to decreased	Defective mucosal barrier due to <i>H. pylori</i> Increased acid production (increased parietal cell mass) BAO and MAO both increased
Location	Single ulcer on lesser curvature of antrum (same location for cancer)	Single ulcer on anterior portion of first part of duodenum followed by single ulcer on posterior portion (danger of perforation into pancreas)
Complications	Bleeding (most commonly in left gastric artery) Perforation	Bleeding (most commonly in gastroduodenal artery) Perforation (air under diaphragm, pain radiates to left shoulder) Gastric outlet obstruction, pancreatitis
Clinical findings	Burning epigastric pain soon after eating	Burning epigastric pain 1-3 hours after eating

Pancreatitis

Pancreatic enzymes: amylase, lipase, phospholipase A2, trypsin, chymotrypsin, elastase, carboxypeptidase A and B. All these enzymes are secreted in pancreas in non-active form and activated in duodenum.

Acute pancreatitis

Acute pancreatitis is an inflammation of the pancreas characterized by autodigestion of the pancreas by pancreatic enzymes. Pancreatic cells are injured or killed, leading to areas of cell necrosis and hemorrhage. Stimulation of the immune and inflammatory systems results in the swelling and edema of the organ.

There is an ability to regenerate after the acute pancreatitis as opposed to chronic pancreatitis.

The key chain of pathogenesis is an activation of pancreatic enzymes.

In 80% of cases acute pancreatitis is caused by a gallstone in the common bile duct. Chronic alcoholism (ethanol action) is associated with pancreatitis because of stimulation of the pancreatic enzyme release.

Trypsin activates pancreatic enzymes: kallikrein, phospholipase A2, and elastase → autodigestion of pancreas, vasodilation, arterial hypotension, increase in vascular permeability.

Pathogenesis of autodigestion

- 1) bile and duodenum contents reflux into the pancreatic ducts
- 2) trypsinogen transformation in trypsin in pancreatic ducts and gland interstitium, presence of gallstones in bile ducts
- 3) activation of zymogens and phospholipase A2 (destruction of cell membrane)
- 4) lysolipin formation (destruction of cell membrane)
- 5) autolysis
- 6) edema and microcirculation impairments

Impairments of intestinal absorption

Causes: insufficient digestion, diarrhea, atrophy of intestinal mucous membrane, enteritis, acute intestinal infection, enterectomy, impairment of intestinal blood and lymph circulation.

Chronic pancreatitis

Etiology:

- idiopathic.
- alcohol abuse is the most common known cause.
- cystic fibrosis is the most common cause in children.
- malnutrition is the most common cause in developing countries.

Pathogenesis

Repeated attacks of acute pancreatitis produce duct obstruction. Calcified concretions occur as well as dilation of the ducts. Radiographic dyes show a "chain of lakes" appearance in the major duct.

Clinical findings

- Severe pain radiating into the back
- Malabsorption
- Type 1 diabetes mellitus
- Pancreatic pseudocyst

Laboratory and radiographic findings

- Increased amylase and lipase
- Pancreatic calcifications (CT scan best study)

Malabsorption

Malabsorption is a failure of the small intestine to absorb certain foodstuffs. There are several types of malabsorption: 1) one type of amino acid, fat, sugar or vitamin, 2) all amino acids, fats, sugars, 3) all fat-soluble vitamins

Malabsorption is a symptom complex result from the selective or total impairments of digestion (maldigestion) and absorption (malabsorption) in the small intestine

Types of malabsorption (according to origin)

- 1) primary: genetically determined or congenital enzymopathias in the small intestine, pathology of the absorbing epithelium in the small intestine (non-tropical sprue, tropical sprue)
- 2) secondary: impairments in the single part of the small intestine, or impairments of the whole small intestine as a consequence of other diseases

Clinical manifestations of malabsorption depend on what is not being absorbed and whether other areas of the bowel can compensate. Specific symptoms are related to the dietary deficiency that occurs. Generalized symptoms usually include those related to the GI tract or to the loss of fat-soluble vitamins: Fat malabsorption results in steatorrhea (fat in the stool). Diarrhea, flatulence, bloating, and cramps often occur. Stools are bulky but of light weight, float, and are malodorous.

Bile salt deficiency results in malabsorption of fat-soluble vitamins, causing the following:

- Vitamin A deficiency — night blindness.
- Vitamin D deficiency — bone demineralization and increased risk of fractures.
- Vitamin K deficiency — poor coagulation with prolonged prothrombin time, easy bruising, and petechia (hemorrhagic spots on the skin).
- Vitamin E deficiency — perhaps resulting in poor immune function.
- Lactose malabsorption results in osmotic diarrhea and flatulence (gas).

Diagnostic Tools

The presence of over 7 g of fat per day in the stool of an adult consuming a typical American diet is considered malabsorption. Weight loss or failure to gain weight in infancy or young childhood may indicate malabsorption.

Complications

Failure to thrive may occur in severe cases, leading to malnutrition, infection, and even death.

Nontropical Sprue

One type of sprue, called variously idiopathic sprue, celiac disease (in children), or gluten enteropathy, results from the toxic effects of gluten present in certain types of grains, especially wheat and rye. Only some people are susceptible to this effect, but in those who are susceptible, gluten has a direct destructive effect on intestinal enterocytes. In milder forms of the disease, only the microvilli of the absorbing enterocytes on the villi are destroyed, thus decreasing the absorptive surface area as much as twofold. In the more severe forms, the villi themselves become blunted or disappear altogether, thus still further reducing the absorptive area of the gut. Removal of wheat and rye flour from the diet frequently results in cure within weeks, especially in children with this disease.

Tropical Sprue

A different type of sprue called tropical sprue frequently occurs in the tropics and can often be treated with antibacterial agents. Even though no specific bacterium has been implicated as the cause, it is believed that this variety of sprue is usually caused by inflammation of the intestinal mucosa resulting from unidentified infectious agents.

Malabsorption in Sprue. In the early stages of sprue, intestinal absorption of fat is more impaired than absorption of other digestive products. The fat that appears in the stools is almost entirely in the form of salts of fatty acids rather than undigested fat, demonstrating that the problem is one of absorption, not of digestion. In fact, the condition is frequently called steatorrhea, which means simply excess fats in the stools. In very severe cases of sprue, in addition to malabsorption of fats there is also impaired absorption of proteins, carbohydrates, calcium, vitamin K, folic acid, and vitamin B12. As a result, the person suffers (1) severe nutritional deficiency, often developing wasting of the body; (2) osteomalacia (demineralization of the bones because of lack of calcium); (3) inadequate blood coagulation caused by lack of vitamin K; and (4) macrocytic anemia of the pernicious anemia type, owing to diminished vitamin B12 and folic acid absorption.

The pathological increase in absorption is associated with the increase in intestinal wall permeability in arterial hyperemia, in irritation of the intestinal epithelium, in small children.

Impairments of intestinal motor function

Types: increase in peristalsis, decrease in peristalsis, intestinal obstruction

Diarrhea

Diarrhea is an increase in fluidity and frequency of stools (more than 2–3 times per day). It may be large or small volume and may or not contain blood. It is associated with the increase in intestinal motor function.

Types and mechanisms of diarrhea

- Exudative diarrhea. It results from inflammatory exudates formation because of the mucosa becomes extensively irritated. And its rate of secretion becomes greatly enhanced. Motility of the intestinal wall usually increases manifold. As a result, large quantities of fluid are made available for washing the infectious agent toward the anus. At the same time strong propulsive movements propel this fluid forward.
- Secretory diarrhea. This type of diarrhea is caused by cholera (and less often by other bacteria such as some pathogenic colon bacilli). Cholera toxin directly stimulates excessive secretion of electrolytes and fluid from the crypts of Lieberkühn in the distal ileum and colon (up to 10–12 liters per day). Although the death can result from loss of fluid and electrolytes.
- Hyperosmotic diarrhea. It results from the increase in intestinal peristalsis and hypersecretion (enterocolitis, syndrome of intestine irritation).
- Hyperkinetic: as a result of hypersecretion and increased peristalsis of intestine (f.e. during enterocolitis)

Clinical manifestations and consequences

Hypohydration up to exicosis, hypovolemia, arterial hypotension, electrolyte imbalance and acid-base imbalance

Constipation

Constipation is defined as difficult or infrequent defecation. Because frequency of stool varies among individuals, the second half of this definition is subjective and should be interpreted as a relative decrease in the number of stools for that particular individual.

In general, however, bowel movements fewer than once every 3 days are considered to indicate constipation.

Types and mechanisms

- Alimentary (small volume). It results from the small volume of the intestinal contents. It is observed in chronic malnutrition, small water intake, lack of fruits and vegetables, light food intake. The small volume of intestinal contents and excrements is not sufficient for defecation activation. Defecation is a reflex process.
- Neurogenic
 - ✓ Spastic constipation. It is caused by high increase in n.vagus influences on the intestinal wall. It results in spasm of the intestinal musculature and decrease in feces evacuation.
 - ✓ Atonic constipation. It is caused by decrease in neuroeffector actions on the intestinal musculature. Decrease in neurotonic actions results in intestinal hypotonia and constipation.
- Rectal constipation. It is a consequence of pathologic processes in rectum (rectal fissure, paraproctitis). It is associated with pain. Pain inhibits defecation.
- Mechanic constipation. It is a result of mechanical stool retention by scar or tumor.

Intestinal obstruction (obstipation)

Intestinal obstruction is an impairment of intestinal passage results from the mechanic stool retention, or impairment of intestinal function (closed-loop obstruction).

Causes of acute intestinal obstruction: hernia, thrombosis, closed-loop obstruction, invagination, tumor, commissure.

Classification of obstipation:

Congenital (associated with malformations) and acquired

By pathogenesis:

- mechanical:
 - ✓ obturation type results from the intestine obstruction by tumor or helminths.

- ✓ strangulation type results from the impairment of intestinal passage results from twist of intestinal loop, compression of mesenteric blood vessel by tumor, scar, inflammatory infiltrate
- dynamic
 - ✓ Spastic type results from the impairment of the intestinal peristalsis results from the spasm of the single part of intestine
 - ✓ Paralytic type results from the paralysis of the single part of intestine
- thromboembolic

Questions for self-control of knowledge:

1. What are main causes of digestive disorders.
2. Describe functional relationships between single parts of digestive system.
3. What is role of psycho-emotional factors in development of gastrointestinal tract pathology?
4. What are different forms of eating dysorexia?
5. Is vomiting act a pathological or protective reaction?
6. What is role of reflux esophagitis in occurrence of heartburn?
7. Describe aggressive and protective factors of stomach and duodenum.
8. What are pathological types of gastric secretion?
9. What is role of neurogenic factors in development of gastric ulcers?
10. What is protective role of gastric mucosa?
11. Describe gastroenteropancreatic endocrine system (GEP) and its role in pathology of digestive system.
12. What is pathogenetic significance of constipation and diarrhea for body?
13. What kind of pathological disorders occur after gastrectomy?
14. What are types and stages of intestinal obstruction?
15. What is maldigestion in hypopancreatism?
16. What are causes of acute pancreatitis?

Tasks for self-managed student work:

1. APUD-system; role in digestion pathology.
2. Role of Helicobacter pylori in gastroduodenal pathology.
3. Postresection syndromes, their pathophysiological substantiation.
4. Principles of prevention and therapy of main disorders of digestive system.

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