Methodical Approaches to Modeling the Pathology of the Digestive System in Animals

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ABSTRACT

The pathology of the digestive system is of great interest to researchers in the field of medicine and physiology. However, today there is no clear understanding of the issues of experimental modeling of diseases of this system. The methods presented in this article for modeling diseases of the digestive system, in our opinion, should provide significant assistance to researchers in this area.

Keywords: Digestive System; Experimental; Animals

Introduction

Pathology of the digestive system is one of the topical topics of modern medical science. Understanding the processes of formation and development of diseases of the digestive system should be considered as a mandatory element of the knowledge of medical professionals who encounter these pathologies in their practice [1-8]. In this regard, there is a need for the existence of methods that allow in experimental conditions to simulate and study certain pathological processes of the digestive organs [9]. The presented article is an overview of the currently existing methods of modeling such processes. To study the secretory and motor functions of the digestive organs, special preparation of animals is required (operation of removal of the ducts of the salivary gland [10], esophagotomy, isolated ventricle, imposition of bass fistula [11-13], etc.), special care and feeding (especially for esophagotomized animals). Of all the operations on the stomach, the most simple is the imposition of a Basov fistula. In particular, such animals can be experimented with imaginary feeding, giving small pieces of meat with an open fistula, into which they fall. This method allows you to collect gastric juice without complicated esophagotomy or isolated ventricle operations. In some cases, the degree of digestion of food and the condition of the stomach and intestines can be investigated by opening the animals after appropriate intervention [1,6].

Technique of Some Surgical Interventions in Experimental Pathology of Digestion

Technique of the Operation of Removing the Duct of the Parotid Salivary Gland

The operation is performed with thiopental anesthesia, the dose is slightly increased. During the operation itself, a tampon moistened with an ether-chloroform mixture is placed in the dog's mouth. The opening of the parotid gland duct is found (against a large carnivorous tooth) and a thin probe (0.3-0.6 mm) with a button-like thickening at the end is inserted into it. The probe is left until the end of the operation. A circular incision of the mucosa

with a diameter of 8-10 mm is formed around the duct . In front and behind the duct, a ligature is applied. The incision of the mucosa is deepened (at this stage it is important not to damage the vessel) and, pulling the formed mucous flap with the mouth of the duct by ligatures, the duct is dissected for 4-5 cm. The pre-shaved cheek is pierced with a scalpel from the inside, tweezers are inserted into the hole, with which the ligatures are captured and the duct is extracted. In order not to twist the duct, the anterior or posterior ligature is marked with a nodule. On the cheek, the ligatures are arranged in reverse order: front – back (to the tail), back – forward. A round flap of mucosa with a duct opening is straightened, the skin is cut off under it, sewn to the skin with 6-8 stitches. The wound in the oral cavity is closed with a continuous suture, without tightening I [9]t.

Technique of Gastric Fistula Surgery

To apply a stomach fistula in an animal under general anesthesia, the abdominal cavity is opened along the midline between the xiphoid process and the navel. The stomach is tightened and in the area of its bottom, retreating 2-3 cm from the edge, a thick string is applied with a pouch seam in the form of an oval (parallel to the blood vessels) with a diameter equal to the diameter of the lower disc of the fistula. The ligature is applied so that it captures the serous-muscular layer without mucosa. The serous membrane and muscles are cut, the protruding submucosa is cut flat together with the mucosa and a fistula tube is screwed into the resulting hole. Tighten the pouch seam. Stepping back from it by 1 cm, a second pouch seam is applied, the tightening of which immerses the first. Then the fistula is strengthened in the abdominal wound by suturing the peritoneum (together with muscles or aponeurosis), on the skin and muscles. For better fixation, the protruding part of the fistula is wrapped with a gauze swab under its outer disc, so that the inner disc fits more tightly to the stomach wall (the swab is removed after a day). During the first two days, the dog is not given any food or water. On the third day, she is given 100-400 ml of warmed water, on the fourth, the same amount of milk diluted with water is added. On the fifth –they give whole milk and water, on the sixth –the same with the addition of 50-100 g of white bread soaked in milk. Then the amount of food is gradually increased by adding pieces of meat [13].

Esophagotomy Surgery Technique

An esophagotomy operation is performed on dogs that already have a fistula, stomach, or simultaneously with the imposition of a fistula. Before the operation, atropine is injected (0.4 mg per 1 kg of weight) to reduce salivation. The skin of the neck along the middle line is cut into 4-6 cm, the muscles are bred in a blunt way. They grab the esophagus with a pean, pull it to the left of the trachea and cut it to half with scissors. The edges of the esophageal wound are deployed, sewn to the edges of the skin incision along the entire circumference and lubricated with iodine, the skin around the wound with vaseline. The dog is fed through the fistula in the usual way. In addition to food, a saline solution (300-500 ml 1-2 times a day) is injected into the stomach to avoid dehydration due to loss of saliva through the esophageal fistula [13].

Preparation for Experience in Experimental Pathology of Digestion

Experiments are performed on an empty stomach (the last feeding for 18-20 hours). Before the experiment, the stomach is washed through a fistula tube. Warm water (30-35 °) is poured into a large (300-400 ml) funnel or a bottle with a tube. The rubber tube from the funnel or bottle is clamped with a clamp and connected to a special stopper for the fistula, into which a glass tube is inserted. Water is allowed into the stomach slowly, rhythmically squeezing the rubber tube, since rapid filling of the stomach can cause vomiting. Water is poured out of the stomach by removing the stopper. Washing is done until the water becomes clean. When all the water drains (after 5-10 minutes), the experiment begins [9].

Digestive Disorders with Lesions of the Nervous System

Demonstration of Gastric Secretion Disorders in Brain Damage

15-18 hours before the demonstration, two frogs are fed with a bloodworm (10-12 pieces of bloodworm are put in the frog's mouth and pushed into the esophagus). After that, the brain of one of the frogs is cut at the level of the visual halls, and the second one is left without damage to the central nervous system. At the demonstration, the stomach cavity is opened. In a normal frog, the bloodworm is digested and turns into a homogeneous grayish gruel, while in a decerebrated one, part of the bloodworm retains its shape and color, and sometimes live worms are found. In the absence of a bloodworm, it is replaced with thinly sliced pieces of meat [3]. During the demonstration, both frogs have their stomachs opened. In a decerebrated frog, individual pieces of food (worms, pieces of meat) that have not been chemically exposed to digestive enzymes are clearly visible in the stomach contents. At the same time, a homogeneous gruel is observed in the stomach of the control frog [9]. Demonstration of violations of the motor function of the stomach with brain damage 15-18 hours before the demonstration, 1-1.5 ml of 40% suspension of barium sulfate in water ($BaSO_4$) is injected into the oral cavity by pipette to two frogs. Then one of them has her brain cut at the level of the visual halls. At the demonstration, both frogs are dissected. In a normal frog, the stomach is free of barium porridge by this time, while in a decerebrated frog, the porridge is still in the stomach. It is also possible to demonstrate the corresponding radiographs (to remove radiographs, frogs are placed in chemical cups with a diameter of

about 7 cm), on which similar phenomena will be observed in the movement of barium suspension through the gastrointestinal tract [5]. Violations of the secretory and motor functions of the stomach in brain lesions can be reproduced in other animals, causing inflammatory changes in the brain (by injecting turpentine, hot water, pathogens of infectious diseases, etc. into its tissue through a trepanation hole) [5]. As the above experiments on frogs show, the inhibition of stomach function with damage to the visual chambers lasts longer than the inhibition of motor reflexes, heart activity or respiration with the same damage to the central nervous system [14].

Demonstration of Unconditionally and Conditionally Reflex Disorders of Gastric Secretion

The experiment is put on a dog with a stomach fistula by Basov and with an esophagotomy (or without it). Operations are performed 3 weeks before the demonstration. Food is taken away 18-20 hours before the experiment. The stomach is washed. Gastric secretion is caused by imaginary feeding. Imaginary feeding (meat) is performed during the demonstration for 5 minutes. Gastric juice is collected after the end of the latent period (duration on average 6-7 minutes). Samples are taken every 15 minutes. Painful irritation of the skin of the hind paw is caused by induction current for 1-2 seconds at a distance between the coils of 0-5 cm 30 minutes after the start of feeding (the time of the greatest increase in gastric juice secretion). Following the painful irritation, the secretion is sharply inhibited for 30-40 minutes. After that, the rise and further attenuation of the secretion follows again. After 2-3 combinations, the secretion of gastric juice is inhibited already with one application of electrodes to the dog or with one blow of the inductor [4,15,16].

Demonstration of Unconditionally and Conditionally Reflex Disorders of the Motor Function of the Stomach

The experiment is put on a dog with a Bass fistula. Preparation for the experience is similar to that described in the previous section. Food is taken away 16-18 hours before the experiment. The stomach is washed. A can of thin rubber, the size of a walnut, is injected into the stomach through the fistula. The can and the rubber tube attached to it are filled with warm water and connected to a water pressure gauge. The other arm of the pressure gauge containing air is connected to the Mareev capsule. The balloon is placed near the fistula, because when it penetrates into the pyloric part of the stomach, not periodic hungry contractions will be recorded, but constant peristaltic contractions of the pyloric part of the stomach. During hunger contractions, the walls of the stomach squeeze the balloon and squeeze the air out of it. The corresponding pressure changes are recorded on the kimograph tape. Hunger contractions occur every 1-1.5 hours and last for 20-30 minutes [9]. If the pain irritation (see previous experience) is

applied at the beginning of the period of hunger contractions, then simultaneously with the general defensive reaction, there is an inhibition of hunger contractions for 4-6 minutes. Then the cuts resume. If pain irritation is applied in the second half of the period of hunger contractions, then they completely stop and do not resume until the next period. After 2-3 combinations, one application of the electrode to the dog or the impact of the inductor slows down the hungry contractions. Due to some methodological difficulties of this demonstration (the possibility of spontaneous inhibition of hunger contractions in a lecture demonstration), we can limit ourselves to showing the curves obtained in previous experiments [9].

Demonstration of Acute Gastric Atony after Vagotomy

The experience is put on the dog. Half an hour before the demonstration, both vagus nerves are prepared on the neck and ligatures are applied to them. Both nerves are cut directly during the demonstration. Immediately after the operation, the abdominal cavity is opened. The stomach is stretched like a sack, the walls of the stomach are sluggish, the tone of their muscles is weakened, peristaltic movements are barely noticeable, and the sphincter is closed. Under normal conditions, the walls of the stomach tightly cover its contents (the animal should be fed before the operation). Due to the presence of intramural ganglia of the Auerbach plexus in the stomach wall, its motor function can be restored with vagus nerve paralysis. The same cutting in rabbits does not lead to stomach atony, since their vagus nerves are not toned [7]. Irritation of the vagus nerve increases the tone of the stomach walls, increases peristalsis and simultaneously weakens the tone of the pylorus, which contributes to the evacuation of stomach contents into the duodenum [15,16].

Violations of Secretory Function when the Salivary Glands are Affected

Demonstration of Violations of Saliva Secretion in Mumps

The experiment is put on a dog with the ducts of the parotid gland removed (right and left). 1-2 days before the demonstration, a skin incision is made over the parotid gland and a suspension of earthen soil or 0.2-0.3 ml of 50% turpentine emulsion is injected into its thickness with a syringe. To excite secretion during the demonstration, 30.0 g of ground crackers are fed to the animal or 30 ml of 0.5% hydrochloric acid solution is washed in the mouth. Saliva is collected in graduated test tubes. 2-3 times less saliva is released from the inflamed gland than from the normal one. This saliva is usually cloudy, contains more organic substances (due to inflammatory exudate). The normal level of saliva secretion is restored after 5-10 days, and on some days the amount of saliva exceeds normal [1]. Histological examination of the affected gland shows that the restoration of secretion occurs even before

the elimination of the inflammatory focus in the tissues of the gland and is possible with a significant replacement of functional glandular tissue with connective tissue. Obviously, the disruption and restoration of the function of the affected gland cannot be explained by structural changes in its tissue alone. They also depend on changes in the nervous regulation of the gland activity caused by irritation from the lesion. The significance of reflex changes in the secretion of the gland, arising under the influence of pathological impulses from the focus of inflammation, can be detected, causing damage not to the gland itself, but to the oral mucosa, which is the receptor zone of the salivation reflex [9].

Demonstration of Violations of Saliva Secretion in Gingivitis

The experiment is put on a dog with the ducts of the parotid gland removed from both sides (according to the Pavlov-Glinsky method). The day before the demonstration, the dog causes a unilateral burn of the mucous membrane of the gums and cheeks with hot water (5-10 ml at 80-90 °). Spontaneous saliva secretion caused by irritation from the burn has been observed for some time. During the demonstration, the secretion of saliva is excited by ground breadcrumbs or weak acid. A sharp asymmetry of salivation from the parotid glands is detected. As a rule, on the side of the lesion, the secretion is increased, on the opposite side it is inhibited. In this experiment, the tissue of the gland itself was not damaged and the violations of its function can only be explained by the reflex action from the focus of inflammation on the centers of salivation. The asymmetry of the salivary glands indicates that the absorption of substances formed in the focus of inflammation is not decisive in the violation of salivation. With gingivitis, the conditionally reflex secretion of the salivary glands is also disrupted. Consequently, irritation from the focus of inflammation extends to the cerebral cortex 6]. Unconditionally- and conditionally-reflex salivation is restored (as in the case of direct damage to the gland itself) usually before the healing of the tissue defect. Irritation from a pathological focus on the oral mucosa leaves a trace aftereffect in the cerebral cortex. Additional irritation of the animal (by anesthesia, examination of conditioned reflexes after a long break, emergency inhibition of conditioned reflexes) soon after the restoration of salivation and elimination of the inflammatory focus in a number of experiments again leads to the same violations of reflex secretion of saliva, which were observed in the acute period. Reflex disorders of salivation can also be observed with inflammation of the gastric mucosa. At the same time, the secretion of saliva is so abundant that it is also visible in a dog without the ducts of the glands removed [9].

Digestive Disorders with Stomach Lesions

Demonstration of Acute Gastritis

Acute gastritis is easiest to cause by burning the gastric mucosa.

If the experiment is performed on a dog without a fistula, then the burn is performed through a probe inserted into the esophagus (you can use a conventional, not too soft rubber tube). To insert the probe into the esophagus, a well-rounded plate with a hole of 1.5-2 cm in diameter is inserted into the dog's mouth (behind the canines). Holding the tablet between the jaws, they bind it to the dog's muzzle. The dog's muzzle is raised so that the esophagus and mouth cavity lie on the same straight line. After calming the animal, a probe soaked in warm water is pushed through the hole in the tablet and injected into the esophagus. If the probe gets into the trachea, a cough begins. Then the probe is pulled back, the dog's head is raised steeply and its end is directed slightly higher. If the probe has entered the esophagus, then it goes on freely, without resistance, and the animal does not worry (it is necessary that it be completely calm at the time of administration). The distance to which the probe needs to be inserted so that the end of it gets into the stomach is determined by eye by the size of the dog [5]. After entering the probe, they clamp its lumen and hold it for 20-30 seconds. If the animal does not suffocate at the same time, then the probe is inserted correctly. Only after that, 100-150 ml of hot water at 80 ° is injected through a funnel connected to the probe. If the experiment is put on a dog with a gastric fistula (which allows you to study in detail the motor and secretory function of the stomach in acute gastritis), then the burn is caused by a test tube-a thermocouter. A glass tube is inserted into an ordinary test tube through which hot water is passed. To isolate the tube from the walls of the fistula and to divert hot water from the test tube, a rubber tube with a hole for a glass tube is put on it, which is fixed at the same time [2].

The dog is put into the machine, fixed, put on a mask. Boiling water is passed through a test tube for warming up, then it is injected through the fistula until it comes into contact with the back wall of the stomach and held for 2 minutes. The amount of mucosal erosion reaches 1.5-2 cm in diameter. The resulting limited inflammatory process allows further examination of gastric juice without a large admixture of exudate, usually observed with diffuse burn of the gastric mucosa. This technique allows you to examine the gastric juice in acute gastritis without prior surgery of the isolated ventricle. 1-2 minutes after the burn, a picture of acute gastritis develops: vomiting, nausea, excessive salivation, loss of appetite. Vomiting movements are usually repeated rhythmically, at first with intervals of 3-5 minutes, then less frequently [9]. The occurrence of vomiting is associated with peculiar changes in the work of skeletal muscles, which should be paid attention to by the audience. The onset of vomiting is preceded by a deep breath and breath retention. However, instead of the usual weakening of the abdominal muscles corresponding to inspiration, the abdominal muscles contract. The combined pressure of the contracted diaphragm and abdominal

muscles contributes to squeezing the contents of the stomach into the esophagus. The cardiac sphincter opens during vomiting, the vomit enters the esophagus and is expelled outwards by its antiperistaltic movements. These movements begin in the intestine, so the contents of the intestine, bile, pancreatic juice are mixed with the vomit. Due to the simultaneous reflex closure of the nasopharynx and larynx, vomit does not enter the respiratory tract. All this complex complex of reflexes is carried out by the vomiting center located in the medulla oblongata, near the respiratory center. The afferent pathways for these reflexes in case of irritation of the gastric mucosa are the vagus and the abdominal nerves. Efferent impulses arrive to the stomach via the vagus nerves, to the diaphragm – via the diaphragmatic nerves and to the abdominal muscles – via the spinal nerves of the corresponding segments of the spinal cord. Cutting the spinal cord under the oblong prevents the possibility of vomiting.

Vomiting is accompanied by nausea. Salivation increases sharply: a very viscous, thick saliva is separated from the dog, usually in large quantities. In addition to changes in the digestive organs, a burn of the gastric mucosa causes shortness of breath and tachycardia. At the same time, the general excitement of the animal is observed, which after 3-4 hours is replaced by sleep. Thus, the body's response to impulses from the lesion in the stomach immediately after the burn depends on the wide irradiation of excitement through the central nervous system (vomiting attacks, hypersalivation, shortness of breath, tachycardia, general excitement, turning into sleep). The process of restoring impaired functions begins shortly after the burn of the mucous membrane and is expressed in limiting reactions to damage (dyspnea, vomiting and hypersalivation disappear). Functional disorders last the longest in the damaged stomach itself. Within 3-7 days, a large amount of bloody viscous mucosal fluid is released from the fistula. The increase in mucus secretion has a protective character. Mucus binds a harmful agent injected into the stomach and, enveloping the mucosa, protects it from direct contact with it [6,7].

Changes in Motor Function in Acute Gastritis

This phenomenon can be studied in detail on a dog with a stomach fistula. If a balloon is injected into the stomach immediately after burning the mucous membrane, then the registration of its movements will show continuous periodic contractions of the type of hungry periodicals. These contractions are, apparently, the cause of one of the characteristic clinical signs of gastritis – pain. Changes in the motility of the stomach when its mucosa is damaged cannot be explained only by local irritation from the lesion: they depend on the reflex excitation of the central nervous system by impulses from a pathological focus. After cutting the vagus nerves, the reaction to the burn of the gastric mucosa is weakened. The clinic also notes that with injections of atropine (the paralyzing end of the vagus nerves), the phenomena of pylorospasm are removed [9].

Changes in Secretory Function

Gastric secretion is caused by imaginary feeding or irritation with food (the first phase of secretion) and subcutaneous administration of 1 ml of 0.1% histamine solution (the second phase of secretion). The first phase of gastric juice secretion after a burn is sharply suppressed. The dog refuses to eat, it does not release juice for food irritation. More greedy dogs (most often males) eat the meat offered to them (which falls into the opening of the fistula). But even with imaginary feeding, a sharp inhibition of gastric juice secretion is detected until its complete cessation. This can be detected by examining the reaction of the separated stomach to litmus or to a piece of paper with the color of a conglomerate. Gastric juice should be collected outside of vomiting attacks when, as a result of antiperistaltic movements, the contents of the duodenum enter the stomach. In acute gastritis, not only the first phase of secretion (for imaginary feeding) is suppressed, but also the second phase – for histamine injection. Gist-min is injected under the skin (1 ml of 0.1% solution). The latent secretion period lasts from 10 to 12 minutes. Hyposecretion is also detected on histamine administration, although not as sharply as on imaginary feeding [11]. On the 2nd-3rd day after the burn, hyposecretion is usually replaced by hypersecretion, which can be shown on the same dog during the next demonstration. With a decrease in the secretion of gastric juice and a decrease in its acidity, the digestion of proteins is mainly disrupted. It depends both on the reduction of the amount of pepsin and on the decrease in acidity. Gastric juice is taken before and after the stomach burn, poured into 3-4 ml test tubes, a small piece of freshly obtained fibrin is added and put in a water bath at 37-40 ° for 30-60 minutes. Taking out the test tubes, they find a complete dissolution of a piece of protein in a test tube with gastric juice taken before the experiment, and incomplete – in a test tube with a detachable burnt stomach. Instead of fibrin, rolled egg white or frog muscles can be used in this experiment [14]. In experiments conducted in the laboratory of I. P. Pavlov, secretion disorders in gastritis were studied on dogs with an isolated ventricle. This made it possible to study changes in the secretion of an intact part of the stomach under the influence of a burn of another part of it. A burn of a large or small isolated ventricle in a dog was caused by the introduction of hot water at 80-90 ° or 1% sulema solution. The secretion was immediately inhibited in both the burnt and unburned parts of the stomach. After some time, hyposecretion was replaced by hypersecretion. Violation of secretion in the unburned part of the stomach occurs reflexively, as a result of extreme pathological irritation of the nerve endings of the gastric mucosa. With repeated damage to the gastric mucosa, there are changes in secretion characteristic of chronic gastritis. Sometimes, in the first hour, a much larger amount of juice is released on a food irritant than in a normal state, but the secretion stops quickly, i.e. the first phase of secretion prevails. In other cases,

much less juice is released in the first hour than normal, but from the second hour, the secretion increases and takes on a protracted character, i.e. the second phase of secretion prevails. The first state of I. P. Pavlov compared it with the state of neurasthenia, with the type of reactions characteristic of the sanguine temperament of the nervous system, and the second with the type of reactions of the choleric temperament [6].

Demonstration of Changes in the Nervous Regulation of Stomach Functions in Acute Gastritis

1. Violation of reflex secretion for imaginary feeding in acute gastritis during the modeling of this pathology described above.

2. Similarly, the reactions of a pathologically altered stomach to pain irritation change. Normally, pain irritation inhibits the secretion and hungry contractions of the stomach. After a burn, these reactions weaken. The experiment is put on a dog with focal gastritis (on the day of the burn). Half an hour after the start of secretion (for imaginary feeding or histamine), electrocutaneous pain irritation is applied to the animal. The motor-defensive reaction in the animal persists, but the inhibition of secretion caused by pain irritation is weaker and less prolonged than in a healthy dog. The reaction to conditioned reflex irritation is also weakened. Obviously, the irritation from the pathologically altered mucosa has spread to the cerebral cortex.

3. Reflex effects on the motor activity of the stomach are also weakened. Neither unconditionally nor conditionally reflex pain irritation slows down those continuous tonic contractions of the stomach that occur after a burn of its mucosa.

This weakening of reflex reactions, which occurs immediately after damage to the gastric mucosa, is then replaced by increased sensitivity to various kinds of additional influences. This explains the fact that a variety of irritations acting on the body of a patient suffering from, for example, a stomach ulcer: mental stress, fatigue or sharp fluctuations in barometric pressure – often provoke pylorospasm, exacerbation of secretion disorders. The functions of the stomach in acute gastritis are restored in the experiment a few days after the burn, as a rule, before the healing of the tissue defect. In addition, direct experiments have established that in case of insufficiency of the central nervous system caused by experimental neurosis in a dog, the restoration of stomach function when its mucosa is affected is significantly delayed compared to the restoration of function with the same lesion in an animal with a normal nervous system [9].

Demonstration of Violations of the Evacuation Function of the Stomach in Achilia

The experiment is put on a freshly fed rabbit. Under local anesthesia, the animal's abdominal cavity is opened. The walls of the stomach tightly cover its contents. The esophagus is cut under the diaphragm and the duodenum at the place of its transition to the small intestine. Despite the cutting of the branches of the vagus nerve (along with the esophagus), the stomach walls do not lose their tone, since the rabbit's vagus nerve is not toned. The stomach is taken out and shown. Rare peristaltic movements in the pyloric part of the stomach are clearly visible. When pressing on it (sometimes up to the rupture of the walls), food does not pass into the intestine. Normally, the pyloric sphincter opens only after neutralizing the next portion of acidic chyme with alkaline juice of the pyloric part of the stomach and duodenum [2]. If 5-10 ml of 10% NaOH solution is injected into the stomach, the pyloric opening opens, the food freely passes into the segment of the intestine and falls out of it. With achilia, the pilorus gapes and the contents of the stomach continuously drain into the duodenum [1]. It should be noted, however, that under natural conditions, achilia can also be accompanied by a delay in emptying the stomach, which apparently depends on the accompanying gastric atony. The intake of insufficiently digested food into the intestines causes further digestive disorders. In the absence of hydrochloric acid in the stomach, microbial flora develops intensively, fermentation processes begin and the accumulated lactic acid is thrown into the esophagus, causing a feeling of heartburn. The spread of microbial flora to the small intestine leads to the development of enteritis. A decrease in acidity also weakens the secretion of the pancreas, which normally occurs reflexively, in response to irritation of the duodenum with acidic stomach contents. With an increase in the secretion of gastric juice, the pyloric reflex increases. The tone of the walls of the stomach increases until the appearance of spastic contractions, especially in the pyloric part of it. Evacuation of food from the stomach to the duodenum slows down. However, evacuation may remain undisturbed, apparently due to increased secretion of saliva, neutralizing the acidic contents of the stomach. In the case of slowing down the evacuation of stomach contents, increased fermentation of carbohydrate food develops. Gases accumulate in the stomach, belching, vomiting, heartburn appear [9].

Demonstration of Gastric Obstruction

On the eve of the demonstration, the rabbit's abdominal cavity is opened under local anesthesia and ligatures are applied to the pyloric part of the stomach. During the demonstration, the animal is examined and then the abdominal cavity is opened. The stomach is sharply swollen, as the food, lingering in it, begins to ferment, releasing gases: carbon dioxide (50-80%), methane (25-30%), hydrogen sulfide, nitrogen, oxygen. Mechanical irritation experienced by the gastric mucosa during its stretching dramatically increases the secretion of gastric juice, its acidity

reaches 120-150 units. The delay of food in the stomach leads to a slowdown in intestinal motility, weakening of pancreatic secretion and separation of bile. If partial patency persists between the stomach and intestines, then gases pass into the intestines, causing general flatulence [8].

Digestive Disorders with Intestinal Lesions

Demonstration of Acute Enteritis

The rabbit's abdominal cavity is opened under local anesthesia. By applying two ligatures to one of the loops of the small intestine at a distance of 10-15 cm from each other, an isolated segment of the intestine is created. The same segment is created at a distance of 5-10 cm from the first one. In one of these isolated segments of the intestine, 2-3 ml of hot water is injected with a syringe at 80°C, in the other – the same amount of saline solution at 38°C. Both isolated loops are lowered into the abdominal cavity. After 30 minutes, they are taken out, opened and their contents are collected in test tubes. The unburned segment is empty, the burnt one contains a large amount of intestinal juice.

At one time, back in the laboratory of I. P. Pavlov, it was shown that the same increase in the secretion of intestinal juice, poor in enzymes, occurs also with mechanical and chemical irritation of its mucosa. Increased secretion of intestinal juice in acute enteritis occurs reflexively in response to irritation from a pathologically altered mucosa. In chronic experiments on dogs with a loop of the small intestine removed under the skin, mucosal burn also leads to increased secretion of intestinal juice, but after denervation of the loop, this effect is absent [3]. Increased secretion of intestinal juice in acute inflammatory bowel processes is one of the reasons for the appearance of liquid feces in diarrhea. Another reason for this is increased intestinal motility, which is common in acute inflammation of it. If diarrhea depends on increased peristalsis not only in the colon, but also in the small intestine, then the absorption processes and nutrition of the body are disrupted. If diarrhea depends only on the increased peristalsis of the large intestine, then such disorders do not occur, since the absorption processes have already been completed in the small intestine. Chronic inflammatory processes of the intestinal mucosa, on the contrary, are characterized by a decrease in secretion and a slowdown in peristalsis, leading to constipation. Constipation, accompanied by a delay in the contents in the large intestine, increases the processes of fermentation and putrefaction, which causes a number of severe functional disorders of the nervous and cardiovascular system. By itself, a decrease in the secretion of intestinal juice probably does not matter much for the digestion of food. The removal of 2/3 of the small intestines in a dog is tolerated by the animal satisfactorily. This is due to the compensatory enhancement of the function of the pancreas and the remaining part of the small intestine. Only the

removal of the duodenum leads to death even when transplanting the ducts of the pancreas and liver flowing into it, which probably depends on the loss of the secretory influence of the duodenum [9].

Demonstration of Intestinal Obstruction

The most severe consequences are caused by complete intestinal obstruction, which occurs when its loop is turned around its axis or when the overlying segment of the intestine is invaginated into the underlying one (which is possible with a sharp increase in peristalsis), when the intestine is compressed by a tumor or scar. In an experiment, the phenomena of mechanical obstruction can be studied by applying a ligature to any part of the intestine in a cat or dog [9]. Peristalsis is inhibited below the ligation site, above it increases up to spastic contractions. In the postoperative period, the animal refuses to eat, vomiting occurs, sometimes with feces (if a ligature is applied to the large intestine), cessation of defecation. The overlying part of the intestines gradually fills with gases, the intestine stretches, the movement of the intestines stops and complete paralysis of the entire intestine occurs. The animal is shown 2-3 days after the aseptic ligature is applied to the intestine and then opened. Local disorders of tissue nutrition near the obstacle lead to necrosis, which causes reactive inflammation of neighboring areas of the intestine and peritoneum, and sometimes general peritonitis. In some cases, the ligation of the bowel loop in a dog does not lead to the death of the animal. Due to the increased peristalsis, the overlying area creeps onto the lower one, covering it with a stocking. The bandaged part of the intestine is digested and thus intestinal patency is restored [17].

Demonstration of Circulatory and Respiratory Disorders in Pathological Changes of the Gastrointestinal Tract

With digestive disorders leading to the accumulation of gases in the gastrointestinal tract (flatulence), respiratory and circulatory disorders occur. The experiment is put on a cat under general anesthesia. Blood pressure in the carotid artery and respiration are recorded. Through a probe inserted into the esophagus, air is pumped into the stomach by a bicycle pump. Initially, filling the stomach with air causes its spastic contractions and pylorospasm, then the air breaks into the intestine and quickly spreads through it. A swollen stomach, by raising the diaphragm, reduces intra-thoracic pressure, thereby preventing diastolic filling of the heart. The flow of venous blood weakens, as the swollen stomach squeezes the hollow veins. Blood pressure drops, heart contractions become more frequent. Opening the peritoneum, the swollen stomach and intestines are shown, as well as the position of the diaphragm [18]. Respiratory and circulatory disorders depend not only on the mechanical pressure of the stomach on the diaphragm, but also on the irritation of the vegetative centers by impulses from the overgrown walls of the gastrointestinal tract. This is proved by

the following experience. The loop of the intestine 35-40 cm long is brought to the surface of the abdominal wall and bandaged at the edges with two ligatures. The loop is inflated with air through a cannula (pump). The possibility of mechanical pressure on the diaphragm and hollow veins in this form of experience is excluded. Breathing and blood circulation are disrupted reflexively. To register these violations on one animal, first put this experience, then the previous one [9].

Digestive Disorders in Lesions Pancreas and Liver

Demonstration of Digestive Disorders in Pancreatic Insufficiency

The experiment is put on a dog who has both pancreatic ducts ligated 1-2 weeks before the demonstration. The large duct enters the duodenum along the common bile duct and is usually 1-2 mm in diameter. The smaller duct is covered with gland tissue and is very thin. The easiest way to approach it is from the side opposite to the entrance of the large duct. The study of feces in these dogs gives an idea of the digestive disorders that occur during this operation [9]. The absence of pancreatic secretions affects the digestion and assimilation of all nutrients. Only 50% of proteins are digested. When examining the feces of a dog under a microscope, muscle fibers are found that have retained transverse striation and nuclei. If a smear of feces is applied to gelatin, then it is not digested, since feces does not contain trypsin. It also contains up to 40% undigested starch. The digestion of fats is sharply disrupted. The absence of pancreatic lipase (steapsine) leads to the fact that up to 60% of fats are excreted in the feces in undigested form. Fatty droplets envelop protein particles, contributing to their rotting. Insufficiency of pancreatic secretion in a growing organism can cause growth disorders, preventing the absorption of fat-soluble vitamins [18,19].

Demonstration of Mechanical Jaundice

8-10 days before the demonstration, the cat's common bile duct is bandaged. The abdominal cavity is opened by an incision along the midline from the end of the xiphoid process to the navel. The stomach and duodenum are moved away from the liver and the hepatoduodenal ligament is found. The ligature is brought under the common bile duct and tightened. Demonstrating the animal, pay attention to the jaundice of the sclera of the eyes, conjunctiva, gum mucosa, skin and the general condition of the animal. A few days after the ligation of the common bile duct, the animal experiences excitement, which then turns into drowsiness and indifference to the environment. The pulse is calculated – the rhythm of cardiac activity is slowed down. Sometimes there is periodic breathing. Then the animal is killed. At the autopsy, it is found that the fatty tissue (subcutaneous fat layer, omentum, perinephrine tissue), mesentery, intima of blood vessels and heart valves are most strongly colored.

The brain does not acquire a yellow color, since the blood-brain barrier prevents the passage of bile pigments. Gland secretions (saliva, tears, milk) in jaundice are usually not colored, which also depends on the presence of histohematic barriers [9]. Collect blood from the heart into a test tube. Blood clotting is reduced. Blood plasma is also colored yellow. The jaundice of the tissues is caused by the deposition of bile pigments in them. Bile pigments are formed from the hemoglobin of decayed red blood cells. The iron–containing part of the hemoglobin molecule breaks down to form hemosiderin, and hematoporphyrin turns into a bile pigment - bilirubin. Decaying erythrocytes and their shells are captured and absorbed by the cells of the entire reticular-endothelial system. Therefore, bilirubin is produced not only in the liver, in merchant cells, but also in the bone marrow and in the spleen. However, the place of bilirubin excretion is only the liver. Arriving with bile in the intestine, bile pigments under the influence of microbes turn into urobilin, staining feces. Part of the urobilin from the intestine is absorbed into the blood and enters back into the liver (where it again turns into bilirubin), part is excreted in the urine, giving it a characteristic color [12]. With mechanical jaundice, bile does not enter the intestine, feces are not stained. The rectum is opened. Feces are clayey, whitish, with a putrid smell, very dense. Bilirubin does not turn into urobilin, but directly passes into urine. Collect urine from the bladder – it is sharply jaundiced, brown in color. Cessation of bile outflow after ligation of the common bile duct causes digestion disorders, mainly fats. Fats are not emulsified and their cleavage by lipase is difficult. Over 50% of the fat coming from food (instead of 5-10% normally) is excreted in the feces. Fat envelops protein particles, which prevents the action of proteolytic enzymes on proteins. The absence of bile weakens intestinal peristalsis, constipation develops. 1-3 months after the ligation of the common bile duct, the animal dies with the phenomena of severe exhaustion. With the complete exclusion of fats from the diet, animals live longer [20,21].

Test for Bile Pigments in Urine: About 1 ml of urine is poured into a test tube. Carefully, the same amount of concentrated nitric acid is layered on the wall. A green ring is formed at the boundary of liquids in the presence of pigments [9].

Test for Urobilin: 8-10 ml of urine is poured into a test tube, acidified with 2% hydrochloric acid. Add 2-3 ml of amyl alcohol and, closing the tube with a rubber stopper, turn it over several times. When the contents settle, a few drops of zinc chloride solution are added to the upper alcohol layer (1 g of zinc chloride is dissolved in 100 ml of ethyl alcohol and alkalized with an ammonia solution). In the presence of urobilin, green fluorescence appears [9].

Test for bile Acids in the Urine: This test is based on lowering the surface tension. Pour about 50 ml of urine into a cup, neutralize it with a 1% solution of caustic soda until pink staining

with phenolphthalein appears (1-2 drops), cool for 10 minutes (lowering the cup into cold water), then pour a little sulfur color on the surface of the urine. If it sinks, then bile acids and salts are not less than 0.01%. If it remains on the surface, there are no bile acids in the urine.

Lowering the Surface Tension of Fat Under the Action of Bile

1.   0.5 ml of vegetable oil is poured into a test tube with 3-5 ml of bile and shaken. It turns out a thin, resistant emulsion.

2.   Filter the fat through 2 filters: one moistened with water, the other with bile. Through the first fat does not pass, through the second – it goes quickly [9].

Demonstration of the Penetration of Fluid from the Gallbladder into the Bloodstream

In a dog or rabbit, under general anesthesia, the abdominal cavity is opened along the middle line and the cystic duct is tied at the gallbladder itself, and the common bile duct is prepared at the place of its entry into the duodenum. A cannula is inserted into it and a warm solution of indigocarmine is injected through it under pressure into the gallbladder. The paint can also be injected with a large syringe (50-100 ml) with a short, wide and blunt needle, if the common bile duct is previously tied below the injection site so that the paint does not enter the intestine. Observe the speed of the passage of paint into the blood, noting the beginning of its introduction and the moment of the appearance of paint in the bladder. After 5-6 minutes, the urine in the bladder turns blue (shown on a white background) [22].

Demonstration of Disorders of the Nervous System in Cholemia

Severe disorders of the functions of the central nervous system, cardiovascular system, respiration with mechanical jaundice are explained not by jaundice, but by poisoning of the body with bile acids absorbed into the blood due to blockage of the common bile duct.

1.   A frog is injected under the skin with 1-2 ml of bile (bovine, dog, rabbit, etc.) or 1-2 ml of deholin. After 5-10 minutes, the frog becomes sluggish, sedentary, covered with foamy mucus. Her reflexes are inhibited.

2.   The acid reflex of the Turk is examined before and after the introduction of bile. 3-5 minutes after the injection, a slowdown in the reflex time to 20-30 seconds or longer is detected.

3.   Irritate the peripheral segment of the sciatic nerve in the same frog by induction current or twitching – they detect a good motor reaction of the limb. Consequently, the inhibition caused by cholemia captures the central part of the reflex arc.

4.   A frog is injected 0.2-0.3 ml of bile directly into the central nervous system, for example, into the brain. Severe tonic and clonic seizures occur [23,24].

Demonstration of Disorders of the Cardiovascular System in Cholemia

1.   The frog is opened. Count or record the number of heart contractions. 0.1 ml of bile diluted in half with water is injected directly into the heart or through the abdominal vein. The activity of the heart slows down, often it stops.

2.   Repeat the same experiment on another frog by injecting it previously (in 20 minutes) 1 ml of atropine (1:1000), paralyzing the end of the vagus nerves in the heart. Bradycardia does not occur. It follows that bradycardia in cholemia depends on the effect of bile salts on the vagus nerves. However, large doses of bile salts cause bradycardia even after cutting the vagus nerves and even on an isolated heart, since they act directly on the sinus node and the conducting system.

3.   The experiment is put on a dog under general anesthesia. The registration of blood pressure in the carotid or femoral artery is being adjusted. The vagus nerves on the neck are prepared and ligatures are placed under them. The femoral vein is prepared for the introduction of bile into it.

The initial blood pressure is measured, then 3-5 ml of dog or bovine bile is injected. Blood pressure drops, but quickly levels out. Continue to slowly inject bile for 15-30 minutes until the appearance of a sharp bradycardia and a decrease in blood pressure. Both vagus nerves are cut – heart contractions become more frequent, blood pressure rises [20].

If you continue to inject bile, then the heart eventually stops, despite the cutting of the nerves, since in high concentration bile acts directly on the heart muscle.

The decrease in blood pressure in cholemia depends not only on the slowing down of the heart, but also on the effect of bile salts on the centers of vascular regulation [23,24].

Demonstration of Respiratory Disorders in Cholemia

The frog's respiration is recorded before and after subcutaneous administration of bile (2 ml). Breathing is recorded by pinching the skin of the chin area with tweezers or simply stitching it with a thread connected to a lever for registration. The frog develops shortness of breath. This experiment can also be carried out on a warm-blooded animal, registering breathing and blood pressure. 5-10 ml of bile is injected into the femoral vein for a dog, 2-4 ml into the jugular vein for a rabbit [9].

Demonstration of Blood Changes in Cholemia

2-3 ml of bile is poured into a test tube with citrate blood. The blood becomes transparent, varnished due to hemolysis of red

blood cells. Bile dissolves cholesterol and lecithin of erythrocyte membranes, causing their decay – hemolysis. In the patient's body, this process is not as pronounced as in a test tube, since red blood cells gradually acquire increased resistance to bile salts. Nevertheless, anemia develops in patients, as bile acid salts inhibit hematopoiesis. Blood clotting with mechanical jaundice decreases, since bile retention also affects the liver tissue, and therefore the production of fibrinogen and fibrin decreases. In addition, the absorption of vitamin K (fat-soluble), which is of great importance for the blood clotting process, is disrupted. A decrease in blood clotting makes surgical interventions very difficult in patients with liver diseases due to severe bleeding [24].

Demonstration of Hepatic Coma

On the eve of the demonstration, 0.2-0.3 g of white phosphorus dissolved in 10-15 ml of vegetable oil (slightly warmed for better dissolution) is injected into the rabbit's stomach through a probe. When preparing the solution, it must be remembered that white phosphorus ignites in the air – it is cut under water and weighed in a closed glass bix. At the demonstration, the animal is examined, stating its extremely serious condition – it lies on its side, does not react to irritation, breathing is difficult. When measuring blood pressure, a significant decrease is detected. The animal is killed by bloodletting. At the autopsy, attention is paid to the liver, which has a yellow color and is easily torn due to pronounced fatty degeneration [25]. The methods of modeling the pathology of the gastrointestinal tract presented in this article cover a wide range of nosological units of gastroenterological, pancreatological and hepatological profile. Allowing the specialists of practical medicine to form an understanding of the development of the main diseases of the organs of the esophageal tract and other organ complexes associated with it, these methods are of high scientific value, since they make it possible to experimentally study lesions of the gastrointestinal tract and violations of their normal physiological processes.

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