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Review Article

Experimental Modeling of the Pathology of the Cardiovascular System in Animals - A Review

Bon LI* and Kokhan NV

Department named DA Maslakov, Grodno State Medical University, Russia

***Corresponding author:** Lizaveta I Bon, Candidate of Biological Science, Assistant Professor of Pathophysiology Department named DA Maslakov, Grodno State Medical University, 80, Gorkogo St, 230009, Grodno, Republic of Belarus, Russia.

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Abstract

The proposed article is an experience of creating a review on the experimental pathology of the cardiovascular system. Much attention is paid to the nervous mechanisms of disturbance and restoration of the functions of pathologically altered organs. It is also important that most of the proposed methods are easily and simply reproducible. For the analysis of functional disorders caused in the experiment, in addition to physiological ones, clinical and pathoanatomical research methods are included. The article will undoubtedly be of interest to a pathophysiologist, a clinician, and even a pathologist. It will prove to be a useful tool for teaching one of the leading disciplines of medical science-pathological physiology.

Keywords: Methodological Approaches; Cardiovascular System; Experimental Animals

Introduction

Experimental animals are often used in studies related to the study of the structure and function of the cardiovascular system in normal and pathological conditions. Information about the morpho functional features of the heart and blood vessels creates a fundamental basis for scientific research, in this regard, it is important analysis and generalization of literature data on methodological approaches for modeling in experimental pathology of the cardiovascular system.

Heart Disorders in Disorders of the Nervous System

Demonstration of Cardiac Arrhythmias in Brain Damage

Experiment of IM Sechenov: 15-20 minutes before the demonstration, the skull is opened in 2-3 frogs, the brain is cut with an eye scalpel at the level of the visual halls (see the description of the operation in the section Pathology of the nervous system). Bleeding is carefully stopped with tampons. The frog is fixed with its stomach up. 2-3 minutes before the demonstration, the work of the heart is checked (the operation itself causes inhibition). A frog with the most frequent heart rhythm is selected, its work is recorded on a kymograph, the surface of the brain incision is carefully dried with filter paper, and a NaCl crystal is applied (for no more than 1 minute) to the incision surface. The heart stops for 30-50 seconds or its rhythm slows down. Sometimes there are uneven intervals between its individual contractions (*sinus arrhythmia*) [1]. An electrocardiographic study reveals: a flat isoelectric line at the time of cardiac arrest, the appearance of a positive T wave (normally weakly expressed in a frog), indicating a violation of the functional state of the myocardium. With the restoration of the

rhythm to the original, the T wave remains invisible. Sometimes (in 20% of experiments) there is a deepening and splitting of the P wave, indicating non-simultaneous coverage of the atrial excitation. The electrocardiogram is restored after 5-6 hours. An electrocardiogram can be taken in advance and demonstrated using an epidiascope.

20 minutes before the experiment, 1 ml of a 1% solution of atropine sulfate is injected under the skin of the frog. Repeat previous experience. Putting a crystal of salt on the visual halls does not slow down the heart rate. Obviously, the influence of pathological irritation of the brain on the heart is carried out through the vagus nerves since atropine paralyzes their endings. Violations of cardiac activity in case of brain damage can be reproduced by causing inflammatory changes by injecting turpentine (0.2-0.3ml), hot water (2-3ml), pathogens of an infectious disease, etc. into the brain of a dog or rabbit through a burr hole in skull. The most dramatic changes in cardiac activity occur when the ventricles of the brain, the hypothalamic region and the brain stem are damaged. In these cases, coronary circulation disorders may appear, giving changes in the electrocardiogram like those in myocardial infarction-a deep Q wave, a deviation of the S-T interval from the isoelectric line, and a negative T wave. In frogs, such changes in the electrocardiogram do not occur due to the lack of coronary circulation [2,3]. Functional changes in the central nervous system can also cause cardiac arrhythmias. Conditioned reflex changes in the rhythm of cardiac activity in the experiment can be induced by a combination of a conditioned stimulus with the introduction of adrenaline, physical work, and other factors that change the heart rhythm [4].

Heart Disorders for Pericardial Damages, Myocardia, and Endocardia

The easiest way to cause cardiac dysfunction is to inject fluid into the pericardium, ligate the coronary vessels, turn off part of the myocardium with a clamp or inject hot saline into the myocardium, traumatic damage to the heart valves (experimental methods are described in the corresponding demonstrations). A wide opening of the chest, undertaken to reproduce certain diseases of the heart (pericarditis, coronary circulation disorders, focal myocardial lesions, etc.), causes a sharp violation of cardiac activity. This difficult operation is accompanied by a huge imposition from the wound, which leads to a loss of vagal tone in those animals in which it is expressed normally (for example, in dogs on which these experiments are usually carried out). The heart rate sharply increases (up to 200-250 beats per minute instead of 70-100) and subsequent transection of the vagus nerves does not cause further acceleration [5]. Such dysregulation of cardiac activity can be avoided by causing appropriate lesions of the heart through a narrow opening in the chest, but this greatly reduces the visibility of the demonstration. In the experiments below, we use both methods-both wide and limited opening of the chest. In rabbits, the tone of the vagus nerves is not normally expressed, and therefore opening the chest does not cause such sharp disturbances in the regulation of cardiac activity in them as in dogs. Many of the experiments that are usually performed on open-chested dogs can be successfully reproduced on rabbits [6].

Technique of operation of wide opening of a thorax. Th e operation is performed on a male dog (in female dogs, when the soft parts are cut, many vessels of the mammary glands have to be tied up, so it is better to avoid taking them for experiments) under general ether-chloroform anesthesia (a two-necked bottle is included in the artificial respiration system, into which, as needed, add ether) or under intravenous anesthesia (5% solution of barb amyl in sterile distilled water is injected at 0.5-0.6ml per 1 kg of weight). Previously, 15 minutes before the dog is administered morphine (0.5-0.75ml of a 1% solution per 1 kg of weight). They establish a record of blood pressure (from the carotid artery), insert a tee for artificial respiration into the trachea. In the absence of a breathing table, artificial respiration is done using an automobile pump connected to the trachea through a tee. On the sides of the sternum, incisions are made, retreating from the top two fingers from the midline. From top to bottom, the incisions diverge to the end of the chest. Above the upper edge of the sternum, the ends of the incisions are connected by cutting the sterno-nipple muscles. Then, at the upper edge of the sternum, the muscles of the shoulder girdle are cut from the sides, ligating the small arteries passing through them. When the ribs open, the musculoskeletal integuments are shifted to the sides and incisions are made in the middle of all intercostal spaces up to the diaphragm along the ribs, first on one side, and then on the other. At the same time artificial respiration is started. Around each rib, except for the top two, a strong twine is circled, and two ligatures are applied to compress the intercostal vessels at about 5 cm from each other. In this case, the lower ligature is applied to the depth at which the ribs are supposed to be cut off after. It is possible, without opening the intercostal spaces, to bring ligatures with a curved conductor [7,5].

When all the ligatures are in place, the ribs are cut with forceps on both sides 1.5 cm above the upper ligature. The anterior wall of the chest is lifted by the upper edge of the sternum, while two mammillary arteries rising from the depths to the sternum become clearly visible, which are tied with a double ligature separately and cut. Then the entire front wall is folded back onto the stomach (the breastbone can be cut across at the diaphragm) and held in place with a paean or suture [4]. Technique of operation of limited opening of a thorax. Anesthesia is given the same as with a wide opening of the chest. For artificial respiration in a dog, a

conventional tracheotomy operation is performed. If they want to keep the animal for a long time, artificial respiration is performed through a tube inserted into the trachea through the larynx. In this case, a glass tube 15-20 cm long and 7-10 mm in diameter with a melted free end is attached to the end of the rubber tube coming from the artificial respiration apparatus. In a dog lying on its back, the mouth is opened wide, the tongue is pulled out, which is then pulled up (to the lower jaw). With the end of the glass tube, the epiglottis is carefully removed to the posterior wall of the pharynx. Then, because of the epiglottis, a diamond-shaped glottis is clearly visible, limited by the vocal cords, which collapse and diverge in time with the breath. A glass tube is inserted through the slit into the trachea at 4-5 cm. After the usual processing of the surgical field, a skin and fascia incision are made 6-8 cm long along the IV or V rib on the left along the axillary line. After the incision of the external intercostal muscles, the rib is exposed and subperiosteally removed for 4-5cm.

The movements of the lungs are clearly visible through the exposed parietal pleura. The pleura is carefully opened with a scalpel (at this moment artificial respiration is turned on). The heart shirt is clearly visible through the surgical wound [7,5]. Pathological changes in the heart can also be caused in a chronic experiment, but this requires long periods and many animals. To obtain experimental myocarditis, adult rabbits are injected into the ear vein with 20g of theophylline (1-2% solution) or 50 mg of nitrobenzoic caffeine. After 2-3 minutes, adrenaline is injected-0.2ml 1:1000 (very slowly-within 3-5 minutes). About a third of rabbits die from acute pulmonary edema. In surviving rabbits, macroscopic changes in the heart are most apparent by the 25th-40th day after the injection. The heart is hypertrophied, its weight increases to 8-14g (normally 5.5-7g). Often there is pericarditis, sometimes with significant adhesions. Microscopically detect focal and diffuse lymphoid infiltrates, vascular sclerosis, cardiosclerosis [8].

Atherosclerosis can be obtained by long-term feeding of animals with cholesterol. Cholesterol is deposited in the intima of blood vessels and endocardium (valves). This leads to a reactive growth of connective tissue and the deposition of lime (sclerosis). The deposition of cholesterol is facilitated by an increase in blood pressure by the administration of adrenaline, compression of the abdominal aorta, narrowing of the renal vessels, etc. Until recently, atherosclerosis was obtained in this way only in rabbits. Relatively recently, it was found that when the basal metabolism is suppressed by thiouracil, feeding with cholesterol causes atherosclerosis in dogs as well. For this purpose, young dogs are administered with food daily for 4 months 0.6-1.2g of thiouracil and 10g of cholesterol, previously dissolved in ether. Feed is given to animals after the evaporation of the ether. The level of cholesterol in the blood reaches 4,000-5,000 mg% (instead of 100-200mg % in the norm). Atheromatous plaques are found in the aorta, valves and coronary vessels of the heart, arteries of the brain, kidneys, etc. Microscopically, pronounced sclerotic changes in the coronary and other vessels are detected [9,6].

Heart Disorders

In Pericardial Lesions

Disorders of cardiac activity with pathological changes in the pericardium are most often caused by the accumulation of fluid in the cavity of the heart shirt. Normally, it contains several milliliters of fluid and the pressure in it, as in the chest, is negative. Under pathological conditions, up to 1 liter of fluid can accumulate in a person's heart shirt. This fluid can be exudate released during exudative pericarditis, transudate-with dropsy of various origins, blood-with rupture or injury of the base of the aorta or heart [5].

Demonstration of a Violation of the Activity of the Heart when Fluid is Injected into the Pericardium

In a dog with a wide-open chest (see the opening technique at the beginning of the section), blood pressure is recorded. The board on which the dog is tied is placed almost vertically, so that the audience can clearly see the heart (good lighting!). So that the lungs that swell during artificial respiration do not block the heart, a bandage, a strip of oilcloth or a sheet of paper is brought under it during a demonstration. Then a heart shirt is cut, a pericardial cannula, a small fistula, or just a glass tube with bent edges is inserted into it. The heart shirt is stitched, retreating 0.5 cm from the edge of the incision with a purse-string suture (the suture can be applied in advance), tighten, and tie the ends of the thread around the cannula or tube. The upper end of the cannula is connected in advance with a rubber tube to a syringe (capacity 100ml) filled with saline heated to 38° (a clamp is applied to the tube, which is removed only before administration). Liquid is injected from the syringe into the pericardial sac (instead of saline, liquid paraffin or air can be injected). The introduction of 20-30 ml does not change blood pressure, while the introduction of 60-80ml leads to its fall. Fluid injected into the pericardium compresses the thin-walled cavities of the atria and right ventricle, preventing their diastole. Blood accumulates in the vena cava and venous pressure rises, which can be established by simultaneously measuring the pressure, for example, in the femoral vein. During the systole of the heart, a venous pulse appears, as part of the blood is thrown back into the vena cava [5,8]. When blood pressure drops sharply, the pericardium is cut open and fluid is drained from it. Blood pressure

is restored, you can see a well-functioning and rhythmically contracting heart [4].

Demonstration of the Role of Nervous Regulation in Pericardial Lesions

Experience put on a dog with a limited opening of the chest. The pericardium is carefully grasped with Kocher's clamps and taken out into the wound, and then cut for 2.5-3cm with a scalpel or pointed scissors. In the manner described above, a pericardial cannula is inserted, and fluid is pumped until a pronounced drop in blood pressure is observed. Then, pre-prepared vagus nerves are cut on the neck. Blood pressure rises, heart rate increases. It is obvious that disturbances in the activity of the heart occur not only from squeezing it with liquid, but also because of irritation of the nerve endings in the pericardium, reflexively, through the centers of the vagus nerves [4]. The functional state of the heart in pericarditis also depends on the speed of accumulation of fluid in the pericardium. With the rapid introduction of relatively small amounts of fluid into the pericardium, more severe disorders occur than with a gradual, chronic accumulation of it. In clinical pathology, it is known that in acute hemorrhage into the pericardium, death occurs already in the presence of 200-250ml of blood in the heart shirt. If the fluid accumulates gradually (for example, with edema), then the regulatory systems have time to adapt to the changed conditions and prevent functional disorders even with a significant accumulation of fluid in the heart shirt. This, apparently, explains the fact that pericarditis often proceeds without dysfunction. At autopsy, in 5% of cases, fusion of the sheets of the pericardium is found due to former pericarditis without a history of corresponding functional disorders [5].

Heart Disorders in Myocardial Disorders and Disorders of the Coronary Circulation

Demonstration of Violations of the Activity of the Heart in Disorders of the Coronary Circulation

The experiment is performed on an animal with a wide-open chest. Ligate the right coronary artery. To do this, a ligature (a sharp, steeply curved intestinal needle) is brought under the artery and tied up. As a rule, the heart rate and blood pressure after a short-term change are restored. Then the common trunk of the left coronary artery (feeding 4 myocardium) is taken for the ligature as close as possible to the place of its discharge from the aorta. The ear must be pushed up and to avoid injury to the left atrium.

Due to acute anemia of the heart, after 30-60 seconds, its contractility is disturbed-strong contractions alternate with weak ones and irreversible fibrillation of the heart occurs. Uncoordinated contractions of individual muscle bundles run along its surface. The animal dies with symptoms of cardiac insufficiency. An autopsy reveals an overflow of blood in the venous vessels and venous hyperemia of the internal organs-a large amount of dark blood flows from the incision of the liver and kidneys.

In humans, blockage of even individual branches of the coronary vessels can cause irreversible cardiac arrest. Of great importance is the speed with which the shutdown of muscle circulation occurs. The heart can work even with significant narrowing of the coronary arteries if it develops slowly and is not accompanied by spasms. The above experiment can also be carried out on a rabbit. Opening the chest in a rabbit is much easier than in a dog. After the tracheotomy operation, with artificial respiration, the skin is opened along the midline, then the sternum, starting from its middle to the end of the chest. The sternum is partially removed on both sides of the incision and the edges of the wound are stretched to the sides with a hook. With this method of operation, bleeding is insignificant. It is only necessary to avoid damage to the mamillary arteries. A board with a rabbit tied to it is placed vertically and the heart is illuminated [4].

On a rabbit with a wide-open chest, some arrhythmias can be shown very defiantly. So, atrioventricular blockade is shown by stopping artificial respiration (causing asphyxia), myocardial fibrillation-by passing an electric current from the network through the heart. Demonstration of arrhythmias in focal myocardial lesions. During physiology, as well as pathological physiology, cardiac arrhythmias are usually demonstrated on the isolated frog heart. This form of experience is very important for understanding the origin and spread of the process of excitation through the conduction system of the heart. However, the mechanism of the occurrence of arrhythmias in this form of experiment is reduced to the local effect of the stimulus on the heart and conduction system. It is possible to establish reflex influences from the lesion in the myocardium on the development of arrhythmias only by electrocardiographic examination of the heart on a warm-blooded animal [8,10].

To study arrhythmias in pathological myocardial lesions, you can use the above methods of heart damage (focal myocardial damage with hot saline, ligation of coronary vessels). These interventions must be performed with a limited opening of the chest, so as not to cause loss of vagal tone [4].

I. Experience put on the dog. Focal myocardial damage is caused through a limited opening in the chest by introducing 1 ml of hot saline solution (90°) into the apex of the heart or ligating one of the small branches of the left coronary artery (see the technique in previous experiments). Examine the electrocardiogram and blood pressure. Experiments are put

in practical classes, and the resulting electrocardiograms and blood pressure curves are demonstrated and analyzed in lectures. Depending on the degree and localization of myocardial damage, a variety of rhythm disturbances occur-*tachycardia, less often bradycardia, extrasystole*, sometimes group, sometimes turning into short-term attacks of *paroxysmal tachycardia*, an average electrocardiogram), blockade (in case of damage to the conduction pathways of the heart) and, finally, *fibrillation* of the whole heart or one of the atria. Along with rhythm changes, qualitative changes in the electrocardiogram appear, which are characteristic of focal lesions of the myocardium such as a heart attack-a shift in the 5-T interval above the isoelectric line, a deep Q wave. T wave (it should be noted that the T wave can normally be negative in a dog) [2,3,10]. With limited damage to the myocardium, blood pressure slightly deviates from the norm (by an average of 20mm). In the case of myocardial fibrillation, it drops sharply.

II. In the same dog, the vagus nerve is additionally irritated with an induction current for 10 seconds (distance between coils 20 cm, voltage 4 V), after which the electrocardiogram and blood pressure are again examined. Irritation of the vagus nerves leads, as a rule, to a slowing of the rhythm and a drop in blood pressure. Often, after irritation of the vagus nerves, extrasystole increases, attacks of paroxysmal tachycardia appear more often, blockades are more pronounced, sometimes immediately after irritation of the vagus nerves, cardiac fibrillation and a sharp drop in blood pressure occur.

III. In the same dog, the vagus nerves are cut. The heart rate quickens, blood pressure rises, extrasystoles and paroxysmal tachycardia disappear. Correct sinus rhythm is established. In some cases, after transection of the vagus nerves, a paradoxical drop in blood pressure and death of the animal occurs. Thus, the lesion in the myocardium, being a source of pathological impulses, can cause changes in the heart rate, extraordinary contractions of the heart-extrasystoles, paroxysmal tachycardia attacks. If the frequency of impulses from the pathological focus is so high that the heart is unable to reproduce the corresponding number of contractions, then uncoordinated contractions of individual muscle fibers may occur-myocardial fibrillation [4].

However, the manifestations of these functional disorders are determined by the state of the nervous regulation of the heart. After transection of the vagus nerves, extrasystoles and paroxysmal tachycardia disappear and a normal sinus rhythm is established, despite the presence of the same morphological changes in the myocardium. On the other hand, additional irritation of the vagus nerves can provoke the appearance of extrasystoles, paroxysmal tachycardia and myocardial fibrillation, which were not there before, despite the presence of the same morphological changes in the myocardium. This is since irritation of the vagus nerve reduces the strength of automatic impulses from the sinus node, lengthens the time of diastole and thereby contributes to the manifestation of a reaction to irritation from a heterotopic focus [4].

The clinic found that, despite the pathological changes in the heart and its conduction system, extrasystoles and paroxysmal tachycardia may be absent. For their appearance, violations of the extracardiac regulation of the heart are also necessary. The cause of this disorder may be additional irritation of the nervous system: emotional and mental experiences, pressure on the carotid sinus or eyeballs, increased inhalation, swallowing, straining, increased blood pressure, changes in climatic and atmospheric conditions [3]. When extrasystoles are provoked (by additional irritation of the nervous system by any method-pressure on the eyeballs, carotid sinus, etc.), only the type of extrasystoles occurs that is observed in this patient and when they occur spontaneously. This indicates that the pathological focus in the myocardium is on a state of a kind of dominant excitation and a variety of stimuli can set it into action. Similar additional stimuli in the presence of extrasystoles can remove them [3,10].

Disorders of the conduction of the heart-blockades caused by myocardial damage also depend on the state of nervous regulation. They also cannot be explained by a single anatomical break in the conduction system of the heart. Irritation of the vagus nerves contributes to the manifestation of blockades, and after cutting their blockades often disappear. Consequently, blockades during pathological changes in the myocardium can occur not only with an anatomical interruption of the conduction system of the heart, but also because of a functional interruption caused by overstimulation of the conduction system or a reflex effect from the lesion on the centers of the extracardiac nerves. With myocardial damage, the thresholds of irritation of the vagus nerve also change. The current strength necessary to slow down cardiac activity in acute myocardial damage must be increased. In chronic myocardial damage (for example, with cardiosclerosis), the sensitivity of the heart to irritation of the vagus nerve, on the contrary, increases. The reactions of the pathologically altered heart to irritation of the sympathetic nerves are more persistent. This, apparently, is explained by the fact that only the vagus nerves are interrupted in the intramural ganglia of the heart, while the sympathetic fibers pass into the myocardium without interruptions. With myocardial damage, the excitability of the intramural ganglia changes, which facilitates the conduction of impulses from the center of the vagus nerves, or, conversely, blocks them [4].

Heart Disorders for Endocardial Lesions (Heart Defects)

Heart defects are a consequence of a gradual change in valves caused by an inflammatory process in the endocardium. In experiment, valve defects are usually caused by tearing them. Demonstration of valve malfunctions (model experiment). The experiment is performed on a heart cut out from a slaughtered animal (dog) or taken in a hospital dissection (the heart is kept in the cold, not fixed in formalin). The heart is opened by inserting one branch of the scissors into the aorta and going along it to its mouth. Then a finger is inserted into the mouth of the aorta and the valves are groped. Make a longitudinal incision of the left ventricle so that it passes between the valves without damaging them. With such an incision, the semilunar valves of the aorta are clearly visible [3,11].

Holding the heart vertically, let a stream of water along the wall of the aorta in the direction opposite to the blood flow. Clearly (it can be seen how the semilunar valves, filling with water, stretch and swell. In the same way, during ventricular diastole, these valves close under blood pressure in the aorta and prevent the return flow of blood into the ventricle. Then, the edge of one of the aortic valves is torn with a hook. The torn valve does not stretch, and part of the water flows through it back into the ventricle. The same happens with heart defects arising from valve insufficiency-during ventricular diastole, when the aortic valves should be closed, blood from the aorta rushes back into the left ventricle, creating an additional load on the heart. In a similar model experiment, mitral valve insufficiency can be shown. The wall of the left atrium is cut, the edges of the incision are turned out and sewn to the round leg of the chemical stand so that the leaflet valves of the left heart are clearly visible. The aorta and pulmonary artery are ligated or clamped with clamps. Water is poured from above-flap valves let it through. Then, squeezing the ventricle, they try to squeeze the water back-the flap valves slam shut and do not let water through. The preparation is tilted and illuminated from the front, so that the valves swollen under the pressure of water can be better seen. Then one of the valves is damaged and the experiment is repeated. When the ventricle contracts, some of the fluid is ejected back through the opening in the valve. Circulatory disorders occur not only with valve insufficiency, but also with stenosis of the opening. Both defects can occur simultaneously since the fusion of the valves can simultaneously prevent the hole from completely closing [4].

Demonstration of Cardiac Dysfunction in Aortic Valve Insufficiency

Experience put on the dog. Adjust the registration of blood pressure in the femoral artery. Having dissected the left carotid artery, two ligatures are brought under it. One of them bandages the peripheral part of the artery as close as possible to the head. Then a Dieffenbach clamp is applied to the central end of the artery, its wall is incised closer to the ligation site, and a conventional probe (or a simple needle) is carefully inserted into the vessel. The thickness of the probe should be such that it freely enters the vessel but does not dangle in it. After inserting the probe, release the clamp. If blood oozes from the artery incision, loosely tighten the second ligature. The probe is pushed inward until it meets the aortic valves. At this moment, they feel resistance to the movement of the probe and notice its jerky oscillations in time with the heartbeats.

It is necessary to break the valve now of greatest resistance (the moment of closing the valves), overcoming it with a sharp movement to the left and up. The movement must be short so as not to damage the walls of the ventricle. Then the probe is removed, the vessel is tied and the change in blood pressure is monitored. If the chair has a special probe for breaking through the valves (a thin rod ending in a spring in the form of a hook inserted into a thin tube), then you need to insert it into the carotid artery, pushing the tube so that the spring is pressed, and wait for the moment of least resistance (opening valves), then insert it into the cavity of the heart (not too deep), move the tube back (the spring will be released) and break the valves, pushing the probe back into the aorta. After the valve ruptures, the tube is pushed back in, and the probe is removed. As soon as the probe is removed, the ligature applied to the central segment of the artery is tightened.

After the valves rupture, blood from the aorta, where it was under high pressure, rushes back into the left ventricle during diastole, where the pressure is negative at the beginning of diastole. The ventricle, which now receives blood not only from the atrium, but also from the aorta, is stretched more than usual. The muscle of the left ventricle during systole contracts more strongly and ejects into the aorta, in addition to the usual amount of blood, also the excess that comes from the aorta [3]. Due to this, blood pressure usually does not decrease. But this applies only to the maximum, systolic pressure. Diastolic pressure drops sharply. A significant difference between systolic and diastolic pressure is also manifested in the fact that the pulse becomes fast, high, and frequent. It is customary to explain the features of this pulse mechanically-by the return of blood into the ventricle during diastole. However, it is also necessary to consider the reflex influences that arise in this case on the vasomotor centers (see the following experiment) [4].

Demonstration of the Role of Nervous Regulation in Aortic Valve Insufficiency

In a dog with torn aortic valves (from prior experience), the vagus nerves in the neck are severed. At the same time, the aortic

nerves that go with them in a common trunk are cut at the same time. Systolic and diastolic pressure rises, and the difference between them is significantly reduced. Obviously, after the breakthrough of the valves, the backflow of blood into the heart is accompanied by an unusual increase in pressure in the aortic arch, which enhances the volley of impulses sent along the aortic nerve to the vasomotor center. In response to this, the arterioles expand reflexively, which explains the sharp drop in diastolic pressure.

Transection of the aortic nerves removes this reflex (V. S. Livshits). Under normal conditions, only the arteries pulsate. Arterioles and capillaries do not pulsate. With insufficiency of the aortic valves, arterioles also begin to pulsate, as the difference between systolic and diastolic pressure increases. Since there is a powerful left ventricle behind the valve defect, this defect is well compensated. If the operation is carried out under aseptic conditions and the wound is sutured, the dog is no different from a healthy one and copes well with physical activity. Due to the increased load on the left ventricle, its hypertrophy develops after 2-3 weeks. If the animal is killed immediately after the experiment, then the heart is removed, opened, and a stream of water is directed to the valves, demonstrating the defect. In some cases, when trying to break through the valve, the myocardium is mistakenly broken through (when the probe slips into the cavity of the ventricle and the moment the valves are open, it rests against the wall of the ventricle and the resistance of the ventricular wall is taken for the resistance of the valves). The death of the animal occurs quickly, as the blood from the heart is poured into the heart shirt and hemopericardium occurs. The animal is quickly opened and a strongly strained cardiac shirt is shown, through which the accumulation of blood in its cavity is clearly visible.

The pericardium is incised-liquid blood with clots pours out of it. Find the place of myocardial breakthrough. Fresh blood clots usually form on the inner surface of the heart in this area. The same picture is observed in clinical pathology with heart rupture (most often due to softening of the infarction). Demonstration of violations of the activity of the heart in the narrowing of the mouth of the aorta . At the mouth of the dog's aorta, an obturator with a rubber cap is inserted through the left carotid artery (see above for a description of the insertion technique). Then air is injected into the obturator with a syringe. A rubber bag placed over the end of the obturator stretches and narrows the aortic orifice. During systole, the left ventricle encounters great resistance to the outflow of blood. With a slight narrowing of the aortic orifice (introduction of 4-5ml of air into the obturator), the stroke volume of the heart increases, but blood pressure does not change. With a large narrowing of the mouth of the aorta, blood pressure is applied. The pulse with this defect is slowly increasing, meager and rare. These features of the pulse are explained by the fact that the aortic arch experiences less than normal fluctuations in blood pressure, because of which the reflex expansion of peripheral vessels is insufficient and blood flow slows down [12].

The same pulse changes can be reproduced with gradual compression of the aorta not at its mouth, but in the abdominal cavity, immediately below the diaphragm, provided that the blood pressure in the femoral artery is measured. To do this, it is enough to open the abdominal cavity with a small incision along the midline, grope for the aorta immediately after it exits from under the diaphragm and partially compress it with a clamp, a loosely tightened ligature, or fingers. The pressure in the femoral artery drops, the pulse becomes like the pulse with stenosis of the aortic orifice. With stenosis of the aortic orifice, due to the increased load on the left ventricle, its hypertrophy occurs. Circulatory disorders in other heart defects are based on the same mechanisms as described above. With insufficiency of the valves of the left *atrioventricular orifice* during ventricular systole, part of the blood from the left ventricle enters the left atrium. The left atrium, which now receives blood not only from the pulmonary veins, but also from the left ventricle, expands. During atrial systole, it contracts and ejects an increased portion of blood into the left ventricle. Consequently, with this defect, the amount of blood entering the left ventricle also increases. As a result, left ventricular hypertrophy occurs, which is of great importance for compensating for this defect, since the left atrium itself is weak. In the future, the overflow of the left atrium with blood is accompanied by the accumulation of blood in the pulmonary veins and leads to an increase in pressure in the small circle, which entails an increase in the load on the right ventricle and its subsequent hypertrophy. With *stenosis* of the left *atrioventricular orifice*, the emptying of the left atrium is difficult. The amount of blood entering the left ventricle and the aorta decreases and blood pressure falls. The left atrium, on which the greatest load falls, expands, and then hypertrophies. In the future, the overflow of the left atrium with blood leads to the accumulation of blood in the pulmonary veins, to an increase in pressure in the small circle and hypertrophy of the right ventricle. The left ventricle, receiving a reduced amount of blood, may undergo atrophy. Stenosis of the left atrioventricular opening is one of the most unfavorable defects of the left heart, since the most powerful part of the heart, the left ventricle, is not involved in its compensation, and the blood supply to the heart itself through the coronary vessels is also disturbed. Organic valvular defects of the right heart are much less common than those of the left heart. This is due to the lower load on the right heart [4].

Demonstration of Tonogenic and Myogenic Expansion of the Heart

Strengthened contractions of the corresponding parts of the heart, which prevent circulatory disorders in case of valve damage, can be clearly shown in the following experiment. In a rabbit with a wide-open chest (with artificial respiration), ligatures are applied to the base of the aorta and pulmonary artery. First, the ligature is tightened at the base of the aorta, thereby narrowing its mouth. Immediately, before our eyes, the boundaries of the left ventricle expand, and its contractions intensify (tonogenic dilation). After removing the ligature from the aorta, tighten the ligature on the pulmonary artery and observe the expansion of the boundaries of the right heart and the strengthening of its contractions [13]. With excessive narrowing of the lumen of the vessels, the boundaries of the heart expand even more, but this expansion is no longer accompanied by increased contraction of the myocardium (myogenic dilation). Heart failure sets in, venous congestion develops in the internal organs.

Heart Disorders in Pathological Changes in Other Bodies and Systems

Demonstration of violations of cardiac activity with a change in blood pressure. With an increase in blood pressure, bradycardia occurs (see demonstration with clamping of the abdominal aorta), with a decrease in pressure, tachycardia (see demonstration of bleeding). A change in blood pressure irritates the baroreceptors embedded in the vessels. Among them, the most important receptors are the aortic arch and carotid sinus. The impulses arising from this, propagating along the aortic and sinus nerves, cause a reflex slowdown of heart contractions with an increase in blood pressure, and, conversely, an increase in their frequency with a decrease in it, which contributes to the restoration of normal blood pressure [4]. However, there are exceptions to this general rule. In hypertension, despite an increase in blood pressure, there is often an increase in cardiac activity. Demonstration of cardiac disorders in case of irritation of the upper respiratory tract when ammonia is brought to the nose of a rabbit, cardiac activity slows down simultaneously with holding the breath. Changes in heart rhythm can be recorded by recording an electrocardiogram, blood pressure, or simply by inserting a flag needle into the apex of the heart. The afferent pathway of the reflex is the trigeminal nerve, the efferent pathway is the vagus nerve. After anesthesia of the nasal mucosa with novocaine or vagotomy, this reflex disappears [6,14]. Demonstration of cardiac disorders in case of damage to the abdominal organs (Goltz's experience in the modification of I. R. Tarkhanov). An hour before the experiment, the frog is immobilized and applied to a board, its abdominal cavity is opened so that the insides dry out in the air and inflammation of their serous membranes develops. Then they open the skin above the sternum, remove the sternum so that the heart is visible, hit 1-2 times with a scalpel handle or tweezers on the insides. A few seconds later, the heart stops.

The afferent pathway of this reflex is the splanchnic nerves: after their transection, a blow to the abdominal organs does not cause cardiac arrest. The efferent pathway is the vagus nerves. After atrophy of the heart, this reflex also disappears. It is important to point out that in warm-blooded animals, reflex cardiac arrest, as a rule, is not observed even with the most severe injuries of the abdominal cavity. At the same time, they have only a slight slowdown, and sometimes an increase in cardiac activity [14].

Vascular Hypotension

The most common causes of an acute drop in blood pressure are bleeding, shocks of various origins (traumatic, burn, blood transfusion, anaphylactic) and collapse. Chronic low blood pressure (hypotension) occurs with adrenal insufficiency.

Bleeding

The most dangerous is bleeding from large arteries. Thus, the loss of blood from the carotid artery is much more dangerous than the same volume of bleeding from a vein or parenchymal organ, since with a rapid outflow of blood, compensatory mechanisms do not have time to fully turn on. As has already been shown in previous experiments (see section "Etiology and pathogenesis") slow bloodletting does not change blood pressure at all, even if it reaches the entire blood volume. Different rates of bleeding from different vessels are demonstrated by the following experiment. Demonstration of bleeding from arteries, veins, capillaries, and parenchyma.

a. A large artery, for example, the carotid, is incised in a rabbit. From its central segment, scarlet blood flows in a strong stream, in jolts corresponding to the contractions of the heart. A clamp is quickly applied to the central segment. Blood also flows from the peripheral segment of the artery, although under less pressure. This is due to the presence of anastomoses between the carotid and vertebral arteries. A clamp is also applied to the peripheral segment of the carotid artery [15].

b. Cut the jugular vein. Blood flows mainly from its peripheral segment, evenly and with very little force. The uniformity of blood flow in the veins is explained by the extinction of pulse waves during the passage of blood through the capillaries.

c. They pierce the rabbit's ear with a needle-they cause capillary bleeding, which is usually limited to the appearance of 1-2 drops of blood.

d. Feel through the skin of the back (on the left, under the ribs) the kidney of the rabbit and squeeze it strongly with the palm of your hand until crushed. Open the rabbit. The blood from the crushed kidney oozes slowly. It flows simultaneously from capillaries, small veins, and arterioles (internal parenchymal bleeding). Having separated the skin over the kidney, they show that, despite the complete crushing of the kidney tissue, the skin and subcutaneous tissue are not changed, due to their high resistance to mechanical pressure [4].

Demonstration of Acute Bleeding

The dog's respiration and blood pressure (in the carotid artery) are recorded. 10-15ml of blood is released into a beaker or measuring cylinder from the femoral artery through a cannula previously tied into it. Blood pressure decreases slightly, but quickly levels off. They release about 25% of the blood volume (the volume of blood in a dog is 6-7% of body weight). There is a persistent drop in blood pressure, increased heart rate and respiration. If bleeding continues (more than half of the blood volume), then, in addition to the usual systolic, diastolic, and respiratory fluctuations in blood pressure, there are wave-like rises and falls of it (waves of the third order), indicating a gradual decrease in the excitability of the vasomotor center. Then they become weaker, and the blood pressure drops sharply. Breathing becomes periodic interspersed with long pauses. General clonic and tonic convulsions develop.

Cardiac activity slows down and then stops-death occurs. The animal is opened, a sharp anemia is found-the skin and mucous membranes are pale, the liver and kidneys are gray, yellow. The spleen is sharply reduced but retains its former color and releases a little blood when cut. This indicates that even with significant blood loss, not all blood from the blood depots enters the bloodstream [15]. Most of the blood is stored in the vessels of the brain and heart. Under the endocardium, under the pleura, and in the mucous membrane of the stomach and intestines, pinpoint hemorrhages (per diapedesis) are found. Why did the animal die? With blood loss, the number of red blood cells decreases, and oxygen starvation develops (although only the oxygen capacity of the blood decreases, but not the O2 tension). However, a decrease in the number of erythrocytes (up to 1 million in 1 mm3) does not yet lead to death. Of great importance is the drop in blood pressure. So, with bleeding, the difference between the pressure at the beginning and at the end of a large circle decreases, because of which the supply of oxygen to the tissues is disrupted and death occurs. If saline solution is administered during acute blood loss, then blood pressure and functional state improve. However, saline administration only briefly raises blood pressure.

Excess fluid is rapidly absorbed by the tissues. Therefore, the best effect is given by the transfusion of blood, plasma, or its substitutes. Blood transfusion not only compensates for its loss during bleeding, but also enhances blood formation, since the blood itself and its decay products irritate the blood-forming organs. An increase in cardiac activity and respiration during bleeding increases the supply of oxygen to the body, the suction capacity of the chest, facilitates the emptying of venous vessels and filling the heart, the blood is enriched with oxygen, and its flow accelerates. Of great importance for maintaining blood pressure during bleeding is a decrease in the lumen of the vessels. It does not apply to all organs. As we saw at the autopsy, it is pronounced in the skin, mucous membranes, in the abdominal organs that serve as blood depots (liver, spleen).

At the same time, the vessels of the lungs, heart and brain do not contract, which provides them with a preferential supply of blood with a general lack of it. The contraction of the vessels of the skin also has the significance that it reduces heat transfer. Therefore, body temperature after blood loss does not fall, but may even increase by 1-1.5°. The increase in cardiac activity and respiration, vascular contraction occurs reflexively, due to irritation of vascular baroreceptors caused by a decrease in blood volume. In compensating for the consequences of bleeding, increased absorption of tissue fluid rich in thrombokinase into the bloodstream is also important, which increases blood clotting and thereby contributes to an early cessation of blood circulation. Bleeding also enhances the hematopoietic function of the bone marrow, which helps to restore the number of red blood cells [4].

Demonstration of Transfusion of Blood, Plasma, and Saline Solution for Blood Loss

Experience put on two dogs. The blood pressure is measured in the carotid artery, then 50-60% of all blood is released from the femoral artery. Dogs are injected into the vein the same volume: one dog-saline, the other-blood. The blood pressure in the first dog, rising, does not reach the initial level and soon decreases again. In the second dog, the blood pressure rises to its original level and holds steady. The same effect is exerted by the introduction of plasma or special blood-substituting fluids [15,16]. Blood-substituting fluid I. R. Petrov. A hypertonic saline solution is prepared (15g of NaCl; 0.1g of CaCl and 0.2g of KC1 are dissolved in 1 liter of water). To 850ml of this solution, add 100 ml of dog blood, previously mixed with 50 ml of 6% sodium citrate [4].

Shock

Demonstration of traumatic shock. Traumatic shock occurs with severe injuries-with fractures of the hip, iliac wings, spine, etc. In the experiment, traumatic shock can be caused by crushing of the limbs, eventration of the abdominal organs, etc.

i. The experiment is set on two rabbits. Before the experiment, the temperature in the rectum is measured, the initial level of blood pressure in the carotid artery is set, and respiration is recorded. In one of the rabbits, 10% of the blood volume is released from the carotid artery (the amount of blood in rabbits is 1/12 of the animal's weight). By itself, *phlebotomy* lowers blood pressure for a short time. After 5-10 minutes it is restored. Then both rabbits inflict the same injury to the limb. One of the hind limbs is pulled out and crushed with two or three blows of a hammer, brick, or stone (the risk of death from fat embolism during crushing of tubular bones is exaggerated-it is quite rare). Both rabbits become agitated, breathing quickens, blood pressure rises, but the further reaction of the animals to a limb injury differs sharply. In a rabbit with preliminary bleeding, oppression quickly develops, breathing becomes weak and superficial, blood pressure decreases by 40-50%, temperature-by 2-4°. In a rabbit without blood loss, shock does not occur [17,18].

Due to the regulatory mechanisms developed during evolution, it is very difficult to induce a persistent decrease in blood pressure during injury. To reproduce traumatic shock in dogs and cats, up to 1,000 blows with an iron rod are applied to the limbs, etc., but even so, shock does not always develop. Of decisive importance in the development of shock is the state of the body preceding the injury. Blood loss weakens the body's compensatory capabilities. In humans, shock is also caused by blood loss, severe mental stress, overwork, lack of sleep, etc. A sharp drop in blood pressure during shock is explained by the accumulation of blood in the capillary network of blood depots-abdominal organs, skeletal muscles. Venous congestion in these organs is accompanied by sweating of the transudate and swelling of the mucous membranes. The blood thickens, the percentage of hemoglobin increases, the color indicator increases. The amount of circulating blood is reduced by 25°/o, and in severe cases even more. Despite the increased heart rate, the heart works almost idle, as a significant amount of blood is retained in the blood depots.

ii. Carrying out the same experiments without recording blood pressure and fixing the animals necessary for this makes it possible to show the general state of the organism more clearly in case of injury to the limb. A rabbit that has not been bled, after a few seconds after the injury, shakes itself and, dragging its injured paw, approaches the beet or cabbage offered to it, sniffs it and begins to gnaw. A rabbit with blood loss after an injury sits as if numb, then falls on its side. His mucous membranes turn pale (turn away and show lips, eyelids), motor reactions to pain irritation of the skin disappear or weaken. The rabbit developed shock [19]. If a rabbit with a crushed paw (which did not develop shock) is left without surgical intervention, then after 1-2 days it dies. At the autopsy, an abundant accumulation of blood is found in the crushed tissues of the limb, which is shown in the lecture. If the rabbit's crushed foot is amputated, the bleeding is stopped and the wound is sewn up, then it remains to live. It should be noted that in practice, the diagnosis of shock is often incorrectly made-in cases of death from damage to vital organs or from heavy bleeding that was not stopped in time in the absence of timely surgical care [4].

Demonstration of Pain Shock

If shock is caused by injuring the limb of the animal, and the currents coming from the peripheral end of the mixed nerve of this limb (for example, the sciatic nerve) are recorded, then a strong impulse is detected now of injury. It continues in the form of asynchronous impulses of small amplitude for many hours after the injury. To elucidate the role of reflex influences of the central nervous system in the development of shock, the following experiment is performed. The experiment is carried out on two rabbits, one of which is preliminarily induced to bleed (10% of the blood volume). Blood pressure and respiration are recorded, the sciatic nerves are exposed, submersible electrodes are placed on them and irritated with an induction current (battery 2-4 V, distance between coils 5-10cm). Irritate the nerve 10-15 times with a break of 0.5-1minute. During irritation, both rabbits experience excitation, shortness of breath, and increased blood pressure. However, the bloodletting rabbit then develops a picture of shock, while the other rabbit does not go into shock. Shock often (especially in dogs and cats) does not develop even after irritation of the sciatic nerve for several hours. If shock occurs when the nerve trunks are irritated, then this occurs against the background of a previous weakening of the body's resistance [20].

Demonstration of the State of Excitability of the Nervous System in Shock

As a result of shock, the excitability of the central nervous system decreases. The experiment is set on the rabbit from the previous demonstration, when the animal has already developed shock and the blood pressure has dropped. Again, cause irritation of the sciatic nerve on the same or opposite paw and compare the degree of increase in blood pressure with data obtained before

the development of shock. This time, the rise in blood pressure is less pronounced, as the vasomotor center is in a state of inhibition. Weakened and painful shortness of breath, which indicates the oppression of the respiratory center during shock. The centers of the vagus nerves are also inhibited-short-term asphyxia caused by compression of the trachea is accompanied by a very slight slowdown in cardiac activity, while normally this causes a sharp bradycardia due to irritation of the centers of the vagus nerves with carbon dioxide accumulating in the blood. The tone of the vagus nerves is also lowered-cutting them causes only a slight increase in blood pressure instead of the usual clear rise in its level (the rhythm of cardiac activity does not change during cutting of the vagus nerves in rabbits and is normal). The motor centers are also inhibited-the motor reaction to skin irritation and the general defensive reaction to irritation of the sciatic nerve are weakened [4].

Demonstration of Histamine Shock

Experience is put on a rabbit. Record blood pressure and respiration, as in the previous experiment. One of the decay products of crushed tissue is histamine. Its solution (1mg of histamine in 1ml of saline) is administered intravenously at the rate of 2mg per 1kg of body weight. Arterial pressure is significantly reduced. Sometimes the animal dies. The pressure drop in this case is explained by the expansion of the capillary network and the increase in the permeability of the capillary walls, while the arterioles narrow [20]. There is no reason to oppose neurogenic factors in the development of shock to humoral ones; to cause shock, humoral substances must act on certain nerve formations that regulate blood circulation. For example, intravenous administration of histamine does not eliminate shock in puppies younger than 2-3 weeks of age, since only from this age do they develop pressor vascular reactions.

Demonstration of Transfusion Shock

The dog under general anesthesia is fixed with the stomach up. The femoral artery and vein are dissected. The artery is connected to a blood pressure recording system. Having established the initial background, 10-50 ml of heterogeneous blood is injected into the femoral vein. Blood pressure drops sharply, shortness of breath appears, convulsions, and the animal dies [11].

Vascular Hypertension

An increase in blood pressure is prevented by neuro-reflex mechanisms. Even with a significant increase in the volume of fluid in the vascular bed, only a short-term increase in blood pressure is observed. Its persistent rise occurs because of several reasons leading to an increase in the tone of arterioles and small arteries (hypertension, certain diseases of the endocrine system, kidneys, etc.). Demonstration of changes in blood pressure in hydremic plethora. The experiment is performed on a rabbit under general anesthesia or without it. Register blood pressure in the carotid artery and respiration. Into the jugular or femoral vein, saline is injected, heated to 37-38°, in an amount exceeding the volume of blood (equal to 1/12 of the rabbit's weight). The solution is injected slowly, 7ml per 1kg of weight per minute.

The amplitude of pulse waves increases, breathing becomes deeper and more frequent. Blood pressure rises slightly during infusion, then decreases, and finally settles at the same level. Restoration of blood pressure occurs reflexively stretching of the vessels by the injected fluid causes a reflex (through the receptors of the cardio-aortic and carotid sinus zones) expansion of the arterioles of the whole body and an increase in blood flow. The speed of blood flow increases by 6-8 times compared with the norm. This can be shown by incising the marginal vein of the rabbit ear or other venous vessel before and after administration of saline. Venous pressure rises. Subsequent opening of the abdominal cavity reveals distended veins and an enlarged liver [21]. Due to the high venous pressure, the filling of the cavities of the heart increases during diastole, and therefore the heart contractions also increase. The pulse rate usually also increases because of significant atrial stretch (Bainbridge reflex). An increase in pressure in the veins and capillaries of the abdominal cavity and an acceleration of blood flow contribute to an increased outflow of fluid into the lymphatic vessels and its removal from the body by the kidneys and through the intestinal mucosa [4].

Demonstration of Reflexogenic Hypertension

Turning off the main regulatory mechanisms of vascular tone (cardio-aortic and carotid sinus zones) leads to an increase in the tone of arterioles and an increase in blood pressure. Half an hour before the lecture, depressor nerves are taken from the rabbit for ligatures and the carotid sinuses are looked for. To do this, the neck muscles are pushed apart in a blunt way at the edge of the lower jaw and between them the place of branching of the common carotid artery into the internal and external branches is found. Register the initial blood pressure in the femoral artery. Cut both depressor nerve. Then, the area of the carotid sinus is carefully dissected from the surrounding tissues, having previously lubricated it with a 3% solution of Novocain, all nerve fibers suitable for the bifurcation are cut, and the carotid glomerulus is removed. Denervation must be done as carefully and carefully as possible, otherwise the animal will die or the blood pressure, instead of rising, will fall.

For complete denervation, ligatures can be applied above and below the carotid sinus and the bifurcation can be excised along with the carotid glomerulus. After sinus denervation, blood pressure is measured. It usually rises and the heart rate becomes faster. A long-term increase in blood pressure depends on an increase in the tone

of arterioles. If the operation is carried out under aseptic conditions and the animal remains alive, then hypertension lasts for 2-3 months. The restoration of blood pressure after transection of the aortic nerves and removal of the carotid sinus is explained by the inclusion of other vascular-receptor zones-vena cava, pulmonary, mesenteric, femoral arteries, etc., which also contain baroreceptors [11].

For demonstration in a lecture, the experience can be simplified. To turn off the carotid sinuses, both carotid arteries are ligated at the neck (below the bifurcation). The aortic nerve is cut along with the vagus and cervical sympathetic nerves, which lie with them in the same bundle. Blood pressure rises sharply. Demonstration of centrogenous hypertension. Experience put on rabbits. Pre-release cerebrospinal fluid in a volume equal to the amount of fluid injected (see "Etiology and pathogenesis" for the technique). Then, a suspension of kaolin powder (20mg per 1kg of weight in sterile saline, about 1-1.5ml) is injected through the same needle. A few days after the injection, some rabbits show an increase in blood pressure (by 50-80 mm above the original), which lasts for several weeks or even months, if the animals survive until this time. This experience can be put on dogs. Kaolin is administered under anesthesia (10mg per 1kg of weight repeatedly, 3-4 weeks after the first injection). After the introduction, the dog's head is lowered down and left in this position for 20 minutes. Surviving dogs develop persistent hypertension within 2-3 months.

Demonstration of Conditioned Reflex Hypertension

The experiment is performed on a dog with a carotid artery brought into the skin flap. For a long time (1-3 months) the dog is taught to stand in the machine. Then she develops a conditioned reflex to the introduction of adrenaline (subcutaneously, 2-3ml of a 1:1000 solution). The conditioned stimulus is a bell, which is turned on 30 seconds before the injection of adrenaline and sounds within 5 minutes after its administration. After 6-12 daily combinations, the conditioned stimulus is turned on in isolation, reinforcing it with the introduction of saline. Arterial pressure rises by 10-15mm Hg. By introducing several conditioned stimuli (positive and negative) and then violating the developed stereotype, some authors managed to cause persistent hypertension [4].

Demonstration of Nephrogenic Hypertension

Restriction of blood flow through both kidneys causes persistent hypertension. The experiment is performed on a dog with a carotid artery brought into a skin flap (for a description of the operation, see the end of the chapter). Several methods have been proposed to restrict blood flow through the kidneys.

a. The animal (dog, rabbit) is fixed with its back up. A roller is placed under the stomach. Departing from the spine by 2 cm, cuts are made 4 cm long, on the right-along the edge of the ribs, on the left-retreating 2 fingers from the edge of the ribs. Dissect the subcutaneous tissue, fascia and muscles and feel for the kidneys. Having prepared the renal artery, special screw clamps or ligatures are applied to them, the vessel lumen is narrowed by 1/4-1/3 of the diameter. Blood pressure begins to rise from the first days and reaches a maximum after 1-3 months.

b. The kidney is enclosed in a thin-walled rubber bag, which is tied up at the mouth of the renal vessels. Then the bag is turned inside out onto the kidney and tied over it again. Connective tissue develops at the mouth of the vessels, which compresses the renal vessels and causes anemia and atrophy of the kidneys.

c. The kidneys are brought out under the skin of the back, the hole in the muscles is pulled together with sutures and the skin wound is sutured. Blood circulation in the kidneys is gradually disturbed, their volume decreases, persistent hypertension develops. An increase in blood pressure with limited blood flow through the kidneys is explained by the release of a protein enzyme, renin, from them into the blood. Renin, acting on blood alpha globulins, converts hypertension into hypertension, which has a pronounced pressor effect. An increase in blood pressure during the formation of hypertensin in the blood occurs more slowly than when adrenaline enters the blood but continues for several hours. Recent studies have shown that after denervation of an anemic kidney, blood pressure decreases. Obviously, in the development of nephrogenic hypertension, reflex changes in blood pressure under the influence of impulses from an anemized kidney tissue are important [21].

Demonstration of Violations of Vascular Regulation in Experimental Hypertension

Regardless of the cause that caused hypertension, the nervous regulation of blood circulation in this disease is invariably disturbed. Experience put on the same rabbit, which was obtained reflexogenic hypertension. Both femoral arteries are dissected and ligated. As you know, such a shutdown of a part of the vascular bed does not increase blood pressure (see "Peripheral Circulatory Disorders"). In a rabbit with experimental hypertension, blood pressure rises during this intervention, since vascular regulation is disturbed. Technique for bloodless blood pressure testing. To remove the carotid artery in dogs, a 4-5cm wide flap is cut out of the skin of the neck (the operation is performed under general anesthesia). The median incision is made from the thyroid cartilage to the manubrium of the sternum, slightly short of it. The side incision is made shorter by 1.5-2cm at each end. After separating

the flap with subcutaneous tissue, the carotid artery is removed and taken aside. The muscles under the artery are sutured, leaving holes in the places where it passes.

Then sutures are applied to the skin of the neck. The artery is placed in the flap and sutured into the subcutaneous tissue and then into the skin of the flap. The corners are especially carefully sewn up, trying not to pinch the artery with sutures (they always check if there is a pulsation). A gauze pad and rollers are placed under the loop on the sides of the loop, then a gauze bandage is applied, and on top of it is a wide bandage or oilcloth apron covering the entire front surface of the neck. The sutures are removed on the 7-8th day. The bandage is left until the wound is completely healed [4]. Frequent complications during this operation are bleeding from the arterial wall and necrosis of the skin flap. Bleeding occurs when suppuration or when the flap is cut incorrectly, when the artery must be pulled hard when it is sutured. Necrosis of the skin flap is due to a violation of its nutrition during separation from the surrounding tissue. 10-15 days after the operation, blood pressure can be measured using a rubber cuff (made of rubber gloves), reinforced with a bandage on a loop and connected to a conventional mercury manometer, Riva-Rocci apparatus, or tonometer. The removal of the artery into the flap in rabbits is done according to the same method. Blood pressure in rats is measured on the tail artery. Before determination, the rat is placed in a thermostat (for 5 minutes, at 5°C) to avoid spasm of the artery. Then the rat is placed in a narrow box, the tail is left outside.

A rubber cuff connected to a tonometer is placed on the base of the tail, and the peripheral part of the tail is placed in a plethysmograph. Air is pumped into the cuff until the pulse disappears, then it is gradually lowered until blood begins to flow into the peripheral part of the tail, which is detected by an increase in its volume recorded by a plethysmograph. At the time of the rise of the water column in the capillary, soldered into the plethysmograph, the systolic pressure is noted on the tonometer (normally 100-130mm) [4]. Thus, the data presented in the review on modeling the pathology of the cardiovascular system in the experiment represent a fundamental basis for further study of this system, deepening and detailing the pathogenesis of diseases, allowing you to create a basis for clinical research.

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