Review Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2022.45.007227

Methodological Approaches to Modeling the Pathology of External Respiration in Animals

Bon LI*, Klimuts TV and Kokhan NV

Grodno State Medical University, Republic of Belarus

***Corresponding author:** Lizaveta I Bon, Candidate of biological science, assistant professor of pathophysiology departme D.A. Maslakov, Grodno State Medical University, 80, Gorky St., 230009, Grodno, Belarus

ARTICLE INFO

Received: July 25, 2022

Published: August 09, 2022

Citation: Bon LI, Klimuts TV and Kokhan NV. Methodological Approaches to Modeling the Pathology of External Respiration in Animals. Biomed J Sci & Tech Res 45(4)-2022. BJSTR. MS.ID.007227.

ABSTRACT

The proposed article is an experience of creating a review on the experimental pathology of the respiratory 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; Respiratory Disorders; Experimental Animals

Respiratory Disorders in Disorders of the Nervous System

Demonstration of Respiratory Disorders in Brain Damage

Experience put on a frog. To register respiratory movements in a frog, the skin of the chin area is captured with a serpentine connected by a thread to the Engelman lever, or simply stitched with a thread. 16–20 minutes before the demonstration, the brain is cut at the level of the visual halls. Then impose a crystal of salt on the surface of the cut. Breathing stops in most cases not immediately, but gradually, or after a preliminary increase. In 30–40 seconds after the complete cessation of breathing, single respiratory movements appear, and then they become more frequent until the initial rhythm is restored. Sometimes there is an increase in amplitude or an increase in the rhythm [1]. In frogs, true respiratory or pulmonary movements of large amplitude and mandibular movements of small amplitude are distinguished. True respiratory movements, being phylogenetically later, are more easily inhibited and later restored in brain lesions [2]. In the process of restoring breathing after Sechenov's inhibition, it is often possible to observe long pauses between individual respiratory movements or their groups – periodic breathing. Respiratory disorders in case of brain damage in other animals can be reproduced by causing inflammatory changes in the brain by injecting turpentine, hot water, pathogens of infectious diseases (staphylococci, meningococci, etc.) through the burr hole. In this case, along with changes in the frequency of breathing, various types of periodic breathing may appear. The most dramatic changes in breathing occur when the brain stem is damaged.

Demonstration of Respiratory Disorders in Bilateral Vagotomy

Experience put on a guinea pig or a rabbit. Before the lecture, under local anesthesia, both vagus nerves are exposed on the neck and ligatures are brought under them. At the lecture, they demonstrate the breathing of the animal and then cut the nerves. Breathing becomes deep and rare. Impulses arising from the expansion of the lungs under normal conditions, enter the respiratory center through the vagus nerves and cause a reflex end of inspiration, preventing overextension of the lungs. Impulses arising from the collapse of the lungs reflexively determine the beginning of inspiration. Transection of the vagus nerves disrupts this self-regulation, lengthening both inhalation and exhalation [3].

Demonstration of Unconditioned and Conditioned Reflex Dyspnea

A. The lateral surface of the thigh is shaved in the dog and plate electrodes are applied. Gauze pads moistened with a 20% saline solution are placed under the electrodes. The electrodes are well fixed with a bandage or rubber band. Breathing is recorded using a pneumograph, a blood pressure cuff or a gas mask tube (closed tightly at one end), connected by air transmission to Marey's drum. Pain irritation is caused within 1–2 seconds by induction current (distance between coils 0–6 cm, voltage 2–4V). The dog develops a motor defensive reaction and painful shortness of breath (expiratory pause followed by hyperventilation). After 2–3 painful stimuli, even one bringing the electrodes to the paw (or the knock of the inductor) causes a similar shortness of breath.

B. Experience put on the dog. Breathing is recorded as in the previous experiment. Bringing a bottle of ammonia to the dog's nose for 1–2 seconds causes a breath hold, followed by shortness of breath. After 2–3 combinations, bringing the same in appearance, but an empty vial causes conditioned reflex shortness of breath. Bringing the bottle is best combined with a sound stimulus (for example, opening a cork). The dog must be accustomed to the stall and the environment of the experiment in advance. In humans, conditioned reflex mechanisms are of great importance in the development of respiratory disorders. So, for example, attacks of shortness of breath in bronchial asthma can appear not only when inhaling pollen from flowers, hay dust, etc., but also as a conditioned reflex, with one kind of picture or photograph of these plants [4].

Respiratory Disorders for Upper Respiratory Injuries

Demonstration of Mechanical Asphyxia

Experience is put on a rabbit or a rat. For a better demonstration of respiratory movements, the muscles of the chest and abdominals are exposed. The skin is cut along the midline from the upper edge of the sternum to the pubis, it is dissected and taken to the sides so that the chest and abdominal muscles are clearly visible. The board on which the animal is fixed is placed vertically and well illuminated. Gradually tighten the ligature previously applied to the trachea. It is noted that as its lumen decreases, more and more large muscle groups are involved in respiratory movements. Inhalation during quiet breathing occurs due to the contraction of the muscle fibers of the diaphragm, pulling the center of the tendon downward (the diaphragm is the main respiratory muscle), and due to the contraction of the external intercostal muscles, raising the ribs. The tone of the abdominal muscles at this time is reciprocally weakened. Tightening the ligature on the trachea makes it difficult to inhale, and the animal develops inspiratory dyspnea.

At the same time, auxiliary muscles are included – the muscles of the shoulder girdle, scapular, pectoral and trapezius. Like the external intercostal muscles, they increase the longitudinal dimensions of the chest. At the same time, the nostrils widen sharply, the neck stretches and the head rises. The narrowing of the airways makes it difficult to exhale, and expiratory dyspnea appears. Exhalation during calm breathing occurs passively due to the inherent elasticity of the chest and lungs, i.e., the desire to occupy the original volume. In this case, the contraction of the internal intercostal muscles is of some importance. The tone of the abdominal muscles during exhalation increases, and they contribute to the depression of the dome of the relaxed diaphragm into the chest cavity. With difficult exhalation, additional muscles are involved, mainly abdominal: transverse, rectus and oblique muscles of the abdomen, pushing the diaphragm upward. At the same time, the volume of the abdomen decreases, the back bends (the animal is shown from the side), depressions along the costal arch are pronounced [5].

Thus, inhalation is enhanced by the inclusion of the muscles of the shoulder girdle, exhalation – due to the abdominal muscles. Due to the inclusion of additional muscles, the depth of breathing and pulmonary ventilation increase. The amount of air inhaled (as measured by a gas watch) remains normal or even increases, despite the reduction of the tracheal lumen to one third. When the ligature is tightened until the trachea is completely closed, breathing stops for a few seconds (this stop occurs reflexively as a result of irritation of the vagus and upper laryngeal nerve). Then shortness of breath increases even more. The exhalation movements become stronger than the inhalation movements and turn into convulsions, in which almost all the muscles of the body are involved. Spasms also extend to smooth muscles (excretion of feces and urine). By the end of the second minute, breathing stops. 1 minute after the cessation of breathing, rare and deep breaths reappear – the animal stretches convulsively, opens its mouth wide, grabbing air. The pauses between breaths are getting longer.

These terminal respiratory movements are a kind of periodic breathing that occurs when the excitability of the respiratory center decreases sharply. At this time, even strong stimuli cannot cause the appearance of reflexes. By the end of the fourth minute, paralysis of the respiratory center sets in and breathing stops. If blood pressure is measured in the same experiment, then a sharp increase in it is found in the initial stages of asphyxia and its fall from the moment breathing stops. Immediately after stopping terminal breathing, open the chest. The heart is still beating. Gradually, atrioventricular block develops (the atria contract more often than the ventricles) and, finally, the heart stops. The heart may still beat for 5 to 15 minutes after breathing has stopped. At autopsy, the lungs are distended and in a state of emphysema. Under the pleura and on the

endocardium, pinpoint hemorrhages are visible, which have arisen by diapedesis, due to malnutrition of the walls of the capillaries and a simultaneous increase in blood pressure. Parenchymal organs are plethoric – from the incisions of the liver, kidneys, dark cherry-colored blood flows abundantly.

Death during asphyxia occurs from hypoxemia, the dark color of the blood depends on the lack of oxygen in it. Some time after the autopsy, the blood of the corpse turns red, as it absorbs oxygen from the air, the percentage of oxyhemoglobin increases and its color becomes scarlet. The change in blood color can be demonstrated by taking a drop of blood from an incision in the liver or kidneys and smearing it thinly on white paper. Absorbing oxygen from the air, the blood changes color before our eyes, within a few seconds. An increase in the concentration of carbon dioxide during asphyxia is of great importance in the adaptation of the body to hypoxemia. The respiratory center is very sensitive to elevated levels of carbon dioxide in the blood. This property contributes to the rapid development of shortness of breath during asphyxia. An increase in the concentration of carbon dioxide during asphyxia also has the significance that its excess in the blood contributes to the deoxidation of oxyhemoglobin and the return of oxygen to the tissues.

At the same time, the accumulation of carbon dioxide reduces metabolism, and therefore oxygen consumption decreases. The minute volume of respiration can therefore increase significantly without a noticeable increase in total gas exchange. The slowing of breathing, which develops towards the end of asphyxia, is explained by a decrease in the excitability of the respiratory center. To excite it, a large concentration of carbon dioxide is required, which accumulates during long pauses between individual respiratory movements. After the next respiratory movement, the oxygen tension in the arterial blood increases, and the amount of carbon dioxide decreases. There is a pause again, during which an excess of carbon dioxide accumulates again. Excess carbon dioxide also changes the functioning of the cardiovascular system. At the autopsy of the animal, immediately after respiratory arrest, we saw a slowdown in the rhythm of cardiac activity. This deceleration depends on irritation of the centers of the vagus nerves with an excess of carbon dioxide.

The latter also excites the vasomotor center, as a result of which, in the first stage of asphyxia, the arterioles narrow. Then, as a result of paralysis of the vasomotor center, the vessels dilate and the blood depots overflow with blood. That is why the autopsy reveals venous plethora of parenchymal organs. After breathing stops, the heart continues to contract. Death occurs from paralysis of the respiratory and vasomotor centers [6]. Simultaneously with irritation of the centers of the medulla oblongata – the respiratory, vasomotor and centers of the vagus nerves during asphyxia, excitation also covers other parts of the nervous system, as a result of which the pupils narrow, the hair ruffles, sweat and saliva are released [7].

Demonstration of Changes in the Excitability of the Respiratory Center During Asphyxia

In a guinea pig, rabbit, or rat, the head is quickly cut off with scissors, placed on the table, and the respiratory movements of the isolated head are observed. Due to the inhibition of the respiratory center caused by the operation itself and anemia from bleeding, respiratory movements are inhibited and do not appear immediately, but 30–40 seconds after the removal of the head. Breathing is rare and deep – the nostrils and mouth open wide. Then the pauses between respiratory movements gradually increase, as in mechanical asphyxia, and breathing stops. This simple experiment clearly demonstrates the dependence of respiratory disorders during hypoxemia on changes in the excitability of the respiratory center [8,9].

Demonstration of Reflex Mechanisms of Shortness of Breath During Asphyxia ("Imaginary Asphyxia")

A rabbit undergoes a tracheotomy operation under local anesthesia. Pay attention to the fact that in a tracheotomized animal, the respiratory movements of the facial muscles and nostrils are completely preserved, despite the fact that air now enters the lungs directly through the trachea, bypassing the upper respiratory tract. These breathing movements can be considered as "imaginary breathing" by analogy with imaginary feeding during the operation of esophagotomy. Just as imaginary feeding reflexively causes the secretion of gastric juice, imaginary breathing is of great importance in the reflex regulation of breathing. This is proved as follows. In a tracheotomized animal, imaginary breathing is turned off by closing the nostrils with a hand or tightly plugging them with cotton swabs. Breathing slows down and becomes deeper (despite the free access of air to the lungs through the tracheotomy tube). After the release of the upper respiratory tract of the tracheotomized animal from squeezing, there is an increase and deepening of breathing – hyperventilation, as if before that the animal really experienced difficulty in breathing [10].

In this experiment with imaginary asphyxia, there are no disturbances in gas exchange and, consequently, shortness of breath is caused by exteroceptive impulses. It should be noted that even in true asphyxia, accompanied by a change in the partial pressure of oxygen and carbon dioxide in the blood, oxygen and carbon dioxide act not only directly on the respiratory center, but also reflexively through vascular chemoreceptors. After denervation of the aortic and carotid sinus zones, inhalation of mixtures with a low oxygen content does not cause a respiratory reaction. Irritation by carbon dioxide of an isolated carotid sinus (which retains only a nervous

connection with the body) leads to a deepening of breathing. The same is observed when carbon dioxide passes through the vessels of the spleen and other organs that have retained contact with the body only through the nervous system. Demonstration of respiratory disorders with spasm of smooth muscles of the bronchi and bronchioles. These disturbances are clearly visible in general anaphylactic shock in a guinea pig. Immediately after the administration of a resolving dose of serum, the guinea pig develops a spasm of the bronchioles and develops expiratory dyspnea. The air accumulated in the alveoli lingers in them and cannot exit through the narrowed bronchioles. There comes an acute expansion of the lungs – emphysema. The breath becomes strong and fast. At the same time, the elastic elements of the lungs pull back the walls of the bronchi, contributing to their opening. Exhalation is slow and long [1].

Respiratory Disorders for Lungs, Pleura, Chest

Demonstration of Respiratory Disorders in Focal Pneumonia

Experience put on a rabbit or dog. Establish breath registration. It is injected into the lung tissue with a syringe, especially bilateral, more severe disorders can be obtained, up to acute pulmonary edema, leading to death. Damage to lung tissue usually does not cause coughing. Cough with pneumonia occurs when the inflammatory process passes to the pleura or bronchi and is most pronounced when the mucous membrane of the upper respiratory tract is affected. Inflammation of the lungs in the experiment can also be reproduced by injection into the lung tissue of 0.5 ml of a 50% emulsion of turpentine, intratracheal injection of pneumococci. In the latter case, inflammatory foci may develop, capturing entire lobes of the lungs. After showing dyspnea, the animal is bled to death and the lungs are removed along with the trachea. Then they are connected with a pump, strengthening the glass tube in the trachea, and inflated. Damaged parts of the lung do not swell. This is especially demonstrative if pneumonia was caused on the eve of the lecture and a sufficient amount of exudate managed to accumulate in the alveoli. The same thing happens if these lungs are placed in a hermetically sealed space with gradually decreasing pressure (Donders model) – the infiltrated areas remain sunken when the lungs expand. Pieces of infiltrated tissue cut from the lungs sink in water, unlike normal airy lung tissue. Consequently, the damaged areas of the lungs are indeed airless and the respiratory surface of the lungs has decreased [11].

Demonstration of Reflex Mechanisms of Shortness of Breath in Focal Pneumonia

Despite the exclusion of part of the lung tissue, gas analysis shows that the oxygen saturation of the blood with pneumonia usually decreases slightly. The tension of carbon dioxide in most cases remains within the normal range or even lowered (due to shortness of breath). Consequently, respiratory disorders in pneumonia cannot be reduced to local shutdown of a part of the respiratory surface and the resulting decrease in lung ventilation and impaired gas exchange. Of great importance in the development of shortness of breath in pneumonia are reflex changes in breathing under the influence of irritation from the focus of damage in the lungs. This is demonstrated by the following experiment. In a rabbit, both vagus nerves are cut in the neck. 20–30 minutes after the transection, the lungs are damaged in the manner described above. In this case, the introduction of hot water does not cause rapid breathing. Deepening of breathing is observed, which, perhaps, depends on irritation from the focus of damage, going along the afferent fibers that are part of the sympathetic system. The experiment can also be done on a rabbit with focal lung damage from a previous experiment. Transection of the vagus nerves leads to a sharp slowing of breathing [12].

Demonstration of Violations of Unconditioned and Conditioned Reflex Regulation of Breathing in Focal Pneumonia

a. Before and after, damage to the lungs, produced, as in the previous experiment, causes painful shortness of breath. To do this, the sciatic nerve of the rabbit is dissected in advance, electrodes are placed on it, and current is passed from the induction coil (voltage 2–4 V, frequency 50 breaks per minute). They cause painful shortness of breath (the irritation threshold is set in advance, in a rabbit it is usually equal to 12–15 cm of the distance between the coils). A typical reflex reaction to irritation of the sciatic nerve is expiratory pauses followed by increased breathing. After damage to the lungs, this reaction is perverted – expiratory pauses weaken or completely disappear, instead of short-term hyperventilation, a longer increase in breathing is observed. The respiratory center, excited by an impulse from the lesion, is unable to give the usual inhibitory reaction (expiratory pauses). To do this, it is necessary to increase the current strength (up to 9–11 cm of the distance between the coils).

b. Experience put on the dog. After injecting 20 ml of hot saline into the lung tissue with a syringe through the chest, the unconditioned and conditioned reflex responses to ammonia inhalation are examined. After 1 hour, inhibition of the conditioned reflex reaction develops, indicating that the irritation caused by impulses from the lesion in the lungs extends not only to the respiratory center, but also to the cerebral cortex. The reflex reactions of the respiratory center are also restored before the restoration of a tissue defect in the lungs and may even be increased. This explains that various kinds of additional irritations in patients with pathological changes in the lungs easily cause shortness of breath. Of great importance in the restoration of breathing is the compensatory role of the nervous system. In case of insufficiency

of the nervous system caused by decortication in an animal, lung damage leads to more severe and longer-lasting respiratory disorders than the same lung damage in animals with a normal nervous system [1].

Demonstration of Violations of the Elasticity of Lung Tissue in Acute Emphysema

Lungs removed from a rabbit corpse are slightly inflated with a pump connected to the trachea. After inflating, they, due to their elasticity, return to their previous volume, as happens during normal inhalation and exhalation. The elasticity of the lungs is provided by a large number of elastic connective tissue fibers in the alveoli and alveolar ducts. If, on the other hand, an excessively large amount of air under pressure is introduced into the lungs several times, the elastic fibers are partly torn, and partly overstretched, and the lungs cannot return to their original volume. They remain inflated, with pressure on the lung tissue, traces of depression do not disappear. With overstretching of the lungs, the alveoli are sharply expanded; alveolar septa and elastic fibers rupture, and the capillaries become empty. All this leads to a decrease in the lung surface. A decrease in the elasticity of the lungs leads to a decrease in negative pressure in the chest cavity. The lungs do not stretch well when inhaling and collapse even worse when exhaling, their vital capacity decreases.

The amount of residual air in the lungs becomes larger, ventilation is disturbed. Disruption of gas exchange contributes to the desolation of capillaries in overstretched alveolar septa and rupture of the alveoli. Due to a decrease in the elasticity of the lungs, exhalation is lengthened and is not performed passively, as usual, but with considerable difficulty. Therefore, during exhalation, the abdominal muscles tense up, expiratory dyspnea develops. With emphysema, in addition to breathing, blood circulation is also disturbed. The desolation of capillaries in a small circle creates obstacles to blood flow. Difficulty in blood flow through the pulmonary circulation in chronic emphysema leads to the development of right heart hypertrophy followed by decompensation, from which patients usually die [13].

Demonstration of Respiratory Disorders in Pleural Lesions

In the pleural cavities, inflammatory exudate (pleurisy), transudate (hydrothorax), blood (hemothorax), air (pneumothorax) can accumulate.

1. Experience is put on a rabbit

Air is introduced into the pleural cavity using a pneumothorax apparatus or a conventional syringe with a capacity of 100 ml. The pleura is punctured with a 5–7 cm long needle with a lumen diameter of 1 mm. To avoid damage to the pleura of the lung, the end of the needle should be with a short, not sharp cut. The puncture is made in the fourth-fifth intercostal space, in the middle between the mamillary and axillary lines, at the anterior edge of the rib. The needle is connected to a mercury pressure gauge with a rubber tube with a clamp. After the puncture, the clamp is removed. The appearance of fluctuations of mercury in the manometer, corresponding to respiratory movements, means that the needle is in the pleural cavity. The absence of hesitation may depend on clogging of the needle with fat or blood, or on the fact that the parietal pleura is not punctured. Normally, the pressure in the pleural cavity is negative, more during inhalation than during exhalation. As air is introduced into the pleural cavity, the negative pressure gradually decreases and becomes positive. Positive pressure in the pleural cavity leads to the collapse of the lung and its exclusion from the act of breathing. In response to this, a compensatory increase and deepening of respiratory movements, an increase in cardiac activity, and an acceleration of blood flow develop reflexively [14]. Limited Closed Pneumothorax is widely used for Therapeutic Purposes in Tuberculosis.

2. Open pneumothorax occurs with penetrating wounds of the chest. In the experiment, it is caused by a small incision of the soft tissues between the ribs (a glass tube is inserted into it to prevent the edges of the wound from collapsing). With open pneumothorax, each breath is accompanied by the suction of air into the pleural cavity. Therefore, the lung collapses during inhalation and expands during exhalation (paradoxical breathing). With bilateral pneumothorax, death occurs from asphyxia. The mechanism of shortness of breath in case of damage to the pleura (as in cases of damage to the respiratory tract or lung parenchyma) cannot be reduced only to compression, a decrease in the lung surface, since shortness of breath is also observed with dry fibrinous pleurisy, when the lung is not squeezed by exudate. When analyzing respiratory disorders caused by pathological changes in the pleura, it is necessary to take into account reflex respiratory disorders under the influence of impulses from the pathologically altered pleura.

Irritation from the pleura also explains the reflex contraction of the intercostal muscles in pleurisy, due to which the affected part of the chest is turned off from breathing. In addition to breathing, with pneumothorax, blood circulation is also disturbed. Normally, respiratory movements contribute to the suction of blood into the large veins and atria, creating a negative pressure in them. When the pleural cavity is filled with liquid or air, the suction of blood to the heart becomes difficult. In addition, the fluid accumulated in the pleura compresses large veins. Arterial pressure in process of development of the phenomena of asphyxia in the beginning rises, and then falls. With a one-sided accumulation of fluid, the heart moves to the side. With such a displacement, a sudden kink of the superior vena cava can cause immediate death of the patient. With

short-term mediastinal shifts that disrupt the flow of blood from large veins to the heart, the pulse may disappear during inspiration – a paradoxical pulse occurs [1].

Demonstration of Respiratory Disorders in case of Chest Injury

The type of breathing in animals is usually mixed – chest-abdominal. If the chest is affected, the type of breathing may change and become abdominal. Experience is easiest to put on a rabbit. At first, the movements of the chest of a calmly lying rabbit are monitored (it is better to observe from the side, at the same time it is possible to write off the respiratory movements mechanographically or using a small pneumograph). Then a fracture of several ribs is made, strongly squeezing the chest with the hands. Respiratory excursions of the chest immediately stop, the movements of the abdominal wall increase. The same consequences, except for a fracture of the ribs, can lead to neuritis of the intercostal nerves and inflammatory changes in the pleura. With the accumulation of fluid in the abdominal cavity, the movements of the abdominal wall, on the contrary, stop and intensify chest excursions – a chest type of breathing appears. This can be shown by introducing air into the abdominal cavity with a syringe or, more simply, by mechanical squeezing of the lower abdomen (towel, bandage). At the same time, the abdominal muscles are immobilized, the viscera support the diaphragm and limit its movements, chest excursions are compensatory intensified. This is especially clearly seen if the hair on the chest and sides of the animal is cut in advance [15]. In severe brain damage, dissociation between the respiratory movements of the chest and muscles may appear– at the time of inhalation, the abdominal wall may be reduced, i.e., in the position of maximum exhalation [1].

Respiratory Disorders when the Quantity and Composition of the Blood is Changed

Demonstration of Respiratory Disorders During Bleeding

The animal is bleeding. With the loss of 40–50% of the blood, a sharp shortness of breath appears. It would seem that the easiest way to explain this shortness of breath is by a decrease in the number of red blood cells and hemoglobin, which binds oxygen. It has been established, however, that despite the decrease in the total amount of oxygen in the blood, its partial pressure in the blood does not decrease. The vascular receptors are sensitive only to changes in oxygen tension in the arterial blood, but not to a decrease in its percentage. Shortness of breath during bleeding depends mainly on the fall in blood pressure. If physiological saline is administered intravenously simultaneously with the release of blood, shortness of breath does not occur. With a drop in blood pressure, the respiratory center is reflexively irritated by impulses following along the afferent nerves from the aortic arch and branches of the carotid arteries. On the contrary, an increase in pressure in these areas depresses and even completely stops breathing [16].

Demonstration of Respiratory Disorders in Carbon Monoxide Poisoning

A mouse or a rat is placed under a glass cap (you can use a bell from a Komozsky pump), into which light gas is passed or a rag is set on fire. Poisoning occurs at a content of 0.03–1% of this gas in the air. Hemoglobin combines with carbon monoxide 300 times faster than with oxygen, forming a very stable compound carboxyhemoglobin. With CO poisoning, muscle weakness gradually develops, plastic tone increases, shortness of breath appears, turning into periodic breathing, convulsions, and coma. Already when half of the blood hemoglobin is replaced with carboxyhemoglobin, severe functional disorders occur. At the same time, a halving of hemoglobin in anemia does not yet lead to such disorders. This difference is explained by the fact that CO poisoning not only reduces the amount of oxyhemoglobin, but the remaining hemoglobin binds more strongly with oxygen and hardly releases it to the tissues. An autopsy of an experimental animal that died from CO poisoning reveals blood of a bright carmine-red color (the color of carboxyhemoglobin). Cyanosis does not develop during this poisoning, even if the animal exposed to CO is taken out from under the cap and additionally subjected to mechanical asphyxia. Consequently, the bond between carbon monoxide and hemoglobin is so strong that even with an acute lack of oxygen caused by asphyxia, the tissues cannot receive it. Carbon monoxide poisoning is often complicated by pneumonia [17,18].

Demonstration of Respiratory Disorders in case of Sodium Nitrite Poisoning

Sodium nitrite-sodium nitrite ($NaNO_2$) is administered intravenously to a rabbit or Yoshka in the form of a 10% aqueous solution at the rate of 0.01–0.02 g per 1 kg of weight or subcutaneously (0.1–0.2 g per 1 kg of weight). Rats, mice and frogs are injected with 2–3 ml of a 10% solution subcutaneously [1]. In case of sodium nitrite poisoning, methemoglobin is formed and blood pressure decreases, oxygen starvation develops, from which the animal dies in a few minutes. At autopsy, blood and tissues have a chocolate tint – the color of methemoglobin. At the lecture, animals that died from CO poisoning, sodium nitrite and asphyxia are simultaneously dissected, and the color of the blood is compared.

Demonstration of Tissue Respiration Disorders in Cyanide Poisoning

Experiments are done on mice. KCN solution is prepared ex tempore as it is very unstable. The minimum lethal dose for mice when administered subcutaneously is 0.004–0.006 mg per 1 kg of

body weight. With this poisoning, the enzyme systems that provide oxidative processes in the tissues are disrupted. The oxygen capacity of the blood remains high, its color at the autopsy of the dead animal is scarlet, since the tissues cannot use the oxygen supplied to them [19].

Respiratory Disorders when the Content Changes Oxygen and Carbon Dioxide in Inhaled Air

Demonstration of Respiratory Disorders in a Confined Space

When breathing in a closed, poorly ventilated room, the amount of oxygen in the inhaled air decreases, the amount of carbon dioxide increases. Respiratory disorders occurring in this case are demonstrated in the following experiment. Experience put on two white mice of the same weight. Each mouse is placed in 100 ml bottles. For tightness, the edges of the lids of the bottles are smeared with petroleum jelly. A chemical CO2 absorber [containing Ca(OH)2] is placed in one of the bottles. The amount of oxygen in both bottles decreases as the animal consumes it, and the amount of CO2 increases only in the bottle without an absorber. The bottles are placed on a dark background and well lit. Gradually, the mice develop shortness of breath (somewhat earlier in the one that sits in the bottle without an absorber), sometimes mild convulsions, then the mice become more and more lethargic and die at the same time (after 10–15 minutes). Therefore, death due to asphyxia occurs from a lack of oxygen, and not from an excess of CO2. However, the solution is prepared with the precautions provided by the pharmacopoeia. shortness of breath develops earlier and is more pronounced in an animal in a bottle without an absorber. This is due to the high sensitivity of the respiratory center to carbon dioxide. At 2% CO2 in the inhaled air (instead of 0.04%) ventilation increases by 50%, and at 6% CO2 – by 750%. Due to this increase in ventilation, the percentage of CO2 in the alveolar air remains within the normal range (5.6%) even at 5% CO2 in the inhaled air [1]. An excessively high concentration of carbon dioxide in the inhaled air (over 8%) does not excite, but depresses the respiratory center – breathing slows down, and pulmonary ventilation decreases. Inhalation of CO2 at higher concentrations (30–40%) leads to death [20].

Demonstration of Respiratory Disorders in a Rarefied Atmosphere

Respiratory disorders that occur when climbing to a height can be reproduced in a pressure chamber. A rat or mouse is placed in a pressure chamber or under a glass dome of the Komovsky pump and the air is gradually rarefied. The degree of rarefaction of air under the bell is determined by a pressure gauge attached to the pump. As the rarefaction develops, the animal first develops motor excitation, then inhibition, shortness of breath, cyanosis, convulsions, respiratory arrest and death. Body temperature usually drops. If the test animal is simultaneously given oxygen while the pressure in the chamber is reduced, it tolerates the pressure reduction without noticeable respiratory disturbances. Therefore, the cause of death is a decrease in the partial pressure of oxygen. With a gradual decrease in pressure in the pressure chamber, it is found that shortness of breath occurs only when the percentage of oxygen in the inhaled air decreases by half, i.e., to 12–13% (instead of 21%), which corresponds to an altitude of 4–4.5 km above sea level. Thus, a lack of oxygen (hypoxemia) excites the respiratory center to a lesser extent than an excess of carbon dioxide.

This is due to the ability of hemoglobin to bind oxygen to a certain extent, regardless of its tension. Only with a decrease in the partial pressure of oxygen below 90–85 mm (instead of 95–96 in the norm), which corresponds to 11–12% O2 in the air, the content of oxyhemoglobin in the blood decreases significantly and severe shortness of breath develops. Animals die at an altitude of about 11 km, where the partial pressure of oxygen does not exceed 35 mm (4.7% > O2). Atmospheric rarefaction is simultaneously accompanied by a decrease in the partial pressure of CO2 in the inhaled air. This explains the difference between shortness of breath in an animal in a rarefied atmosphere and that which occurs during mechanical asphyxia. The effect of excess CO2 is mainly to deepen breathing. Hypoxemia causes a distinct increase in respiratory rate and only a slight increase in its depth. Superficial, although frequent breathing is less advisable than rare and deep. It requires a lot of energy for respiratory movements, causes fatigue, but does not provide sufficient ventilation of the lungs, since air circulation is largely limited to the so-called dead space, i.e., the upper part of the respiratory tract.

A decrease in the partial pressure of CO2 during breathing in a rarefied atmosphere reduces the excitability of the respiratory center, as a result of which periodic breathing often occurs [1]. After denervation of the aortic and carotid sinus, inhalation of a mixture with a low oxygen content does not cause shortness of breath, which proves its reflex nature [21]. Hypoxemia also changes the state of the cardiovascular system. Tachycardia appears, a spasm of blood vessels (skin, liver, spleen), which enhances blood circulation and compensates for the lack of oxygen. This also contributes to the strengthening of hematopoiesis. Death in hypoxemia occurs from paralysis of the respiratory and vasomotor centers. Immediately after breathing stops, the animal is opened. An autopsy reveals hemorrhages characteristic of hypoxemia by diapedesis on the mucous membrane of the respiratory tract, under the pleura, on the mucous membrane of the gastrointestinal tract [1]. Thus, the data presented in the review on modeling the pathology of the respiratory 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.

References

1. Frankstein SI(1956) Demonstration course of pathological physiology. Moscow.
2. Shafer GD (1924) Respiratory Exchange of the Frog. Science 60(1547): 179-181.
3. Farber S (1937) Studies on pulmonary edema: I. The consequences of bilateral cervical vagotomy in the rabbit. The Journal of Experimental Medicine 66(4): 397-404.
4. Andrew Salter (2001) Conditioned reflex therapy. – Wellness Institute, Inc.,.
5. Suzuki T (1996) Suffocation and related problems. Forensic Science International 80(1-2): 71-78.
6. Kleinert HD, Scales JL, Weiss HR (1980) Effects of carbon monoxide or low oxygen gas mixture inhalation on regional oxygenation, blood flow, and small vessel blood content of the rabbit heart. Pflügers Archiv 383: 105-111.
7. Heymans C (1950) Survival and revival of nervous tissues after arrest of circulation. Physiological Reviews 30: 375-392.
8. Henderson Y (1933) Fundamentals of asphyxia. Journal of the American Medical Association 101(4): 261-266.
9. Lawson EE, Thach BT (1977) Respiratory patterns during progressive asphyxia in newborn rabbits. Journal of Applied Physiology 43: 468-474.
10. Breckenridge CG, Hoff HE (1954) Reflex respiration. American Journal of Physiology-Legacy Content 178: 521-528.
11. Bachofen H, Hildebrandt J, Bachofen M (1970) Pressure-volume curves of air-and liquid-filled excised lungs-surface tension in situ. Journal of applied physiology 29: 422-431.
12. Glogowska M, PS Richardson, JG Widdicombe, AJ Winning (1972) The role of the vagus nerves, peripheral chemoreceptors and other afferent pathways in the genesis of augmented breaths in cats and rabbits. Respiration physiology 16: 179-196.
13. Karlinsky JB, Snider GL (1978) Animal models of emphysema. American Review of Respiratory Disease 117: 1109-1133.
14. Permar HH (1923) The pathogenesis of experimental pneumonia in the rabbit. The Journal of Medical Research 44: 1-26.
15. Jekl V (2021) Respiratory Disorders in Rabbits. Veterinary Clinics: Exotic Animal Practice 24: 459-482.
16. Head H (1889) On the reglation of respiration: Part I. Experimental. The Journal of physiology 10: 1.
17. Piantadosi CA (2019) Toxicity of carbon monoxide: hemoglobin vs. histotoxic mechanisms. Carbon monoxide. CRC Press, pp. 163-186.
18. Rose JJ, Wang L, Xu Q, Mc Tiernan CF, Shiva S, et al. (2017) Carbon monoxide poisoning: pathogenesis, management, and future directions of therapy. American journal of respiratory and critical care medicine 195: 596-606.
19. Graham DL, Laman D, Theodore J, Robin ED (1977) Acute cyanide poisoning complicated by lactic acidosis and pulmonary edema. Archives of Internal Medicine 137: 1051-1055.
20. Hill L, Flack M (1908) The effect of excess of carbon dioxide and of want of oxygen upon the respiration and the circulation. The Journal of physiology 37: 77-111.
21. Bouverot P (2012) Adaptation to altitude-hypoxia in vertebrates. Springer Science & Business Media, p. 16.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2022.45.007227

Bon LI. Biomed J Sci & Tech Res