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TRANSLATION

INFLUENCE OF ELEVATED INTRAPULMONARY PRESSURE ON RESPIRATION AND CIRCULATION

By

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FOREIGN TECHNOLOGY DIVISION

AIR FORCE SYSTEMS COMMAND

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UNEDITED ROUGH DRAFT TRANSLATION

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INFLUENCE OF ELEVATED INTRAPULMONARY PRESSURE ON RESPIRATION AND CIRCULATION

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Cases in which there is a substantial difference between atmospheric and intrapulmonary pressure are encountered among persons engaged in certain occupations and individuals with various pathological conditions. Thus, for example, this phenomenon occurs in wind-instrument players, glass-blowers, and persons subject to protracted fits of coughing or dyspnea as a result of stenosis of the upper respiratory passages. A brief discrepancy between intrapulmonary and external pressure may develop during diving; it is more prolonged and more severe when a dive or an ascent to high altitude is made with self-contained breathing apparatus, which hermetically seals the respiratory passages off from the surrounding water or air.

An increase in intrapulmonary pressure is occasionally resorted to in the clinical treatment of certain forms of pulmonary edema and fits of asthmatic dyspnea.

Artificial elevation of intrapulmonary pressure has recently come into wide use in thoracic surgery. The increased pressure in the lungs keeps them from collapsing when the thoracic cavity is opened and makes it possible both to maintain sufficient arterialization of the patient's blood and to employ intratracheal inhalation anesthesia (Grigor'yev and Anichkov, 1948).

An increase in intrapulmonary pressure undoubtedly influences the

entire body, particularly the activity of the respiratory and circulatory organs. Study of the character and mechanism of the changes in respiration and circulation which occur in this case and establishment of the conditions under which these changes can prove intolerable is of great theoretical and practical interest for modern medicine.

These problems, however, have not been the subject of sufficient research. Physiology has available a rather large number of data on the remote sequelae of altered intrapulmonary pressure (respiratory and circulatory reflexes to irritation or compression of the lungs, impairment of blood flow and increased pulmonary-vessel pressure, etc.). It also has at its disposal fundamental facts regarding the regulation of blood pressure and the relationship between respiratory and circulatory functioning, which undoubtedly bear directly on the aforementioned problems. However, all these data still do not constitute a complete picture of the changes which occur in respiration and circulation under the influence of a more or less prolonged discrepancy between external and intrapulmonary pressure. V.A. Vinokurov (1944) described the pattern of these changes when pulmonary pressure was increased for a comparatively brief time. However, in conducting these experiments the author aimed not so much at studying and analyzing the respiratory and circulatory changes which occurred as at determining the role of the sympathetic nerve fibers which innervate the lungs in the development of these reactions.

The aforementioned problems of the character and mechanism of the respiratory and circulatory changes and of the maximum magnitudes and exposure times critical for these changes thus required special investigation. Our work, which consisted of a series of acute and a series of chronic experiments on dogs, was conducted toward this end.

ACUTE EXPERIMENTS

Method

Figure 1 shows a schematic diagram of the apparatus for breathing under elevated pressure employed in our experiments.

The principal component of the device is a gas tank with floating bell, which has a volume of 1.6 m^3, a height of 1.9 m, and a diameter of 0.95 m. The stationary gas-tank reservoir is filled with water to approximately half its height, the floating bell being held down with weights; the size of the weights varies in accordance with the pressure which must be applied. Compressed air is supplied to the bell from a tank, through a reduction valve. As it enters the gas tank the bell floats at a definite height; an elevated pressure, whose magnitude is governed by the size of the weight and recorded with a water manometer, is created beneath the bell. The air space of the gas tank is connected through corrugated rubber tubing and a three-way stopcock to the inhalation valve. The experimental animal thus carries out inhalation under the pressure present in the gas tank. The latter remains unchanged, since as the experimental animal consumes air in breathing the bell sinks lower into the water; this ensures that the air in the gas tank is under a strictly constant pressure. For the reason noted above, this constancy is not disrupted during each individual inhalation, a phenomenon which ordinarily occurs when different methods are used to supply an inhaled gas mixture under pressure.

The second part of this device for maintaining pressure in the respiratory passages is a specially fabricated tin cylinder 85 cm high and 25 cm in diameter equipped with a water gauge and a tube through which it can be filled with water. To the top of the cylinder are soldered two tubes 2.5 cm in diameter; one ends just after it enters the cylinder, while the other reaches to within 2 cm of its bottom. The

long tube is connected to the exhalation valve. The height of the water column in the cylinder governs the pressure which must be set up in the lungs in order for air to be expelled from the respiratory passages. The pressure in the pulmonary passages during inhalation is thus equal to that in the gas tank, while the pressure during exhalation is governed by the height of the water column in the cylinder. The short tube soldered to the cylinder top is connected to a gas-meter through a three-way stopcock, whose third branch is in turn connected to the exhalation-tube system before it reaches the cylinder. The air exhaled by the animal can be released directly into the atmosphere, be passed through the meter, avoiding the resistance, or be passed first through the resistance and then through the meter.

This setup makes it possible to create various ratios of inhalation pressure to exhalation pressure. It does, however, exclude versions involving large inhalation pressures, since in this case the air can pass through the valves and escape through the water in the cylinder. The three-way stopcocks on either side of the inhalation-exhalation valves permit switching on or off of the inhalation or exhalation pressure. The inhalation-exhalation valves with mica sheets which we used in our first experiments proved to be insufficiently reliable with respect to maintenance of elevated pressure, so that in subsequent experiments we were forced to resort to leaf valves in metal housings (Fig. 2). These maintained the hermetic sealing of the inhalation and exhalation portions of the device with complete reliability. The intervalve space was connected to a mercury manometer, which kymographically recorded the magnitude and direction of the changes in respiratory-passage pressure.

This device was employed in both the acute and chronic experiments. The methods by which the experiments in each series were conducted had

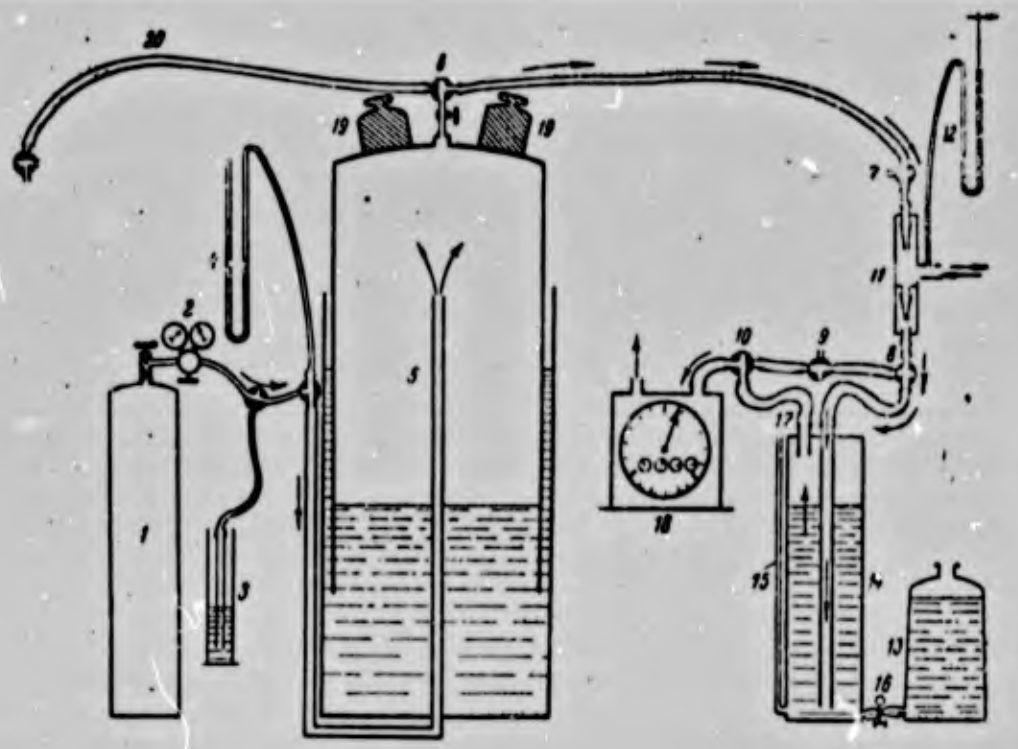

Fig. 1. Diagram of apparatus for respiration under elevated pressure. 1) compressed-air tank; 2) reduction valve; 3) glass cylinder filled with mercury, with tube immersed in it (supplemental device for varying pressure in gas tank); 4) water manometer; 5) gas tank; 6-10) three-way stopcocks; 11) inhalation-exhalation valves; 12) mercury manometer for recording changes in pressure in intervalve space; 13) bottle containing water; 14) tin cylinder with tube connected to exhalation valve extending to its bottom; 15) water gauge; 16) clamp for disconnecting bottle and cylinder; 17) tube for air to escape from cylinder; 18) gas meter; 19) weights on gas-tank bell; 20) corrugated tube which permits simultaneous performance of two experiments.

their own characteristics, which requires that they be described separately, in the appropriate sections of this paper.

All the acute experiments were performed on dogs. Chloralose anesthesia (10 cm^3 of a 0.7% solution per kg of body weight), administered intravenously after preliminary stunning with ether, was employed in 16 experiments. Hexenal (a 5% solution administered intravenously in doses of 0.8-1 cm^3 per kg of body weight) was used in 5 experiments.

In all the experiments arterial pressure, the pressure in the intervalve space (in the respiratory passages), thoracic and abdominal respiration, and ventilation were recorded kymographically. The pressure in the abdominal cavity and in the jugular vein was also recorded

in a number of cases.

Respiration (the changes in thoracic and abdominal volume) was recorded with the aid of corrugated-tubing cuffs connected to Mareyev capsules. The recording arms of the capsules were specially converted to first-order levers, which enabled us to obtain an ordinary kymogram (with inhalation at the top). The cuffs were always applied at the same points, one to the medial portion of the chest and the other to the abdomen, at the level of the navel.

Blood pressure was recorded in the right femoral artery, with an ordinary mercury manometer. In individual cases we made a parallel record with a Sechenov manometer, which enabled us to evaluate the mean arterial pressure. We also used the membrane manometer, which permits more precise recording of the pulse-induced fluctuations in blood pressure.

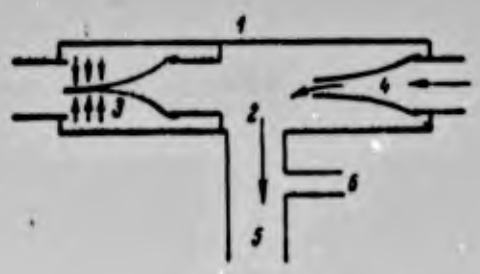

Fig. 2. Diagram of inhalation-exhalation leaf valves. 1) Valve housing; 2) intervalve space; 3) rubber leaves of exhalation valve; 4) rubber leaves of inhalation valve; 5) tube communicating with respiratory passages; 6) tube communicating with manometer which records the pressure in the intervalve space.

In order to record venous pressure in the left jugular vein we inserted a cannula connected to a water manometer by a system of citrate-filled tubes; the manometer was in turn connected to an ordinary Mareyev capsule. In using this system we did not try to obtain absolute values for the venous pressure, but recorded only the dynamics of its relative changes.

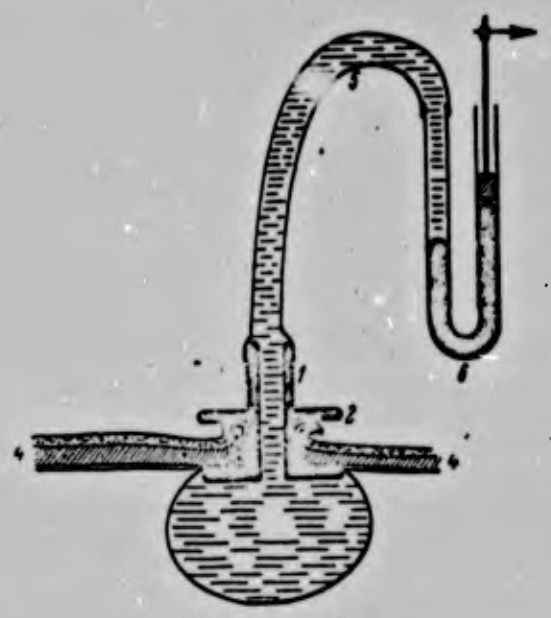

Fig. 3. Schematic diagram of system for recording intraperitoneal pressure. 1) Threaded metal cannula; 2) flat nut screwed on; 3) rubber bulb; 4) animal's abdominal wall; 5) rubber tube; 6) mercury manometer.

In order to record the intraperitoneal pressure in the upper right-hand region of the abdomen we made a longitudinal incision 2 cm long through all the layers of the abdomenal wall 4-5 cm below the costal margin. A special metal cannula with a water-filled rubber bulb at its end was inserted into the aperture thus formed. The peritoneum, muscles, and skin were then drawn together with three rows of purse-string sutures and the flat nut on the cannula was then screwed down, the area of abdominal wall surrounding the instrument thus being compressed between the nut and the flat portion of the cannula (Fig. 3). A rubber tube was used to connect the cannula to a mercury manometer and the entire system, including the rubber bulb inserted into the abdominal cavity, was filled with water.

The experiments were conducted in the following sequence. The animal was immobilized on the table and given ether, the left femoral vein was exposed, and the chloralose (hexenal) solution was administered. The tracheotomy was performed, the tracheotomy cannula was connected to the valve housing through a large rubber tube (1.2 cm in diameter), and the equipment for recording arterial and venous pressure, the pressure in the abdomina cavity and intervalve space, and thoracic and abdominal respiration was set up. Pharmaceutical ligatures were usually used to isolate the vagus nerves in the neck and they were subsequently transected during the course of the experiment. These preparations occupied approximately an hour.

In the experiments we employed: 1) resistance to exhalation only (unilateral pressure); 2) various ratios of low inhalation pressure to high exhalation pressure (intermittent pressure); 3) equal inhalation and exhalation pressures (constant pressure). Pressures of from 5-10 to 60 mm Hg were used in the acute experiments. The exposure time varied from several minutes to 2 hr.

All cases in which pressure was employed involved breathing through a gas-meter. Brief periods of respiration under elevated pressure were recorded continuously on kymograms. When pressure was applied over an extended period records were made at definite time intervals. All the experiments were conducted during the morning, on dogs last fed at the end of the preceding day.

EXPERIMENTAL RESULTS

Experiments involving respiration with exhalation under pressure. Respiration with exhalation under pressure caused a number of characteristic physiological changes in the functions of the respiratory and cardiovascular systems in the anesthetized dogs.

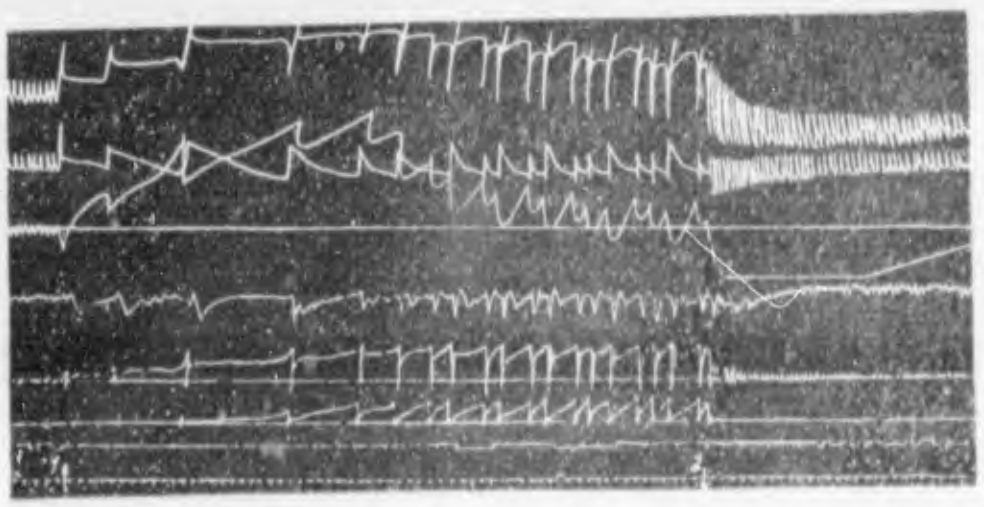

Fig. 4. Respiration in the presence of resistance to exhalation. Experiment No. 20. Dog's weight – 12 kg. Chloralose anesthesia. From top to bottom the curves represent thoracic respiration, abdominal respiration, venous pressure in the left jugular vein and its null line, blood pressure in the right femoral artery, pressure in the intervalve space and its null line (the same as the arterial-pressure null line), pressure in the peritoneal cavity and its null line, pulmonary-ventilation marker (250 cm^3), and time marker (5 sec). The arrow at the left indicates ap-

plication of exhalation pressure (38 mm Hg) and the arrow on the right indicates discontinuation of this pressure.

The kymograms shown below (Figs. 4-6) represent the typical pattern of these changes on application of substantial pressure (25-38 mm Hg) during exhalation. In reading and analyzing these kymograms one must be guided primarily by the pressure curves for the intervalve space (respiratory passages). These curves reflect the direction and magnitude of the changes in intrapulmonary pressure, give a quite precise indication of the duration of inhalation and exhalation and permit us to determine the instant at which one respiratory phases passes into the other (a drop in pressure in the intervalve space indicates inhalation, while a rise in pressure indicates exhalation).

Application of resistance to exhalation was accompanied by a substantial decrease in respiration rate in all cases without exception. Breathing later underwent a relative acceleration, but remained slow until the action of the resistance was discontinued. The respiration rhythm did not return to its initial level even when the animal was subjected to exhalation resistance for 1.5-2 hr.

Discontinuation of resistance had the opposite effect: breathing was greatly accelerated, the respiration rate usually exceeding its initial level by several times. The extent of the acceleration usually increased with the duration of the prior period of resistance-hampered breathing. The respiration rate returned to its normal level 10-15 or occasionally 30-50 sec after the resistance was discontinued. Table 1 presents numerical data relating to these changes in respiration.

In all cases the retardation of respiration under the action of resistance to exhalation was accompanied by a more or less substantial rise in thoracic volume and a smaller increase in abdominal volume.

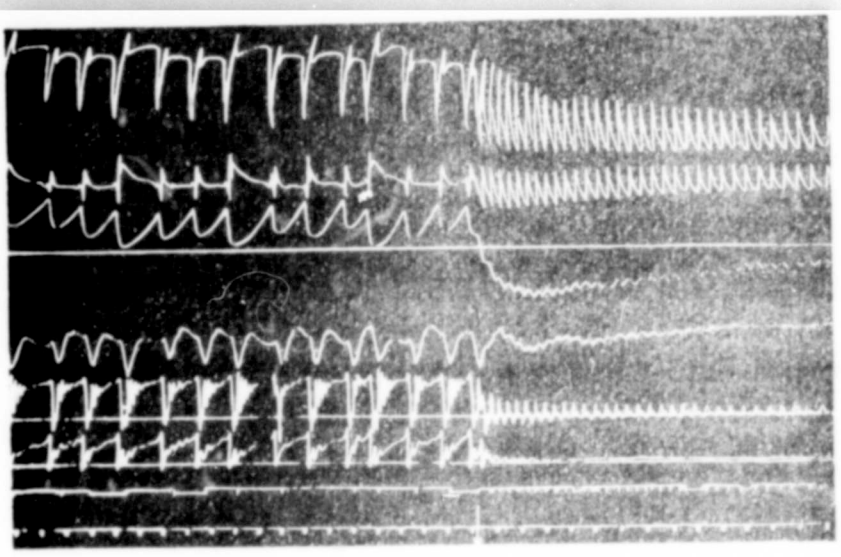

Fig. 5. Respiration in the presence of resistance to exhalation. Experiment No. 19. Dog's weight – 4.3 kg. Chloralose anesthesia. From the top down the curves represent thoracic respiration, abdominal respiration, pressure in the left jugular vein, mean initial venous pressure, pressure in the right femoral artery, pressure in the intervalve space and its null line (the same as the arterial-pressure null line), pressure in the abdominal cavity and its null line, pulmonary-ventilation marker (250 cm³), and time marker (5 sec). The arrow indicates discontinuation of the pressure (38 mm Hg).

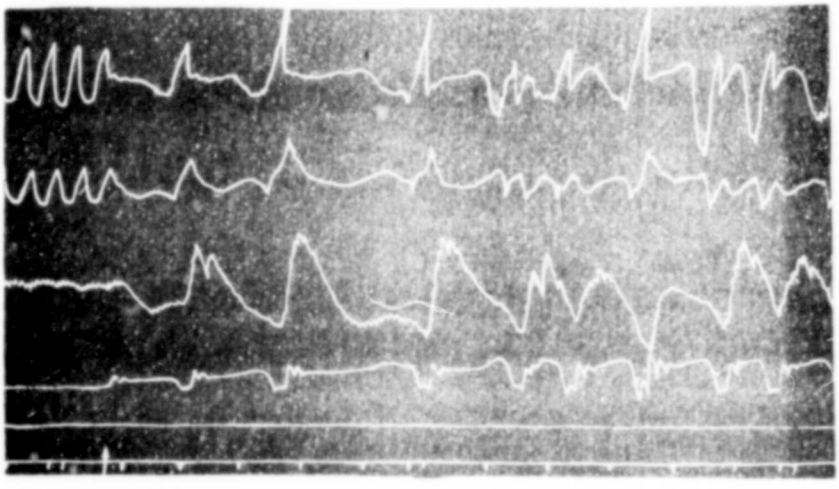

Fig. 6. Respiration in the presence of resistance to exhalation. Experiment No. 4. Dog's weight – 14 kg. Chloralose anesthesia. From top to bottom the curves represent thoracic respiration, abdominal respiration, blood pressure in the right femoral artery, pressure in the intervalve space (for the null level see the left-hand portion of the curve), blood-pressure null line, and time marker (5 sec). The arrow represents application of the inhalation resistance (24 mm Hg).

TABLE 1

Changes in Respiration rate on Application and Discontinuation of Exhalation Pressure in Animals with Intact Vagus Nerves

1 № опыта	2 Частота дыхания: 3 исходная	2 Частота дыхания: 4 после включения давления	5 Давление (в мм рт. ст.)	1 № опыта	2 Частота дыхания: 6 перед выключением давления	2 Частота дыхания: 7 после выключения давления	5 Давление (в мм рт. ст.)
А А	23	7	14	А А	9	30	23
В Б	26	18	22	8 Б	7	15	25
С В	28	9	20	2	8	20	17
1	21	16	14	3	22	34	54
2	26	8	17	3	20	34	58
2	17	7	17	3	14	31	22
5	9	5	12	6	17	26	20
6	22	6	20	8	6	16	14
8	16	2	18	8	7	24	14
8	26	6	12	10	22	43	24
10	51	14	24	11	68	72	30
11	84	58	30	11	7	68	30

1) Experiment No.; 2) respiration rate; 3) initial; 4) after application of pressure; 5) pressure (mm Hg); 6) before discontinuation of pressure; 7) after discontinuation of pressure.

The increase in thoracic and abdominal volume occurred in stages after the resistance was applied, over 3-4 inhalations; the resultant distension persisted throughout the entire period for which the resistance acted. When the latter was discontinued the phenomenon underwent involution, but somewhat more rapidly: the thoracic and abdominal volume returned to normal within 15-20 sec.

The character of the respiration curves was materially altered. These changes essentially reduced to a disruption of the normal relationships of the respiratory phases. Inhalation became rapid and brief in duration (the recording-pen traces were almost vertical), while, conversely, exhalation was prolonged; respiratory pauses disappeared altogether. The ratio of the durations of the individual respiratory phases was most precisely reflected by the pressure curve for the intervalve space. In considering this curve it becomes quite clear that each exhalation (rise in the curve) occupied an incomparably greater time than the corresponding inhalation. Hence it follows that in breathing

against an exhalation resistance the total time for which the lungs are subject to elevated pressure substantially exceeds the total time for which the intrapulmonary pressure is normal.

The synchronous change in the thoracic and abdominal volumes which occurs in ordinary respiration was usually disrupted in breathing against an exhalation resistance. Under normal conditions, each inhalation is accompanied by an increase in thoracic and abdominal volume and each exhalation by a decrease in their volume. When resistance was applied the changes in the thoracic and abdominal volumes were opposite in direction during the individual periods of the respiratory cycle. Figure 7A shows the typical relationships between thoracic and abdominal respiration under the action of exhalation pressure. Proceeding from the assumption that the true exhalation and inhalation times were recorded in the pressure curve for the intervalve space we may draw the following conclusion regarding the character of respiration in this case. The rapid increase in the thoracic and abdominal volumes occurs synchronously and coincides with inhalation, but these volumes then begin to decrease, synchronously at first; the decrease coincides with the very beginning of exhalation. The abdominal volume then continues its steady drop, but the thoracic volume increases, even though the animal has completed its exhalation, as is confirmed by the fact that the pressure in the intervalve space increases or remains at the level which it has reache. The final stage of exhalation, which in the majority of cases corresponds to expulsion of air from the lungs, was detected from the bubbling of the exhaled air through the water and the movement of the gas-meter needle and was accompanied by a synchronous decrease in the thoracic and abdominal volumes. These relationships are illustrated more graphically in Fig. 8, where the kymogram under consideration (Fig. 7A) is reproduced on a larger scale, taking into account the coincidence of the re-

cording pens. We are thus faced with a sort of paradox: exhalation is accompanied by distension of the thoracic cavity.

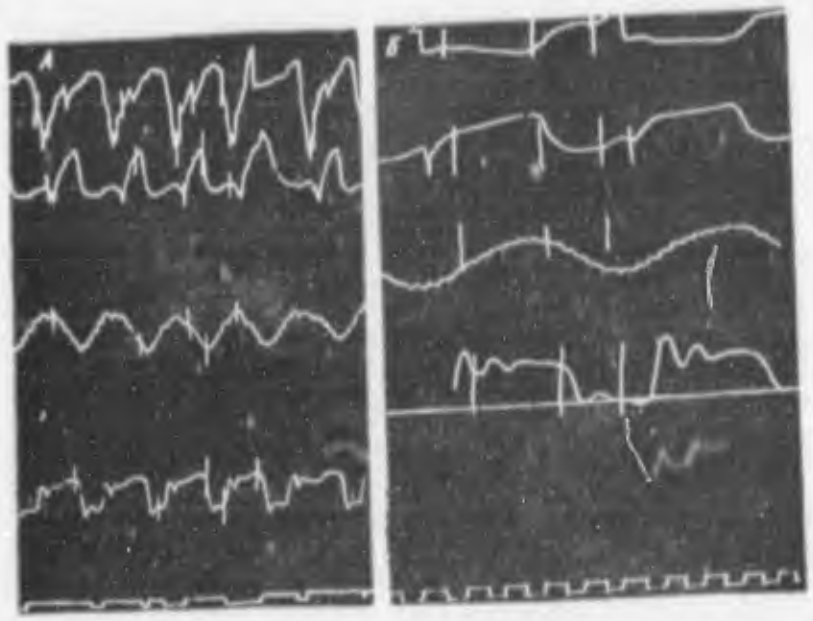

Fig. 7. Relationship between thoracic and abdominal respiration under the action of resistance to exhalation. A) Experiment No. 3. Dog's weight – 10.7 kg. Control markers (at 30 mm Hg) are superimposed on the curves for checking pen coincidence. From top to bottom the curves represent thoracic respiration, abdominal respiration, blood pressure in the right femoral artery, pressure in the intervalve space, and time marker (5 sec). B) experiment No. 8. Dog's weight – 8 kg. Control markers (at 18 mm Hg) are superimposed on the curves to check pen coincidence. From top to bottom the curves represent thoracic respiration, abdominal respiration, blood pressure in the right femoral artery, pressure in the intervalve space and its null line, and time marker (1 sec). Chloralose anesthesia was employed in both cases.

In our opinion, the only explanation of this phenomenon is the dominant role of the prelum abdominale in the act of exhalation. The expiratory muscles of the thoracic cavity obviously play a secondary role in this type of respiration. Active contraction of the abdominal muscles leads to an increase in intraperitoneal pressure. This pressure is transmitted through the diaphragm to the lungs and, since it is an obstacle to expulsion of air, causes an increase in intrapulmonary pressure, which in turn leads to pulmonary distension and an increase in the volume of the thoracic cavity. At a certain passive distension the thoracic cavity begins to counteract the pressure acting on it, which causes the pressure in the abdominal cavity and lungs to increase under

the continued action of the prelum abdominale; as soon as this pressure exceeds the resistance air is expelled from the lungs. Whether the reduction in thoracic volume at the end of exhalation results from the decreasing pressure in the lungs (since the prelum abdominale immediately becomes less intense) or from renewal of the action of the expiratory muscles is difficult to decide in a number of cases. This pattern is confirmed by Figs. 4 and 5, which simultaneously show the changes in intraperitoneal pressure. In evaluating the latter we must take into account the fact that the intraperitoneal-pressure recording system did not ensure absolute hermitic sealing in a number of cases. The absolute pressure in the thoracic cavity is thus frequently not represented on the kymogram, while the relative changes are recorded with sufficient accuracy. In many cases the latter correspond precisely to the pressure changes in the lungs, while the character of respiration indicates the dominant role of the prelum abdominale. All these cases confirm the considerations advanced above.

In our view, the dominant role of the prelum abdominale and the paradoxical dilitation of the thoracic cavity during exhalation are thus indisputable in these cases. This gives rise to one important consequence, which must be taken into account in analyzing the blood-pressure reaction, i.e., that the pressure in the abdominal cavity cannot be less than that in the lungs during exhalation in this type of respiration.

In several experiments involving resistance to exhalation we detected inverse relationships between the changes in the thoracic and abdominal volumes (Fig. 7B). The expiratory muscles of the thoracic played the dominant role in these cases. We do not feel, however, that the importance of the muscles of the prelum abdominale can be excluded in this type of respiration. It seems more correct to assume that they

exhibit a greater or lesser tonus during the exhalation phase. This tonus, which ensures rigidity of the abdominal wall, prevents extreme depression of the diaphragm, since the increase in pulmonary pressure

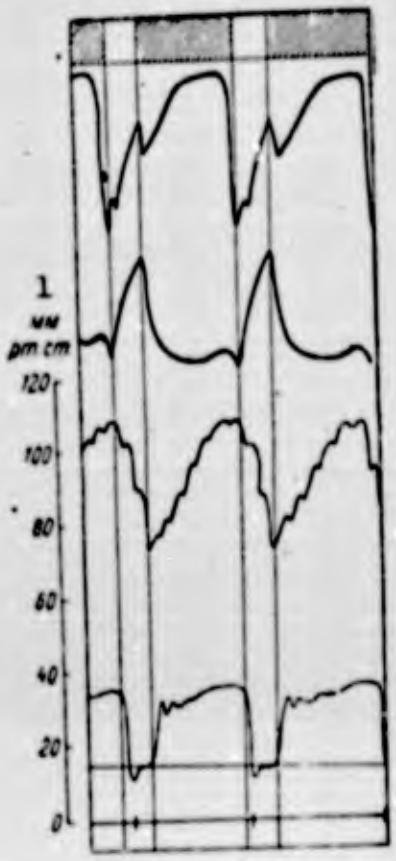

Fig. 8. Copy of kymogram obtained during respiration in the presence of resistance to exhalation. Pen coincidence is taken into account. Experiment No. 3. Dog's weight - 10.7 kg. Chloralose anesthesia. From top to bottom the curves represent thoracic respiration; abdominal respiration, arterial blood pressure, pressure in the intervalve space, and time marker (5 sec). The hatched sections indicate periods of exhalation, the unhatched areas indicating inhalation.

forces the diaphragm downward only until the intraperitoneal pressure equals the intrapulmonary pressure. This line of reasoning is supported by the fact that the rise in abdominal volume during exhalation is usually not of material extent. It must thus be assumed that the intraperitoneal pressure is approximately the same as the intrapulmonary pressure during the exhalation phase.

It should be noted that predominance of thoracic or abdominal breathing under the action of resistance to exhalation was obviously re-

lated to the animal's individual characteristics. In separate experiments involving breathing under exhalation pressure of various magnitudes the same animal usually exhibited some one type of variation in respiration. The role of the prelum abdominale was dominant in the overwhelming majority of cases.

The amplitude of the respiratory movements of the chest generally increased during respiration in the presence of resistance to exhalation; the amplitude of the respiratory movements of the abdomen varied in the same direction, but to a somewhat lesser extent. We unfortunately did not obtain any precise numerical data for the changes in pulmonary ventilation, because of the great inertia and insufficient precision of the gas-meters which we had at our disposal. However, our data give us a basis for concluding that these changes generally corresponded to those in respiration rate under the action of resistance to exhalation. When the resistance was applied ventilation decreased, but subsequently rose somewhat, although remaining reduced until the end of the impaired-respiration period despite the increased respiratory-movement volume during this period. Pulmonary ventilation increased sharply when the resistance was discontinued, frequently exceeding its initial level; it then gradually reverted to its original value.

The changes in respiration under the action of resistance to exhalation thus essentially reduced to substantial distension of the thoracic cavity, somewhat lesser distension of the abdomen, severe retardation of respiration, a relative decrease in pulmonary ventilation, a disruption of the relationship of the respiratory phases, and dominance of the prelum abdominale in exhalation.

A sharp increase in the respiratory fluctuations in blood pressure was extremely characteristic of the action of resistance to exhalation. In ordinary breathing the amplitude of these fluctuations ranged from

3-4 to 10-13 mm Hg; they increased by factors of 5.8 and 10 during respiration in the presence of resistance to exhalation. The respiratory fluctuations in blood pressure increased as soon as the resistance was applied, soon reached their maximum, and remained at this level until the resistance was discontinued. In the majority of cases there was a quite clear direct dependence between the magnitudes of the respiratory blood-pressure fluctuations and the resistance to exhalation. When the resistance amounted to 40-50 mm Hg the respiratory waves reached amplitudes of 70-80 mm Hg, this being 50 and occasionally even 60% of the mean blood-pressure level.

We were unable to detect any regular relationship between the time at which each respiratory blood-pressure wave developed and a given phase of respiration under normal conditions. We most frequently found that the beginning of the rise in the respiratory blood-pressure wave corresponded to inhalation, while its maximum occurred during the respiratory pause. These relationships generally varied widely in ordinary breathing. On the other hand, they were absolutely regular when resistance to exhalation was applied. Detailed analysis of the kymograms showed quite definitely that in all cases of respiration against a resistance the maximum rise in blood pressure corresponded to the exhalation phase. The minimum blood pressure, i.e., the negative peaks of the respiratory waves, corresponded to inhalation in the overwhelming majority of cases. In all cases the beginning of the rise in the respiratory waves corresponded quite precisely to the beginning of exhalation.

Thus, in respiration in the presence of exhalation resistance the changes in blood pressure during a single respiratory cycle generally reduced to the following. The beginning of exhalation was marked by a rise in blood pressure. This rise reached its maximum toward the middle of exhalation and ordinarily began an immediate decrease. This drop

frequently became sharper during inhalation and blood pressure reached its minimum at this point; the latter again began a sharp rise at the beginning of the next exhalation. The respiratory waves which occurred under the action of exhalation pressure were consequently characterized by unusually high amplitude and regularity with respect to development time. Discontinuation of the resistance was followed by a sharp reduction in the amplitude of the respiratory waves, which reverted to their normal value.

In breathing against substantial exhalation resistance mean blood pressure decreased somewhat in the majority of cases. However, this drop was relatively slight, as a result of the presence of unusually large respiratory waves. While the minimum blood pressure was frequently substantially less than the initial value, its maximum frequently exceeded this level and the mean value consequently dropped only slightly.

The changes in mean blood pressure on discontinuation of the resistance were very regular. Blood pressure immediately rose, exceeding its initial level. This rise lasted 3-5 sec and the blood pressure then decreased over the next 10-15 sec, only subsequently beginning a slow, uniform increase to its initial level. The typical changes in mean blood pressure on shifting to normal conditions thus consisted in a rapid rise, a subsequent drop, and a second slow increase, usually to the initial level.

Venous pressure increased in all cases when exhalation resistance was applied. This rise was gradual: the pressure increased slightly with each exhalation, the minimum level corresponding to each inhalation also increasing substantially in comparison with its initial value. Mean venous pressure thus increased steadily and usually reached its maximum when faster and more rhythmic respiratory movements began. At this point it started to drop, at a rate which increased with respiration rate.

This drop was characteristic of all cases of respiration in the presence of exhalation resistance, but in some venous pressure decreased to its initial level and stayed there, while in others it remained somewhat elevated. It also occasionally exhibited a temporary drop to below its initial level and then regained this level. In respiration against exhalation resistance the initial rise in venous pressure was thus succeeded by a marked tendency toward a reversion to its initial level. The amplitude of the fluctuations in venous pressure proved to be substantially increased throughout the entire period of breathing against exhalation resistance. In the majority of cases discontinuation of the resistance caused the venous pressure to drop below its initial level and regain it slowly. This drop was very substantial in individual cases, the reversion to the initial level requiring several minutes.

The changes in pulse rate during respiration in the presence of exhalation resistance were very unusual. Determinations made over 1-min periods showed that in the majority of cases pulse rate was reduced after application of the resistance. This deceleration generally progressed with time and the pulse rate was as a rule slower at the end of the resistance period than initially. There was occasionally no deceleration of pulse rate and in individual cases we even detected an acceleration during breathing against exhalation resistance. Such cases were rare and were usually characterized by high arterial pressure during the resistance period. General bradycardia ordinarily appeared against a background of extremely infrequent arrhythmia. The arrhythmia developed when the resistance was applied and was somewhat uncommon. On the one hand, this arrhythmia was related to respiration, since periods of rapid and slow pulse alternated during each respiratory cycle. On the other hand, we did not detect any direct relationship between these changes in pulse rate and the various respiratory phases. It was quite

obvious that in all cases tachycardia was noted during the rise in blood pressure and bradycardia always began at the height of this rise, being accompanied by a drop in blood pressure. Since both the rise and fall in blood pressure generally took place during exhalation, the alternation of fast and slow pulse also occurred within a single respiratory phase, i.e., exhalation. In those cases where exhalation was due to the prelum abdominale and the above-described paradoxical dilitation of the thoracic cavity occurred, the latter coincided with the beginning of the period of bradycardia and of the respiratory blood-pressure wave.

The changes in pulse rate on discontinuation of the exhalation resistance were not regular. In some cases there was a still greater retardation, while in others pulse rate was sharply accelerated immediately after discontinuation and then gradually decelerated to its initial level. There was occasionally a uniform acceleration of pulse rate which resulted in its reaching its initial level within 2-3 min.

Generalizing the data presented above, we may conclude that the changes in cardiovascular functioning during respiration against exhalation pressure generally reduce to a slight drop in mean blood pressure, a sharp increase in the amplitude of the respiratory blood-pressure waves, regular development of these waves at the beginning of each exhalation, an initial rise and subsequent relative decrease in venous pressure, and an unusual arrhythmia, which in the majority of cases proceeds against a background of general bradycardia.

In the majority of cases the extent of these changes in respiration and circulation was a direct function of the magnitude of the exhalation resistance. Pulmonary pressures of less than 5-6 mm Hg had virtually no effect on respirator and cardiovascular functioning. At such resistances the changes in this functioning generally took the form of

a slight retardation of respiration rate, with no material disruptions of the relationships between the respiratory phases, and a slight increase in the amplitude of the respiratory blood-pressure fluctuations, its initial mean value being maintained and no severe arrhythmia or bradycardia occurring.

All the aforementioned changes in respiration and circulation usually developed at exhalation pressures of 10-15 mm Hg, but became less marked as the resistance increased, this being especially obvious at resistances of 35-45 mm Hg, as is indicated by Fig. 7.

It must be noted that anesthetized dogs withstood these resistances for quite prolonged periods without catastrophic disruptions of respiratory or cardiovascular functioning. Thus, in certain experiments we subjected the animals to breathing against a resistance of 40 mm Hg for 1.5-2 hr, then shifting to ordinary respiration; after the transition cardiovascular and respiratory activity were quite normal for acute experimental conditions.

We can thus conclude that exhalation resistances of up to 35-40 mm Hg are completely tolerable for anesthetized dogs.

Resistances of 50-55 mm Hg are maximum for anesthetized dogs. In a number of cases such animals withstood these pressures, but usually only for several minutes. Exposure for longer periods caused a steady retardation of respiration, loss of the ability to expel air from the lungs, bradycardia passing into a marked vagal pulse, a drop in blood pressure, and death.

Experiments involving breathing under inhalation and exhalation pressure. In breathing under inhalation and exhalation pressure the character of the respiratory and circulatory changes depended primarily on the ratio of the inhalation pressure to the exhalation pressure (resistance). The lower the difference between these values, i.e., the more

nearly constant the applied pressure, the greater were the differences between the changes which developed and those which arose under the action of exhalation pressure of corresponding magnitude. In order to emphasize these differences let us consider cases of respiration under the following types of pressure: 1) strictly constant (Fig. 9); 2) approximately constant (Fig. 10).

Inhalation and exhalation pressure caused a rapid and more substantial distension of the thorax and abdomen, followed by more or less prolonged apnea.

Our attention is struck by the fact that the abdominal volume began to decrease during the course of the apnea, while the thoracic volume changed little after its initial increase; the intraperitoneal-pressure record indicated that it rose. This rise was parallel to the decrease in abdominal volume. It was consequently associated with contraction of the muscles which produce the prelum abdominale, whose dominant role in respiration under pressure is manifest as soon as the pressure is discontinued. The threshold inhalation pressure required to produce apnea varied from 8-10 to 12-15 mm Hg in our experiments. At lower pressures apnea generally did not develop at all; at pressures above 30-35 mm Hg the apnea lasted several minutes and was irreversible in a number of cases.

At moderate pressures the apnea was followed by establishment of a slow respiratory rhythm, breathing having all the peculiarities characteristic of exposure to exhalation resistance alone; however, these were more marked and the retardation of respiration was greater in extent. Table 2 presents numerical data on this respiratory retardation.

The arterial-pressure reaction differed materially from that observed under the action of exhalation resistance alone, both immediately after application of pressure and at later intervals. Blood pressure

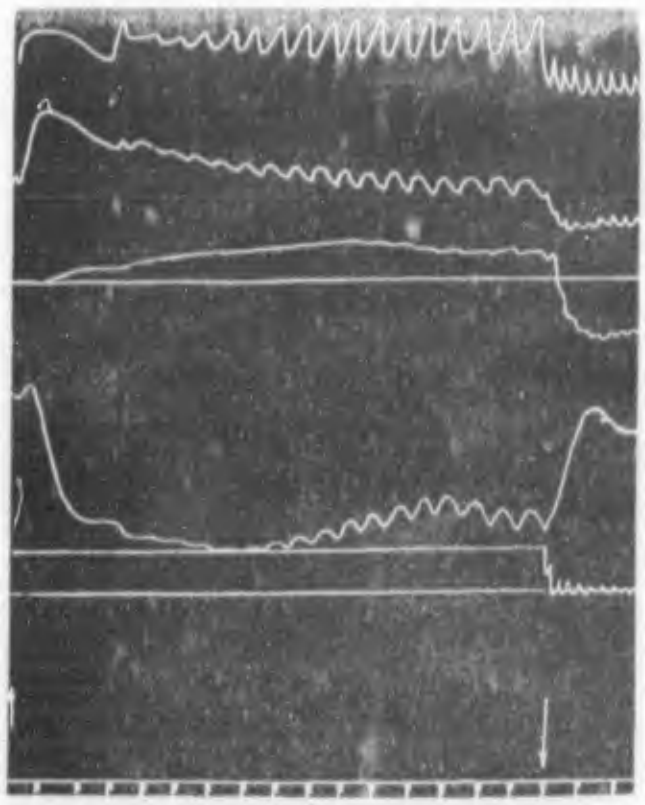

Fig. 9. Respiration under strictly constant pressure. Experiment No. 17. Dog's weight – 10.25 kg. Chloralose anesthesia. From top to bottom the curves represent thoracic respiration, abdominal respiration, pressure in the left jugular vein and its null line, blood pressure in the left femoral artery, pressure in the intervalve space (which remains unaltered, despite the occurrence of respiratory movements), the null line for the pressure in the intervalve space and the arterial pressure, and time marked (5 sec). The arrow at the left indicates application of pressure and that at the right indicates discontinuation of pressure (27 mm Hg).

dropped sharply, to half or occasionally 30% of its initial level, after application of inhalation and exhalation pressure (20-25 mm Hg). The extent of the decrease depended on the inhalation pressure, while the time for which it persisted varied from 4 to 20 sec and increased with its magnitude. A drop in blood pressure then began against the background of the continuing apnea; by the time the apnea disappeared the mean blood pressure had ordinarily reached 50-60% of its initial value. There were no respiratory blood-pressure waves during the apnea period and the amplitude of the pulse fluctuations was minimal. Respiratory waves developed when respiratory movements reappeared. Their amplitude

was incomparably less than in breathing under exhalation pressure alone and, in a number of cases, differed little from the initial level. The changes in blood pressure during the respiratory cycle usually corresponded to those observed under the action of exhalation resistance. Mean blood pressure remained substantially reduced throughout the entire period of respiration under bilateral pressure. When the pressure was discontinued the changes in blood pressure were basically similar to those observed on discontinuation of exhalation resistance.

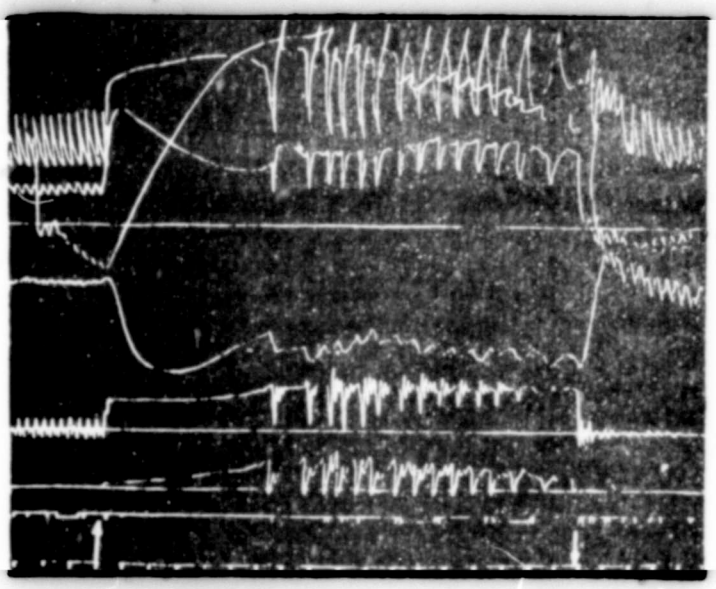

Fig. 10. Breathing under inhalation and exhalation pressure (inhalation pressure of 22 mm Hg and exhalation pressure of 37 mm Hg). Experiment No. 20. Dog's weight – 12 kg. Chloralose anesthesia. From top to bottom the curves represent thoracic respiration, abdominal respiration, pressure in the left jugular vein and its null line, blood pressure in the right femoral artery, pressure in the intervalve space and its null line (the same as the arterial-pressure null line), pressure in the abdominal cavity and its null line, pulmonary-ventilation marker (250 cm^3), and time marker (5 sec). The arrow at the left indicates application of pressure and that at the right discontinuation of pressure.

Just as in respiration against exhalation resistance, the venous pressure increased in all cases. The only difference lay in the fact that it rose sharply, reached its maximum toward the end of the experi-

ment, and then never reverted to its initial level, remaining elevated until the conclusion of the period of breathing under pressure. This is quite marked when the corresponding kymograms are compared (compare Fig. 10 with Figs. 4 and 5).

Venous pressure dropped even more sharply when inhalation and exhalation pressure was discontinued than when exhalation resistance was discontinued; it then rose slowly, reaching its initial level only after 4-5 min.

The changes in pulse rate during respiration under inhalation and exhalation pressure essentially differed little from those observed under the action of exhalation resistance, except for the initial changes. These, corresponding to the typical drop in arterial pressure against a background of apnea, reduced to a slight brief retardation of pulse rate immediately after application of pressure. This retardation was quite rapidly succeeded by a sharp acceleration, which rose in proportion to the drop in blood pressure and reached its maximum at the minimum pressure. The subsequent rise in blood pressure began against a background of an extremely rapid pulse; there was an especially great retardation of pulse rate at the end of this rise, before the first breath. The action of inhalation and exhalation pressure was subsequently accompanied by still greater general bradycardia and arrhythmia, which was the same in character as that described above. In a large number of cases discontinuation of the pressure was accompanied by marked bradycardia and a subsequent gradual acceleration of pulse rate, which returned to its initial level (Fig. 10).

Summarizing the material presented above, we may conclude that the changes in cardiovascular and respiratory functioning under the action of inhalation and exhalation pressure differ in a number of respects from those observed under the action of exhalation pressure alone.

TABLE 2

Changes in Respiration Rate on Application and Discontinuation of Inhalation and Exhalation Pressure in Animals with Intact Vagus Nerves

1 № опыта	2 Частота дыхания: исходная (3)	после включения давления (4)	5 Давление (в мм рт. ст.): выдох (6)	вдох (7)
СВ	18	2	20	11
5	12	5	20	20
6	21	9	30	16
6	22	14	36	22
7	26	5	24	12
7	12	5	22	14
8	24	3	14	10
9	10	8	30	12
10	22	22	24	10
11	75	40	30	18
11	38	30	30	18
11	54	2	30	26
11	36	35	30	10
12	21	19	32	24
12	24	14	34	26
12	24	16	30	20
19	18	Апноэ	26	
19	18	10 "	24	

1 № опыта	2 Частота дыхания: перед выключением давления (8)	после выключения давления (9)	5 Давление (в мм рт. ст.): выдох (6)	вдох (7)
8	3	15	—	—
[illegible]	36	38	30	12
10	22	31	30	16
11	2	36	36	22
12	30	36	24	12
12	3	18	24	12
12	39	22	18	8
12	20	24	34	26
13	19	20	32	24
13	14	24	34	20
13	16	27	30	20
17	10	34	24	24
17	10 14	30	24	24
19	Апноэ	11	20	
19	"	12	26	
19	"	16	24	
19	4	17	24	24
19	5	30	20	20

1) Experiment No.; 2) respiration rate; 3) initial; 4) after application of pressure; 5) pressure (mm Hg); 6) exhalation; 7) inhalation; 8) before discontinuation of pressure; 9) after discontinuation of pressure; 10) apnea.

These differences consist in a typical initial drop in blood pressure against the background of apnea, comparatively low-amplitude respiratory blood-pressure fluctuations and establishment of these fluctuations at a lower mean level, a more substantial and stable increase in venous pressure, greater bradycardia, and a more substantial change in the character and rate of breathing. These differences enable us to understand why, all other conditions being equal, it is more difficult to withstand constant pressure than exhalation resistance.

A constant pressure of 30-35 mm Hg was found to be maximum with respect to tolerance; if the animal is able to breathe under such a pressure it is only for a very short time. The principal symptom indicating inability to withstand this intrapulmonary pressure, a steady

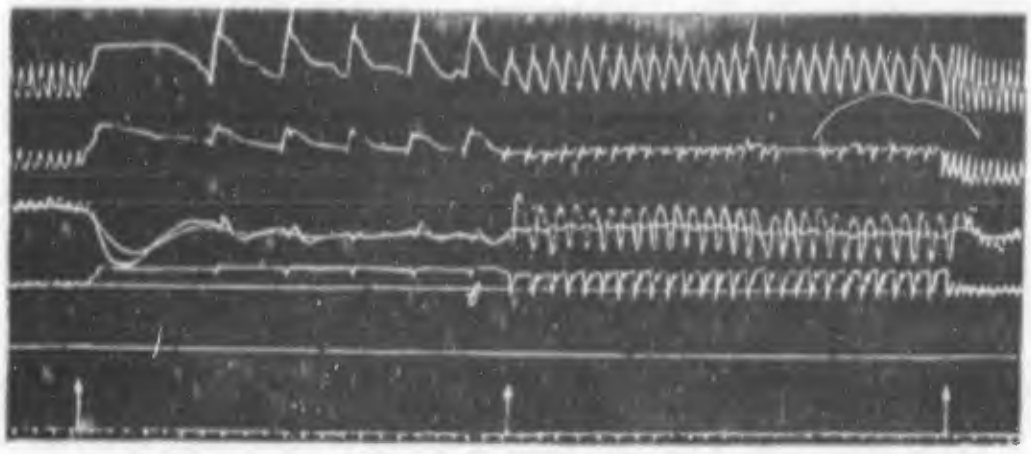

Fig. 11. Transition from respiration under inhalation and exhalation pressure (left-hand portion of kymogram) to breathing against exhalation resistance (right-hand portion of kymogram). Experiment No. 7. Dog's weight – 10.25 kg. Chloralose anesthesia. From top to bottom the curves represent thoracic respiration, abdominal respiration, blood pressure in the right femoral artery (ordinary manometer), the same (Sechenov manometer), pressure in the intervalve space and its null line, arterial-pressure null line, and time marker (5 sec). The arrow at the left indicates application of inhalation (18 mm Hg) and exhalation (24 mm Hg) pressure, that in the center indicates elimination of inhalation pressure (the exhalation pressure remaining as before), and the arrow at the right indicates elimination of the exhalation pressure.

drop in blood pressure accompanied by respiratory disturbances and arrest, then appears. In a number of cases application of a constant pressure of this magnitude caused irreversible apnea, breathing not reappearing at all.

All other factors being equal, the maximum time for which the animals were able to breathe under a low-magnitude constant pressure was substantially shorter than that observed during breathing against exhalation resistance.

Experiments involving a low inhalation pressure and a high exhalation pressure yielded intermediate results in comparison with the two aforementioned extreme variants. The pattern of physiological changes did not as a rule have any characteristic peculiarities, approximating that observed under the action of constant or unilateral pressure, depending on the ratio of the inhalation and exhalation pressures. All

other conditions being equal, the retardation of respiration increased, the amplitude of the respiratory blood-pressure fluctuations decreased, and mean blood pressure dropped as the inhalation pressure increased. As the kymograms in Figs. 11 and 12 indicate, the latter regularity was especially marked when the animal was shifted from breathing under one form of pressure to breathing under the other.

Figure 11 shows a rapid transition from breathing under inhalation and exhalation pressure to breathing under exhalation pressure alone. Discontinuation of the inhalation pressure caused a sharp increase in the respiratory blood-pressure fluctuations, which in turn produced a marked rise in mean blood pressure; at the same time there was a slight drop in the thoracic and abdominal volumes and a relative acceleration of respiration rate.

Figure 12 shows a case in which the inhalation pressure was reduced to zero. This kymogram also indicates that the amplitude of the respiratory waves increases and the mean arterial pressure steadily rises as the inhalation pressure is reduced (see the curve representing the pressure in the intervalve space).

This regularity is also quite strikingly confirmed by numerical data representing the mean blood-pressure level as a percentage of its initial level at equal intervals after application of bilateral and unilateral pressure (Table 3).

The data in Table 3 also indicate that the mean blood pressure is incomparably higher during breathing against exhalation resistance than during respiration under inhalation and exhalation pressure, despite equal exhalation pressures in both cases.

It may thus be concluded that the extent of the changes observed in respiratory and cardiovascular functioning were greatest during breathing under constant pressure and least during breathing under ex-

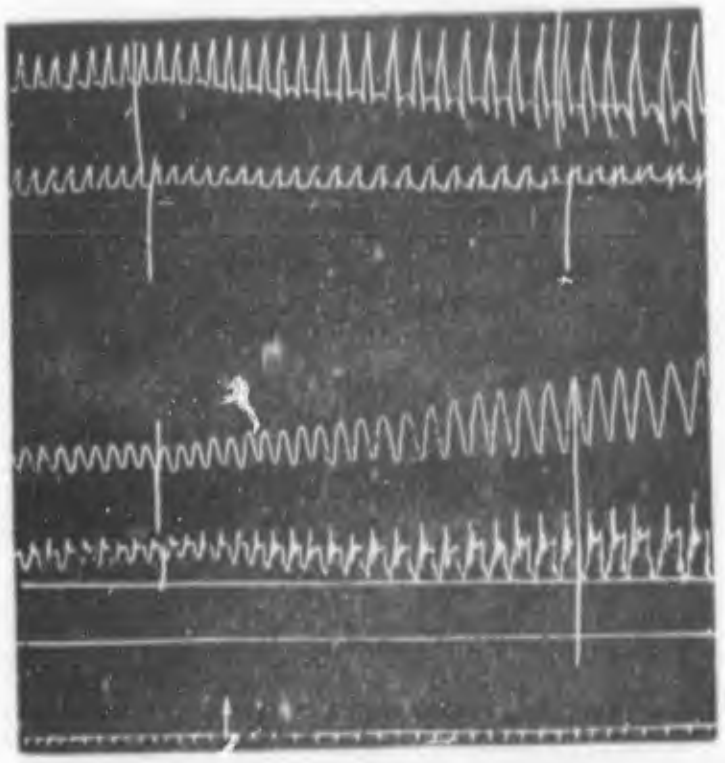

Fig. 12. Gradual transition from breathing under inhalation and exhalation pressure to breathing against exhalation resistance. Experiment No. 9a. Dog's weight – 6.5 kg. Chloralose anesthesia. From top to bottom the curves represent thoracic respiration, abdominal respiration, blood pressure in the right femoral artery, pressure in the intervalve space and its null line, blood-pressure null line, and time marker (5 sec). The arrow represents the beginning of the decrease in inhalation pressure (which was gradually reduced to zero, the exhalation resistance remaining unaltered). Lines for checking pin coincidence are superimposed on the curves.

halation pressure alone.

Before moving on to a description of experiments involving vagotomy we must consider another phenomenon observed in a number of cases of respiration under intermittent pressure. This consisted of two-phase blood-pressure waves, blood pressure rising and falling twice during each respiratory cycle. The left-hand portion of the kymogram shown in Fig. 13 can serve as an example of such changes in blood pressure. In considering this illustration we first conclude that the highest respiratory peak, i.e., the maximum rise in blood pressure, once again coincides with exhalation, most frequently with the beginning of the expiratory phase. A lower peak occurs at the end of exhalation in such

TABLE 3

Changes in Mean Arterial Pressure During Respiration Under Intermittent and Constant Pressure

№ опыта	Давление (в мм рт. ст.)		Средняя величина давления (в % к исходному)		Давление на выдохе (в мм рт. ст.)	Средняя величина давления (в % к исходному)	
	вдох	выдох	1-я минута	2-я минута		1-я минута	2-я минута
6	13	27	89	90	24	93	93
7	18	24	86	81	24	92	90
8	16	30	70	77	32	91	114
17	27	27	31	31	29	82	66
17	26	26	32	34	—	—	—
20	35	40	58	58	40	93	96
20	32	38	74	60	40	100	100
21	22	30	52	38	32	98	83
21	25	28	41	49	28	78	63

1) Experiment No.; 2) pressure (mm Hg); 3) inhalation; 4) exhalation; 5) mean pressure (% of initial level); 6) 1st minute; 7) 2nd minute; 8) exhalation pressure (mm Hg).

cases. Inhalation is accompanied by a brief drop in blood pressure. The changes in blood pressure during each respiratory cycle thus reduce to the following pattern: pressure begins to rise half-way through exhalation, decreases briefly during inhalation, undergoes a still sharper increase at the beginning of exhalation, and then decreases, reaching its minimum at the half-way point of exhalation. In considering such respiratory waves one gets the impression that they are essentially a single large wave. The rising trend of this latter wave is interrupted by the brief drop in blood pressure during inhalation. Inhalation is consequently accompanied by a drop and exhalation by an increase in blood pressure. This respiratory-wave configuration generally occurred during very slow breathing and was most frequently encountered under intermittent pressure, when the inhalation pressure was substantially less than the exhalation resistance.

Experiments involving respiration under pressure after bilateral vagotomy. In order to clarify the physiological mechanisms of the various respiratory and circulatory changes we transected the vagus nerves

in the cervical region and forced the animal to breathe under pressure. It was found that the respiratory reaction to elevated intrapulmonary pressure had a number of material differences in these cases, being directly opposed to that described earlier with respect to individual indices (Figs. 14 and 15). We did not observe apnea in a single case in which pressure was applied after vagotomy. Conversely, we usually observed a slight acceleration of respiration in vagotomized dogs when inhalation and exhalation pressure was applied and only the exhalation pressure was discontinued. This acceleration generally took place against a background of negligible dilitation of the thoracic cavity and was always accompanied by a sharp reduction in the amplitude of the respiratory movements of the chest and abdomen. As a rule, when the pressure was continued the respiration rate remained almost unchanged or decreased slightly. Discontinuation of the pressure was for the most part followed by a retardation of respiration. The initial respiratory rhythm subsequently ceased. Tables 4 and 5 confirm this regularity. In considering them we see that cases in which it was absent are the exception. It is very interesting that we observed apnea after discontinuation of the pressure in several experiments on vagotomized dogs. It may thus be assumed that the most typical changes in respiration rate in vagotomized dogs during respiration under elevated pressure are generally opposite in trend to the corresponding changes in intact animals.

Analysis of the thoracic- and abdominal-respiration curves enables us to state that in a number of the vagotomized dogs exhalation under pressure was initiated by a strong contraction of the abdominal muscles, which caused a brief, obviously passive expansion of the thoracic cavity; the subsequent changes in thoracic and abdominal volume generally bore no regular relationship to the functioning of the expiratory muscles or the muscles controlling the prelum abdominale. In any event, we

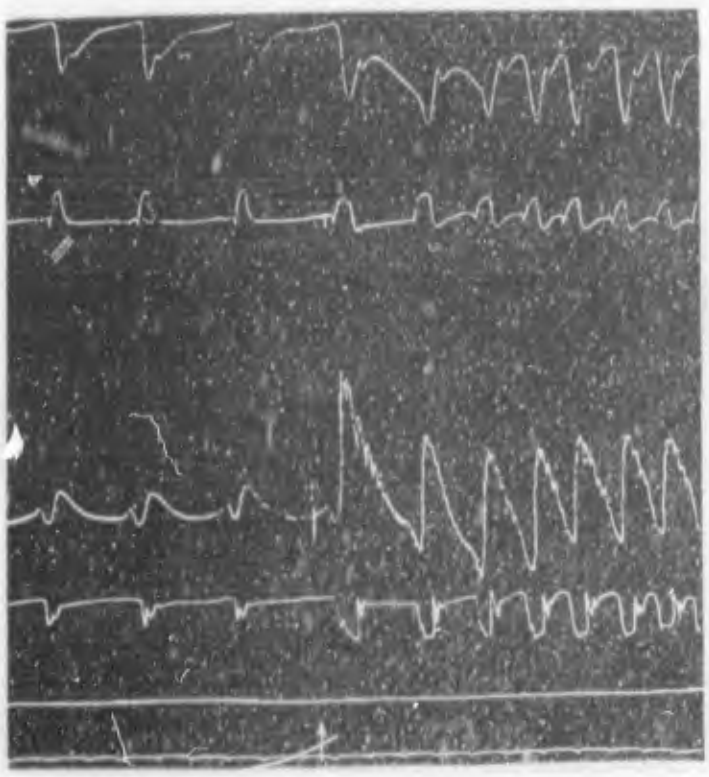

Fig. 13. Transition from breathing under inhalation and exhalation pressure (left-hand portion of kymogram) to respiration with exhalation resistance only (right-hand portion of kymogram). Experiment No. 3. Dog's weight – 10.7 kg. Chloralose anesthesia. From top to bottom the curves represent thoracic respiration, abdominal respiration, blood pressure in the right femoral artery, pressure in the intervalve space, blood-pressure null line, and time marker (5 sec). The arrow indicates the shift in breathing.

did not observe the previously described dominance of the abdominal muscles throughout the entire course of exhalation, which was most characteristic of animals with intact vagus nerves, in a single case after vagotomy. Transection of the vagus nerves ordinarily led to some nonconformity and discoordination in the functioning of the two respiratory musculature and the abdominal muscles during breathing under elevated pressure.

As for the relationship of inhalation and exhalation time, the latter was less altered during respiration under pressure after vagotomy. In a number of cases the breathing of the vagotomized animal was characterized by suppression of inspiration both before and during application of pressure, which must be specially emphasized, considering

TABLE 4

Changes in Respiration Rate on Application and Discontinuation of Exhalation Pressure in Vagotomized Animals

№ опыта 1	Частота дыхания 2		Давление (в мм рт. ст.) 5	№ опыта 1	Частота дыхания		Давление (в мм рт. ст.) 5
	исходная 3	после включения давления 4			перед выключением давления 6	после выключения давления 7	
4	7	8	23	8	12	13	20
4	4	5	23	4	10	6	24
5	7	7	14	4	7	4	28
5	12	14	17	5	14	—	14
5	8	10	15	10	4	2	24
6	7	13	20	11	12	14	30
9	5	7	20	11	15	10	30
11	9	12	30	19	15	18	10
11	14	16	30	19	14	15	20
19	21	15	10	19	12	10	18
19	16	14	20				
19	10	9	18				
19	8	10	18				
19	10	10	20				
20	14	18	20				

1) Experiment No.; 2) respiration rate; 3) initial; 4) after application of pressure; 5) pressure (mm Hg); 6) before discontinuation of pressure; 7) after discontinuation of pressure.

the extreme rapidity with which the exhalatory phase succeeds the inhalatory phase in animals with intact vagus nerves under similar conditions. The curves representing the pressure in the intervalve space indicate that during breathing under pressure inhalation was slower and more gradual in the vagotomized dogs, while, conversely, exhalation was very rapid and the pressure rose immediately to its maximum. For the most part we observed an opposite pattern in the intact dogs. From the passage of exhaled air through the water and the movement of the gasmeter indicator we found in the majority of experiments that expulsion of air from the respiratory passages occurs at the beginning of exhalation in most vagotomized animals and at the end of exhalation in intact animals.

It must be noted that in a number of cases application of bilateral pressure after vagotomy did not, strictly speaking, cause expansion

of the thoracic cavity, but only reduced the extent of its exhalatory excursions (see Fig. 14). This indicates that in the case in question each inhalation made by the vagotomized animal before the pressure was applied distended the thoracic cavity ad maximum, to its limit of elasticity, since the applied inhalation pressure was not sufficient to increase the inspiratory volume of the chest.

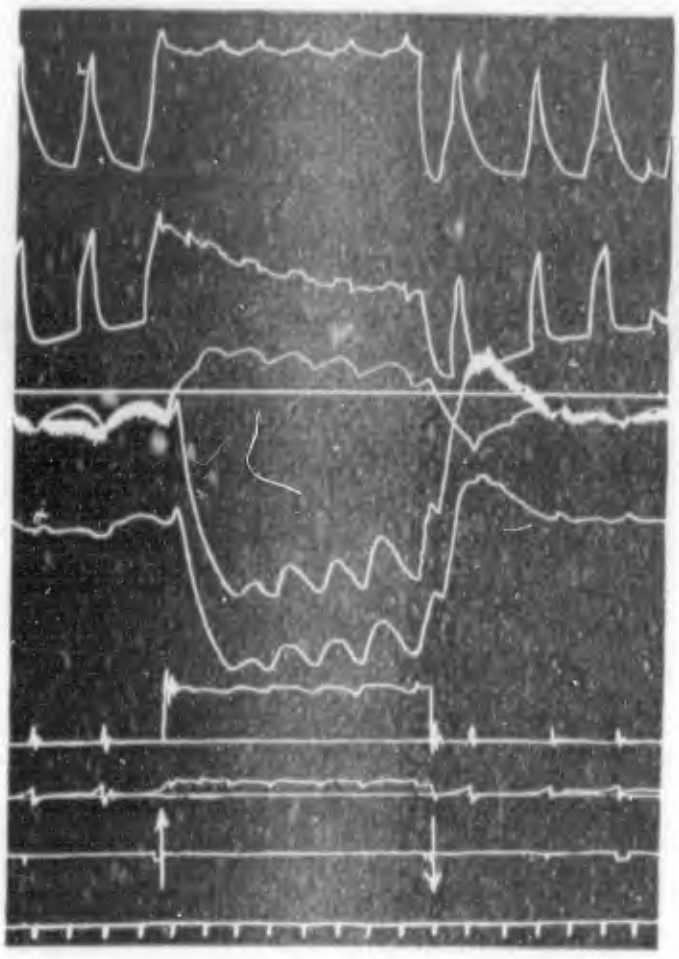

Fig. 14. Respiration under inhalation and exhalation pressure after bilateral vagotomy. Experiment No. 19. Dog's weight – 4.3 kg. Chloralose anesthesia. Vagus nerves transected. From top to bottom the curves represent thoracic respiration, abdominal respiration, initial venous pressure, venous pressure in the left jugular vein, blood pressure in the right femoral artery (membrane manometer), the same (ordinary manometer), pressure in the intervalve space and its null line, pressure in the abdominal cavity and its null line (system not hermetically sealed), pulmonary-ventilation marker (250 cm^3; the same as arterial-pressure null line), and time marker (5 sec). The arrow at the left indicates application of pressure (28 mm Hg on inhalation and 31 mm Hg on exhalation), while the arrow at the right represents discontinuation of the pressure.

In a number of vagotomized dogs abdominal volume did not increase

at all when the intrapulmonary pressure was raised; quite the contrary, it slowly and gradually decreased during respiration under pressure.

Pulmonary ventilation underwent essentially the same changes in the vagotomized animals as in the intact subjects. The reduction in pulmonary volume during breathing under pressure after vagotomy obviously resulted primarily from the decrease in respiratory-movement amplitude.

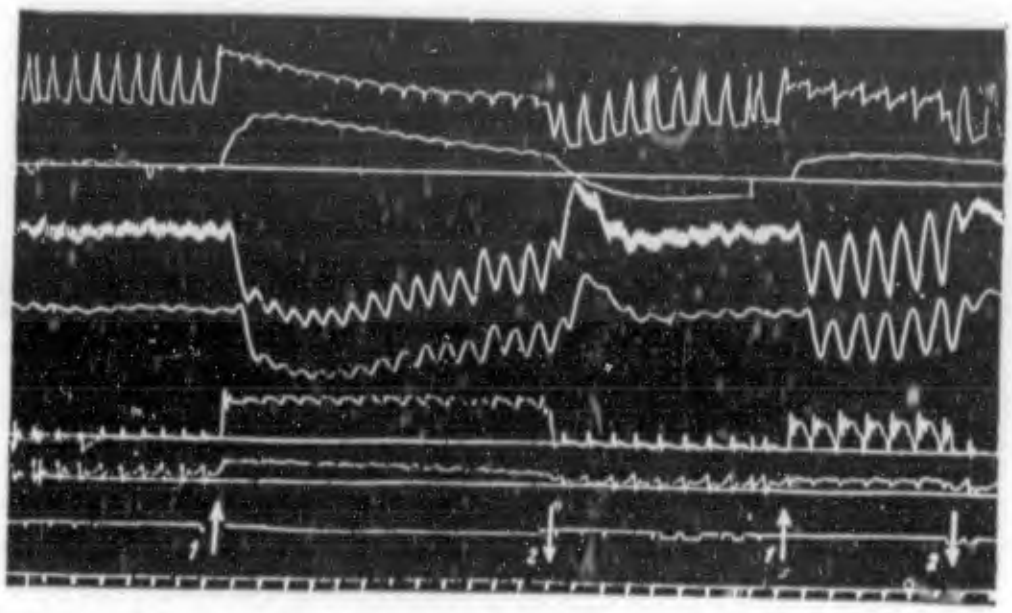

Fig. 15. Respiration under bilateral (left-hand portion of kymogram) and unilateral (right-hand portion of kymogram) pressure after vagotomy. Experiment No. 19. Dog's weight – 4.3 kg. Chloralose anesthesia. Vagus nerves transected. From the top down the curves represent thoracic respiration, venous pressure in the left jugular vein and its null line (initial), blood pressure in the right femoral artery (membrane manometer), the same (ordinary manometer) pressure in the intervalve space and its null line, pressure in the abdominal cavity and its null line (system not hermetically sealed), pulmonary-ventilation marker (250 cm^3;not recorded during respiration under pressure), the same – arterial-pressure null line, and time marker (5 sec). Arrows 1 and 2 at the left indicate bilateral pressure (28 mm Hg on inhalation and 32 mm Hg on exhalation), while arrows 1 and 2 at the right represent unilateral exhalation pressure (28 mm Hg).

Bilateral vagotomy also caused material changes in the reaction of the cardiovascular system to elevated pressure in the respiratory passages. All other conditions being equal, breathing under elevated pressure (both bilateral and unilateral) led to a more substantial decrease in mean arterial pressure in the systemic circulatory system in the va-

TABLE 5

Changes in Respiration Rate on Application and Discontinuation of Inhalation and Exhalation Pressure in Vagotomized Animals

1 № опыта	2 Частота дыхания: исходная	3 Частота дыхания: после включения давления	4 Давление (в мм рт. ст.): выдох	5 Давление (в мм рт. ст.): вдох	1 № опыта	8 Частота дыхания: перед выключением давления	2 Частота дыхания: после выключения давления	9 Давление (в мм рт. ст.): выдох	5 Давление (в мм рт. ст.): вдох
5	4	7	28	18	8	7	4	30	20
5	4	6	30	20	5	7	4	30	20
6	9	12	30	16	7	16	10	30	24
6	12	11	30	18	10	8	10	22	17
7	12	16	30	22	11	13	10	30	16
7	13	19	28	24	11	10	8	30	16
10	10	8	22	17	11	12	9	30	16
11	8	10	30	16	11	12	14	30	16
11	8	22	30	16	11	16	4	30	16
11	14	12	30	16	19	22	21	28	26
11	10	16	28	26	19	16	16	30	11
19	24	22	28	26	19	12	10	24	18
19	18	16	28	26	19	10	8	30	30
19	10	12	28	26	19	10	8	30	26
19	8	10	—	—	19	11	10	32	28
19	8	10	28	26					
19	8	10	28	26					

1) Experiment No.; 2) respiration rate; 3) initial; 4) after application of pressure; 5) pressure (mm Hg); 6) exhalation; 7) inhalation; 8) before discontinuation of pressure; 9) after discontinuation of pressure.

gotomized animals.

Application of bilateral pressure after vagotomy led to a rapid drop in blood pressure, but no subsequent rapid rise. Since apnea did not occur in the vagotomized animals, the respiratory blood-pressure waves appeared immediately and then always were more substantial than in animals with intact vagus nerves. During breathing under exhalation pressures of 30-40 mm Hg they occasionally reached 70% of the mean blood pressure; the character of the kymographic curve varied so widely as to be unrecognizable. However, not even such substantial respiratory waves could ensure maintenance of mean blood pressure at the level characteristic of intact animals, since the fluctuations in the vagotomized animals were in large measure due to a decrease in the minimum

blood pressure. It must also be pointed out that the respiratory blood-pressure fluctuations during ordinary respiration were more substantial in the vagotomized animals. The time at which these waves developed in breathing under pressure remained unaltered after vagotomy.

In all cases the beginning of the rise of the respiratory wave coincided with the beginning of exhalation, its maximum occurred midway through exhalation, and its minimum generally coincided with inhalation. Figure 16 shows an expanded record of the changes in blood pressure during one respiratory cycle. The kymogram indicates that these changes correspond to the variation in pressure in the intervalve space. This regularity was completely confirmed in the vagotomized animals: those cases in which the intrapulmonary pressure was more or less constant were characterized by respiratory waves of lower amplitude and a relatively low mean blood pressure. Conversely, cases of unilateral pressure were characterized by relatively large respiratory blood-pressure waves and a higher mean level (Fig. 15). The blood-pressure reaction to shifting to ordinary respiration remained unaltered after vagotomy. Just as when the vagus nerves were kept intact, it generally consisted in a rapid rise in blood pressure, a subsequent slight drop, and a slow rise to the initial level. The character of the changes in venous pressure in the vagotomized animals was the same as before, but they were usually of lesser extent than in the intact animals. As a rule, pulse rate was the same in the vagotomized animals during breathing under elevated pressure and no arrhythmia appeared.

We can thus state that the differences in the reaction of the cardiovascular system to elevated intrapulmonary pressure in vagotomized animals reduce to absence of arrhythmia and bradycardia, a large increase in the amplitude of the respiratory blood-pressure fluctuations, absence of any rapid rise in blood pressure after the initial drop, and

subsequent maintenance of low blood-pressure levels.

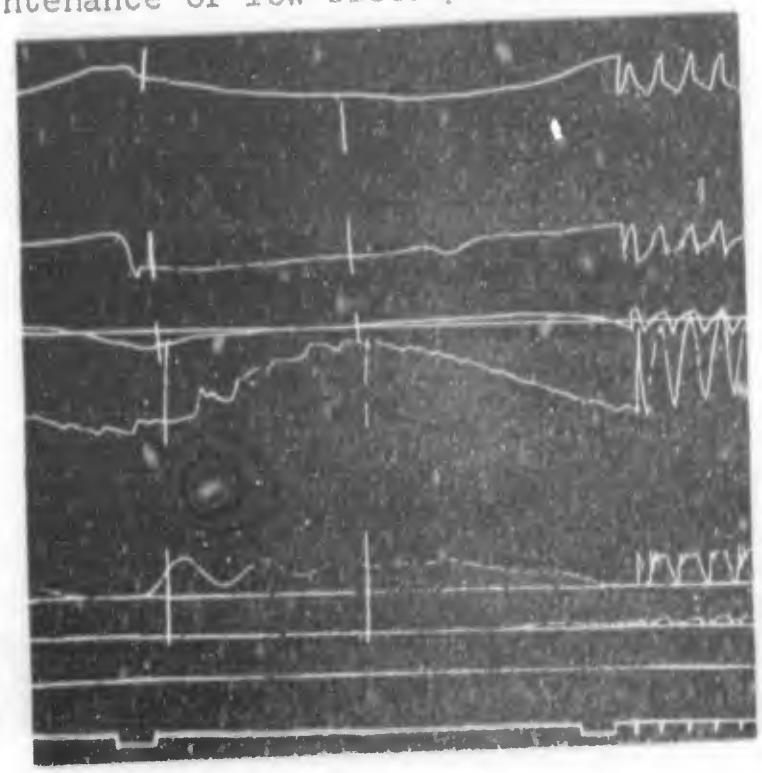

Fig. 16. Relationship between breathing and respiratory blood-pressure waves during respiration against exhalation resistance after bilateral vagotomy. Experiment No. 19. Dog's weight – 4.3 kg. Chloralose anesthesia. Vagus nerves transected. The left-hand portion of the kymogram represents rapid movement of the kymograph drum, while the right-hand portion represents slow movement. Check marks are superimposed on the curves. From top to bottom the curves represent thoracic respiration, abdominal respiration, venous pressure and its null line, blood pressure in the right femoral artery, pressure in the intervalve space and its null line, pressure in the abdominal cavity and its null line (system not hermetically sealed), arterial-pressure null line, and time marker (5 sec).

By altering the character of the body's reaction vagotomy had a material influence on the subjects' ability to withstand elevated pressure. This influence was manifested not so much in a decrease in the maximum withstandable pressure as in a decrease in the time for which the vagotomized animals were able to breathe under pressure. In other words, all other conditions being equal, the critical respiratory and circulatory disturbances produced by elevated intrapulmonary pressure required less time to develop in the vagotomized than the intact animals. In the vagotomized dogs the distinguishing characteristics of these preagonal disturbances were respiratory arrest with no prior

changes in the character or extent of the respiratory movements and a sharper drop in blood pressure with no vagal pulse.

CHRONIC EXPERIMENTS

In this series of experiments we set ourselves the task of determining the character of the physiological changes induced in intact, unanesthetized animals by respiration under elevated pressure.

In our case it was absolutely necessary to conduct acute experiments on anesthetized animals in order to make a thorough physiological analysis of the reactions observed and to determine the mechanism by which they developed.

It is quite clear that anesthesia substantially alters the body's reaction to external factors. It affects primarily the central nervous system, particularly depressing the activity of its higher branches, and so reduces the organism's functional capacities. The data in the pharmacological literature indicate that a number of anesthetics have a considerable toxic effect on the respiratory center. Vascular reflex reactions are also materially altered by different types and degrees of anesthesia, as the work of M.P. Brestkin (1928) indirectly indicates. There is no doubt that anesthesia has an unfavorable influence on the functional capacities of the heart. It is thus obvious that the functions which interest us most, i.e., respiration and circulation, were subject to unfavorable conditions during the acute experiments. It was consequently necessary to check the data obtained by experimentation on intact animals, to determine the pattern of physiological changes under the action of elevated intrapulmonary pressure in the normal organism, and then to evaluate the material yielded by the acute experiments.

METHOD

The chronic experiments were conducted on two dogs. One of them (Dzhek) served as the subject of 20 experiments, thoracic and abdominal

respiration, the pressure in the intervalve space, and pulmonary ventilation being recorded kymographically. The other dog (Reks) was the subject of one experiment, in which the blood pressure in the femoral artery was recorded in addition to the aforementioned indices, local novocaine anesthesia being employed and the roles of asepsis being observed as far as possible.

The dog's respiratory passages were connected to the elevated-pressure apparatus by a special composite mask equipped with inhalation-exhalation valves. The mask was fastened to the animal's muzzle with an elastic rubber bandage, which ensured sufficiently tight hermetic sealing. It must be emphasized that application of pressure through a mask was a methodological departure from the acute experiments, in which a tracheotomy was performed and the action of the elevated pressure did not extend to the larynx and upper respiratory passages. In all 20 experiments the dog Dzhek was placed on a table with which he had systematically been familiarized over a period of one month before experimentation began. In the experiment involving recording of blood pressure the dog Reks was immobilized on a vivisection table. All the experiments were conducted at approximately the same time, 2-3 hr after the dog's morning feeding. Elevated pressure was applied in the same variance as in the acute experiments. The pressure ranged from 5-10 to 50-60 mm Hg and its action time from 30 sec to 20-25 min.

Experimental Results

It must first be noted that the dog Dzhek, who was accustomed to standing on the table and breathing through the mask, became extremely restless and began to vomit during our first attempts to create an elevated intrapulmonary pressure, especially when inhalation and exhalation pressure was applied simultaneously. It is very interesting that no less marked anxiety symptoms occasionally appeared in the initial experiments when the pressure was relieved. These phenomena disappeared as the experiments were repeated and toward the end of the work the dog generally tolerated both application and discontinuation of the pressure without any active resistance. One thus gets the impression that

it is possible for dogs to adapt to breathing under elevated pressure.

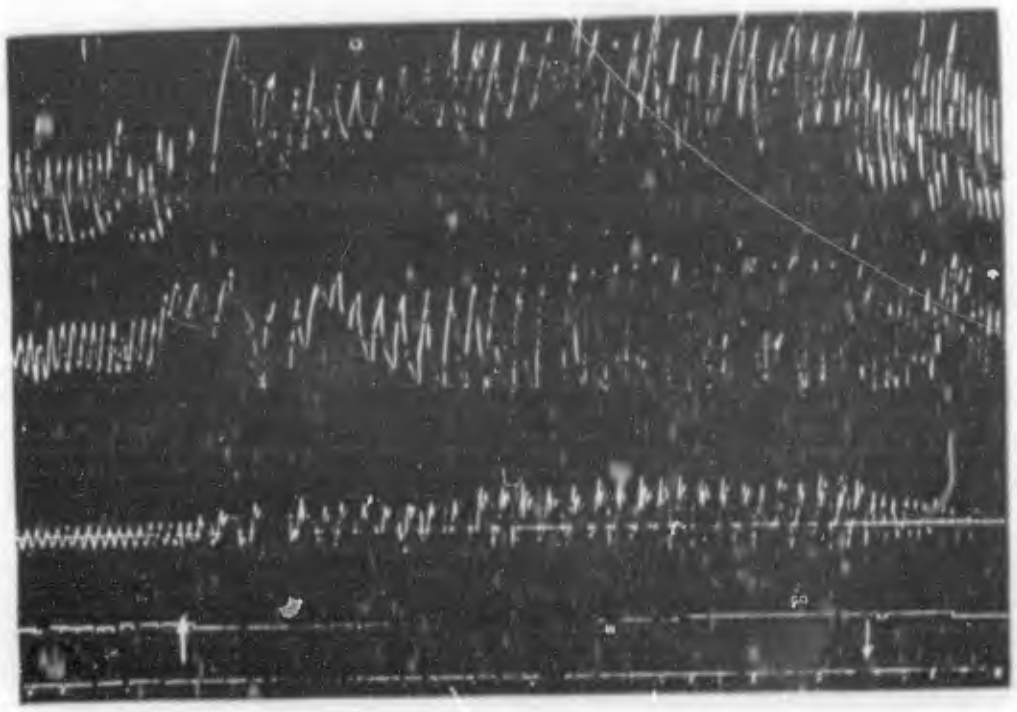

Fig. 17. Breathing against exhalation resistance. Experiment No. 6. Dog Dzhek, weighing 25.5 kg. No anesthesia. From the top down the curves represent thoracic respiration, abdominal respiration, pressure in the intervalve space and its null line, pulmonary-ventilation marker (250 cm^3; the gas meter did not operate during application of the pressure), and time marker (5 sec). The arrow at the left represents application of the pressure (18 mm Hg), while that at the right represents its discontinuation.

Moving directly to consideration of the material obtained, we must mention still another circumstance manifested to some extent in the experimental data. The gist of the matter lies in the fact that our experimental dog frequently developed dyspnea involving a respiration rate of 70-80 breaths per min during the experiments for no apparent reason. We are still not completely clear regarding the causes of this phenomenon. It is possible that the tachypnea expressed the animal's excited state and was a reaction to the somewhat unusual circumstances; we cannot exclude the possibility that the dyspnea observed was associated with the temperature conditions (the experiments were conducted in May, at a room temperature of 20-21°) and was a thermoregulatory reaction ("thermal dyspnea"). It is important to emphasize that the data obtained

in experiments in which dyspnea occurred cannot be identified with those yielded by the other experiments, in which dyspnea was absent. The latter constituted the overwhelming majority of the experiments and provided the following results.

The changes in respiration rate under the action of elevated pressure were very regular in both experimental dogs and were in complete agreement with the analogous changes in the anesthetized animals. Resistance to exhalation (Fig. 17) was accompanied by a substantial retardation of respiration (by a factor of 1.5-2 in comparison with the initial rate); the extent of this retardation was greatest at the beginning of the resistance period and least at its conclusion. A substantial but transient acceleration of respiration occurred when the resistance was discontinued. Respiration under both inhalation and exhalation pressure (Fig. 18) was distinguished by the fact that application of bilateral pressure generally caused apnea, while, all other conditions being equal, the subsequent retardation of respiration was more substantial.

The duration of the apnea depended on the inhalation pressure and ranged from several seconds (at pressures of 10-15 mm Hg) to 1.5 min (at pressures of 30-35 mm Hg).

In all cases of breathing under unilateral or bilateral pressure there was a substantial expansion of the thoracic cavity, which persisted throughout the entire experimental period. This expansion occurred rapidly and suddenly when inhalation and exhalation pressure was applied, being followed by apnea. When exhalation pressure was applied alone the thoracic cavity expanded gradually. Analysis of the kymograms corresponding to this latter case enabled us to establish an interesting regularity (Fig. 19).

Application of unilateral pressure has absolutely no effect on the

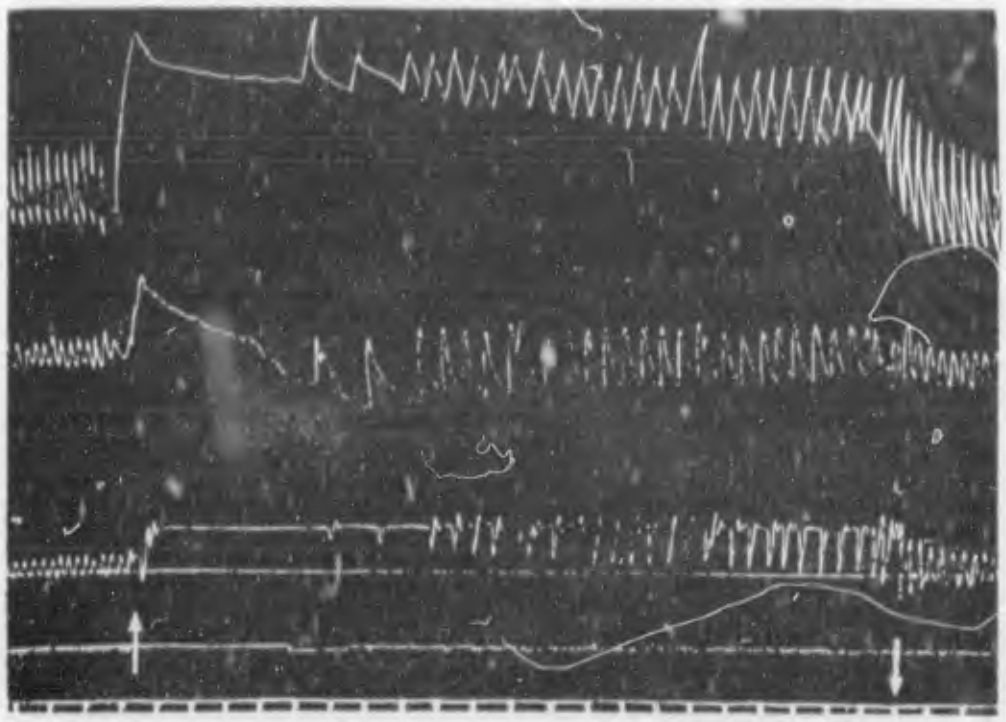

Fig. 18. Respiration under inhalation and exhalation pressure. Experiment No. 5. Dog Dzhek, weighing 25.5 kg. No anesthesia. From the top down the curves represent thoracic respiration, abdominal respiration, pressure in the intervalve space and its null line, pulmonary-ventilation marker (250 cm^3), and time marker (5 sec). The arrow at the left indicates application of pressure (16 mm Hg on inhalation and 34 mm Hg on exhalation), while the arrow at the right represent discontinuation of pressure.

inhalation occurring at the time. The first exhalation meets with a resistance which the animal cannot overcome, since the pressure set up in the lungs is not sufficient to expel the air from the respiratory passages. As a result, the exhalation is shallower and the expiratory contraction of the thoracic cavity does not reach its usual level. The next inhalation starts with the thoracic cavity somewhat dilated in comparison with its ordinary state and leads to still greater expansion. The corresponding exhalation again encounters resistance: the intrapulmonary pressure rises somewhat higher than during the first exhalation, but is still insufficient for expulsion of the air from the lungs. The extreme expiratory position of the chest now approximates the normal inspiratory position. After 3-4 inhalations, which cause the thoracic cavity to reach its greatest dilitation and thus the lungs their great-

est distension, there is a marked expiratory depression of respiration, reminiscent of brief apnea in a number of cases. Breathing then becomes slower, an intrapulmonary pressure sufficient to overcome the resistance and expel the air being set up during each exhalation. After gradually reaching its maximum expansion the thoracic cavity is somewhat reduced in volume, but remains enlarged throughout the entire period of breathing under pressure.

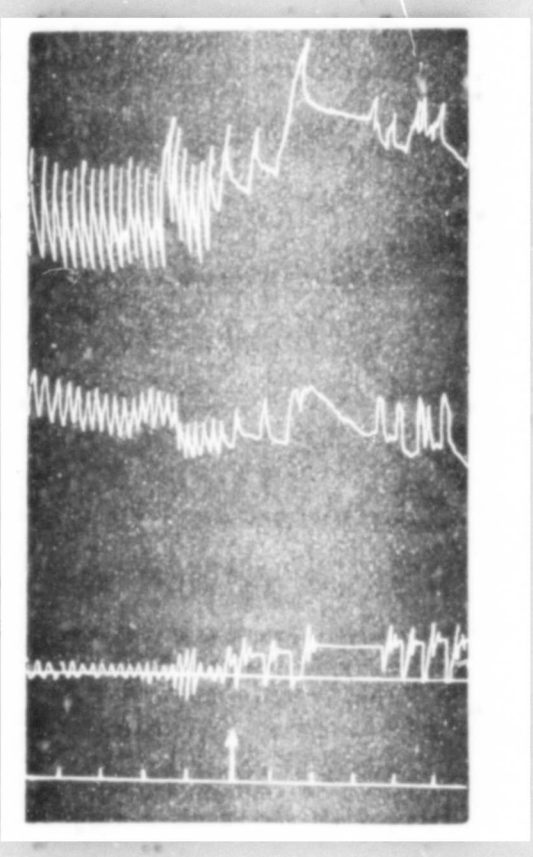

Fig. 19. Respiratory reaction to application of exhalation resistance. Experiment No. 8. Dog Dzhek, weighing 25.8 kg. No anesthesia. From the top down the curves represent thoracic respiration, abdominal pressure, pressure in the intervalve space and its null line, and time marker (5 sec). The arrow indicates application of exhalation resistance (23 mm Hg).

These changes occur in reverse order but more rapidly during the shift to ordinary respiratory conditions; the thoracic cavity regains

its initial volume.

Abdominal volume remained essentially unchanged under the action of both unilateral and bilateral pressure; the abdomen occasionally expanded immediately after the pressure was applied, but, very characteristically, underwent an immediate decrease in volume, which obviously indicates active contraction of the abdominal muscles.

The amplitude of the respiratory movements of the abdomen increased very substantially during the action of the pressure, to a greater extent than the amplitude of the respiratory movements of the thorax. Just as in the acute experiments, there was a substantial decrease in inhalation time, disappearance of respiratory pauses, and an increase in exhalation time. We thus found in these experiments as well that elevated intrapulmonary pressure is markedly predominant during respiration against exhalation resistance.

Analysis of the thoracic- and abdominal-respiration curves showed that the changes in thoracic and abdominal volume during the action of the pressure agreed in trend and were temporally coincident. The volumes of the chest and abdomen increased during inhalation and decreased during exhalation. This forces us to assume that the respiratory and abdominal muscles participate equally in exhalation when the latter encounters resistance.

The changes in pulmonary ventilation corresponded completely to those observed in the acute experiments, but pulmonary-ventilation volume dropped to a lesser extent during respiration under pressure in the intact animals, obviously as a result of the relatively less marked retardation of respiration in unanesthetized dogs under these conditions.

The threshold inhalation pressure necessary for development of apnea ranged from 5 to 10 mm Hg. The apnea disappeared at inhalation pressures of greater than 40-45 mm Hg: the dog began to thrash about on the

table and clearly could not breathe any longer. The animals were capable of withstanding somewhat greater exhalation resistance. In certain cases we observed uniform slow breathing accompanied by expulsion of air from the lungs with each exhalation for a number of minutes at resistances of 55 and even 60 mm Hg. The dogs were capable of withstanding exhalation resistances of 35-40 mm Hg for 20-25 min, remaining completely at ease.

The changes in cardiovascular activity observed in the unanesthetized dog Reks during respiration under elevated pressure differed materially in several respects from those observed in the acute experiments. One of these differences lay in the fact that there was no substantial or prolonged decrease in mean arterial pressure except the initial reversible drop under the action of various unilateral and bilateral pressures (from 10 to 30-35 mm Hg). At individual times during breathing under elevated pressure the mean arterial pressure was even somewhat greater than its initial level.

A second peculiarity of the cardiovascular reaction of the unanesthetized animals was the absence of any material changes in pulse rate during respiration under elevated pressure. The pulse rate per min generally remained unchanged, even exhibiting a slight acceleration during individual periods. The unusual arrhythmia observed in the unanesthetized dogs in the acute experiments was immeasurably weaker and was difficult to detect in a number of cases. The other changes in cardiovascular activity during breathing under pressure also displayed substantial differences from those noted in the acute experiments. This was true both of the initial blood-pressure reaction and of the typical changes in blood pressure during each respiratory cycle. In the chronic experiments (Reks) we also detected regular, substantial rises in blood pressure with each exhalation: all other factors being equal, the res-

piratory waves increased in magnitude with the difference between the inhalation and exhalation pressures.

The experiments in which dyspnea developed yielded the following results with respect to changes in respiration. If the animal began to exhibit dyspnea we waited for it to end and pressure was almost always applied against a background of normal respiration. As a result, in all such cases the reaction to application of elevated pressure was initially the same as that described above. The subsequent differences reduced to sudden development of severe dyspnea involving a respiration rate of from 65 to 85 breaths per min against the background of the slow breathing established after apnea, this conditions continuing until the pressure was discontinued. Discontinuation of the pressure against a background of dyspnea generally halted the latter; breathing was slower than initially during the first 15-20 sec, but then accelerated sharply or returned to its normal level. Application of pressure against a background of dyspnea caused apnea in some cases and a severe initial retardation of respiration in others; the reaction to discontinuation of the pressure was similar to that just described.

DISCUSSION OF RESULTS

One of the basic indices of external respiration is respiration rate, which usually undergoes diametrically opposite changes in intact and vagotomized animals under intermittent and constant elevated intrapulmonary pressure. The immediate respiratory reactions to application and discontinuation of pressure in acute experiments are also opposite in character in the cases in question. We are consequently forced to two conclusions: first, that the vagus nerves play the primary role in the formation of the reaction characteristic of the intact animal and, secondly, that when the vagus nerves are deactivated the action of certain other mechanisms, which produce opposite changes in the respira-

tion rate, is manifested. Since both mechanisms are activated by the same factor, i.e., elevated intrapulmonary pressure, we must conclude that they can both participate in the formation of the reactions in question, but that the former (i.e., that represented by the vagus nerves) is dominant in the intact animal. We are thus completely justified in attributing the apnea which develops in the intact animal under elevated intrapulmonary pressure, the subsequent retardation of respiration, and the acceleration of respiration when the pressure is discontinued to the functions of the vagus nerves, this being in complete accord with the data in the literature.

It is well known that expansion of the lungs stimulates the vagus receptors located in the pulmonary tissue: under normal conditions these are excited with each inhalation and ensure that the inhalatory phase is succeeded by the exhalatory phase. Respiration under elevated pressure is always accompanied by distension of the lungs, regardless of the character of the pressure, as is indicated by the expansion of the chest which occurs in all cases. In this case it must be taken into account that during breathing under pressure the volume of the thoracic cavity at the end of exhalation is frequently greater than its inspiratory volume during ordinary breathing, i.e., throughout the entire period of breathing under pressure the lungs are distended to an extent sufficient to ensure continuous excitation of the corresponding vagus receptors. Breathing under elevated pressure thus obviously causes the vagus nerves to have a continual inhibitory reflex influence on the respiratory center. As has already been noted, the effects associated with these receptors cause cessation of inhalation and promote exhalation. The extremely rapid replacement of the brief, pressure-facilitated inhalation by protracted exhalation is thus understandable. The occurrence of inspiratory arrest in vagotomized animals despite the ex-

treme distension of the lungs during breathing under pressure confirms the correctness of this explanation. It is quite obvious that the apnea which develops in intact animals when inhalation and exhalation pressure is applied must similarly be attributed to the rapid expansion of the lungs and the stimulation of these receptors. The rate at which the lungs expand is clearly of material importance in the development of the apnea, since this condition generally does not arise on application of exhalation resistance, when the lungs expand gradually, despite the fact that in a number of cases the extent of thoracic distension is greater than under the action of bilateral pressure, which causes apnea.

These changes in respiration become still more understandable if one agrees with the authors who also recognize a reflex stimulation produced by each inhalation after a normal exhalation (Hammounda and Stella, 1934; Hammounda and Wilson, 1935a, 1935b). We are forced to conclude that, in addition to the intensified functioning of the inhibitory fibers of the vagus nerves, the fibers which stimulate respiration and prevent prolonged exhalation completely stop functioning throughout the entire period for which the pressure acts, since even during exhalation the lungs are more distended than during inhalation under ordinary respiratory conditions. They consequently fail to reach the threshold state for development of the inhalation-stimulating reflex.

We cannot exclude the possibility that the relative acceleration of respiration during the period for which the pressure acts results from a certain adaptation of the respiratory center to the continuous inhibitory influence of the vagus nerves. It is also possible that this acceleration is caused by the decrease in pulmonary-ventilation volume during the action of the pressure and by the slight increase in the carbon dioxide content of the blood.

The changes in respiration rate in the vagotomized dogs require

special analysis. Our data on the nature of this mechanism only enable us to advance a number of suppositions.

Firstly, it may be assumed that the afferent link in this mechanism lies in the thoracic branch of the sympathetic trunk. V.A. Vinokurov demonstrated the possibility of transmission of afferent impulses from the lungs by this pathway. Secondly, we can consider it probable that the reflexes produced by stimulation of the sensory receptors of the pleura, which are subjected to pressure from the distended lungs, participate in this process. Finally, we can attribute the mechanism of the observed respiratory changes to proprioceptive reflexes from the respiratory musculature. It may be that the pressure which expands the thoracic cavity during inhalation promotes rapid and substantial extension of the inhalatory muscles (mm. intercostales externi), which, by virtue of reciprocal relationships, must lead to inhibition in the nerve centers of these muscles and to excitation in the centers of their antagonists. A pressure-facilitated and accelerated inhalation may thus stimulate the following exhalation.

In addition to the aforementioned reflex mechanisms, we must again take into account the possible humoral action of carbon dioxide on the respiratory center in analyzing the changes in respiration rate in the vagotomized dogs.

We can conclude that the character of respiration is always sharply altered under pressure, being in a certain sense inverted. While inhalation is active under normal conditions, since it is carried out by contraction of the inhalatory muscles, and exhalation is passive, since it is effected by virtue of the elastic properties of the thoracic cavity, without contraction of the exhalatory muscles, during respiration under pressure these relationships are inverted: exhalation is active, even the auxiliary muscles being involved, while inhalation is to some

extent passive or, in any case, is facilitated by the pressure in the lungs. An intrapulmonary pressure corresponding to the resistance overcome is set up toward the end of exhalation under both bilateral and unilateral pressure. When exhalation ends, i.e., as soon as the tonus of the exhalatory musculature disappears, this pressure is sufficient to act on the thoracic cavity from the lungs and facilitate its expansion. This force does not exclude active participation of the exhalatory musculature in inhalation, but makes it by no means obligatory. The character of respiration is consequently always altered. As for the physiological activity of the nerve centers associated with respiration (the respiratory center and the spinal centers of the intercostal muscles), the processes taking place in these structures, which correspond to inhalation and exhalation, are active under both normal and elevated-pressure conditions. However, it must be assumed that their character is also altered in the latter case.

In speaking of the change in the character of respiration under the conditions in question we must give this fact a negative significance and use it as a proof of the severely unfavorable action of elevated pressure on the organism. It indicates only the high functional lability of respiration, which is reorganized under the influence of certain conditions. This reorganization ensures that the reserve musculature, particularly the abdominal muscles, is used in respiration.

On the basis of our experiments involving vagotomy it must be assumed that the vagus nerves play a definite role in coordinating the activity of the abdominal muscles with that of the true respiratory musculature.

Moving on to an analysis of the changes in cardiovascular activity during breathing under elevated pressure, we must first note that the blood-pressure reaction was identical in general outline in all the

acute experiments, including those in which vagotomy was performed. Essentially, the latter influences primarily the character of the pulse, which in turn affects the two most characteristic changes in blood pressure, the drop in pressure level and the increase in respiratory fluctuations, both of them being more marked after the vagus nerves are severed. There is consequently no basis for assigning the leading role in the etiology of these reactions to the vagus nerves, as we did in analyzing the respiratory changes. Quite the contrary, it seems more correct to assume that participation of the vagus nerves in the reactions of the cardiovascular system partially obliterates the changes occurring in it.

In analyzing the development of these changes we must first consider the purely mechanical action of elevated pressure on circulation. As we have repeatedly emphasized, intraperitoneal pressure also increases during breathing under elevated pressure, the variations in its character and magnitude coinciding with those in intrapulmonary pressure in the majority of cases. The mechanical action of elevated pressure thus extends both to all the organs in the thoracic cavity and all the structures in the abdominal cavity. We are interested primarily in the effect of elevated pressure on the blood vessels. We must take into account the fact that all the vessels of the pulmonary circulatory system and some of those of the systemic circulatory system (those supplying the lungs and abdominal organs) are subject to elevated pressure. It may be assumed that external pressure most materially affects the capillary and venous networks of a given vascular system. It is obvious that the veins and the venous segments of the capillaries may even be partially compressed if the pressure from outside exceeds that within the vessels plus the resistance of their elastic walls. As a result, the venous blood will be forced toward the heart because of the valves

in the veins and the outflow of blood from the arterial system into the venous system through the constricted capillaries will be greatly reduced. The action of pressure on the arterioles, regardless of the change in their lumen size, will increase blood-flow resistance in direct proportion to its magnitude, this in turn promoting a rise in arterial pressure in the vascular system in question.

The immediate consequences of elevated pressure acting externally on a given vascular system are thus a rise in arterial and venous pressure, and obstruction of flow from the arterial to the venous system. This circumstance affects the vessels of the pulmonary and systemic circulatory systems (particularly those supplying the lungs and abdomen in the latter case) equally, although the effects of pressure on the general circulatory regime differ in individual cases. The action of pressure on the vessels of the pulmonary circulatory system initially causes a brief increase in blood flow to the left auricle from the pulmonary veins and then an obstruction of blood flow through the capillaries of the pulmonary system, a rise in blood pressure in the pulmonary arteries, and a decrease in blood flow to the left auricle. This results in a drop in arterial pressure in the vessels of the systemic circulatory system. The action of pressure on the vessels of the systemic system (those supplying the abdominal organs and pulmonary tissue) causes an obstruction of flow from the arterial to the venous system and consequently promotes an increase in arterial pressure in the system. An additional consequence is an intensification of venous flow to the right auricle and a rise in venous pressure.

The fact that exposure of the heart to pressure causes a reduction in its volume, as the works of Hill and Flack (1909) showed, must be taken into account. These authors used x-ray techniques to establish that cardiac volume decreases to 40% of its initial magnitude during

Valsalva's experiment, i.e., under sharply elevated intrapulmonary pressure. The action of pressure obviously extends to the coronary vessels, i.e., is limited to the shunting role of the coronary system and consequently promotes an increase in blood pressure in the aorta and its ramifications.

Proceeding from the hypotheses presented above, let us attempt to analyze the changes in blood pressure during each respiratory cycle under the action of exhalation resistance. In this case the direct mechanical influence of elevated pressure on all the vessels of the abdominal and thoracic cavities, of both the systemic and pulmonary circulatory systems, is eliminated.

However, it is quite evident that the arterial pressure in the systemic system is affected primarily by elimination of the resistance from the ramifications of its arterial network (the abdominal and true pulmonary vessels). The decrease in resistance and possibly the increase in capacity as well are directly related to the system in which the pressure is measured. Simultaneous discontinuation of elevated pressure on the vessels of the pulmonary system facilitates blood flow through this system and increases flow to the left auricle. However, this is reflected in the arterial pressure in the systemic system only after a certain interval, during which the blood must pass through the left auricle and be forced into the systemic system by several contractions of the left ventricle.

Predominance of outflow of blood from the arterial portion of the systemic system, through the capillaries freed from elevated pressure, over inflow of blood through the left auricle is thus obviously a direct consequence of inhalation. The drop in blood pressure noted during inhalation in all cases must be attributed to this phenomenon.

Since inhalation has been found to be very brief during breathing

under pressure the aforementioned difference between inflow and outflow cannot be eliminated during this phase, although there is undoubtedly partial relief of the venous system through the pulmonary vessels during inhalation, the left auricle consequently receiving more blood at the beginning of exhalation.

Exhalation begins against this background, i.e., the pressure begins to act simultaneously on all the aforementioned vascular systems of both the systemic and pulmonary circulatory systems. This immediately reduces the possibility of relief of the systemic system through the coronary and abdominal vessels, increases the resistance of the arterial portion of the systemic system, and consequently hampers blood flow to the periphery, while inflow of blood is increased, since the left auricle received an increased amount of blood as a result of inhalation. Inflow is probably also greater because the first result of the increase in intrapulmonary pressure during exhalation is expulsion of blood from the pulmonary veins into the left auricle.

Because of the predominance of inflow in the arterial portion of the systemic system and perhaps because of the decrease in its capacity arterial pressure is sharply increased in this system. The latter should then decrease, since the pressure begins to act on the vessels of the pulmonary system, i.e., blood flow to the left auricle is reduced. This actually occurs in a number of cases: arterial pressure begins to drop after reaching its maximum at the beginning of exhalation. The next inhalation again intensifies this pressure, but at the same time sets up all the prerequisites for a further rise in arterial pressure in the systemic system. It is evident that in those cases where intrapulmonary pressure remains elevated during inhalation instead of dropping to atmospheric level less blood passes through the pulmonary circulatory system, there is less blood in the left-hand side of the heart at the

beginning of the next exhalation, and the blood-pressure wave during this exhalation is consequently lower in amplitude. In the case of intermittent pressure each inhalation thus ensures relief of the right-hand portion of the heart: the extent of this relief and of the rise in arterial pressure during the next exhalation increased as the inhalation pressure decreases.

The action of intermittent pressure on the vessels of the pulmonary system can be compared with that of a stopcock between the right-hand and left-hand halves of the heart. It is closed to some extent during exhalation and open during inhalation.

Mean arterial pressure is thus maintained at higher levels under intermittent or unilateral pressure, because of the intensification of respiratory fluctuations.

If we visualize the vessels of the systemic and pulmonary circulatory systems as being subject to a strictly constant external pressure during inhalation and exhalation, it becomes clear that blood flow in both sets of vessels is obstructed at all times, that the respiratory fluctuations are minimal, since the requisite conditions for their generation are not satisfied, and that mean arterial pressure is substantially lower than under intermittent intrapulmonary pressure.

The blood flow in the vessels of the pulmonary system is of decisive importance under constant pressure. This is quite understandable, since the pressure acts only on some of the vascular ramifications of the systemic system, but on all the ramifications of the pulmonary system. Blood flow through the former system can consequently be effected partially along vessels not subjected to pressure, while blood flow through the lungs encounters resistance in all areas of the pulmonary vascular network. In this case relief of the venous system is always difficult and flow to the left-hand side of the heart is always re-

duced. A clear proof of this is the difference in the changes in venous pressure under constant and intermittent intrapulmonary pressure. This gives rise to still another very important hypothesis: the functioning of the right ventricle must be intensified to a far greater extent than that of the left ventricle in order to compensate for the circulatory disturbances which develop during respiration under elevated pressure. In other words, this type of respiration makes increased demands primarily on the right ventricle.

Generalizing the material presented above, we must first conclude that the mechanical component of the pressure, which acts directly on the vessels, is basic and decisive in producing the changes in the cardiovascular system. This is indicated by the fact that the changes in blood pressure are a direct function of the form and magnitude of the pressure under which breathing is carried out. However, there is no doubt that a number of mechanisms other than the decisive mechanical factor participate in producing the cardiovascular reaction to elevated pressure. Prime among these is the reflex originating in the venae cavae. The substantial increase in venous pressure during each exhalation obviously is the cause of the severe tachycardia at the beginning of each exhalation, this in turn promoting an immediate rise in arterial pressure.

In explaining the increase in blood pressure at the beginning of exhalation we must also take into account the possibility of irradiation of excitation from the respiratory center to the vasomotor center. The depressor reflex which develops as a result of the increase in arterial pressure in the pulmonary circulatory system is an additional factor preventing a rise in blood pressure in the systemic system during exhalation against resistance (Schweigk, 1935).

In addition to the aforementioned reflexes and irradiation phen-

omena, a number of circulatory-regulation mechanisms which are activated secondarily and intended to eliminate the changes which arise in the cardiovascular system must be taken into account in analyzing the fluctuations in blood pressure. The reflexes originating in the aortic arch and the sinocarotid zones and the reaction of the vasomotor center to the changes in blood pressure are thus limited to a rise in pressure during each exhalation and a drop in pressure during each inhalation.

The effect of the mechanical factor is therefore based on a number of reflex influences, which either coincide with or oppose this factor in the character of their effect. When the mechanical factor is clearly dominant the aggregate of all these elements forms the basis for the changes in arterial pressure under the action of elevated intrapulmonary pressure.

On the basis of the foregoing material we can assume that the unusual arrhythmia which appears in dogs during breathing under elevated pressure must be attributed to the pressor-depressor reflexes developing during the sharp fluctuations in arterial pressure and to the reflex originating in the venae cavae during the sharp fluctuations in venous pressure. This makes it evident that the variation in pulse rate results primarily from the changes in blood pressure and is not directly related to the succession of the respiratory phases.

Since the periods of retarded pulse are more prolonged than those of accelerated pulse the ultimate result is bradycardia. We cannot exclude the possibility that the latter is maintained reflexively by the continual distension of the lungs and the stimulation of the vagus receptors, whose influence on cardiovascular activity can obviously be exerted both through the respiratory center and independently of it.

The fact that bilateral vagotomy prevents both the bradycardia and the arrhythmia completely confirms our hypotheses, since reflexes from

the aortic arch, the venae cavae, and the lungs are effected through the vagus nerves. The increase in the amplitude of the respiratory blood-pressure fluctuations after vagotomy is also in complete accord with our explanations. This operation deactivates the overwhelming majority of regulatory mechanisms; neither the increase nor the decrease in blood pressure are faced with reactions intended to eliminate them.

In developing his concept of the regulation of circulation I.P. Pavlov emphasized the enormous importance of the physiological mechanisms of reflex cardiovascular regulation, which are associated with the functions of the vagus nerves. Breathing under elevated pressure promotes unusual great activity on the part of these mechanisms, since it causes sharp fluctuations in blood pressure as a result of mechanical factors. Transection of the vagus nerves, which, as I.P. Pavlov showed, regulate general blood pressure, causes these fluctuations to become still more substantial.

According to the data of V.A. Vinokurov (1948), vagotomy also facilitates irradiation of excitation from the respiratory center, which can promote intensification of the respiratory blood-pressure waves.

Both the basic mechanical factor and reflex mechanisms obviously participate in the reaction of the cardiovascular system to application and discontinuation of pressure. When inhalation and exhalation pressure is applied an intact animal yields a greater, but smoother drop in blood pressure and a characteristic subsequent rise. The decrease in blood pressure resulting from mechanical compression of the vessels of the pulmonary circulatory system is evidentally intensified by the reflex originating in the pulmonary rteries. However, pressor reflexes undoubtedly also participate in the reaction, being secondarily by the decrease in blood pressure and working to prevent a further drop. Finally, the reflex originating in the venae cavae as a result of the

sharp increase in venous pressures produces extremely severe tachycardia during the drop and subsequent rise in blood pressure. The latter is obviously due to a substantial extent to active contraction of the muscies which produce the prelum abdominale and to the increase in intraperitoneal pressure.

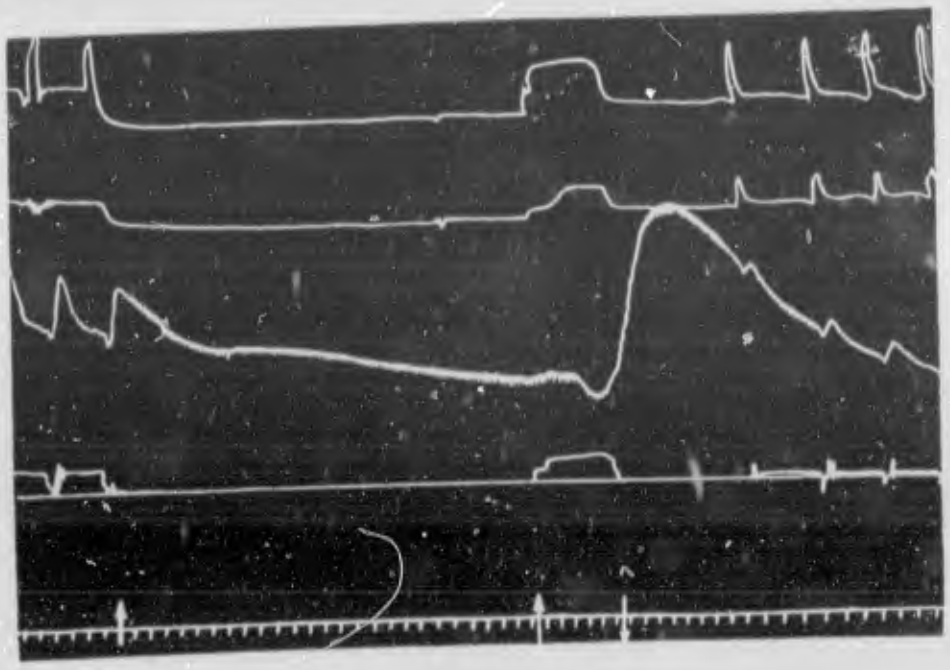

Fig. 20. Blood-pressure reaction to application of resistance. From top to bottom, the curves represent thoracic respiration, abdominal respiration, blood pressure in the intervalve space and its null line (the same as the blood-pressure null line), and time marker (5 sec). The arrow at the left represents application of exhalation pressure (25mm Hg), while the arrows in the center and at the right represent inhalation pressure (25 mm Hg), and exhalation pressure (25 mm Hg).

The increase in blood pressure during the period of apnea is obviously also due to the increase in the tonus of the respiratory and cardiovascular centers in response to the increasing carbonic acid concentration. The majority of the aforementioned reflexes are deactivated and the participation of the prelum abdominale is reduced after vagotomy; as a result, blood pressure drops more quickly and does not undergo a subsequent rapid rise. The initial swift increase in blood pressure to an above-normal level on shifting to ordinary respiratory conditions is evidently associated with some reflex mechanism not related

to the vagus nerves, since vagotomy does not prevent this phenomenon. It is possible that it is associated with the action of the thoracic segment of the sympathetic trunk, as V.A. Vinokurov believes. In any case, there is no doubt regarding its reflex nature, which is demonstrated by the kymogram shown in Fig. 20. On shifting to ordinary breathing conditions the vagotomized dog developed apnea (a frequently-observed phenomenon) and exhibited a progressive drop in arterial pressure. Elevated pressure was applied against this background for a brief time, but did not cause any substantial reaction. Discontinuation of the pressure caused an extremely sharp rise in blood pressure, which subsequently underwent a rapid decrease, despite the restoration of respiration. In V.A. Vinokurov's opinion, the second portion of the reaction to discontinuation of elevated pressure (the slow rise) results from restoration of blood flow through the lungs.

The severe bradycardia which developed in the intact animal when the pressure was discontinued must obviously be attributed to the sharp drop in venous pressure and the reflex originating in the venae cavae.

Before moving on to a discussion of the results of the chronic experiments we must consider two more problems. The first is the question of irradiation from the respiratory center during respiration under elevated pressure. We observed irradiation on very diverse scales, ranging from slight twitching of the neck muscles to severe contractions of the animal's entire musculature during each exhalation. In a number of cases there was no doubt that we were witnessing irradiation of excitation from the respiratory center to the skeletal-muscle and vasomotor centers, also during exhalation. Thus, for example, in one experiment we noted that during breathing against exhalation resistance typical high-amplitude blood-pressure waves developed during each exhalation. The resistance was then reduced and the subsequent record was

continued for 3 min. We found that uniform blood-pressure waves appeared both during each exhalation and during the corresponding inhalation. The number of waves was double the respiration rate. On making another kymogram 6-7 min after the resistance was discontinued we noted only blood-pressure waves corresponding to each inhalation. In our opinion, this proves beyond doubt that the respiratory center functioned actively during exhalation and that irradiation of excitation to the vasomotor center occurred coincidentally with exhalation during the period of breathing against resistance. When the resistance is discontinued inhalation is activated, but the respiratory center reverts gradually to its normal activity and for some time is active during both inhalation and exhalation, so that there are two blood-pressure waves per respiratory cycle. These obviously correspond to irradiation during inhalation and exhalation. Exhalation is subsequently not accompanied by excitation of the respiratory center and the blood-pressure waves develop only during inhalation. It must be noted that V.A. and B.A. Vinokurov observed essentially similar phenomena in studying the mechanisms of irradiation of excitation from the respiratory center. All these data confirm both the participation of irradiation in producing the respiratory waves and the aforementioned hypothesis regarding the reorganization of respiratory-center activity during breathing under elevated pressure.

The second problem relates to the action of elevated pressure on the upper respiratory passages. In several experiments we hermetically sealed the animal's mouth and increased the pressure in the oral and nasopharyngeal passages through the trachea, maintaining normal pressure in the lungs. We observed a substantial acceleration of respiration and, in a number of cases, fluctuations in blood pressure. This reaction generally decreased in strength and in some cases disappeared on

repeated application of elevated pressure to the upper respiratory passages. When a 20-30-minute interval was left between successive applications of pressure to the oral and nasopharyngeal cavities the reaction normally reappeared with its original strength. A similar reaction occurred when the pressure in the upper respiratory passages was increased during respiration under pressure through a tracheotomy tube. Vagotomy did not alter this pattern. It must be noted that application of pressure to the upper respiratory passages generally caused air to pass through the esophagus into the stomach, so that the latter was more or less distended at the end of the experiment.

These observations indicate that we must take into account the action of the pressure on the upper respiratory passages in analyzing the changes which develop during respiration under elevated pressure when a mask is employed.

In evaluating the data obtained in the chronic experiments we must first conclude that the changes in respiration in the unanesthetized dogs were essentially the same as the corresponding changes in the anesthetized dogs. Proceeding from this, it must be assumed that the changes are based on the same mechanisms in both cases, the distension of the lungs and the stimulation of the vagus receptors located in the pulmonary tissue being of prime importance. The constant expansion of the thoracic cavity and the subsequent expiratory arrest observed in the chronic experiments when exhalation pressure was applied are of interest from this standpoint. The expiratory arrest is obviously also a consequence of reflexes produced by the distension of the lungs and the stimulation of the vagus receptors. However, the pulmonary distension necessary for development of apnea is reached gradually in this case, while under constant pressure it is attained immediately, within an immeasurably shorter time. If we take into consideration the fact that

both the extent and rate of pulmonary distension play roles in the development of apnea it becomes clear that there is less possibility of apnea on application of unilateral pressure at a lower respiration rate (as was observed in the anesthetized dogs), because of the gradual distension of the lungs.

As has been mentioned, application of pressure against a background of dyspnea does not produce an effect comparable to that observed under ordinary conditions. From this standpoint the cases in which dyspnea occurred are not directly related to the problems with which we are concerned: hence we may conclude that a materially elevated intrapulmonary pressure is no obstacle to development of tachypnea and that application and discontinuation of pressure inhibit and temporarily eliminate any existing dyspnea.

The mechanism of the changes in cardiovascular activity in unanesthetized animals during breathing under elevated pressure are obviously basically similar to those described above. This is shown by the existence of respiratory blood-pressure fluctuations, their relationship to the variation in intrapulmonary pressure (and evidently in abdominal pressure as well) during each respiratory cycle, and their dependence on the applied pressure and the ratio of the inhalation and exhalation pressures. Nevertheless, general blood-pressure level usually remains unaltered in unanesthetized dogs, while pulse rate is not as greatly affected, occasionally increasing.

These deviations from the regularities noted in the acute experiments do not contradict what we have said above. They only prove that anesthesia materially alters the reactivity of the entire organism. Since it acts primarily on the higher branches of the central nervous system and selectively depresses cortical activity, anesthesia deactivates a number of the most precise mechanisms for regulation of respira-

tory and cardiovascular activity and reduces the functional reserves of the cardiovascular system. The absence of any drop in blood pressure and the retardation of pulse rate in unanesthetized animals must obviously be evaluated from the standpoint that the functional capacities of the cardiovascular system are completely adequate to compensate for the unfavorable influence of the elevated pressure on circulation. All other conditions being equal, a pattern of more or less marked decompensation is created under anesthesia; this is probably also a result of the depression of the higher branches of the central nervous system and the deactivation of a number of the most delicate neuroregulatory mechanisms.

In summing up the results obtained, we must conclude that, from the standpoint of changes in respiration and circulation, elevated inhalation and exhalation pressure imposes greater requirements on the cardiovascular and respiratory systems than intermittent pressure during exhalation. We must also note the extremely high resistance of dogs to elevated intrapulmonary pressure. These animals are capable of withstanding not only pressures of up to 30-35 mm Hg, but even those of up to 50 mm for prolonged periods with no critical disruptions of bodily functions. These data are interesting because such intrapulmonary pressures exceed the normal blood pressure in the capillaries of the pulmonary circulatory system. The increased blood-flow resistance is nevertheless obviously overcome by the intensification of the functioning of the right ventricle.

These facts consequently again indicate the extremely strong functional reserves of the organism, which enable it to maintain its viability under very unfavorable conditions.

CONCLUSIONS

1. The changes in respiration under elevated intrapulmonary pres-

sure, which take the form of an initial respiratory arrest, a subsequent retardation of respiration rate, and disruption of the normal relationships of the time and character of inhalation and exhalation (activation and intensification of exhalation), result principally from stimulation of the vagus receptors located in the pulmonary tissue.

2. The extent and character of the respiratory changes depend on the exhalation and inhalation pressure.

3. The principal role in exhalation during respiration under pressure is played by the muscles of the prelum abdominale. The coordination of the functioning of the abdominal muscles and the true respiratory musculature during respiration under pressure is disrupted after bilateral vagotomy in the cervical region.

4. At identical elevated intrapulmonary pressures the changes in circulation depend on the character of the pressure.

5. In contrast to intermittent pressure, constant pressure causes more substantial circulatory disturbances, as manifested in a greater decrease in arterial pressure and a larger increase in venous pressure.

6. In contrast to respiration under constant pressure, breathing against exhalation resistance creates the requisite conditions for relief of the venous system and development of unusual respiratory fluctuations in arterial pressure, this being accompanied by a substantial rise in arterial pressure with each exhalation; the mean arterial-pressure level is consequently higher, while venous pressure returns to normal after an initial rise.

7. The principal role in the development of these respiratory blood-pressure fluctuations is played by the mechanical factor – the intermittent pressure in the thoracic and abdominal cavities and the active participation of the muscles of the prelum abdominale in respiration. The action of this mechanical factor is conjoined with irradia-

tion of excitation from the respiratory center to the vasomotor center during exhalation, which intensifies the rise in blood pressure with each respiratory wave. A number of reflex mechanisms participate in producing the blood-pressure waves, acting in different directions but generally tending to limit the possibility of any extreme increase in pressure.

8. The unusual cardiac arrhythmia which arises during respiration under elevated pressure is not directly associated with the succession of respiratory phases, but is due principally to the fluctuations in arterial and venous pressure, which affect the pressoceptive reflex mechanisms.

9. All the disruptions of respiratory and circulatory functioning are less severe during breathing under exhalation pressure and more severe during breathing under both inhalation and exhalation pressure.

10. Increasing the intrapulmonary pressure to 10 mm Hg does not cause any material changes in respiration or circulation in anesthetized dogs. Pressures of from 10 to 35 mm Hg cause substantial respiratory and circulatory changes, but can be withstood for several hours. Exhalation pressures of greater than 50-55 mm Hg and combined inhalation and exhalation pressures of greater than 35 mm Hg are intolerable for anesthetized dogs.

11. Elevated intrapulmonary pressure causes smaller respiratory and circulatory disturbances in unanesthetized dogs; such animals can withstand somewhat greater pressures than anesthetized animals.

12. Bilateral vagotomy reduces the capacity of animals to withstand elevated intrapulmonary pressure.

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