SHORTENING OF REFLEX APNEA WITH EXPERIMENTALLY INDUCED HEART DEFECT

F. Z. Meerson

From the Department of Nervous System and Higher Nervous Activity Physiology (Head – V. V. Parin, Active Member of the AMS USSR), The Central Institute of Advanced Medical Training (Director – Prof. Z. P. Lebedeva), Moscow

(Received January 18, 1957. Presented by V. V. Parin, Active Member of the AMS USSR)

Earlier conducted investigations have shown that changes in the functional condition of the centers regulating cardiac activity develop during compensated experimental aortic stenosis in rabbits. These changes are essential to the maintenance of continuous, compensating cardiac hyperfunction [1] as they are expressed by an increase in the reflexes intensifying cardiac activity, which are realized through sympathetic innervation, and by a decrease to 1/4-1/5 of the original level of the vagus reflexes inhibiting cardiac activity. Taking into account the close intercommunication of the circulation and respiration functions and especially the data indicating the reflex effect on the respiration center from the cardiac and vascular interoceptors [2, 3, 4, 5, 6, 8], one can propose that changes develop in the nervous regulation of respiration as well as in cardiac activity in experimentally induced heart defect. To prove this proposition, in this work we studied the effect of experimental aortic stenosis on respiration and on the development of unconditioned reflex apnea in animals.

EXPERIMENTAL METHODS

The experiments were done on 16 male rabbits weighing 2-2.5 kg. Aortic stenosis was induced by an earlier described method [1]. The characteristic functional, morphological and biochemical changes resulted from the constriction of the aortic orifice to 1/4-1/6 of its normal size by means of a lateral ligature. Respiration was electromyographically recorded; a cuff attached to a Marey's capsule was placed on the region of the chest and abdomen. The animal was fixed in position, lying on its stomach. Reflex apnea was induced by stimulating the upper respiratory tract with ammonia fumes. This was done by blowing air from a balloon through a double-necked jar, on the bottom of which was 100 ml of 25% ammonium hydroxide, into the rabbit's nostrils through a small tube, 3 mm in diameter. The receptors of the trigeminal nerve were stimulated, and this stimulation spread through the trigeminal centers to the respiration center, causing apnea. The duration of the apnea was measured in seconds on kymograms. We first conducted comparative experiments, comparing the duration of apnea in normal rabbits with that in 5 animals of the same weight and sex in which a heart defect had been experimentally induced one month before. Then dynamic experiments were done on 5 rabbits; the duration of the apnea was determined before the heart defect was developed and one month after its development. Three rabbits were used as a control; they were given an operation similar to that which was used to induce the aortic stenosis but the ligature on the aorta was not tightened, and therefore did not constrict the lumen. The animals were observed every other day; in each experiment, the stimulant was used 4-6 times at inervals of 2-3 minutes. The duration of apnea in each animal was determined a total of 110-140 times.

In part of the experiments recording the respiration during reflex apnea, the changes in oxygen saturation of arterial blood were observed by means of a Krebs oxyhemometer, with the photoelement placed on the rabbit's ear. The readings of the apparatus were recorded every 5 seconds for 3 minutes before the use of the ammonia fumes and for 5 minutes after their use. Oxyhemometry, when used without direct determination of blood hemoglobin saturation with oxygen according to Van Slyke, is known to be inadequate to establish the true oxygen

content in the blood. However, it does give a good idea of how this index fluctuates, counting off from a representative original level. We used 96% as the original oxygen content of the hemoglobin in these experiments. During reflex apnea, this index decreased to 92-88%, and then gradually returned to normal.

EXPERIMENTAL RESULTS

There was considerable variation among the different animals as to how long the apnea lasted, but apnea duration was more constant in the same animal, varying by 2-3 seconds from experiment to experiment. The Table gives the average apnea duration in 5 normal animals and in 5 rabbits with a heart defect, computed on a basis of 100 determinations per animal.

Duration of Reflex Apnea

Rabbit with heart defect		Normal rabbits	
No. of animal	Apnea (in sec.)	No. of animal	Apnea (in sec.)
1	9	11	16.5
2	7.5	12	15.5
3	12.5	13	21
4	7.5	14	18
5	10.5	15	16.5

The Table shows that the reflex apnea lasted from 15½ to 21 seconds in the normal animals and from 7½ to 12½ seconds in the animals with the compensated defect. Therefore, apnea duration in the animals with the defect was approximately half as long as in the normal animals.

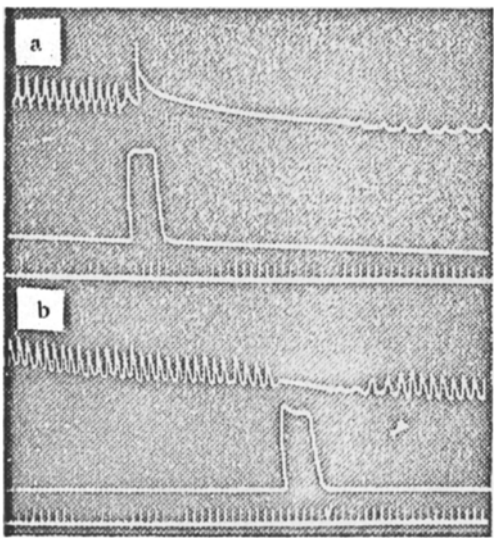

Fig. 1. Reflex apnea in rabbit No. 6 before creation of heart defect (a) and 1½ months after creation of heart defect (b). Curves from top to bottom show: respiration, indicated of stimulation, indication of time (in 1 second marks).

A month after the defect had been developed in all of the animals, dynamic experiments also showed a considerable shortening of the reflex apnea. The pneumograms of rabbit No. 6 made before the creation of the defect (Fig. 1, a) and 1½ months afterwards (Fig. 1, b) show that apnea duration in this animal was almost three times as short in the second pneumogram. In evaluating the fact of reflex apnea shortening, one should remember that the surplus of CO_2, which appears during the apnea, acts reflexively through the chemoreceptors and directly on the nerve cells to cause rhythmic activity in the given center; the apnea is shortened, and normal respiration is restored. In a given animal, the faster the concentration of carbon dioxide reaches the threshold level and the greater the excitability of the respiration center, the shorter reflex apnea will be, other conditions being equal. Therefore, the fact that the reflex apnea observed in the rabbits with the experimental heart defect was 2-3 times shorter must be due to either increased excitability of the respiration center, or the fact that the minute volume of the blood is decreased in aortic stenosis, while the CO_2 content of the blood increases faster than normally. However, the latter explanation contradicts the known fact that, in the animals with heart defect, the shortened apnea was attended by slighter and shorter decline in the O_2 content (Fig. 2). Moreover, even short apnea will probably cause the O_2 content of the blood to decrease sharply when the minute volume is decreased and the arteriovenous difference of O_2 saturation correspondingly increased. According to the experimental data of C. Wiggers [9], there is no

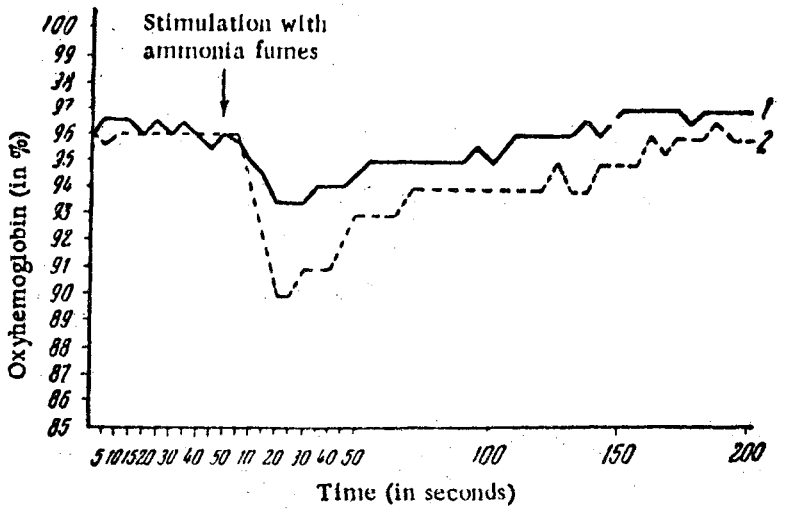

Fig. 2. Decrease of oxyhemoglobin content in blood during reflex apnea in rabbit with experimentally induced heart defect (1) and in the same animal before the creation of the defect (2).

decrease in the minute volume even when the aorta, where it leaves the heart, is 60-70% smaller in diameter, i.e., when the cross-section of the aorta is 8-9 times smaller than normally. Goldberg, Bacst and Bally [7], conducting a clinical physiological study on 26 patients with clear aortic stenosis, showed that the minute volume, the stroke volume and the arteriovenous difference in the oxygen saturation of the blood remain normal even when the degree of stenosis is considerable. These data allow the proposition that constricting the aortic cross-section by 4-6 times, as we did in our animals, i.e., by less than in Wigger's experiments, did not cause the minute volume to decrease either. Consequently, the shortening of the reflex apnea is due to the increased excitability of the respiration center.

SUMMARY

A shortening of the reflex apnea is observed in rabbits with compensated experimentally induced aortic stenosis in stimulation of the upper respiratory tract by ammonia.

Evidence obtained from oxyhemometric investigation gives base for conclusion that this phenomenon is the result of increased excitability of the respiratory center.

LITERATURE CITED

[1] F. Z. Meerson, Arkh. Patol., 1954, No. 4, pp. 30-43.

[2] V. V. Parin, The Role of the Pulmonary Vessels in the Reflex Regulation of Circulation,* 1946.

[3] V. N. Chernigovsky, Fiziol. Zhur. SSSR, 1940, Vol. 29, No. 1, 2, 3, 6.

[4] V. N. Chernigovsky, Byull. Ekspt. Biol. i Med., 1943, Vol. 1, 2.

[5] O. M. Aviado and K. F. Shmidt, Physiol. reviews, 1955, Vol. 35, No. 2.

[6] G. S. Dawes and Feldberg, Brit. J. Pharmacol., 1953, 5, 323.

[7] H. Goldberg, A. A. Bacst and C. P. Bally, Am. Heart J. 1954, 47, 527-559.

[8] A. Larish and Zotterman, Acta physiol. Scandinav., 1948, 16-31.

[9] C. Wiggers, Bureps Circle. J. Amer. Heart Ass., 1952, 5, 321-346.

* In Russian.