

THE EFFECT OF DISTURBANCE OF EXTERNAL RESPIRATION ON RENAL FUNCTION

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(Received May 6, 1957. Presented by V.N. Chernigovskii, Active Member Acad. Med. Sci. USSR)

An important aspect of the problem of the pathology of external respiration is the connection between dyspnea arising in the upper part of the respiratory tract and disturbance of the function of various organs and systems of the body.

The explanation of actual forms of disturbance of the activity of the body in cases of embarrassment of external respiration is very important from both the theoretical and practical points of view. The latter is concerned with the necessity of ascertaining the character and mechanism of the disturbances of certain functions of the body in cases of stenosis of the trachea and larynx resulting from various acute and chronic diseases. However, in pathological physiology the study of the effect of difficulty in the passage of air through the trachea and larynx on various functions of the body is mainly concerned with embarrassment of external respiration of such a degree that it is accompanied by the manifestations of asphyxia; of all the various functions of the body the only ones which have been subjected to any detailed study are respiration and the circulation of the blood. Nevertheless, it is a fact that other functions may be disturbed during embarrassment of respiration, and the character and degree of these disturbances must be determined by the intensity and duration of the dyspnea on the one hand and by the characteristic features of the reaction of the respective organs and tissues to the dyspnea on the other.

It must be thought that the appearance of a disturbance in the activity of various organs and systems of the body during embarrassment of external respiration (stenoses of the trachea and larynx) must be determined in the first place by the anoxia which arises in certain forms of stenosis. In addition, it must be borne in mind that difficulty in the passage of air through the trachea or larynx is accompanied by disturbance of the character of the air circulation in various parts of the upper respiratory tract - the nasal cavities, the accessory sinuses and the larynx, i.e., where disturbance of the air circulation is usually connected with stimulation of nerve receptors and reflex changes in the most widely differing regions of the body as a result [2, 3, 4, 9, 13].

On the question of in what cases do what mutual relationships between these factors determine the development of disturbance in the activity of a particular organ or system, we have evidence from actual examples of the development of stenosis and of some peculiarity of regulation of a certain organ or system of the body. Investigations carried out in this direction in the laboratory of pathological physiology of the State Research Institute for the Ear, Nose and Throat have revealed a number of relationships governing the effect of acute and chronic stenosis of the trachea and larynx on the function of the circulatory and digestive systems and have shown the importance of anoxia and of disturbance of the pattern of respiration in the upper respiratory tract [12, 14].

We set ourselves the task of studying the character and mechanism of the effect of various forms of disturbance of respiration in chronic tracheal and laryngeal stenosis on the excretion of urine by the kidneys.

That this is a reasonable problem for investigation is suggested by the fact that the excretory function of

the kidneys is affected on the one hand by lack of oxygen in the inspired air [1, 7, 8, 15], and on the other hand by disturbance of the character of the air circulation in the upper respiratory tract [5, 6, 9, 11].

EXPERIMENTAL METHOD

Experiments were performed on dogs with exteriorization of the ureters separately under the skin by the I.P. Pavlov-L.A. Orbell method. The present paper deals with experiments on nine dogs.

The excretion of urine by the kidneys was investigated in these animals while on a high intake of water and milk. The renal function was assessed by the volume of urine collected every 5 or 20 minutes (depending on the experimental conditions) for a period of four hours. Separate determinations were made of the glomerular filtration and the tubular reabsorption from the creatinine clearance. For this purpose the endogenous creatinine of the blood and the urinary creatinine of the animals were determined before the production of stenosis in the trachea, during stenosis and at various times after its removal. Calculation of the glomerular filtration and of the tubular reabsorption was made by Rehberg's formula. In all the experiments the content of protein and blood in the urine was determined.

The obstruction to the passage of air through the trachea and larynx was created in the experiments of long duration by introducing a tracheotomy tube into the trachea through a preliminary tracheotomy. Closure of the tracheotomy tube allowed the degree of obstruction to respiration to be regulated. Thus, in these experiments nose breathing was impossible. In experiments in which nose breathing was preserved stenosis was produced by tightening up a special clamp made of stainless steel previously applied to the exposed trachea. With the aid of this clamp it was possible to produce any desired degree of stenosis of the trachea as quickly and for as long as necessary.

Stenosis of the larynx was produced by injection of liquid paraffin under the mucous membrane, thereby diminishing the lumen of the larynx. In all the experiments a kymographic tracing of the respiration was made by means of a cuff applied to the thorax. The respiration was recorded before the application of the stenosing device, during stenosis and after its removal. The chronic experiment required the reapplication of stenosis to the same animal, and so we systematically checked the renal function as revealed by the above-mentioned indices in these animals during normal respiration before the reapplication of the stenosing device.

EXPERIMENTAL RESULTS

The study of the effect of transient stenosis of the trachea on the excretion of urine by the kidneys showed that the character of the changes in renal function depend on the severity of stenosis. We subdivided the stenosis according to its duration into four groups. The first group included stenosis lasting from one to ten minutes, the second from ten minutes to one hour, the third from one to five hours and the fourth from one to three days. According to its severity the stenosis was classified in three categories - severe, moderately severe and slight. The severity of stenosis was determined by the character of the tracing of respiration on the drum of the kymograph and by the clinical picture of stenosis which was sufficiently characteristic of each category.

The experiments showed that in stenosis lasting up to ten minutes and belonging to the severe category, the disturbance of excretion of urine by the kidneys was characterized by a severe fall in diuresis, and in some cases by its complete cessation, which took place either at the same time as or a few minutes after the onset of stenosis. In these cases a compensatory increase in excretion of urine appeared with complete regularity, starting a short time after removal of the stenosis; thus, the total urinary excretion throughout the whole period of the experiment with stenosis of this duration and severity did not differ substantially from the urinary output under normal conditions (Figure 1). With this severity and duration of stenosis, profound disturbances of urinary excretion appeared in some animals in the form of the appearance of protein in the urine, and in some cases of blood. If the stenosis of this duration belonged not to the severe but to the moderately severe category, the changes in renal function as a rule were rather less marked, but the fall in diuresis was always clearly marked, while the compensatory increase in diuresis arising a short time after removal of the stenosis was less pronounced but constant (Figure 2).

In cases of stenosis of the same duration but of slight severity (dyspnea appeared in the animals only on physical exertion), usually no essential changes appeared in the renal function.

In experiments set up to study the effect of renal function in which stenosis lasted from ten minutes to one

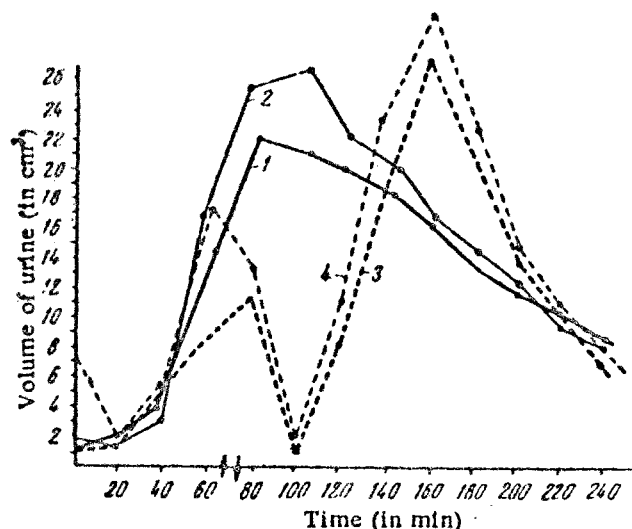


Fig. 1. Diuresis in the dog Mamasha in normal conditions and during severe acute stenosis of the trachea lasting five minutes (high water intake): 1) normal diuresis of the left kidney; 2) normal diuresis of the right kidney; 3) diuresis of the left kidney during the stenosis experiment; 4) diuresis of the right kidney during the stenosis experiment; ↑ - beginning of stenosis; ↓ - end of stenosis.

hour, we found that in its general features the change in the excretory function of the kidneys was the same as in the case of the stenosis of shorter duration - up to ten minutes.

The results of the effect of stenosis lasting several hours on the urinary excretion are particularly interesting. Whereas stenosis lasting for several minutes or tens of minutes (in the two previous groups) was produced during a period of increased excretion of urine following the high fluid intake or else was brought to an end immediately after the diuresis began to fall, stenosis lasting more than one hour occupied a much greater proportion and in some cases the whole of the time of the experiment, i.e., covered the time both of the rise and fall

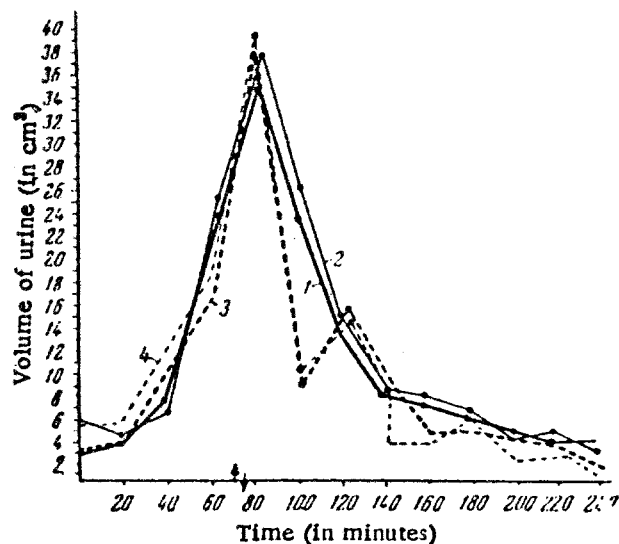


Fig. 2. Diuresis in the dog Chernushka in normal conditions and during stenosis of the trachea of moderate severity lasting five minutes (high water intake). Conventional signs as in Figure 1.

In the output of urine. Under these conditions it was found (and this is most important) that, in spite of the fact that stenosis applied before the intake of water continued for the whole period of the experiment (four hours or more), the diuresis followed the same curve as in cases where stenosis lasting a few minutes ended at the moment of maximum increase of excretion of urine following intake of water: at first there was a sharp fall in diuresis and immediately afterwards a compensatory rise, although the obstruction to respiration (severe stenosis) still continued. Figure 3 shows the curves of urinary output from which it is clear that although stenosis was applied be-

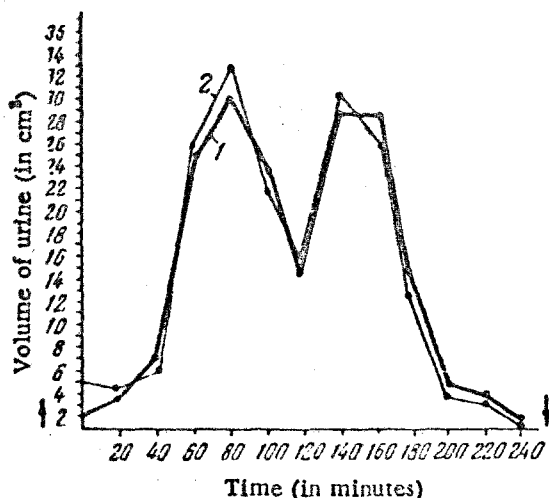


Fig. 3. Diuresis in the dog Mamasha during stenosis of the trachea produced before a high intake of water and lasting throughout the whole experiment. Conventional signs as in Figure 1.

fore the water intake, both kidneys reacted to this water intake normally by an increase in diuresis reaching a maximum at the beginning of the second hour, after which the diuresis diminished considerably, as was observed in stenosis lasting a few minutes. Later the diuresis rose, giving a compensatory reaction similar to that observed in the previous series of experiments after removal of the stenosis. In this case, this compensatory reaction of the kidneys appeared during continuing severe stenosis of the trachea. A similar picture was observed in experiments in which the stenosis produced was of the same duration but of moderate severity.

As in the series of experiments in which the stenosis was of short duration, in the more prolonged stenosis the fall in diuresis and its subsequent compensation were less pronounced in moderately severe stenosis than in severe, but they were always clearly present. When stenosis lasting one hour did not start before the water intake but after it, its effect on diuresis was conditioned by yet another factor: if the onset of stenosis preceded maximum diuresis or coincided with it the diuresis usually underwent further modification in the form of suppression and subsequent compensatory increase, so that the total output of urine remained within normal limits during the experiment; if this type of stenosis began after the diuresis had reached its maximum and had started to fall, no clearly marked suppression of urine excretion nor subsequent compensatory reaction ensued.

It is natural that absence of this type of diuretic reaction should be observed not only in case of slight or moderate stenosis but also in severe stenosis.

It is thus quite clear that the character of the reaction of the excretory function of the kidney to transient stenosis depends on the period of renal activity during which the stenosis arises: if it develops during the period of maximum renal activity during the period of greatest elimination of water taken into the body, then it is accompanied by clear and regular changes in the urine-excreting function of the kidneys in the form of suppression of diuresis and subsequent compensatory increase. These changes are not observed however, in cases where stenosis of this sort arises during diminished renal activity in the period after the maximum excretion by the kidneys of water taken into the body.

What explanation of this fact can be given? The finding that in general the kidneys react only to tran-

slent, severe stenosis or to moderately severe stenosis and do not react to slight degrees of stenosis suggests that kidney function is adequately resistant to embarrassment of external respiration, or in any case is more resistant than the secretory and motor function of the stomach and especially the function of the heart, as can be seen by comparing our findings with those of A.I. Iunina and I.B. Kholmatorov from our laboratory. The resistance of the kidneys to obstruction of the passage of air through the trachea is related, obviously directly, to the resistance of the kidney tissues to oxygen lack.

Leaving for a while the relative importance of anoxia and disturbance of the pattern of respiration in the upper respiratory tract in the mechanism of development of renal functional disturbances during obstruction of the passage of air through the trachea (which is the subject of special study) we can nevertheless consider that the manifestations of anoxia in the kidney tissue must develop particularly acutely in cases where stenosis coincides with the time of maximum renal function, i.e., with maximum diuresis, for at this time the oxygen demand of the kidney tissue increases fourfold.

It can be understood from these facts why stenosis arising before the intake of water is not reflected at all in the first phase of excretion of urine before maximum diuresis, and on the other hand produces characteristic changes in diuresis always after a definite interval of time — immediately after diuresis has reached its maximum. It must be supposed that before the kidneys develop their maximum activity, i.e., before maximum diuresis, the kidney tissue can cope with the oxygen lack; but as soon as the work of the kidneys reaches a maximum (maximum diuresis) and the oxygen demand is several times greater, the compensatory ability of the kidney tissue is exhausted and reactions appear, in the form of rapid and marked (depending on the severity of the stenosis) falling-off in diuresis.

In their turn the falling diuresis and the lowered intensity of work of the kidneys entail a reduced oxygen demand of the kidney tissue; this makes possible the appearance of renewed compensatory powers in the kidney, in the form of increase of diuresis. This ability of the kidneys to compensate for disturbance of the diuretic function immediately after its marked diminution may also account for another of our findings — the leveling-off of the diuretic function of the kidneys when the stenosis is not removed for a period of four hours, i.e., throughout the whole experiment. Thus, besides revealing the importance of disturbance of external respiration to the diuretic function of the kidneys, our findings give also some idea of the nature of the compensatory reactions of the kidneys when the intake of oxygen by the body is disturbed.

SUMMARY

Experiments were performed on dogs with ureters lead out under the skin by the I.P. Pavlov-L.A. Orbelli method. The renal urinary excretion was studied under conditions of disturbance of external respiration in tracheal and laryngeal stenoses of variable duration (lasting from several minutes to a few hours). Reaction of the kidney to stenosis depends on the length and severity of the latter, as well as on the functional state of the kidneys when the experiment was started. The peculiarities of the renal compensatory reaction to the disturbance of external respiration were demonstrated. These characteristic features depended on the degree of the functional strain of the kidneys and thus on the oxygen requirement of the renal tissue.

LITERATURE CITED

- [1] P. Al'bitskii, The Effect of Oxygen Lack on the Nitrogen Metabolism of the Body. Dissertation* (St. Petersburg, 1884).
- [2] V.A. Bukov, *Biull. Eksptl. Biol. i Med.* 6, 543-545 (1941).
- [2a] V.A. Bukov, *Arkh. Patol.* 1, 18-31 (1952).
- [3] V.A. Bukov and K.A. Drenova, *Arkh. Patol.* 2, 18-25 (1951).
- [4] K.R. Viktorov, *Collected Transactions of the 6th All-Union Congress of Otorhinolaryngologists** (Leningrad, 1937), pp. 38-64.
- [5] V.I. Kharacharovskii, *Treatment of Wounds and Diseases of the Ear, Nose and Throat** (Kazan, 1946), pp. 27-29.

*In Russian.

- [6] R.A. Karpova, Transactions of the Research Institute of the Physiology of the Upper Respiratory Tract* (Stalingrad, 1934), Vol. 1, pp. 11-12.
- [7] E. Kartashevskii, The Effect of Oxygen Lack on Metabolism and Heat Production in Animals. Dissertation* (St. Petersburg, 1906).
- [8] A.G. Kuznetsov, Functions of the Body and Changes in the Gaseous Environment* (Moscow, 1955), pp. 173-199.
- [9] E.N. Pavlovskii, Transactions of the Tatar Research Institute of Theoretical and Clinical Medicine* (Kazan', 1937), 4, pp. 135-258.
- [10] E.N. Pavlovskii, Transactions of the 4th All-Union Congress of Physiologists, Biochemists and Pharmacologists* (Moscow, 1947), pp. 508-510.
- [11] M. Fursov, Transactions of the Iu.I. Bazanova Clinical Hospital for the Ear, Nose and Throat (of Moscow University)* 1903, pp. 340-351.
- [12] I.B. Kholmatoev, Transactions of the Research Institute of the Ear, Nose and Throat* (Moscow, 1956), No. 7, pp. 110-122.
- [13] M.F. Tsytovich, Diseases of the Ear, Nose and Throat* (Saratov, 1927).
- [14] A.I. Iunina, Transactions of the State Research Institute for the Ear, Nose and Throat* (Moscow, 1956), No. 7, pp. 123-135.
- [15] F. Detering, Arch. f. ges. Physiol. 214, 744-756 (1926).

*In Russian.