PHASES OF THE NITROGEN WASHOUT CURVE UNDER DIFFERENT GAS MIXING CONDITIONS IN THE LUNGS

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Disturbance of the conditions of gas mixing in the lungs is the main cause of hypoxemia in various stress situations under normal and pathological conditions. In order to detect the early forms of inequality of gas mixing in the lungs, a test has recently been introduced which is based on recording the nitrogen concentration and the volume of expired air after deep inhalation of oxygen [1, 2, 6-8]. Most attention has been paid to the final phase of expiration, with an appreciable rise in the nitrogen concentration. However, not only the last phase of the nitrogen washout curve (NWC) is interesting, but also all its other phases.

The object of this investigation was to compare the particular features of all phases of the NWC during deep expiration in normal persons and under various conditions of gas mixing in the lungs.

EXPERIMENTAL METHOD

The NWC was recorded by means of an "azotograph" (from the Medfizpribor Special Design and Engineering Bureau) and the "gasograph" attachment to it [3]. The gasograph was used to record curves with the nitrogen concentration plotted along the ordinate and the volume of expired air (V) along the abscissa. During inspiration the gasograph tape is stationary; during expiration it moved through a distance proportional to the expired volume.

The experimental procedure was as follows: The sitting subject breathes through a mouthpiece and value unit. After two or three preliminary slow deep inhalations of room air and expirations up to the point of involuntory rejection, the subject was connected to the system by turning a spigot, after which he inhaled pure oxygen deeply from the moist oxygen supply unit, then breathed out to the limit into the gasograph. The test inspirations and expirations were as deep, slow, and quiet as possible; the rate of expiration must not exceed

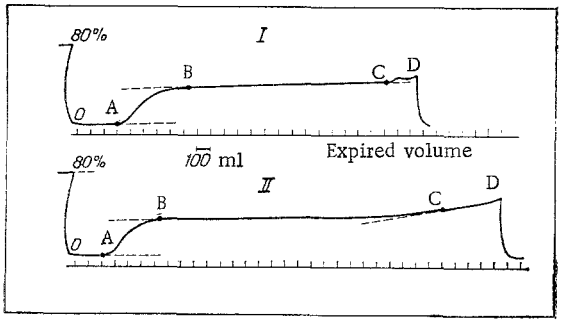

Fig. 1. NWC for healthy subjects. I) Subject K., aged 35 years; II) subject Sh., aged 65 years. Vertical axis—nitrogen concentration (in %); horizontal axis, volume of expired gas (in ml). Points indicated on curves: A) end of phase I; B) end of phase II; C) end of phase III; D) end of phase IV. Broken lines (zero and tangent) drawn to locate these points.

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TABLE 1. Volume of Phases of NWC and Nitrogen Gradients

Groups of subjects	Statistical Index	Relative volume of phases, in % of VC					ΔV_2/100 ml phase III	ΔV_2/100 ml phase IV
		I – DSP	II – MP	III – AP	IV – LCV	LCV		
Healthy	*M*	8,5 (14,2—4,3)	12,9 (19,2—9,8)	66,8 (78,7—59,4)	11,8 (21,5—5,8)	11,8	6,85 (10—6)	5,57 (13—3)
	n	7	7	7	7	7	7	7
Patients with heart diseases	*M*	7,9 (25,2—2,2)	11,4 (30,2—5,1)	73,6 (88,3—44,6)	7,1 (26,1—0)	21,2	10,90 (26—7)	2,0 —
	n	15	15	15	15	5	15	5
Patients with lung diseases	*M*	8,2 (17,6—2,4)	9,5 (20,1—3,7)	72,4 (93,2—27,3)	9,9 (42,4—0)	16,6	14,53 (39—6)	6,73 —
	n	32	32	32	32	19	32	19

Legend. Limits of variations shown in parentheses. ΔV_2/100 ml) Nitrogen concentration gradient, in %, per 100 ml expired air in phases III and IV

TABLE 2. Phases of NWC (in % of VC)

Phase	Healthy			Patients		
	A	B	Difference B – A	A	B	Difference B – A
I – DSP	7,6	5,0	—2,6	9,9	5,1	—4,8
II – MP	16,8	17,5	+0,7	14,9	17,5	+2,6
III – AP	60,0	64,5	+4,5	67,1	68,8	+1,7
IV – LCV	15,6	13,0	—2,6	8,1	8,6	+0,5

Legend. A) Without breath holding in inspiration, B) after breath holding for 10 sec at inspiration

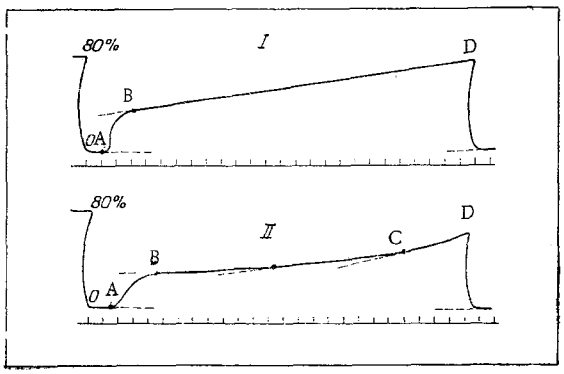

Fig. 2. NWC during disturbances of gas mixing in the lungs. I) Patient Kh., aged 45 years; II) patient P., aged 42 years. Remainder of legend as in Fig. 1.

0.5 liter/sec [8]. After a short rest the investigation was repeated. As a special test, 12 subjects had to hold their breath for 10 sec at the height of inspiration.

The total number of subjects was 54: seven healthy persons (three men and four women) aged from 20 to 65 years and 47 persons with various disturbances of the conditions of gas mixing in the lungs.

EXPERIMENTAL RESULTS

The NWC was divided into four principal phases: I) the dead space phase (DSP); II) the mixed phase (MP), when nitrogen comes partly from the terminal part of the dead space and partly from the alveoli; III) the alveolar phase (AP), i.e., a slow rise of the nitrogen concentration or plateau; IV) the phase of the final, steeper rise in the oxygen concentration. The beginning of this phase in healthy subjects occurs at the time when the intrathoracic

pressure is higher than the pressure in the small bronchioles, so that some of the lung zones, especially the lower zones, are closed [2]. The volume of expired air from the beginning of closure until the limit of the total capacity of the lungs, i.e., the volume of phase IV, has been called the lung closing volume (LCV).

Certain difficulties arise when each of these phases is distinguished on the smooth curve. The phase volumes calculated from the NWC by two investigators differed by 3-8%; the greatest differences applied to phases II and IV. For a more definite calculation of the volume of each of the phases, it is suggested that straight lines be drawn: a zero line and the tangent to the alveolar plateau, as shown in Figs. 1 and 2. By the use of this method the differences in the dead-off values were considerably reduced.

The mean volumes of DSP and LCV obtained for healthy subjects agreed with those given in the literature. For instance, when the vital capacity (VC) of the lungs was 3000 ml, the volume of DSP was 250 ml, of MP and AP together 2390 ml, and of LCV 360 ml. The increase in nitrogen concentration in AP in healthy subjects averaged 6.8%; in phase IV it rose stepwise or with a slope of more than 45° (Fig. 1). The relative values of the phases of NWC are given in Tables 1 and 2 as percentages of VC, taken as 100%. The scatter of the values of the separate phases from maximum to minimum in the healthy subjects can be explained by differences in their age. In elderly persons the LCV fraction is known to increase. The fact that in three subjects over 50 years of age LCV accounted for more than 15% of VC, whereas in young subjects it was much less, is therefore consistent with this rule. The highest value was obtained in subject Sh., aged 65 years (Fig. 1). The increase in the LCV fraction took place chiefly on account of a decrease in the volume of AP.

A group of patients with acquired heart defects, in whom the compliance of the lung tissue was sharply reduced because of stasis in the pulmonary circulation, and a group of patients with lung diseases, who had local disturbances of ventilation because of an inflammatory focus (bronchiectases, abscesses, etc.), were investigated as models changing the conditions of gas mixing in the lungs. An experiment with breath holding for 10 sec at the height of inspiration, increasing the time for gas mixing in the lungs through diffusion, served as the third model.

In patients with cardiac defects the volumes of the phases of NWC (represented by mean values) did not apparently differ very greatly from normal (Table 1). However, the scatter between maximum and minimum in all phases was considerably wider than in healthy subjects. In cases when VC was sharply reduced, DSP was relatively increased and AP reduced. In most cases the plateau in AP was well-marked; the increase in the nitrogen concentration under these circumstances was actually smaller than in the healthy subjects (a few patients were exceptions). Special attention was paid to phase IV: It was discovered in only five of 15 patients with heart defects, but was twice the normal value (700 ml, or 21.2% of VC). The increase in the nitrogen concentration in phase IV in these five patients was below normal (only 2%). In the presence of a diffuse decrease in the compliance of the lung tissue due to stasis in the lungs, gas mixing was thus uniform.

Considerable changes in the shape of NWC during deep expiration were observed in patients with lung diseases. The basic changes were connected with the character of the increase in the nitrogen concentration in phases III and IV. Two types of NWC could be distinguished: 1) a continuous and large increase in the nitrogen concentration from the beginning to the end of AP (Fig. 2); in this case phase IV as a rule was absent and LCV could not be determined; 2) AP had two or three areas with different rates of rise of the nitrogen concentration; a phase IV could be conventionally distinguished at the end of such a curve. In 13 of 32 patients of this group phase IV was absent and in the other 19 it was much larger than normal, amounting on average to 16.6% of VC.

With a large increase in the nitrogen concentration in AP, it can tentatively be suggested, there was thus a wide scatter of the regional ratios of $\Delta V/V$: from high to very low levels of ventilation. With a steady rise in the nitrogen concentration in phase III there was probably a continuous change in $\Delta V/V$, whereas in the case of an NWC with several angles of slope of phase III the distribution of $\Delta V/V$ was more complex (bi- or trimodal). The absence of phase IV or its indistinctness in half of the patients with lung diseases indicates that against the background of regional disturbances of gas mixing in the lungs the closing of a small zone because of the gravitational distribution of intrathoracic pressure may remain unnoticed. The possibility likewise cannot be ruled out that the pneumosclerotic changes found in such patients may prevent closure of the terminal bronchioles even when the intrathoracic pressure is considerably increased at the end of expiration.

Data on the effect of an increase in the time for gas mixing by diffusion on the ratio between the phases of NWC are given in Table 2. The recorded volume of DSP decreased quite regularly, as was shown previously [4, 5]. The decrease in the volume of DSP took place on account of an increase in the volumes of MP and AP of expiration. As regards phase IV, in healthy subjects of the older age group, with a small LCV, this volume was reduced somewhat after breath holding, whereas in eight patients taken at random it showed hardly any change.

To conclude, it must be pointed out that recording NWC between coordinates of volumes gives a clear picture of the process of gas mixing in the lungs during deep inhalation of oxygen. The volumes of DSP, AP, and LCV can be expressed quantitatively as percentages of VC. The gradient of the rise in the nitrogen concentration per unit volume in AP points to differences in the regional levels of ventilation of the lungs. The higher this gradient, the wider the range of possible ventilation of the lungs—from very high to sharply reduced, as occurs mainly in patients with lung diseases. The mechanism of closure of the lung zones, which is connected with gravitational aspects of ventilation, was clearly revealed in healthy subjects, much less so and less frequently in patients with heart diseases, and particularly badly in patients with lung diseases. In the last group disturbances of gas mixing were connected with regional changes in ventilation due to disease. An increase in the time of gas mixing by diffusion during breath holding at inspiration leads to a decrease in the volume of the dead space and to the entry of gas into the alveolar volume. In the presence of regional inequality, however, this does not improve the gas exchange in the worst ventilated zones.

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MECHANISM OF RHYTHMIC RESPIRATION DURING HYPOCAPNIA

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KEY WORDS: hyperventilation; hypocapnia; sensitivity of the respiratory center to CO_2; strychnine.

At the beginning of this century Haldane [5] established the stimulating action of CO_2 on the respiratory center. This was based on the fact that hyperventilation in anesthetized animals causes apnea. However, in later years attention was drawn to phenomena which, in the light of Haldane's discovery, seemed paradoxical. Not only hypercapnia, but also hypocapnia stimulates the respiratory center. In man, for instance, after voluntary hyperventilation hyperpnea often arises. In waking animals after passive hyperventilation, hypocapnic polypnea arises [3].

It was found comparatively recently that active hyperventilation in anesthetized animals due to crushing of the gastrocnemius muscle or stimulation of the nerve to the carotid sinus, by contrast with passive hyperventilation, likewise does not cause apnea. This led to the view that active respiration itself, as a result of reverberation of excitation in the network of respiratory neurons, can maintain rhythmic respiration [4].

The present investigation showed that passive hyperventilation also does not necessarily give rise to apnea in anesthetized animals if the excitability of the respiratory center is raised beforehand. Experiments were carried out on ten cats anesthetized with pentobarbital (30 mg/kg). The electromyogram of the diaphragm was recorded. In full agreement with published data artificial hyperventilation (60 breaths/min, volume 40 ml)

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