THE EFFECT OF BREATHING OXYGEN-ENRICHED AIR DURING EXERCISE UPON PULMONARY VENTILATION AND UPON THE LACTIC ACID CONTENT OF BLOOD AND URINE

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The marked increase of pulmonary ventilation during exercise is caused primarily by the more rapid formation of carbon dioxide, which causes an increased tension of this gas in the blood and alveolar air. Douglas and Haldane (1) showed that if the exercise were not too strenuous the increase in pulmonary ventilation and the increase in alveolar carbon dioxide tension bore approximately the same relation to each other as when the ventilation was increased by the addition of carbon dioxide to the respired air. Thus, according to Haldane (2) the hyperpnea of mild or moderate exercise can be attributed solely to the increased tension of carbon dioxide. When the exercise is more strenuous, the pulmonary ventilation increases out of proportion to the increase of alveolar carbon dioxide tension. Under these circumstances some factor, or factors, additional to the carbon dioxide tension contributes to produce the hyperpnea. One of these contributory factors is the excessive formation of lactic acid in the exercising muscles. Its accumulation produces a lactic acid acidosis; and during strenuous exercise lactic acid salts escape into the blood and urine. A second cause of excessive hyperpnea during moderate and strenuous exercise is oxygen want, for Briggs (3) showed that oxygen inhalations lessen the hyperpnea, at least in individuals who are not in excellent physical condition. Since removal of the lactic acid formed during exercise is an oxidative process, the inhalation of oxygen during exercise might influence the pulmonary ventilation through lessening the accumulation of lactic acid in the muscles and in the body at large. In the following

investigation the subjects performed measured exercises and the effect of breathing oxygen-enriched air upon the lactic acid content of blood and urine was studied.

Method. Exercise was performed on a treadmill, the steps of which were 7 inches high. This treadmill was driven by an electric motor acting through a worm gear. The rate was such that approximately 85 to 90 steps were ascended per minute. This rate varied slightly from day to day. Also the rate became slightly more rapid as the exercise proceeded. In each experiment the number of steps ascended was counted each minute so that the effect of slight variations in rate could be estimated. While the rate of climbing the treadmill remained approximately constant, the amount of work performed was varied either by altering the duration of the exercise or by having the subject carry a load of 30 or 45 pounds.

During the exercise the subject breathed through a rubber mouthpiece, with the nose closed by a clip. Flutter valves directed the expired air to a series of Douglas bags. Minute collections were made, and the minute volumes later determined by passing the air from the bags through a gas meter. The intake tube was connected either with outside air or with a tank containing either pure oxygen or a mixture of outside air and oxygen (approximately 40 per cent oxygen).

Urine was collected for a period of one-half to one hour before the exercise, and for a period of approximately one hour after the exercise. Blood was drawn from the arm vein immediately before the exercise and again at about four minutes after the exercise. The concentration of lactic acid and related bodies in each specimen of blood and urine was determined by the method of Clausen (4) using permanganate oxidation as recommended by Long (5). In the case of the blood, comparisons were made between the concentrations before and after the exercise. In the case of the urine, the rate of lactic acid excretion before the exercise was determined, and the subsequent excess above the resting rate was attributed to the exercise. Blood specimens were drawn into a syringe moistened with a saturated solution of potassium fluoride. In drawing the blood the veins were temporarily obstructed, for we were unable to confirm the observation of Mendel, Engel and Goldscheider (6) that venous stasis materially alters the concentration of lactic acid in the blood drawn.

The experiments on A. W. H. and J. K. L. were performed in the morning after the usual breakfast; those on M. S. L. before breakfast. No attempt was made to alter the usual daily activity of the subjects either before or after the exercise. J. K. L. is 27 years old, weight 64.8 to 65.9 kilos without coat and vest, height 183 cm. and vital capacity 4,500 cc. A. W. H. is 50 years old, weight 70.8 to 72.3 kilos without coat and vest, height 168 cm. and vital capacity 3,400 cc. M. S. L. is 24 years old, weight 63 kilos, height 168 cm. and vital capacity 4,500 cc. All the subjects were accustomed to take a moderate amount of exercise, but none was in training.

EFFECT OF OXYGEN ON LACTIC ACID

Preliminary experiments with A. W. H. showed that in order to produce an unmistakable rise in the urinary output of lactic acid considerable exercise was necessary. Climbing the treadmill for five minutes without load or climbing for one minute with a load of 45 pounds caused no definite alteration in the lactic acid of the urine. On the other hand when thirty pounds were carried up the treadmill for five minutes at an average of 80 or more steps per minute, or when 45 pounds were carried for three minutes, there was uniformly a considerable increase in the concentration in the blood and in the urinary output of lactic acid. For this reason we first adopted the exercise of carrying 30 pounds up the treadmill for five minutes as that with which to test the effect of breathing oxygen-enriched air upon the lactic acid in the blood and urine.

The inhalation of oxygen-enriched air during this fairly strenuous exercise produced subjective sensations of less effort, less shortness of breath and less fatigue. Objectively, as Briggs (3) has shown, the volume of air breathed was less (table 1).

The increases of lactic acid in the blood and urine produced by this exercise are shown in table 1. Of the three subjects J. K. L. showed a much greater rise of lactic acid in the urine. This was probably due to his being unaccustomed to this particular exercise, for the experiment of March 18, 1925, was the first that he had performed on the treadmill, whereas A. W. H. had climbed the steps on many previous occasions. Table 1 shows how J. K. L.'s output of lactic acid in the urine decreased as he repeated the exercise. By regular exercise he subsequently reduced his lactic acid output to a low level (12). The inhalation of oxygen-enriched air during this exercise produced a definite increase in the blood level and in the urinary elimination of lactic acid.

We have stated that in preliminary experiments no definite increase in the urinary output of lactic acid could be demonstrated after walking up the treadmill for five minutes without a load. Nevertheless a slight though definite increase occurred in the blood lactic acid after this exercise (table 2). This increase was lessened by inhalation of oxygen, as were also the minute volumes of the respiration.

TABLE 1

Effect of moderately strenuous exercise (carrying 30 pounds on treadmill for 5 minutes) on pulmonary ventilation and upon the lactic acid content of the blood and urine

Subject	Date	Breathed	Work done	Pulmonary ventilation: Minute of exercise: Second	Third	Fourth	Fifth	Lactic acid: Urinary excess	Blood: Before	After	Increase
	1925		*kgm.*	*liters*	*liters*	*liters*	*liters*	*mgm.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*
A. W. H.	March 13	Air	6,257				75.6	47			
A. W. H.	March 16	Air	6,439	53.1	70.9	75.9	80.5	141			
A. W. H.	April 1	Air	6,438	51.6	65.9	77.0		51			
A. W. H.	April 7	Air	6,362	52.0	67.5	71.6	79.3	54			
Average		Air	6,374	52.2	68.1	74.8	78.4	73			
A. W. H.	March 17	O_2	6,469	51.1	60.5	60.2		43			
A. W. H.	March 23	O_2	6,265	47.9	61.7	66.8	69.6	33			
A. W. H.	March 31	O_2	6,293	49.2	60.5	65.4		5			
A. W. H.	April 6	O_2	6,386	45.2	59.9		69.4	15			
Average		O_2	6,353	48.3	60.6	64.1	69.5	24			
J. K. L.	March 18	Air	5,802	54.6	66.6	68.9	71.3	458			
J. K. L.	March 19	Air	5,570	49.4	58.8	63.4	68.3	329			
J. K. L.	April 2	Air	5,949	53.4	63.8	67.4		309			
J. K. L.	April 10	Air	5,827	46.9	55.1	65.9	65.5	199			
Average		Air	5,787	51.1	61.1	66.4	68.4	324			
J. K. L.	March 20	O_2	5,823	42.1	47.7	48.7	64.1	282			
J. K. L.	March 24	O_2	5,775	40.6	50.7	50.4	56.2	208			
J. K. L.	April 3	O_2	6,006		60.2	61.4		157			
J. K. L.	April 8	O_2	5,831	43.1	49.8	55.4	56.0	145			
Average		O_2	5,859	41.9	52.1	53.9	58.8	198			
	1926			First, second and third minutes							
M. S. L.	April 9	Air	6,040	221.6		82.8	83.5	11	16	66	50
M. S. L.	April 12	Air	5,966	208.7		84.9	87.5	7	20	105	85
M. S. L.	April 14	Air	6,136	218.0		91.0	91.5	20	9	63	54
M. S. L.	April 21	Air	6,253	209.4		85.0		76	7	70	63
Average		Air	6,099	214.4		85.9	87.5	28			63

TABLE 1—*Continued*

Subject	Date	Breathed	Work done	Pulmonary ventilation: Minute of exercise: First, Second and third minutes	Pulmonary ventilation: Minute of exercise: Fourth	Pulmonary ventilation: Minute of exercise: Fifth	Lactic acid: Urinary excess	Lactic acid: Blood: Before	Lactic acid: Blood: After	Lactic acid: Blood: Increase
	1926		*kgm.*	*liters*	*liters*	*liters*	*mgm.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*
M. S. L.	April 13	O_2	6,229		72.5	84.6	4	10	47	37
M. S. L.	April 16	O_2	6,277		82.6	86.6	37	6	48	42
M. S. L.	April 20	O_2	6,158		74.5	81.0	16	13	60	47
M. S. L.	April 23	O_2	6,058		69.0	76.4	12	7	53	46
Average.		O_2	6,180		74.6	82.1	17			43
				First and second minutes	Third minute					
*M. S. L.	April 26	Air	4,282	147.8	87.0		166	7	88	81
M. S. L.	April 28	Air	4,210	135.5	99.1		200	6	78	72
Average		Air	4,246	141.6	93.0		183			76
M. S. L.	April 27	O_2	4,226		83.4		47	7	59	52
M. S. L.	April 30	O_2	4,143	118.7	72.6		88	10	59	49
Average		O_2	4,184	118.7	78.0		67			50

* Carried 45 pounds for 3 minutes.

TABLE 2

Effect of moderate exercise (walking on treadmill for 5 minutes) on pulmonary ventilation and upon the lactic acid content of the blood and urine

Subject	Date	Breathed	Work done	Pulmonary ventilation: Minute of exercise: Second	Pulmonary ventilation: Minute of exercise: Third	Pulmonary ventilation: Minute of exercise: Fourth	Pulmonary ventilation: Minute of exercise: Fifth	Lactic acid: Urinary excess	Lactic acid: Blood: Before	Lactic acid: Blood: After	Lactic acid: Blood: Increase
	1925		*kgm.*	*liters*	*liters*	*liters*	*liters*	*mgm.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*
A. W. H.	June 23	Air	5,459	47.1	60.0	60.4	65.6	0	19	46	27
A. W. H.	June 25	Air	5,436	47.5	60.0	62.5	69.5	4	14	48	34
A. W. H.	June 27	Air	5,414	49.0	59.0	63.9	69.0	4	19	46	27
Average		Air	5,436	47.9	59.7	62.3	68.0	3			29
A. W. H.	June 18	O_2	5,412	43.0	45.6	51.7	56.8	1	21	30	9
A. W. H.	June 24	O_2	5,716	37.3	52.1	57.0	60.8	1	16	35	19
A. W. H.	June 26	O_2	5,405	40.6	48.4	56.5	60.6	2	20	28	8
Average		O_2	5,511	40.3	48.7	55.1	59.4	1			12

RENAL THRESHOLD FOR LACTIC ACID EXCRETION

These observations indicate that exercise may increase the blood lactic acid as determined by the Clausen method without appreciably influencing the urinary output. Inspection of our lactic acid determinations in table 2 indicates that if the lactic acid in blood specimens taken from three to five minutes after exercise was less than 30 mgm. per 100 cc. no excess appeared in the urine, whereas if the lactic acid in the blood exceeded 40 mgm. urinary excesses appeared. Apparently then an excess of lactic acid in the urine cannot be demonstrated after exercise unless the level in the blood, by the method that we used, has been considerably increased over the normal level. The urinary output began to increase when the blood figures lay between 30 and 40 mgm. of lactic acid per 100 cc. of blood. We do not wish to insist upon the absolute value of these figures because the Clausen method probably determines substances other than lactic acid both in the blood and urine. But the evidence indicates that the concentration of lactic acid or related compounds in the blood may be definitely raised as a result of exercise without a demonstrable change in their excretion in the urine. It appears, therefore, that blood studies are better suited than urinary studies to show lesser changes in the lactic acid metabolism after exercise.

EFFECT ON PULMONARY VENTILATION

The inhalation of oxygen-enriched air during the exercise that we have employed lessened the subjective sense of dyspnea during and immediately after the exercise. Objectively the minute volumes of respiration were reduced and the concentrations of carbon dioxide in the expired air were increased. These changes were observed both in the experiments which caused lactic acid excesses to appear in the urine (table 1) and in those which caused no demonstrable change in the lactic acid content of the urine (table 2). We found, then, in complete accord with the experiments of Briggs (3) that oxygen inhalations lessen the pulmonary ventilation during exercise, at least in untrained individuals. This occurs even when the exercise used does not increase the urinary output of lactic acid.

DISCUSSION

In our experiments the inhalation of oxygen-enriched air while carrying a 30-pound load for five minutes up a treadmill lessened the subjective discomfort, reduced the pulmonary ventilation, lessened the concentration of lactic acid in the blood and diminished its output in the urine. In similar experiments without a load the respiratory effects of oxygen inhalations were similar, and the blood showed less increase when oxygen was breathed. The latter exercises, however, were not sufficient to produce a demonstrable increase in the urinary output of lactic acid even when air was breathed, probably because the blood increase was not sufficient to exceed the kidney threshold.

How do oxygen inhalations lessen the hyperpnea of muscular exercise? Douglas and Haldane (1) found that some factor or factors other than increased carbon dioxide tension contributed to the production of the hyperpnea of strenuous muscular exercise. In his discussion of these other factors Haldane (2) concluded that where an increase of lactic acid appeared in the urine this acid played a rôle in producing the hyperpnea. He pointed out, however, that in less strenuous exercise no excess of lactic acid appears in the urine and that here also the hyperpnea is lessened by oxygen inhalations. Haldane, therefore, concluded that the hyperpnea of exercise is in part due to an anoxemia which acts upon the respiratory center in a manner comparable to the anoxemia of high altitudes.

It seems probable that inhalations of oxygen produce their effect by increasing the amount and tension of oxygen in the arterial blood and by supplying more oxygen to the body. But the relief of exercise hyperpnea by oxygen is not comparable to the relief of high altitude hyperpnea by oxygen. At high altitudes there is definite arterial anoxemia, whereas Himwich and Barr (7) on man, in agreement with the animal experiments of Geppert and Zuntz (8) and Hastings (9) found no arterial anoxemia during and after vigorous exercise at sea level. On the contrary such exercise raised the oxygen saturation of arterial blood somewhat above the resting level. A fall in the oxygen saturation apparently occurs only as a result of prolonged and exhausting exercise (Harrop (10), Himwich and Barr (7)). There is then no reason to assume that an arterial anoxemia

exists during moderately strenuous exercises such as we employed. Barr and Himwich (11) using exercises of approximately the same severity as ours found no fall in the oxygen saturation of arterial blood even though the lactic acid concentration in the blood was increased.

The absence of an arterial anoxemia during moderately strenuous exercise does not preclude an oxygen shortage in the active tissues which may be lessened by oxygen inhalations. During exercise the utilization of oxygen by the heart and by the active voluntary muscles is extraordinarily rapid and the supply of oxygen can be maintained only by a much more rapid rate of blood flow through the active tissues. If the necessary blood flow is not maintained, an oxygen shortage might readily appear in these tissues even though the arterial blood is well saturated with oxygen. The inhalation of oxygen during exercise may increase the oxygen supply to the active muscles in two ways: first by raising the oxygen saturation of arterial blood and second by enabling the heart through this better oxygen supply to maintain a more rapid circulation. Thus as a result of oxygen inhalations the active muscles may receive both a better quality and a greater quantity of blood.

The oxygen utilized by the muscles during exercise serves to remove lactic acid which has been formed during the period of contraction (A. V. Hill (13); Meyerhof (14)). An inadequate removal of this lactic acid leads to its accumulation in the muscles and to its escape into the blood and the urine. We have shown that the concentration of the lactic acid in the blood and the escape of lactic acid in the urine during strenuous muscular exercise are both lessened by oxygen inhalations. This lessened accumulation of lactic acid in the body would lessen the pulmonary ventilation, for the accumulation produces an acidosis which stimulates the respiratory center to increased activity. We have seen that oxygen inhalations may also lessen the pulmonary ventilation during exercises which are not sufficiently strenuous to increase the output of lactic acid in the urine. Since a certain amount of lactic acid is always formed in the muscles as a result of exercise it seems probable that the inhalation of oxygen under these circumstances influences the respiration through lessening the accumulation of acid in the muscles and the consequent change in the acid-base equilibrium of the body.

SUMMARY

1. The increase in lactic acid in blood and urine resulting from measured treadmill exercises was determined.

2. A smaller rise of blood lactic acid and a smaller excretion of lactic acid were found when oxygen-enriched air was breathed.

3. Excess excretion of lactic acid over the resting level was only demonstrated in experiments in which the blood lactic acid rose to 30 or 40 mgm. per 100 cc.

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