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THE PHYSIOLOGICAL MEANING OF THE MAXIMAL OXYGEN INTAKE TEST [1]

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According to Hill, maximal oxygen intake is reached when oxygen intake per unit time has attained ". . . its maximum and remains constant . . . owing to the limitation of the circulatory and respiratory systems (1)." In more definitive terms, when one subjects a normal individual to progressively increasing workloads, allowing sufficient time for recovery between each increment of work, a linear relation between workload and oxygen intake is found. Ultimately, maximal oxygen intake per unit of time is reached; beyond this point the workload can usually be increased still further but, ordinarily, oxygen intake levels off or declines.

The maximal oxygen intake which a normal individual can achieve is sometimes taken as an index to maximal cardiovascular function provided pulmonary function is normal. If this concept is sound, the test may come to be of enormous value in the critical evaluation of normal and abnormal cardiovascular function. The superiority of a test that measures cardiovascular capacity, over one that determines whether or not an individual can attain a single arbitrarily chosen workload, is apparent. A value for cardiovascular capacity should characterize a given individual precisely; use of a single workload merely places him in one of two groups. The difficulty, insofar as maximal oxygen intake is concerned, is simply that its physiological meaning is imperfectly understood. The view that cardiac capacity is the determinant of maximal oxygen intake is surmise, not established fact. Ventilatory factors, for example, are usually said not to be involved in determining maximal oxygen intake but have not really been ruled out. For that matter, the various studies that demonstrate some degree of arterial desaturation during heavy work are often thought to suggest that a pulmonary factor, either ventilatory or diffusive, may be involved. Finally, the interplay between cardiac output and AV oxygen difference during heavy work needs further scrutiny. There can be no doubt, theoretically, that the degree to which AV oxygen difference can expand is, like cardiac output, a determinant of maximal oxygen intake.

It is the purpose of this presentation to examine some of these relationships by direct measurement in the hope that the physiological meaning of the maximal oxygen intake test can be clarified.

METHOD

In order to establish normal data for this laboratory, a maximal oxygen intake test similar to that described by Taylor, Buskirk, and Henschel (2) was applied to 65 normal men. A motor-driven treadmill was used for the exercise. For normal subjects, a 10 minute warmup period (3 mph at 10 per cent grade) was followed by a 10 minute rest period. The first test run was then carried out, usually at 6 mph and zero grade. Before the treadmill was started, the subject was connected to a Rudolph two-way breathing valve by means of a rubber mouthpiece, his nose being completely closed with a nasal clamp. For the first minute of the run, expired air was used to wash out a Douglas bag connected to the expiratory side of the valve. Expired air for analysis was collected for the last minute of a two and one-half minute run. The use of this time period was based on the data of Taylor, Buskirk, and Henschel (2), Robinson (3), and Donald, Bishop, Cumming, and Wade (4). Analysis of the expired air was immediately carried out using a Beckman E-2 magnetic oxygen analyzer and a Liston-Becker infrared carbon dioxide analyzer. Duplicate analyses were carried out with a Scholander apparatus at regular intervals. The volume of expired air was measured in a Tissot gasometer and was corrected to STPD. These data permitted calculation of oxygen consumption either by using change in nitrogen content for correction of expired (to inspired) volume, or by use of a nomogram (5). Pulse rate during exercise was measured electrocardiographically. Respiratory rate was

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obtained by use of a strain gauge assembly connected to the expiratory side of the Rudolph valve. After a 10 minute rest period, the workload was increased by raising the grade to 2.5 per cent, the speed being held at 6 mph, and the procedure repeated. Subsequently, the subject performed work at increasing levels, the load being increased each time by raising the grade 2.5 per cent, until oxygen intake per minute leveled off. In most subjects, the entire test required about an hour and a half.

Ordinarily, the point at which the oxygen intake curve (plotted against workload) ceased to rise was taken as maximal oxygen intake. In most instances (72 per cent), when the workload was increased beyond that producing maximal oxygen intake, the value either remained unchanged or declined. In some cases, however, a relatively slight rise occurred, necessitating the formulation of strict criteria for deciding whether or not maximal, or near maximal, intake actually had been reached. Plots of oxygen intake against workload for the entire material (Figure 1) showed that, until a maximal value was attained, oxygen intake rose 142 ± 44 ml. with each increase in workload. If the rise was less than 142 minus 88 (twice the standard deviation), or 54 ml., the final value was accepted as the maximal intake, the assumption being that the subject had attained his true maximal value or had reached the beginning of a plateau and could not increase his intake very much more.

With most younger normal subjects, it was found to be unnecessarily time-consuming to use 2.5 per cent grade increases at the lower levels, since most of them did not attain maximal intake until grades of 10 per cent or more were reached. It was also noted that values for oxygen intake sometimes varied erratically at lower workloads, especially in anxious individuals or in those given to hyperventilation. In some young normal subjects, maximal oxygen intake was not reached even at the highest grade possible (14.75 per cent), making it necessary to increase the speed as well as the grade. The highest workload required was 9 mph at 14.75 per cent grade. With older subjects, no such problem arose. In fact, in some instances slower speeds were used if the 6 mph setting proved to be too troublesome for the subject.

In order to test the repeatability of the method as performed in our laboratory, first and second trials were done on 15 normal subjects and the data analyzed by standard statistical techniques (6).

The method for determining maximal oxygen intake was essentially unchanged when it was combined with determination of cardiac output and blood studies (15 normal subjects). Subjects for the more elaborate procedures were chosen at random. Maximal oxygen intake was first determined by the usual method. At a later date both cardiac output and maximal oxygen intake were determined at rest and at three workloads. The dye dilution technique was employed for estimating cardiac outputs. Prior to beginning the tests, a PE 90 catheter was inserted through a thin-walled 16 gauge needle into the left antecubital vein and was passed proximally to the upper brachial. Then a similar, but shorter, catheter was introduced into the brachial artery of the same arm, also through a thin-walled 16 gauge needle. Finally, the same method was used to introduce a long PE 90 catheter retrograde into the femoral vein to the midthigh level. Local anesthesia was routinely used before inserting the 16 gauge needles. The catheters were attached to three-way stopcocks and were kept filled with normal saline solution containing a small amount of heparin. For the actual measurement of cardiac output, 10 mg. of Evans blue (T-1824) was delivered at the end of the catheter in the brachial vein about one and one-half minutes after the beginning of exercise (during the collection of expired air), it having been shown by Donald, Bishop, Cumming, and Wade (4) that cardiac output and AV oxygen difference reach a steady state after the first minute of exercise. Arterial blood samples were collected at one second intervals in tubes containing powdered heparin, using either a manual collection device or an electrically operated collector. During the final 20 to 30 seconds of the exercise, blood samples were collected anaerobically from all three catheters (brachial artery, brachial and femoral veins) for measurement of oxygen tension and content, carbon dioxide content and pH. Oxygen tension was determined polarographically (7), oxygen content and carbon dioxide content by the Van Slyke and Neill method, and pH by use of a Cambridge Research model pH meter. Carbon dioxide tension was calculated from a Singer and Hastings nomogram (8).

Analysis of blood for dye content was carried out according to a previously published method (9), using a Beckman model DU spectrophotometer. The data were plotted and extrapolated by the method of Hamilton,

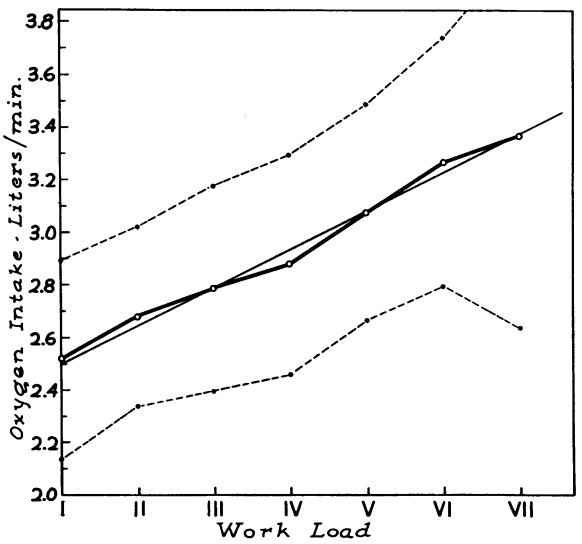

FIG. 1. RELATION BETWEEN SUCCESSIVE INCREMENTS IN WORKLOAD AND OXYGEN INTAKE IN NORMAL MEN

Heavy black line represents mean values at each load. Dashed lines represent standard deviation about each point.

TABLE I

Maximal oxygen intake in liters per minute— Duplicate trials in 15 normal men

Subject	Trial I	Trial II
A. G.	2.94	2.89
J. M.	3.86	3.77
C. D.	3.46	3.34
J. D.	2.84	2.60
J. B.	2.99	2.93
B. A.	3.34	3.39
S. W.	2.45	2.40
C. M.	3.20	3.57
C. J.	3.51	3.65
L. C.	3.46	3.23
C. McR.	2.95	3.08
W. M.	2.99	3.27
J. W.	2.77	2.52
F. H.	3.13	3.14
N. H.	2.07	2.24
Mean	3.06	3.07
S.D.	0.46	0.44

Moore, Kinsman, and Spurling (10). Mean circulation time, "central" blood volume, and cardiac output were then determined, also by the method of Hamilton and co-workers.

RESULTS

Comparisons of gas analyses done by the gas analyzers, on the one hand, and the Scholander method (11), on the other, showed the former to be highly reliable. Mean values for oxygen content in 17 gas samples chosen at random as the work proceeded were 16.38 ± 0.84 per cent for the gas analyzers and 16.42 ± 0.90 per cent for the Scholander method. Corresponding values for carbon dioxide were 4.86 ± 0.78 and 4.85 ± 0.76 per cent, respectively. The polarographic technique, as employed (7), has been shown to be highly reliable at all levels of oxygen tension. More specifically, the method yields values over physiologic venous and arterial ranges that correspond closely to pO_2 values calculated from simultaneous Van Slyke analyses and from determinations by the microbubble technique of Riley, Proemmel, and Franke (12). In very low ranges (3 to 10 mm. Hg) the error is about 5 per cent if values are calculated from the polarographic equation (7) instead of being read off a calibration curve. From 20 to 100 mm. Hg, the percentage error drops to about 2.5 per cent and is still lower at higher oxygen tensions. Repeatability of the method at relatively low oxygen tensions can be judged from first and second trials done on eight blood samples from different sources, equilibrated with known gas mixtures containing 6.1 and 12.6 per cent oxygen (42 and 89 mm. Hg partial pressure), respectively. The first trials on the mixture containing 6.1 per cent oxygen yielded a mean value of 43.2 ± 0.9 mm. Hg; the mean for the second trials was 42.9 ± 0.8 mm. Hg (n = 8 in both trials). For the second mixture, the corresponding mean values were 88.7 ± 1.3 and 89.4 ± 2.0 mm. Hg.

The repeatability of the maximal oxygen intake test, if rigid criteria for determining the point at which the maximal value has been attained are

TABLE II

Oxygen intakes in normal men of various ages at increasing workloads, including that producing maximal oxygen intake

Age group		6 mph, 0 grade		Premaximal		Maximal		Postmaximal	
		L./min.	*ml./Kg./min.*	*L./min.*	*ml./Kg./min.*	*L./min.*	*ml./Kg./min.*	*L./min.*	*ml./Kg./min*
20–29	Mean	2.59	34.6	3.15	41.8	3.37	44.7	3.18	42.7
	S.D.	0.27	2.7	0.49	4.8	0.51	3.9	0.42	4.3
	n	33		35		36		28	
30–39	Mean	2.54	32.7	2.88	37.3	3.04	39.3	2.91	36.6
	S.D.	0.31	3.2	0.38	3.3	0.39	3.3	0.54	4.6
	n	18		18		18		18	
40–49	Mean	2.51	30.4	2.79	33.6	2.94	35.4	2.77	32.9
	S.D.	0.44	2.9	0.59	4.3	0.60	3.3	0.46	3.5
	n	8		8		8		8	
Over 50	Mean			2.13	27.7	2.46	32.0	2.26	29.4
	S.D.								
	n			3		3		3	

TABLE III

Ventilation and oxygen removal rates in normal men at increasing workloads

Age group		6 mph, 0 grade		Premaximal		Maximal		Postmaximal	
		A*	B*	A	B	A	B	A	B
20–29	Mean	61.3	43.0	81.7	39.2	94.9	36.0	95.2	34.0
	S.D.	8.7	6.3	14.6	6.4	15.9	5.6	17.3	5.2
	n	33	33	35	35	36	36	28	28
30–39	Mean	66.1	39.3	80.5	36.8	89.4	35.0	88.5	33.3
	S.D.	13.3	6.4	14.9	6.8	17.3	5.7	18.8	5.7
	n	18	18	18	18	18	18	12	12
40–49	Mean	66.3	38.2	81.0	35.2	88.8	32.7	82.7	34.3
	S.D.	11.0	5.3	19.8	5.1	21.3	4.4	18.6	5.1
	n	8	8	8	8	8	8	5	5
Over 50	Mean			57.0	38.2	65.5	38.7	60.6	38.4
	S.D.								
	n			3	3	3	3	3	3

* A: Total ventilation (expired volume) in liters per min. (BTPS). B: O_2 removal rate expressed as ml. of O_2 (STPD) removed from each liter of air (BTPS) respired.

applied, is demonstrated in Table I, in which the results of first and second trials, weeks to months apart, are shown for 15 subjects. Variance analysis discloses that almost all the variance is attributable to interindividual differences; the random component is quite small and the intraindividual component virtually negligible.

The mean values for maximal oxygen intake obtained in normal men aged 20 and over are given in Table II.

In Table III are presented the mean values for ventilation and oxygen removal rates in normal men at increasing workloads including the maximal and postmaximal levels.

The values for oxygen intake, cardiac output, AV oxygen difference and other hemodynamic variables at rest and at the maximal oxygen intake load are shown in Table IV.

Table V presents mean values for arterial and venous oxygen content, oxygen tension, per cent oxygen saturation, and pH, both at rest and at maximal oxygen intake.

The values for cardiac output and AV oxygen difference at the maximal oxygen intake and at a higher workload are presented in Table VI.

DISCUSSION

The need for an effective measure of circulatory capacity is undisputed. The maximal oxygen intake test, to judge from the views of Hill (1) and of Bainbridge (13), may fill the need but its determinants have not been sufficiently clarified to enable one to accept the test as a measure of circulatory capacity with assurance. The term *maximal oxygen intake* must, itself, be viewed skeptically. It seems clear from the work of Christensen and Högberg (14) and Taylor, Buskirk, and Henschel (2) that the actual value reached for a given individual depends on the nature of the physical activity. It is, therefore, maximal relative to a given set of conditions, which must be carefully defined, rather than in an absolute sense.

For one thing, the actual technique used is far from standard. In the present work, the technique used by Taylor was followed fairly closely except that the subject was required to grip a supporting shelf with his left hand while he ran. Another difference was the time interval between each workload. In our own work, 10 to 15 minutes is allowed; Taylor, however, runs only one workload per day and requires several days to complete a full determination. Buskirk and Taylor's figure for an 18 to 29 year group of sedentary students and soldiers was 3.44 ± 0.46 liters per minute (15). For our 20 to 29 year group the corresponding figure is 3.37 ± 0.51 liters per minute. These groups were not actively in training and neither appears to have been biased toward excessively fat or excessively lean individuals. Åstrand's value for 33 Swedish athletes aged

TABLE IV

*Cardiac output, stroke volume, calculated A V O_2 differences, and other items in 15 normal subjects at rest and at maximal O_2 intake**

	Standing resting	Maximal O_2 intake level
O_2 intake (L./min.)	0.340 ± 0.04	3.22 ± 0.46
n	5	15
Cardiac output (L./min.)	5.4 ± 0.8	23.4 ± 5.5
n	14	15
Pulse rate	91 ± 17	187 ± 10
n	14	13
Stroke volume (ml.)	62 ± 18	125 + 25
n	13	13
AV O_2 diff. (ml./100 ml.)	6.5 ± 0.7	14.3 ± 2.5
n	5	15
"Central" volume (liters)	1.71 ± 0.32	3.49 ± 0.83
n	14	15
Appearance time (seconds)	11.9 ± 2.2	5.9 ± 1.3
n	14	15
Mean circ. time (seconds)	18.5 ± 3.1	9.4 ± 2.0
n	14	15

* Mean maximal O_2 intake determined previously on same group: 3.15 ± 0.31 L./min.

20 to 29 (4.15 ± 0.36 liters per minute) (16), and that of Slonim, Gillespie, and Harold (4.05 ± 0.39) (17) for 65 young trained men, were presumably determined to some extent by the high degree of physical training their subjects had reached (18). Buskirk and Taylor's comparable figure for a group of young trained subjects was 3.95 ± 0.43.

In order to render the test as reliable as possible, rigid criteria for determining the point at which maximal oxygen intake is reached must be established. If this is done, the test is quite repeatable (Table I) and a given value characterizes an individual for several months at least.

The effect of age on the maximal oxygen intake can be seen in Table II. At the initial exercise level the oxygen intake is the same for the first three age groups but the *maximal* intake values for all four age groups show a decrease with age. These results are comparable to those of Robinson (3). It is clear, therefore, that the age trend must be taken into account if the test is used for functional evaluation of human subjects.

In Table III it is noted that ventilation reaches its highest value at the maximal oxygen intake level. There is no significant difference in the ventilation at the maximal and the postmaximal level in a given age group. With increasing age the level of ventilation at maximal workloads tends to decline. Oxygen removal rates decline with increasing workloads in the first three age groups. In the oldest group, the oxygen removal rate ap-

TABLE V

Mean values for O_2 content, O_2 tension, per cent saturation, pH and hematocrit from one arterial and two venous sites at rest and during exercise at maximal oxygen intake level

Site	State	O_2 content *ml./100 ml.*	O_2 tension *mm. Hg*	Per cent sat.	pH	Hct. *per cent*
Brachial artery	Resting	18.1 ± 1.4	87 ± 9	97.1 ± 3.1	7.40 ± 0.04	46.5 ± 3.8
	n	14	15	9	15	14
	Max. O_2	19.3 ± 1.9	88 ± 12	94.7 ± 2.6	7.19 ± 0.09	48.3 ± 3.4
	n	14	15	9	15	14
Brachial vein	Resting	9.3 ± 2.4	31 ± 7	52.6 ± 12.9	7.36 ± 0.03	43.8 ± 2.7
	n	8	8	8	8	8
	Max. O_2	4.5 ± 1.2	29 ± 8	24.9 ± 7.8	7.13 ± 0.04	48.3 ± 3.0
	n	6	6	6	6	6
Femoral vein	Resting	6.6 ± 2.5	30 ± 11	37.9 ± 16.2	7.35 ± 0.07	45.3 ± 2.6
	n	8	8	8	8	7
	Max. O_2	3.9 ± 1.3	30 ± 7	19.9 ± 6.8	7.11 ± 0.05	48.2 ± 3.2
	n	8	8	8	7	8

TABLE VI

Values for cardiac output and A V O_2 difference in six normal subjects at the maximal oxygen intake and at a higher workload

	Maximal oxygen intake level			Beyond maximal oxygen intake level		
	O_2 intake	Cardiac output	AV O_2 diff.	O_2 intake	Cardiac output	AV O_2 diff.
J. B.	2.56	20.6	12.4	2.42	15.6	15.5
L. C.	3.23	25.9	12.5	3.03	21.1	14.4
A. G.	2.89	15.6	18.5	2.90	14.7	19.7
F. H.	3.01	23.2	13.0	2.96	17.1	17.3
C. Mc.	3.08	26.3	11.7	3.05	25.8	11.8
J. W.	2.47	14.1	17.5	2.52	15.1	16.7
Mean	2.87	21.0	14.3	2.81	18.2	15.9
S.D.	0.31	4.7	2.7	0.34	4.1	2.5

pears to remain constant with increasing workloads.

The primary purpose of the study was not, however, merely to re-examine previously established characteristics of maximal oxygen intake but, rather, to inquire into its physiological meaning. It is obvious that, in terms of the Fick equation, the main circulatory determinants must be cardiac output on the one hand, and AV oxygen difference on the other (19). The relative role played by each of these factors in determining the maximal oxygen intake is seen in Table IV. Oxygen intake increased 9.5 times from the resting state to the workload producing the maximal figure; the corresponding figure for cardiac output is 4.3. Proportionately, pulse rate and stroke volume increased equally—about two times. At the time the cardiac output reached its maximal level, the "central" blood volume, as calculated by the Hamilton method, had doubled. The appearance time of the dye and the mean circulation time had decreased by one-half.

On the face of all this, one might assume with Bainbridge (13) that cardiac capacity is the primary determinant of maximal oxygen intake. Such an assumption, however, ignores the fact that the AV oxygen difference makes a contribution of its own to oxygen intake. Simple increase in cardiac output by 4.3 times, AV oxygen difference remaining at 6.5 ml. per 100 ml., would increase oxygen intake from 340 ml. (resting), to no more than 1,500 ml. Widening of the AV oxygen difference by 2.2 times (from 6.5 to 14.3 ml. per 100 ml.), however, permits oxygen intake to exceed 3 liters under the same conditions. Were it not for the ability of the organism to widen its AV oxygen difference, cardiac output would have to increase nearly 10 times to supply 3,200 ml. of oxygen per minute to the tissues. Our mean value for AV oxygen difference during heavy work is in close agreement with that found by Asmussen and Nielsen (20), and Freedman, Snider, Brostoff, Kimelblot, and Katz (21), but higher than that found by Christensen (22).

The magnitude of the maximal AV oxygen difference is determined by the maximal level

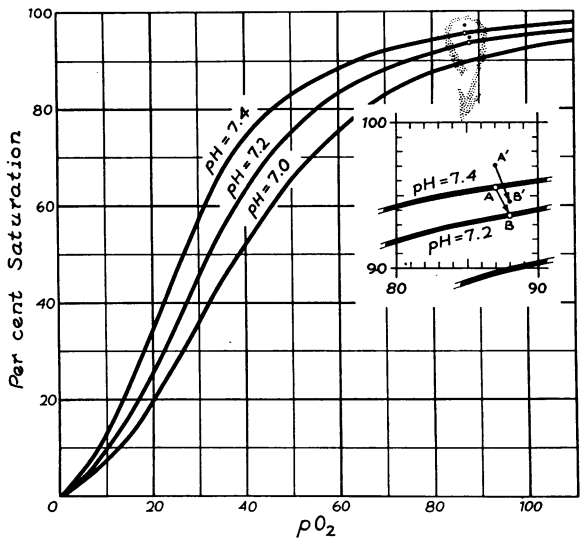

FIG. 2. OXYGEN DISSOCIATION CURVES AT THREE LEVELS OF pH (33)

Insert shows A and B (open circles), representing values for per cent saturation corresponding to two observed values for arterial pO_2 (87 mm. Hg at rest, and 88 mm. Hg during heavy work). A′ and B′ represent per cent saturation, calculated from Van Slyke determinations, for the same two pO_2 values. The fall in per cent saturation is about 2 per cent in each case.

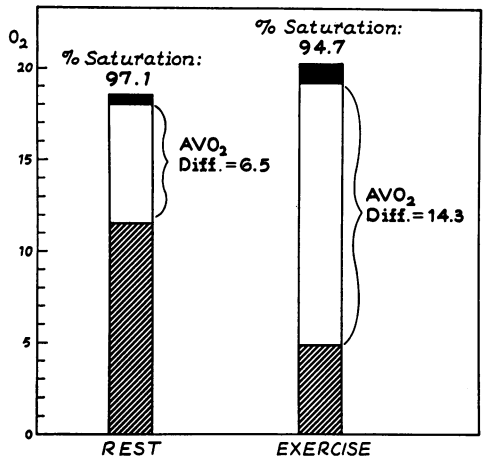

FIG. 3. THE AV OXYGEN DIFFERENCE AT REST AND DURING EXERCISE

Total height of each column represents oxygen capacity. Black areas at top are unoxygenated hemoglobin. Shaded areas at bottom represent mixed venous oxygen content.

reached by the oxygen content of arterial blood on the one hand, and the lowest level reached by the oxygen content of mixed venous blood on the other. In Table V it is noted that there is a 1.2 ml. per 100 ml. rise in arterial oxygen content and a slight fall in per cent saturation (about 2.4 per cent) between rest and heavy exercise. These items are easily understood when it is noted that the exercise also induces a fall in arterial pH, a rise in hematocrit, and no significant change in arterial oxygen tension (Figure 2). In any event, the small increases in arterial oxygen content induced by exercise can contribute very little to the widening of the AV oxygen difference (Figure 3).

The magnitude of the AV oxygen difference is influenced most markedly by encroachment on the mixed venous oxygen content (23). Mixed venous oxygen content (calculated from oxygen intake, cardiac output, and arterial oxygen content) decreased from 11.6 ml. per 100 ml. at rest to 5.0 ml. per 100 ml. during exercise at the maximal oxygen intake level. This encroachment on the mixed venous oxygen content is made possible by two mechanisms: One is the extent to which blood perfusing working tissue can surrender its oxygen; the other is the shunting of blood away from inactive areas as noted by Donald, Bishop, and Wade (24). The lowest level to which the oxygen content of blood flowing through strenuously working muscle may fall is not known but it seems unlikely that it ever approaches zero in normal subjects (25). An approach to these problems was made in the present study by comparing oxygen content and tension of blood from brachial and femoral veins during running. The brachial vein blood was drawn from the stationary arm. It is seen in Table V that heavy exercise reduced venous oxygen content to less than half its resting value in both samples, the femoral sample showing slightly greater reduction than the brachial. The oxygen content of the femoral venous sample (3.9 ± 1.3 ml. per 100 ml.) is probably near the lowest value that can be reached since it is made up primarily of blood from working muscle. But the drop in oxygen content of blood from the brachial vein of the stationary arm is almost as large (4.5 ± 1.2 ml. per 100 ml.) and is in keeping with the report of Donald, Bishop, and Wade (24) to the effect that during moderate exercise the oxygen content of venous blood from a resting extremity falls as low as that from one which is exercising. These findings, along with their observation that the volume of a resting arm is decreased during leg exercise, are most readily explained on the basis of physiological shunting of blood away from resting tissue during exercise. Such blood as continues to perfuse resting tissue may be so small in amount that it must surrender as much oxygen, relatively speaking, as blood perfusing exercising muscle. In any case, oxygen content of femoral and brachial venous blood during heavy exercise draws very close, as exercise proceeds, to the calculated mixed venous oxygen content (5.0 ml. per 100 ml.).

The most striking feature of the blood gas studies is the relative constancy of oxygen tension, both arterial and venous, during heavy exercise (Table V). In contrast, a decrease in arterial oxygen tension during low grades of exercise has been reported by other observers (26–28). Blount, McCord, and Anderson (29), however, found no change in arterial oxygen tension during similar exercise loads. Hickam, Pryor, Page, and Atwell (30), and Asmussen and Nielsen (31) noted a slight drop (about 2 per cent) in arterial oxygen saturation during heavy exercise but the first group (30) felt that the phenomenon might be due to pH changes and not to a decrease in ar-

terial oxygen tension. Our results support the latter view (Figure 2). Oxygen tension of brachial and femoral venous blood also tended to remain at or near the resting value even though oxygen content and per cent saturation are both markedly depressed during heavy work. Teleologically, it would seem that an adequate level of oxygen tension is vigorously protected so that an effective pressure gradient from capillary to tissue cell can be maintained. The decrease in pH and the increase in carbon dioxide tension during exercise combine to cause a temporary shift of the oxygen dissociation curve to the right in the systemic capillary, but the pH changes alone were not large enough to explain the magnitude of the shift as actually observed (Figure 3). The carbon dioxide tension of brachial venous blood increased from a mean value of 45 mm. Hg at rest to 65 mm. Hg at the maximal oxygen intake level of exercise; the corresponding figures for femoral venous blood were 50 mm. Hg and 65 mm. Hg. It may be, as suggested by Roughton (32), that increase in carbon dioxide tension tends, independently of change in pH, to cause a shift to the right of the oxygen dissociation curve. In any case, the shift makes it possible, as blood traverses the capillary, for oxygen to be given up more readily without disturbing the pressure gradient from capillary to cell. In the pulmonary capillary, the situation reverses itself, facilitating oxygenation of venous blood.

The maintenance of arterial oxygen tension during heavy exercise is adequate evidence against the possibility that pulmonary factors, ventilatory or diffusive, determine maximal oxygen intake. Nor did timed vitalometry, carried out at rest in some of the subjects, provide evidence of impairment of pulmonary function. One might well go further and hold that a definite decrease in arterial oxygen tension during heavy exercise, far from being a normal finding, is actually an indication of abnormal response to exercise.

In Table VI are presented the data on six normal men whose oxygen intake leveled or actually declined at workloads beyond that producing maximal intake. It is noted that as oxygen intake declined, the cardiac output also declined. The AV oxygen difference, however, appears to have increased still further. The possibility that the organism can increase AV oxygen difference even after cardiac output and oxygen intake have leveled off or are declining is open to several interpretations. It may mean that cardiac output is the more important determinant but the data at hand do not rule out the possibility that, in some subjects, further widening of the AV oxygen difference may permit oxygen intake to increase even after cardiac output has reached its peak.

In any event, the full meaning of maximal oxygen intake is in terms not merely of the ability of the heart mechanically to propel blood, but also of the ability of the tissues to extract oxygen from blood perfusing them. It seems unnecessary, therefore, to invoke the view that an important determinant of maximal intake is the inability of peripheral arteries and arterioles to take up all the blood pumped out by the vigorously contracting left ventricle (2, 16). The evidence now available suggests that maximal oxygen intake is a measure of cardiac capacity and the ability to increase the AV oxygen difference, not of the ability of the vascular bed to accommodate left ventricular output. With this in mind, the test may indeed have clinical usefulness in evaluating patients with certain types of cardiovascular disease.

CONCLUSIONS

1. The maximal oxygen intake is dependent on both cardiac output and AV oxygen difference. When the oxygen intake increased by 9.5 times from rest to the workload producing the maximal figure, the corresponding figure for cardiac output was 4.3 and for AV oxygen difference 2.2. The widening of the AV oxygen difference was due principally to diminution in mixed venous oxygen content.

2. There was no significant change in arterial oxygen tension from rest to heavy work; the slight decrease in oxygen saturation that was observed can be explained by the pH change of the blood and the resulting shift in the oxygen dissociation curve.

3. The venous oxygen tension showed no significant change, even though the venous oxygen content and saturation fell appreciably. The shift in the oxygen saturation curve to the right was due, in part, to decrease in pH, and (possibly) to an increased carbon dioxide tension as well.

The end result of the phenomenon is to maintain an adequate oxygen tension gradient from capillary to cell.

4. In ascertaining the physiological meaning of the maximal oxygen intake, the relative importance of cardiac capacity and increase in AV oxygen difference must be determined. It is probable that in the normal individual the ability to increase cardiac output is the more important of the two factors.

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