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Research Article

THE GASEOUS CONTENT OF THE BLOOD AND THE OUTPUT OF THE HEART IN NORMAL RESTING ADULTS

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I. GASEOUS CONTENT OF THE BLOOD

In a previous paper (Burwell and Robinson, 1924) we have described a respiratory procedure by which a gas mixture is obtained in which both oxygen and carbon dioxide are in equilibrium with those gases in the blood entering the lungs (the mixed venous blood). The equilibration of this gas with blood of the subject allows, therefore, the determination of the oxygen and carbon dioxide content of the mixed venous blood. We used the analytical method of Van Slyke and Stadie. The data thus obtained, together with those obtained by measuring the gas exchange in the lungs, and by counting the pulse, allow the output of the heart per minute and per beat, by a method to be described in the second part of this paper.

Material. In the present paper we wish to report the results of a study of eleven normal resting subjects, all of whom are members of a hospital staff, ranging in age from twenty-five to forty-five years. All observations were made in the morning, after about half an hour's rest in a reclining chair, and at least twelve hours after taking food. As nearly identical conditions as possible were obtained in all determinations.

Gaseous tension of the mixed venous blood. In table 1 are brought together the results of a number of observers. In all instances the principle of using the lungs as an aerotonometer, as suggested by Pflüger has been employed. Loewy and v. Schrötter (1905) measured the tension of oxygen and carbon dioxide in gas withdrawn from an occluded portion of a lung by means of a lung catheter. All other observers have used some modification of the rebreathing method introduced by Plesch (1909).

The figures of Loewy and v. Schrötter are the average of a number of determinations with fairly wide variations, while the figures of others are either determinations on one subject or show the limits found in small series. Our own findings show a somewhat greater

TABLE 1

Oxygen and carbon dioxide tension of the mixed venous blood

Authors	Oxygen tension	CO_2 tension
	mm. Hg	*mm.* Hg
Loewy and v. Schrötter (1905)	37.5	42.5
Fridericia (1918)	35.1–44.5	45.2–46.3
Barcroft, Roughton and Shoji (1922)	32.6	49.5
Douglas and Haldane (1922)	46.1	44.0
Meakins and Davies (1922)		44.4–49.1
Redfield, Bock and Meakins (1922)	31.0–36.0	45.0–50.0
Burwell and Robinson	31.6–43.7	41.0–47.0

TABLE 2

Oxygen and carbon dioxide content of the blood

Subject	Arterial blood		Mixed venous blood		Oxygen utilized		Respiratory quotient		pH of mixed venous blood
	O_2	CO_2	O_2	CO_2		Of total oxygen capacity	From blood gases	Gas exchange	
	vol. per cent	*vol. per cent*	*vol. per cent*	*vol. per cent*	*vol. per cent*	*per cent*			
1 A.	21.76	46.01	15.23	50.70	6.53	31	0.72	0.76	7.34
2 R.	22.23	44.75	16.26	49.61	5.97	25	0.81	0.85	7.33
3 H.	22.60	45.02	17.01	49.52	5.59	23	0.80	0.81	7.32
4 F.	21.80		16.10		5.70	24		0.72	
5 B.	23.04	46.43	18.15	49.80	4.89	21	0.69	0.71	
6 L.	21.80	47.36	16.55	51.18	5.25	23	0.73	0.75	7.34
7 G♀	17.36	46.26	13.08	49.52	4.28	24	0.76	0.82	7.34
8 M.	22.59		17.14		5.45	23		0.76	
9 P.	21.11	50.30	15.95	54.00	5.16	24	0.72	0.78	7.35
10 K.	21.30		17.21		4.09	18		0.71	
11 Bu.	21.00	47.29	17.86	49.63	3.14	14	0.75	0.75	7.33

variation than previously reported, but our figures are of the same order as those obtained by others. Our own figures, of course, are individual determinations.

The gaseous content of the blood. The oxygen and carbon dioxide content of the blood was determined by the method described in the previous paper. Table 2 shows the results of these analyses in the eleven subjects. The oxygen utilized in the passage of the blood through the body is shown in cubic centimeters utilized from each 100 cc. of blood and also as the percentage of the total oxygen capacity of the blood. The respiratory quotient has been calculated from the blood gases by dividing the amount of the CO_2 lost by 100 cc. of blood by the amount of oxygen gained by 100 cc. of blood in passing through the lungs. The figures so obtained may be compared with the respiratory quotient calculated from the gas exchange in the lungs, which was determined by the Tissot method during each experiment. The fairly close agreement that exists may be taken as evidence of the accuracy of the blood gas determinations. A rational respiratory quotient is obtained only when the four determinations for arterial and venous oxygen and carbon dioxide are substantially correct.

The percentage saturation of the blood exposed to the "venous gas mixture" has in general fallen within the limits of previously published dissociation curves. Sufficient variation exists, however, to render the use of so-called standard dissociation curves unsatisfactory.

The pH figures calculated from the CO_2 tension and content agree with those of others for normal subjects, although they are slightly lower than the average determinations of several recent observers. This agreement indicates that no outspoken error occurred in the CO_2 analyses of the venous blood, and that as a rule no pronounced acid change occurred during the handling of the blood.

II. THE OUT-PUT OF THE HEART

During the past hundred years the problem of the actual volume of the blood expelled by the heart has been attacked frequently by both speculation and experiment. The shrewd guess of Thomas Young (1808) put the output of the heart per beat at an ounce and a half. Such estimations, which were based chiefly upon postmortem measurement of the capacity of the ventricles, were followed by experimental observation upon animals and application of the data so obtained to the calculation of the output of the heart in man. These calculations have resulted in figures so confused and variable that it is quite clear that acceptable determinations must be made upon human subjects.

Many workers have made observations upon human subjects and various types of data have been the bases of the calculation of the volume of the circulation per minute and per beat in man: (1) the volume flow in the arm, determined by plethysomgraphic methods (Müller, 1909); (2) the measurements of instantaneous x-ray photographs of the heart in systole and diastole (Meek and Eyster, 1923); (3) the amount of some inert gas taken up by the blood in a given time, when the absorption coefficient of the gas for blood is known (Bornstein, 1910; Krogh and Lindhard, (1912); (4) the application of the principle of Fick (Fick, 1870; Loewy u. v. Schrötter, 1905; Plesch, 1909; Douglas and Haldane, 1922). Of these the last two types of data are at present the most acceptable.

It would serve no useful purpose to present again the diverse figures for the circulatory minute volume that have been obtained by different workers using different methods. Not only were the methods widely different but also the conditions of the experiments; the activity, position, and external temperature of the subjects were so varied that the results are in no strict sense comparable. It is worthwhile, however, to point out certain general tendencies in these widely divergent figures. The recorded minute volume varies from 2,800 cc. to 9,000 cc. per minute for normal resting adults. There are roughly speaking two groups; in the first are subjects with minute volumes of from 3,000 to 5,000 cc., having usually an output per beat of 45 to 75 cc. In the second group are those with minute volumes of 6,500 to 8,500 cc., having an output per beat of 100 cc. or more. The existence of these two groups of figures has been partly responsible for the development of two contrasting beliefs as to the method of response of the circulation to demand for increased blood supply, a question that will be discussed in a subsequent paper dealing with the response of the circulation to exercise.

The measurements of the output of the heart which we wish to report have been obtained by the application of a method based upon Fick's principle; a principle best described in the words of its originator:

. . . . Man bestimme, wie viel Sauerstoff ein Thier während einer gewissen Zeit aus der Luft aufnimmt und wie viel Kohlensäure es abgibt. Man nehme ferner dem Thiere während der Versuchzeit eine Probe arteriellen und eine Probe venösen Blutes. In Beiden ist der Sauerstoffgehalt und der Kohlensäuregehalt zu ermitteln. Die Differenz des Sauerstoffgehaltes ergibt, wie viel Sauerstoff jedes Cubiccentimeter Blut beim Durchgang durch die Lungen aufnimmt, und da man weiss, wie viel Sauerstoff im Ganzen während einer bestimmten Zeit aufgenommen wurde, so kann man berechnen, wie viel Cubiccentimeter Blut während dieser Zeit die Lungen passirten, oder wenn man durch die anzahl der Herzschläge in dieser Zeit dividirt, wie Cubiccentimeter Blut mit jeder Systole des Herzen aufgeworfen wurde. Die entsprechende Rechnung mit den Kohlensäueremengen gibt Bestimmung desselben Werthes, welche die erstere controllirt . . . .

As the gases of the blood are now commonly calculated as volumes of gas per 100 cc. of blood, a formula conveniently employed is as follows:

$$\frac{O}{U} \times 100 = M$$

when O = cc. of oxygen absorbed per minute.
U = volumes per cent of oxygen utilized.
M = minute output of the heart in cubic centimeter.

In table 3 are shown the oxygen consumed and the carbon dioxide produced per minute, as measured by the Tissot method, the heart rate per minute, the oxygen utilization and the carbon dioxide accumulation in the blood, and the blood flow as calculated from these data. For reasons pointed out in our previous paper, the circulation minute volume calculated from the oxygen figures is considered more reliable than that calculated from the carbon dioxide figures. Therefore, in three experiments in which there was discrepancy between the two and in which there was reason to believe that the fault lay with the carbon dioxide results, only the oxygen figures are included.

It is seen that most of the subjects, under the conditions of the experiment, gave figures for the output of the heart per minute and per beat which agree well with each other. It may be said that the usual minute out-put of the normal resting adult is 3,500 to 4,500 cc., and the usual out-put per beat is 60 to 70 cc. But there are exceptions and one very satisfactory experiment (Subject Bu.) is a marked exception. This individual had a minute volume of 6,780 cc. and an output per beat of 103 cc., in spite of the fact that his basal metabolic rate was low rather than high. It is clearly necessary, therefore, to bring evidence as to the constancy or variability of the volume flow in a given individual under similar conditions but at different times. Table 4 shows the results of successive studies on two individuals;

TABLE 3

Blood flow in normal resting adults

Subject	Oxygen consumed per minute	Oxygen utilization	Minute output	Heart rate per minute	Output per beat	Carbon dioxide produced per minute	Carbon dioxide accumulation	Minute output	Output per beat
	cc.	*vol. per cent*	*cc.*		*cc.*	*cc.*	*vol. per cent*	*cc.*	*cc.*
A.	231	6.53	3,520	54	65	175	4.69	3,730	69
R.	236	5.97	3,950	68	58	200	4.86	4,120	61
H.	230	5.59	4,120	64	64	187	4.50	4,160	65
F.	243	5.70	4,270	64	67	176			
B.	212	4.89	4,340	64	68	150	3.37	4,450	70
L.	235	5.25	4,480	64	70	176	3.82	4,610	72
G ♀	192	4.28	4,490	65	69	156	3.26	4,790	74
M.	249	5.45	4,570	66	69	189			
P.	240	5.16	4,650	56	83	187	3.70	5,050	90
K.	245	4.09	6,000	68	88	175			
Bu.	213	3.14	6,780	66	103	159	2.34	6,800	103

TABLE 4

Successive determinations of two individuals; all under standard resting conditions

Date	Minute output	Output per beat
Subject R		
	cc.	*cc.*
March 31, 1923	3,700	59
April 17, 1923	3,940	60
April 19, 1923	3,950	58
June 2, 1923	3,960	55
March 13, 1924	3,760	57
Subject B		
January 4, 1924	6,780	103
January 7, 1924	6,260	100
March 7, 1924	4,540	73
March 10, 1924	5,340	83

one of whom had the largest blood flow in table 3. This individual showed wide variation, his minute volume being 6,780 on one occasion and 4,540 on another; with a change in the ouput per beat from 103 to 73 cc. This variation was not associated with a change in pulse rate, metabolic rate, activity, or external temperature. The other subject showed a remarkable constancy of minute volume and output per beat over a period of a year.

Quantitative studies of such a matter as the output of the heart, which is controlled by factors not well understood, are better studied as individual results than as averages. Many determinations of the venous oxygen tension of Subject Bu. indicate that his usual resting blood flow is 6,000 to 7,000 cc. although occasionally it may fall

TABLE 5

Blood flow compared with other measurements

Subject	Minute output				Respiratory minute volume / Circulatory minute volume	Output per beat		
	Total	Per square meter body surface	Per kilogram body weight	Per 100 cc. oxygen absorbed		Total	Per square meter body surface	Per kilogram body weight
	cc.	*cc.*	*cc.*	*cc.*		*cc.*	*cc.*	*cc.*
A.	3,520	1,970	53	1,525	0.90	65	36	1.1
R.	3,950	2,000	45	1,670	0.99	58	29	0.7
H.	4,120	2,190	62	1,780	0.98	64	36	1.0
F.	4,270	2,400	64	1,750	0.82	67	38	1.0
B	4,340	2,320	64	2,050	0.66	68	36	1.0
L.	4,480	2,500	72	1,900	0.67	70	39	1.1
G ♀	4,490	2,750	90	2,340	0.60	69	42	1.4
M.	4,570	2,430	67	1,830	0.90	69	37	1.0
P.	4,650	2,470	63	1,940	0.68	83	44	1.1
K.	6,000	3,470	100	2,450	0.55	88	51	1.5
Bu.	6,780	3,720	103	3,180	0.53	103	57	1.6

much below this. The existence of such wide difference in different healthy people is corroborated by a scrutiny of earlier work. The careful studies of Douglas and Haldane (1922), for example, demonstrated an output per beat of 128 cc. in one subject and of 66 cc. in another, under similar conditions; and these differences were quite constant in many determinations.

In an effort to study the factors controlling the cardiac output, the minute volume and the output per beat of these normal subjects have been compared with some other measurements.

In table 5 it is seen that neither the minute output nor output per beat has any exact or noteworthy relation to body weight, to body surface area, or to the volume of oxygen absorbed. The net respiratory minute volume[1] has not varied directly or inveresly with the circulatory minute volume. There is of course no doubt that the volume of blood flow is a function of metabolic rate, but it is equally clear that there are other factors of potent if subsidiary influence. A study of a series of normal adults such as this, shows that even with favorable and, in a sense, trained subjects—so that basal conditions were well maintained—and with earnest efforts to secure identical surroundings in successive experiments, the minute volume may vary widely in different subjects. Even on the same subject at different times the output of the heart per minute may vary as much as 30 per cent.

COMMENT

Our figures for the minute output of the heart and the output per beat are smaller than many appearing in the literature. This may be due in part to our insistence upon rest and fasting. Even so our figures lend support to the view that the output of the heart per beat is not fixed but variable, since an output of 60 to 70 cc. per beat is not enough to transport the large volume of oxygen required during strenuous exertion, even at very rapid heart rates. Observations bearing on this problem are reserved for a subsequent paper.

The significance of the variations in volume flow in Subject Bu. is not clear. As the broad physiological viewpoint of Haldane (1922) has emphasized, one object of changes in the volume of blood flow is to maintain the optimum condition of gas pressure in all parts of the body. Changes in blood flow without change in total metabolism suggests the influence of some other factor, or the redistribution of the blood in various parts of the body.

SUMMARY

In a series of normal adults at complete rest the volume of blood expelled by the heart has varied from 3,500 cc. per minute and 58 cc. per beat to 6,800 cc. per minute and 103 cc. per beat.

[1] The net respiratory minute volume has been calculated from the total amount of air expired per minute with an allowance of 130 cc. per respiration for the dead space.

In one individual, tested repeatedly over a period of one year, the circulatory minute volume varied only from 3,700 to 3,960 cc. In a second individual, during a period of two months the circulatory minute volume varied from 6,780 to 4,540 cc.

The significance of these findings is discussed. The oxygen and carbondioxide content of the arterial and of the "mixed venous" blood have been determined in the series of eleven adults, and the results are given.

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