STUDIES OF OXYGEN IN THE VENOUS BLOOD.

V. Determinations on Patients with Anemia.

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In the first four articles of this series (1–4) facts were discussed which indicate that the oxygen content of the venous blood depends on a number of factors: (1) the total oxygen-combining power, or the hemoglobin content of the blood; (2) the degree of oxygen saturation of the blood in the lungs; (3) variations in the metabolism of the tissues drained by the vein tapped, as compared with the metabolism of the rest of the body; (4) variations in the rate of blood flow through the tissues drained compared with the rest of the body; (5) variations in the minute volume of the heart.

In order to find the effect of one of these factors on the oxygen content of the venous blood, it is necessary to control the other factors or keep them constant.

In Papers II, III, and IV we studied in cardiac patients the effect of the fifth of the above factors. It was not possible to exclude completely the effects of the other four factors, but by choosing suitable subjects, *viz.* decompensated cardiac patients and normal controls, and by excluding the other factors as nearly as possible, or by correcting for them, we were able to observe with a certain degree of accuracy the effect of the cardiac output on the venous oxygen. In particular, variations in the hemoglobin content were corrected for by basing our conclusions not on the absolute value of the venous oxygen, but on the oxygen unsaturation, or the difference between the venous oxygen and the total oxygen capacity of the blood. The correctness of following this procedure in individuals with varying hemoglobin content was assumed rather than exactly proved.

This paper presents the proof in a study of the venous oxygen content and unsaturation in a series of patients in whom the hemoglobin varied over a wide range.

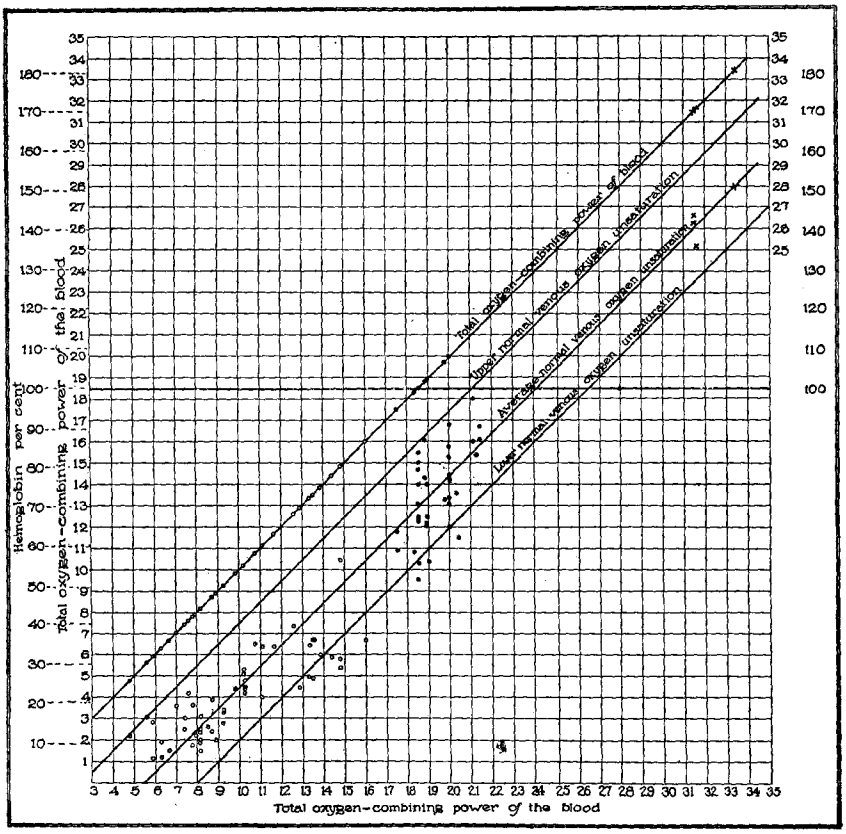
Nine patients with anemia and one patient with polycythemia[1] were selected for this purpose. The hemoglobin in these cases varied from 181 to 27 per cent. The oxygen-combining power of the blood varied consequently from 33.40 to 5.00 volumes per cent. The lungs were examined before each determination and did not show any pathological changes, which might influence the saturation of the blood. The blood samples were drawn at least 2 hours after a meal and after 10 minutes rest in bed. Nothing was found to indicate any abnormality in the circulation, apart from a slight increase in the pulse rate in some of the patients. The diuresis and the blood pressure were found to be normal.

The technique in drawing the blood samples was exactly the same as described in Paper I of this series. In determining the oxygen of the venous blood Van Slyke's method was used (5). The total oxygen-combining power of the blood was either determined directly—Van Slyke's method—or calculated from the hemoglobin determined by Haldane's method.

The results on the patients with anemia are given in Tables I to X. As a whole, the values of the oxygen in the venous blood increase proportionally with the increase in the hemoglobin, giving values for the oxygen unsaturation, which vary within the ordinary normal limits—2.5 and 8 volumes per cent. In a few instances the unsaturation has been between 8 and 10 volumes per cent. This was found only in patients in which hemoglobin had increased rather quickly from low values to about the normal. In other words, the amount of oxygen taken away from the blood during passage through the body capillaries in resting individuals is practically independent of the hemoglobin content of the blood. In order to make the relations more clear the results are presented in Text-fig. 1, where the abscissæ and the ordinates indicate oxygen-combining power in volumes per cent and hemoglobin in per cent. The corresponding percentages are also indicated, as calculated on Haldane's average, 18.5 per cent oxygen equalling 100 per cent hemoglobin. On the upper oblique line are the values for the total oxygen-combining power in each given instance

[1] The details on this patient will be published in the next number of this *Journal*, but the values for unsaturation are given in Text-fig. 1 of this paper.

and on the ordinate belonging to this point is indicated the value for the oxygen of the venous blood; the distance from this figure to the base-line gives the venous oxygen content, while the distance from the point to the upper oblique line measures the venous unsaturation.



TEXT-FIG. 1. Values for the total oxygen-combining power and the venous oxygen in individuals with different amounts of hemoglobin. The circles with light centers indicate values for anemic patients, the solid black circles values for normal individuals, and the crosses values for a polycythemic patient.

The values of the oxygen-combining power lie, of course, on a straight line which goes through the zero point at an angle of 45° with the base-line. If the oxygen unsaturation were absolutely constant the values for the oxygen of the venous blood would also lie on a

straight line, which would be parallel to and below the upper one. This is, however, not to be expected. Even in normal individuals, as previously shown, rather extensive variations occur. On the diagram the results reported in the present paper are combined with those obtained in a series of normal individuals and published in Paper I. The earlier figures cover the middle area between the anemic patients and the polycythemic patient reported below. The diagram shows that it was justifiable to use the oxygen unsaturation in order to exclude the influence of variations in the hemoglobin content of the blood. The variations in the oxygen unsaturation in these cases are probably due to small variations in one or several of the other previously named factors. Of these, oxygenation in the lungs is probably the most constant (in these patients), the minute volume and the local blood flow probably the most variable.

These results are of interest not only for the interpretation of oxygen determinations in general, but also for the understanding of the circulatory mechanism in patients with anemia.

The fact that the hemoglobin is the only bearer of oxygen from the lungs to the tissues has made it a question of moment in what way anemic patients are able to compensate for the decrease in oxygen-combining power of the blood. For a considerable period of time it was supposed that no compensation was necessary, for the reason that the total metabolism was considered to be lower in anemic patients. This theory was based on experiments on dogs by Bauer (6) and on conclusions from fatty degenerations in the organs of patients dying from anemia, the fat being considered the result of lack of oxygen. Experiments by Kraus (7) and others showed that the metabolism is not diminished in patients with anemia. This being the case, a compensatory mechanism for the lack of hemoglobin was thought necessary.

Three theories were put forward: (*a*) an increased oxygen capacity of the hemoglobin—increased "specific capacity" (Hoppe-Seyler (8), Bohr (9), and his pupils), (*b*) an increase in the blood flow, (*c*) an increased percentile consumption of the oxygen in the blood. After Butterfield (10), Barcroft and Morawitz (11), Masing and Siebeck (12), and von Reinbold (13), who proved the proportionality between the color index and the oxygen-combining power of the hemoglobin, the theory about the "specific oxygen capacity" is untenable.

From the experimental data in the literature it is impossible to decide between the other two theories. In some experiments the blood flow has been found increased (Kraus (14) and Plesch (15)). Other experiments are interpreted as showing increased consumption; for instance, experiments of Finkler (16). Morawitz and Roehmer, who have determined the oxygen in the venous blood in eighteen patients with anemia and one with polycythemia, interpret their results to indicate that both methods of compensation are used by the anemic organism.

In discussing the problem it is evidently necessary to distinguish between the resting and working organism. In a resting organism the rate of oxygen consumption is approximately a constant for each particular individual, and for different individuals within the same species it is constant except for variations caused by differences in the surface and weight of the body. The increase caused by exercise is, of course, dependent on the extent of the work. From the determination of the minute volume of the heart and the oxygen unsaturation of the venous blood, we know that the normal resting organism on the average uses 5.5 volumes per cent oxygen in the capillaries. The normal oxygen capacity of the blood being 18.5 volumes per cent, the normal individual consequently has 13 volumes per cent of unused oxygen in his veins. This amount of oxygen may be termed the reserve oxygen, and looked upon as analogous to the reserve force of the heart. When the organism for one reason or another needs more oxygen, or when the blood flow in the capillaries is slower than normally, the organism uses the reserve oxygen. Anemia is in this respect simply a condition where the amount of reserve of the blood is diminished in the same degree as the hemoglobin; the opposite takes place in polycythemia. From a purely mechanical point of view it is clear that in a resting individual no compensation is needed until the hemoglobin has fallen so low that all the reserve oxygen is used in each circulation. This occurs when the oxygen-combining power of the blood has fallen to 5.5 volumes per cent, which corresponds to 30 per cent hemoglobin. Above this value no compensation seems necessary; below this the organism must compensate for the lack of reserve oxygen storage in the blood, and this can be done only in one way, by an increased output of the heart.

The results of the determination in this paper show that this viewpoint is as a whole correct. The last residuum of the oxygen in the blood—the last part of the reserve oxygen—is taken away by the body cells in resting individuals just as easily as the first part. This, of course, is of great importance for the body, especially for the heart.

Clinical experience agrees with the experimental results in this paper; a bodily and mentally resting anemic patient usually does not show any marked reaction from the circulation, until the hemoglobin percentage has fallen below about 30. In patients whose hemoglobin is below that value we usually find an increased pulse rate and palpitation of the heart even at rest.

SUMMARY.

1. Determinations of the oxygen content and the oxygen unsaturation of the venous blood have been performed on patients with varying amounts of hemoglobin.

2. The oxygen unsaturation of the venous blood is independent of the oxygen capacity, unless the latter is reduced below the normal value for oxygen unsaturation (about 5 volumes per cent). In a polycythemic patient,[1] for example, with 33.4 volumes per cent oxygen capacity (181 per cent hemoglobin), the venous oxygen content was 28 volumes per cent, giving an unsaturation of 5.4 volumes per cent. Similarly, in an anemic patient with only 6.7 volumes per cent oxygen capacity (36 per cent hemoglobin), the venous oxygen was 1.5, giving an unsaturation of 5.2 volumes per cent. This means that the tissues extract from the blood all the oxygen they need with apparently equal readiness, regardless of whether the extraction leaves a great oxygen reserve in the blood as in polycythemia, or practically no reserve as in anemia.

3. The results seem to show that the resting organism does not increase its circulation until all the reserve oxygen is used. This means that the resting anemic organism does not need or use any compensation for its anemia until the hemoglobin has sunk below 30 per cent. Below that value the organism increases the blood flow in order to secure to the tissues the normal amount of oxygen.

TABLE I.

Oxygen Unsaturation of the Venous Blood in a Patient with Severe Anemia.

Housewife, age 38 years.

Determination No.	Date.	Oxygen content of venous blood.			Hemoglobin (Haldane's method).	Calculated oxygen capacity (a).	Oxygen unsaturation (a-v).	Pulse.	Respirations per min.
		Sample 1.	Sample 2.	Average (v).					
	1918	*vol. per cent*	*vol. per cent*	*vol. per cent*	*per cent*	*vol. per cent*	*vol. per cent*		
1	July 12	4.40	4.00	4.20	41	7.58	3.38	98	22
2	" 18	3.54	3.64	3.59	38	7.03	3.44	96	20
3	Aug. 3	3.04		3.04	40	7.41	4.37	96	22
4	" 14	1.62	1.34	1.48	44	8.15	6.67	92	22
5	" 22	2.17	2.53	2.35	44	8.15	5.80	90	20
6	" 25	3.08	3.08	3.08	44	8.15	5.07	90	22
7	Sept. 9	2.53		2.53	44	8.15	5.62	90	22
8	" 14	1.75	2.21	1.98	44	8.15	6.17	92	20
9	" 21	1.74	2.20	1.97	48	8.88	6.91	86	20
10	Oct. 5	3.96	3.96	3.96	50	9.25	5.29	90	18
11	" 19	4.01	4.93	4.47	53	9.82	5.35	90	16

TABLE II.

Oxygen Unsaturation of the Venous Blood in a Patient with Severe Anemia.

Housewife, age 41 years.

Determination No.	Date.	Oxygen content of venous blood.			Hemoglobin (Haldane's method).	Calculated oxygen capacity (a).	Oxygen unsaturation (a-v .	Pulse.	Respirations per min.
		Sample 1.	Sample 2.	Average (v).					
	1918	*vol. per cent*	*vol. per cent*	*vol. per cent*	*per cent*	*vol. per cent*	*vol. per cent*		
1	Aug. 29	4.63	5.54	5.09	55	10.20	5.11	66	18
2	Sept. 3	6.46	6.46	6.46	75	13.87	7.40	60	16

TABLE III.

Oxygen Unsaturation of the Venous Blood in a Patient with Severe Anemia from Hematemesis.

Male, engineer, age 20 years.

Determination No.	Date.	Oxygen content of venous blood.			Hemoglobin (Haldane's method).	Calculated oxygen capacity (a).	Oxygen unsaturation (a–v).	Pulse.	Respirations per min.
		Sample 1.	Sample 2.	Average (v).					
	1918	*vol. per cent*	*vol. per cent*	*vol. per cent*	*per cent*	*vol. per cent*	*vol. per cent*		
1	Oct. 29	1.19		1.19	34	6.30	5.11	72	24
2	Nov. 5	1.27	1.05	1.16	32	5.93	4.77	80	18
3	" 14	2.20	2.20	2.20	43	7.96	5.76	62	18
4	Dec. 3	1.70	2.15	1.93	44	8.15	6.22	84	18
5	" 15	3.32		3.32	50	9.25	5.93	90	22

TABLE IV.

Oxygen Unsaturation of the Venous Blood in a Patient with Severe Anemia from Metrorrhagia.

Housewife, age 47 years.

Determination No.	Date.	Oxygen content of venous blood.			Hemoglobin (Haldane's method).	Calculated oxygen capacity (a).	Oxygen unsaturation (a–v).	Pulse.	Respirations per min.
		Sample 1.	Sample 2.	Average (v).					
	1918	*vol. per cent*	*vol. per cent*	*vol. per cent*	*per cent*	*vol. per cent*	*vol. per cent*		
1	Aug. 3	2.82		2.82	50	9.25	6.43	86	26
2	" 13	4.86	5.66	5.26	55	10.17	4.91	86	24
3	" 19	3.95	3.95	3.95	60	11.09	7.14	88	24
4	" 27	5.84	6.76	6.40	63	11.65	5.25	86	20
5	Sept. 9	6.68	6.68	6.68	73	13.50	6.82	86	20

TABLE V.

Oxygen Unsaturation of the Venous Blood in a Patient with Severe Anemia from Hemorrhagic Colitis.

Male, workman, age 33 years.

Determination No.	Date.	Oxygen content of venous blood.			Hemoglobin (Haldane's method).	Calculated oxygen capacity (a).	Oxygen unsaturation (a-v).	Pulse.	Respirations per min.
		Sample 1.	Sample 2.	Average (v).					
	1918	*vol. per cent*	*vol. per cent*	*vol. per cent*	*per cent*	*vol. per cent*	*vol. per cent*		
1	Sept. 19	1.73	1.73	1.73	42	7.78	6.05	76	24
2	" 25	4.54		4.54	55	10.27	5.78	80	24
3	Oct. 8	4.75	4.99	4.87	55	10.27	5.40	68	20
4	" 31	5.92	5.92	5.92	75	13.87	7.95	76	20

TABLE VI.

Oxygen Unsaturation of the Venous Blood in a Patient with Severe Anemia from Miscarriage.

Housewife, age 26 years.

Determination No.	Date.	Oxygen content of venous blood.			Hemoglobin (Haldane's method).	Calculated oxygen capacity (a).	Oxygen unsaturation (a-v).	Pulse.	Respirations per min.
		Sample 1.	Sample 2.	Average (v).					
	1918	*vol. per cent*	*vol. per cent*	*vol. per cent*	*per cent*	*vol. per cent*	*vol. per cent*		
1	Nov. 19	2.21	2.21	2.21	26	4.81	2.60	100	24
2	Dec. 4	3.05		3.05	30	5.55	2.50	112	24
3	" 8	3.87	3.87	3.87	43	8.70	4.93	100	26

TABLE VII.

Oxygen Unsaturation of the Venous Blood in a Patient with Severe Anemia from Hematemesis.

Male, carpenter, age 39 years.

Determination No.	Date.	Oxygen content of venous blood.			Hemoglobin (Haldane's method).	Calculated oxygen capacity (a).	Oxygen unsaturation (a–v).	Pulse.	Respirations per min.
		Sample 1.	Sample 2.	Average (v).					
	1918	*vol. per cent*	*vol. per cent*	*vol. per cent*	*per cent*	*vol. per cent*	*vol. per cent*		
1	Sept. 17	3.56	3.56	3.56	42	7.78	4.22	60	15
2	" 24	3.11	3.57	3.34	50	9.25	5.91	60	14
3	Oct. 3	4.07	4.97	4.52	55	10.27	5.75	60	14
4	" 12	4.04	4.86	4.45	55	10.27	5.82	60	14
5	Nov. 11	4.22		4.22	55	10.27	6.05	72	14
6	" 14	6.30	6.70	6.50	58	10.73	4.23	60	15

TABLE VIII.

Oxygen Unsaturation of the Venous Blood in a Patient with Severe Anemia.

Housewife, age 44 years.

Determination No.	Date.	Oxygen content of venous blood.			Hemoglobin (Haldane's method).	Calculated oxygen capacity (a).	Oxygen unsaturation (a–v).	Pulse.	Respirations per min.
		Sample 1.	Sample 2.	Average (v).					
	1918	*vol. per cent*	*vol. per cent*	*vol. per cent*	*per cent*	*vol. per cent*	*vol. per cent*		
1	Nov. 14	2.20	3.10	2.65	46	8.52	5.97	80	20
2	Dec. 29	10.55	10.35	10.45	80	14.80	4.35	76	19

TABLE IX.

Oxygen Unsaturation of the Venous Blood in a Patient with Pernicious Anemia.

Male, porter, age 44 years.

Determination No.	Date.	Oxygen content of venous blood.			Hemoglobin (Haldane's method).	Calculated oxygen capacity (a).	Oxygen unsaturation (a-v).	Pulse.	Respirations per min.
		Sample 1.	Sample 2.	Average (v).					
	1918	*vol. per cent*	*vol. per cent*	*vol. per cent*	*per cent*	*vol. per cent*	*vol. per cent*		
1	Aug. 13	7.46	7.38	7.42	68	12.57	5.15	72	22
2	" 21	4.90	4.90	4.90	73	13.50	8.60	84	24
3	" 28	5.86	5.96	5.92	78	14.42	8.50	82	22
4	Sept. 3	5.82	5.82	5.82	80	14.78	8.86	82	20
5	" 10	5.42	5.42	5.42	80	14.78	9.36	72	18
6	Oct. 14	6.70		6.70	87	16.03	9.33	70	18
7	Dec. 14	9.85	10.41	10.13	93	17.20	7.07	80	16

TABLE X.

Oxygen Unsaturation of the Venous Blood in a Patient with Pernicious Anemia.

Male, cab driver, age 53 years.

Determination No.	Date.	Oxygen content of venous blood.			Hemoglobin (Haldane's method).	Calculated oxygen capacity (a).	Oxygen unsaturation (a-v).	Pulse.	Respirations per min.
		Sample 1.	Sample 2.	Average (v).					
	1918	*vol. per cent*	*vol. per cent*	*vol. per cent*	*per cent*	*vol. per cent*	*vol. per cent*		
1	Aug. 3	2.82	2.82	2.82	32	5.92	3.10	70	30
2	" 13	2.61	2.43	2.52	40	7.41	4.89	66	20
3	" 25	1.63	1.37	1.50	36	6.67	5.17	68	20
4	Sept. 3	2.06		2.06	27	5.00	2.94	84	24
5	" 10	2.17	1.69	1.93	34	6.30	4.37	70	20
6	" 23	2.65	2.19	2.42	47	8.70	6.28	66	20
7	Oct. 5	6.31	6.59	6.40	60	11.09	4.69	60	20
8	" 19	4.46		4.46	70	12.94	8.48	60	20
9	Nov. 18	4.98	4.90	4.94	72	13.31	8.37	64	18
10	Dec. 16	7.17	6.27	6.72	74	13.58	6.86	60	20

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