

STUDIES IN MUSCULAR ACTIVITY.

VI. Response of several individuals to a fixed task.

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Introduction.

EXPERIENCE teaches that individuals are not equal in physical ability. From prehistoric times contests in war and in sport have given convincing evidence of this fact. The question as to how one individual can surpass another in capacity and in skill is at least partially susceptible of analysis in the laboratory. This has been demonstrated by Hill and his associates⁽¹⁾, and by many others.

There remain, however, many unanswered questions raised by the rearguard runner. Does he fall behind because of inadequate physical endowment or because of insufficient training? His coach may ascribe his failure to his musculature, to his heart, to his "wind" or to his "guts." Since the empirical observations of the runner and his coach certainly have an objective foundation, it has been our aim to seek a basis for these ideas in physiological and physico-chemical facts.

Experimental.

Ten men, normal but not in active training, have performed the same task under controlled conditions. Each came to the laboratory without breakfast and rested for 30 minutes on a bed. With the subject in this state, respiratory and pulse rates were observed, expired air was collected in a 100 litre gasometer over a 10 minute period and then samples of alveolar air and "virtual venous" air were collected. Gas samples were analysed on the Haldane apparatus.

The method used for estimating blood flow is in basic principle that of Christiansen, Douglas and Haldane⁽²⁾. Y. Henderson and Prince⁽³⁾ modified it in important details and introduced the term "virtual venous" air. Field, Bock, Gildea and Lathrop⁽⁴⁾ added further modifications. It is now necessary to modify it still further, for recent determinations⁽⁵⁾ indicate that Haldane-Priestley samples collected in rest at the end of expiration have, without correction, the same pressure of carbonic acid as that in arterial

blood. Accordingly the carbonic acid pressures of alveolar air and of "virtual venous" air are applied directly to the carbonic acid dissociated curve of oxygenated whole blood. The difference between the indicated contents, diminished by 0.3 volume p.c. on the assumption that arterial blood is 95 p.c. saturated, represents carbon dioxide transport in volumes p.c. Rate of dioxide output divided by rate of transport gives rate of blood flow.

Of course this method for determining rate of blood flow, being indirect, is unsatisfactory. Yet many arguments of the kind commonly advanced for indirect methods may be presented in its defence. It yields results, particularly in exercise, of the same order of magnitude as those obtained by other methods; results in certain pathological conditions are qualitatively similar to blood velocity determinations¹; repeated observations on a given individual in the same state give good checks; wholly improbable results are not obtained. So long as the evidence for the absolute accuracy of this and other indirect methods is of such a character, estimates of rate of blood flow must be accepted with reserve.

When all these observations were completed, about 65 c.c. of venous blood was drawn without stasis: 5 c.c. was set aside for serum calcium determination and the remainder was treated with heparin. Determinations made on blood will be described below.

Within an hour of the time resting blood was drawn, the subject, still fasting, began exercise. This consisted in running for 20 minutes on a treadmill, motor-driven in a horizontal plane at a rate of 9.3 km. per hour. Outside air was inspired through a large-size Henderson-Haggard valve (6) and alveolar air samples were collected automatically, since it is not practicable in exercise of this character to use the heavy system of valves suitable in rest or in exercise on the ergometer. The subject breathed continuously through the mouthpiece from the start until the 9th minute, and again from the 12th through the 17th minute. Other details, such as the method of collecting "virtual venous" air in exercise of this sort, are given by Hochrein, Talbott, Dill and Henderson (7).

Expired air was measured in a 600 litre gasometer, and six samples were taken by the mixing chamber method as described by Bock, Dill and Talbott (8). Pulse rate was recorded by a cardiometer which will be described by Paul S. Bauer, its designer, in detail at another time. It resembles in many particulars the instrument of Boas (9). The nature

¹ Reference may be made to the series of papers by H. L. Blumgart and Soma Weiss, *J. Clin. Inv.* 4. 15 (1927) *et seq.*, in which velocity was measured by injecting radioactive material and detecting its arrival at a distant point. The recent velocity measurements by Soma Weiss, G. P. Robb and H. L. Blumgart, *Amer. Heart J.* 4. 1 (1929), involved use of the effect of histamine on the minute vessels and gave similar results. W. O. Thompson, J. M. Alper and P. K. Thompson, *J. Clin. Inv.* 5. 605 (1928), have demonstrated posture effects on velocity from ankle to arm by the dye injection method; and A. V. Bock and associates, in an investigation in the course of publication, have obtained similar results with the histamine method. All the above experiments on blood velocity agree qualitatively with our determinations of rate of blood flow.

of other observations made during exercise will be disclosed in tables of data.

After running for 20 minutes the subject jumped on to the bed, and another 65 c.c. portion of venous blood was withdrawn. A sample of blood obtained within 1 minute of cessation of work of this intensity represents blood circulating during work in nearly every respect, except for different contents of oxygen and of carbonic acid. This is borne out by unpublished observations made in this laboratory on oxygen capacity, carbonic acid capacity and lactic acid content of blood taken during the course of, and within 1 minute of, cessation of exercise on the bicycle ergometer.

Each of the 60 c.c. portions of blood treated with heparin was kept in ice water until equilibration. Two 5 c.c. portions were removed for determination of lactic acid and oxygen combining capacity. The remainder was divided into a 45 c.c. and a 5 c.c. portion and equilibrated at 37.5° with sufficient oxygen for saturation at carbon dioxide pressures of about 40 and 80 mm. respectively. After 15 minutes' equilibration, blood was drawn into sampling tubes for carbon dioxide determination and about 40 c.c. of the larger portion, without exposure to air, were divided between two calibrated centrifuge tubes of 20 c.c. capacity. This technique and other determinations carried out on serum and cells have been described in detail by Dill, Talbott, Edwards and Oberg⁽¹⁰⁾. The only new method used was Van Slyke's micro total nitrogen method⁽¹¹⁾. Single 10 c.c. portions of equilibrated serum and cells were dried to constant weight for total solid determination, and then ashed and used for sodium and potassium determination. Previous determinations of sodium and of potassium carried out in duplicate, using the same method⁽¹⁰⁾, usually agreed within 1 mEq. per litre. In these experiments determinations were not carried out in duplicate, but rest and work serum and cells were analysed side by side, and it is likely that a difference between rest and work greater than 1 mEq. per litre is significant.

Table I records ventilation, pulse rate, respiratory rate, composition of expired air, metabolic rate (M.R.) and respiratory quotient (R.Q.). Composition of alveolar air and carbon dioxide pressure in gas samples equilibrated *in vivo* with oxygenated venous blood are shown in Table II. Four samples of each were taken in rest, and only the averages of these are shown. Alveolar samples were collected at about the 4th, 8th, 13th and 17th minutes in work, and each determination is given in order to show change of state if such occurred. Two "virtual venous" samples

TABLE I. Metabolic rate, respiration, and pulse.

Time (min.)	Remarks	Total ventilation (l. per min.)	Composition of expired air		Oxygen used (c.c. per min.)	Respiratory quotient	Pulse rate	Respiratory rate
			CO ₂ (p.c.)	O ₂ (p.c.)				
0	Work begun	5.38	3.77	16.53	246	0.82	62	10
4-5		41	4.43	15.95	2100	0.86	—	—
6-7		41	4.44	15.99	2080	0.87	138	21
12-13		48	4.17	16.46	2180	0.91	140	24
14-15		50	4.10	16.50	2260	0.90	135	22
16-17		45	4.02	16.53	2020	0.89	138	22
0	P. F. P. Basal	7.90	2.65	17.58	277	0.75*	68	15
0	Work begun							
2-3		45	4.12	16.64	2180	0.95	—	37
4-5		52	4.09	16.89	2100	1.01	172	38
6-7		53	4.06	16.91	2130	1.00	164	44
14-15		67	3.81	17.10	2570	0.98	166	46
16-17		62	3.78	17.15	2350	0.99	164	45
17-18		62	3.72	17.01	2470	0.93	—	47
0	A. A. McC. Basal	5.23	3.23	16.77	276	0.72*	50	15
0	Work begun							
3-4		65	4.23	16.55	2880	0.95	—	36
4-5		64	4.35	16.43	2900	0.95	—	—
6-7		59	4.29	16.22	2830	0.88	—	—
13-14		59	4.27	16.09	2950	0.85	—	34
15-16		59	4.45	15.88	3080	0.85	132	—
17-18		58	4.42	16.05	2900	0.88	132	36
0	J. H. T. Basal	5.89	3.33	16.94	242	0.80	64	9
0	Work begun							
3-4		50	3.84	16.60	2220	0.85	153	—
5-6		52	3.75	16.90	2130	0.90	153	25
7-8		53	3.72	17.03	2100	0.93	153	—
11-12		54	3.70	17.04	2150	0.93	153	—
13-14		52	3.76	16.91	2120	0.91	153	37
16-17		53	3.57	17.15	2020	0.92	153	36
0	W. C. Basal	7.23	3.35	16.90	305	0.79	69	15
0	Work begun							
3-4		63	4.68	16.45	2790	1.04	174	41
5-6		71	4.06	17.06	2720	1.05	168	—
7-8		70	3.91	16.90	2850	0.95	174	—
13-14		74	3.93	17.06	2850	1.01	174	42
15-16		80	3.63	17.38	2830	1.02	180	—
16-17		82	3.45	17.60	2710	1.03	176	49
0	O. S. L. Basal	5.94	3.39	16.96	246	0.81	71	12
0	Work begun							
2-3		44	4.93	15.63	2380	0.91	144	14
4-5		45	5.19	15.28	2600	0.90	146	—
7-8		46	5.13	15.48	2560	0.92	160	12
14-15		49	4.86	15.71	2610	0.91	163	15
15-16		50	4.74	15.95	2530	0.93	156	18
16-17		51	4.69	16.04	2520	0.94	159	19

* Probably a fallacious value due to abnormal breathing.

TABLE I. Metabolic rate, respiration, and pulse (continued).

Time (min.)	Remarks	Total ventilation (l. per min.)	Composition of expired air		Oxygen used (c.c. per min.)	Respiratory quotient	Pulse rate	Respiratory rate
			CO ₂ (p.c.)	O ₂ (p.c.)				
	J. L. S. Basal	6.12	3.22	17.40	222	0.88*	69	14
0	Work begun							
3-4		53	4.59	16.22	2520	0.96	—	25
5-6		55	4.30	16.51	2450	0.95	—	—
7-8		53	4.36	16.39	2460	0.94	—	29
11-12		54	4.34	16.40	2470	0.94	—	30
14-15		53	4.25	16.41	2420	0.92	—	—
17-18		53	4.12	16.47	2390	0.90	—	30
	H. T. E. Basal	4.15	4.32	15.66	232	0.78	66	10
0	Work begun							
3-4		35	5.24	14.91	2180	0.84	153	15
5-6		39	4.80	16.95	1950	0.95	154	—
7-8		42	4.77	15.75	2220	0.90	156	19
12-13		46	4.50	16.15	2210	0.92	154	21
14-15		44	4.62	15.90	2260	0.90	156	—
16-17		43	4.69	15.58	2380	0.84	—	20
	A. V. B. Basal	4.90	4.02	16.26	237	0.82	61	5
0	Work begun							
2-3		47	4.03	16.41	2190	0.86	—	21
5-6		52	4.02	16.80	2170	0.96	142	—
7-8		55	3.96	16.60	2440	0.88	144	32
11-12		60	3.87	16.92	2430	0.95	144	33
14-15		57	3.72	16.98	2290	0.92	—	—
17-18		56	3.75	16.78	2380	0.87	142	33
	W. J. G. Basal	5.02	3.60	16.83	212	0.83	62	14
0	Work begun							
2-3		55	4.16	16.78	2280	1.00	156	27
3-4		55	4.12	16.75	2290	0.97	170	—
7-8		55	3.92	16.90	2230	0.96	168	31
12-13		55	3.82	16.82	2300	0.91	168	30
16-17		56	3.99	16.80	2340	0.95	169	31

* Probably a fallacious value due to abnormal breathing.

TABLE II. Determination of blood flow.

Remarks	Respiratory quotient	Alveolar air		Virtual venous air (pCO ₂ mm. Hg)	CO ₂ transport (mEq. per l. blood)	O ₂ transport (mEq. per l. blood)	O ₂ saturation of blood (p.c.)	Blood flow (l. per min.)
		(pCO ₂ mm. Hg)	(pO ₂ mm. Hg)					
D. B. D. Basal	0.82	40.2	105	47.6	1.35	1.65	75	6.7
Work	0.89	42.0	106	—	—	—	—	—
	0.94	40.2	110	65.4	4.44	4.99	38	18.9
	0.92	39.4	110	—	—	—	—	—
	0.92	40.5	109	62.7	3.95	4.44	44	21.3
Average Δ	+0.10	+ 0.3	+ 4	+16.5	+2.85	+3.07	-34	+13.4
P. F. P. Basal	0.82	36.3	106	43.3	1.30	1.73	75	7.1
Work	0.96	39.8	108	71.5	4.72	4.82	41	21.1
	0.97	37.4	111	—	—	—	—	—
	0.88	36.8	109	66.8	5.12	5.22	37	19.4
Average Δ	+0.12	+ 1.7	+ 3	+25.8	+3.62	+3.29	-36	+13.1

TABLE II. Determination of blood flow (continued).

Remarks	Alveolar air			Virtual venous air (pCO ₂ mm. Hg)	CO ₂ trans- port (mEq. per l. blood)	O ₂ trans- port (mEq. per l. blood)	O ₂ satura- tion of venous blood (p.c.)	Blood flow (l. per min.)
	Respira- tory quotient	(pCO ₂ mm. Hg)	(pO ₂ mm. Hg)					
A. A. McC. Basal	0.81	38.0	103	46.1	1.53	2.12	69	5.9
Work	0.88	42.3	102	—	—	—	—	—
	0.81	42.1	99	67.0	4.23	4.75	43	27.3
	0.83	42.0	100	—	—	—	—	—
	0.87	40.3	103	69.7	5.00	5.61	34	23.1
Average Δ	+0.04	+ 3.7	- 2	+22.3	+3.09	+3.06	-31	+19.3
J. H. T. Basal	0.80	39.5	103	45.8	1.12	1.40	80	8.8
Work	0.86	37.2	112	—	—	—	—	—
	0.95	35.5	112	62.6	4.81	5.28	46	17.9
	0.92	34.3	112	—	—	—	—	—
	0.85	34.3	110	60.1	4.63	5.09	48	18.7
Average Δ	+0.09	- 4.2	+ 8	+15.6	+3.60	+3.79	-33	+ 9.5
W. C. Basal	1.02	35.6	113	45.0	1.65	2.09	72	6.7
Work	1.05	45.2	105	—	—	—	—	—
	0.99	37.3	110	75.1	5.48	5.32	35	24.4
	1.00	32.7	116	72.9	—	—	—	—
	1.01	33.5	115	—	5.66	5.50	33	21.8
Average Δ	-0.01	+ 1.6	- 2	+29.0	+3.92	+3.32	-38	+16.4
O. S. L. Basal	1.11	38.2	114	45.0	1.12	1.38	79	8.0
Work	0.84	42.9	101	—	—	—	—	—
	0.87	45.4	99	67.8	3.64	3.96	52	28.8
	0.86	43.4	102	—	—	—	—	—
	0.87	42.1	103	66.3	4.00	4.35	48	26.3
Average Δ	-0.25	+ 5.2	- 13	+22.1	+2.70	+2.78	-29	+19.6
J. L. S. Basal	1.06	39.3	111	46.6	1.44	1.63	78	6.0
Work	0.94	42.0	106	—	—	—	—	—
	1.07	40.6	104	70.9	5.00	5.38	41	20.7
	0.92	39.7	107	—	—	—	—	—
	0.92	39.7	107	67.7	4.76	5.12	44	20.8
Average Δ	-0.11	+ 1.2	- 5	+22.7	+3.44	+3.62	-36	+14.8
H. T. E. Basal	0.72	40.3	98	46.8	1.15	1.47	78	7.4
Work	0.78	47.0	94	—	—	—	—	—
	0.61	43.2	87	69.7	4.22	4.74	44	21.2
	0.85	41.0	103	—	—	—	—	—
	0.81	42.1	100	69.3	4.42	4.96	42	20.4
Average Δ	+0.04	+ 3.0	- 2	+22.7	+3.17	+3.38	-35	+13.4
A. V. B. Basal	0.87	38.1	100	45.9	1.39	1.70	76	6.3
Work	0.88	38.4	102	—	—	—	—	—
	0.87	38.0	102	63.0	4.59	4.99	45	20.7
	0.88	34.7	106	—	—	—	—	—
	0.86	34.7	105	60.3	4.86	5.28	42	19.5
Average Δ	0.00	- 1.7	+ 4	+15.8	+3.34	+3.44	-33	+13.8
W. J. G. Basal	1.04	43.7	108	49.5	1.04	1.24	82	7.8
Work	0.90	38.6	109	—	—	—	—	—
	0.94	37.8	111	66.2	5.16	5.43	43	19.1
	0.92	35.7	112	—	—	—	—	—
	0.88	36.9	110	59.7	4.55	4.79	49	21.6
Average Δ	-0.13	- 6.5	+ 1	+13.6	+3.82	+3.87	-36	+12.5

were collected during the 9th to 12th minutes, and two more during the 18th to 20th. The average of each pair is given. Values for carbon dioxide transport and rate of blood flow, calculated from the data of Tables I and II, are also given in Table II. Experimental observations on blood equilibrated with oxygen and carbon dioxide are given in Table III.

Under the conditions of our experiments it was not practicable to secure arterial blood nor to equilibrate venous blood at precisely the carbonic acid pressure of arterial blood. From our knowledge of shift of anions and water between cells and plasma with change in acidity and from the present experimental observations, it is possible to recalculate the data to a basis more convenient for comparison.

Thus it is possible to recalculate to the basis of (*a*) a given pH_s value; (*b*) a given carbonic acid pressure, say 40 mm. Hg; (*c*) the estimated carbonic pressure of arterial blood; or (*d*) the estimated carbonic acid pressure of mixed venous blood.

Consideration of these procedures brings to mind the discussion by L. J. Henderson (12) of corresponding states. Any attempt to bring two or more individuals, or even specimens of their blood, to the same state in all probability will fail because of the interdependence of the variables involved. When a given variable has been brought to a common value others will be disturbed. This is well illustrated in the present case. Thus we may bring all specimens of blood to the same pH_s value for rest and work. Calculated values for pH of arterial serum in rest and work are shown in Table IV. These calculations involve the assumptions that

TABLE IV. pH of arterial serum in rest and at the end of work.

Subject	pH_s		ΔpH_s	Ventilation per kg. body weight (litres)
	Rest	Work		
D. B. D.	7.42	7.39	-0.03	0.58
P. F. P.	7.44	7.32	-0.12	0.80
A. A. McC.	7.42	7.37	-0.05	0.72
J. H. T.	7.40	7.44	+0.04	0.67
W. C.	7.44	7.29	-0.15	1.19
O. S. L.	7.41	7.31	-0.10	0.67
J. L. S.	7.39	7.37	-0.02	0.72
H. T. E.	7.39	7.30	-0.09	0.59
A. V. B.	7.40	7.40	0.0	0.70
W. J. G.	7.36	7.38	+0.02	0.81
Average...	7.41	7.36	-0.05	0.75

arterial blood is 95 p.c. saturated in work of this character, and that alveolar carbon dioxide pressure measures accurately arterial carbon

dioxide pressure. Arterial punctures in exercise reported by Dill, Laurence, Hurxthal and Bock⁽¹³⁾ fully justify these assumptions when one is considering the average of a series of observations on the ergometer but such general agreement does not ensure that every individual observation is correct. The values in Table IV show clearly that, on the average, there is a decrease in pH of arterial serum of about 0.05. However, it is equally clear that some individuals show slight change and others large change in pH_s . This variation as well as related physiological changes would be masked by comparing properties of blood in rest and work at a common pH_s value.

TABLE V. Carbon dioxide pressure in alveolar air in rest and work.

Subject	Rest (mm. Hg)	Work		ΔpCO_2 from rest to end of work (mm. Hg)
		Average (mm. Hg)	End of work (mm. Hg)	
D. B. D.	40.2	40.5	40.5	+0.3
P. F. P.	36.3	38.0	36.8	+0.5
A. A. McC.	38.0	41.7	40.3	+2.3
J. H. T.	39.2	37.4	37.1	-2.1
W. C.	36.4	37.3	33.5	-2.9
O. S. L.	38.2	43.4	42.1	+3.9
J. L. S.	39.3	40.5	39.7	+0.4
H. T. E.	40.3	43.4	42.1	+1.8
A. V. B.	38.1	36.4	34.7	-3.4
W. J. G.	43.7	37.2	36.9	-6.8
Average...	39.0	39.6	38.4	-0.6
Median ...	38.7	39.7	38.2	+0.3

Table V has been compiled in order to test the second method of recalculation suggested above. Two columns are given for work. One contains an average of all four samples taken during work and the other gives values for the last work sample only. It appears that in exercise of this character (*a*) there is not usually much change in alveolar pCO_2 from rest to work nor during progress of work, and (*b*) the changes which do occur have no distinct relation to degree of lactic acid accumulation. The evidence for the latter statement will be given later.

Accordingly this method of recalculation was finally decided upon, viz. on the basis of a carbonic acid pressure of 40 mm. Hg. While open to some objection, it involves no doubtful assumptions, it is simple and it gives values at least approximately the same as if arterial blood had been used; in short, it gives values approximately of the order of corresponding states. The recalculations for serum are given in Table VI and for whole blood in Table VII.

TABLE VI. Electrolytes of true plasma at a carbonic acid pressure of 40 mm. Hg. Concentrations are expressed in mEq. per litre of serum, excepting hydrogen ion.

Subject	(Total CO ₂)	pH	Serum vol. (p.c.)	(HCO ₃) ⁻ (Lactate) ⁻ (Cl) ⁻ (HPO ₄) ⁻ + (H ₂ PO ₄) ⁻ (Protein-ate) ⁻	Σ anions	Σ cations*
D. B. D. Rest	27.20	7.42	58.5	25.96 1.0 104.0 2.3 17.4	150.7	147.5
Work	25.62	7.40	56.1	24.38 1.8 104.4 2.6 19.5	152.7	148.8
Δ	-1.58	-0.02	-2.4	-1.58 +0.8 +0.4 +0.3 +2.1	+2.0	+1.3
P. F. P. Rest	26.57	7.41	54.3	25.33 1.1 104.4 2.2 17.1	150.1	147.3
Work	20.68	7.30	52.2	19.44 5.8 105.2 2.6 18.0	151.0	151.6
Δ	-5.89	-0.11	-2.1	-5.89 +4.7 +0.8 +0.4 +0.9	+0.9	+4.3
J. H. T. Rest	25.58	7.40	53.9	24.34 1.6 107.2 1.8 16.7	151.6	148.6
Work	25.24	7.39	52.3	24.00 2.1 107.6 2.1 17.4	153.2	150.3
Δ	-0.34	-0.01	-1.6	-0.34 +0.5 +0.4 +0.3 +0.7	+1.6	+1.7
W. C. Rest	26.08	7.40	55.7	24.84 1.3 105.7 2.5 17.5	151.9	144.2†
Work	18.12	7.24	54.3	16.88 7.2 106.2 3.3 17.5	151.1	150.4
Δ	-7.96	-0.16	-1.4	-7.96 +5.9 +0.5 +0.8 0.0	-0.8	
O. S. L. Rest	26.08	7.40	58.2	24.84 1.3 108.7 2.2 17.4	154.4	149.6
Work	22.59	7.34	55.2	21.35 3.7 108.2 2.7 18.5	154.4	152.1
Δ	-3.49	-0.06	-3.0	-3.49 +2.4 +0.5 +0.5 +1.1	-0.0	+2.5
J. L. S. Rest	25.13	7.39	51.8	23.89 1.3 106.6 2.1 16.8	150.7	151.8
Work	23.96	7.37	50.5	22.72 2.1 107.3 2.8 17.7	152.6	146.9†
Δ	-1.17	-0.02	-1.3	-1.17 +0.8 +0.7 +0.7 +0.9	+1.9	
H. T. E. Rest	25.67	7.40	56.0	24.43 1.2 106.6 2.4 16.9	151.5	149.9
Work	21.15	7.31	53.3	19.91 3.8 107.6 2.8 18.0	152.1	153.7
Δ	-4.52	-0.09	-2.7	-4.52 +2.6 +1.0 +0.4 +1.1	+0.6	+3.8
A. V. B. Rest	25.19	7.39	56.3	23.95 1.1 106.4 2.3 15.8	149.6	149.3
Work	23.81	7.36	51.2	22.57 3.4 104.8 2.6 18.8	152.2	150.0
Δ	-1.38	-0.03	-5.1	-1.38 +2.3 +1.6 +0.3 +3.0	+2.6	+0.7
W. J. G. Rest	25.31	7.39	55.9	24.07 1.1 107.6 1.9 15.2	149.9	150.3
Work	23.11	7.35	52.6	21.87 3.4 108.0 2.6 16.9	152.8	153.5
Δ	-2.20	-0.04	-3.3	-2.20 +2.3 +0.4 +0.7 +1.7	+2.9	+3.2
Average, Rest	25.87	7.40	55.6	24.63 1.2 106.1 2.2 16.7	151.2	149.3
Work	22.70	7.34	53.1	21.46 3.7 106.3 2.7 18.0	152.5	151.3
Δ	-3.17	-0.06	-2.5	-3.17 +2.5 +0.2 +0.5 +1.3	+1.3	+2.0

* Concentration of magnesium is assumed to be 2 mEq. per litre of serum.

† Doubtful result. Not included in the average.

TABLE VII. Electrolytes of oxygenated blood at a carbonic acid pressure of 40 mm. Hg. Concentrations are expressed in mEq. per litre of blood.

Subject	Total Hb	Total CO ₂	(HCO ₃) ⁻	(Lactate) ⁻	(Cl) ⁻	(HPO ₄) ⁻ + (H ₂ PO ₄) ⁻	Protein-ate ⁻	(Na) ⁺	(K) ⁺	Σ anions	Σ cations*
D. B. D. Rest	8.27	22.44	21.30	0.80	83.5	1.7	30.1	86.8	41.1	137.4	132.9
Work	8.76	21.00	19.86	1.47	82.5	1.9	31.6	84.1	44.6	137.3	133.7
Δ	+0.49	-1.44	-1.44	+0.67	-1.0	+0.2	+1.5	-2.7	+3.5	-0.1	+0.8
P. F. P. Rest	9.92	21.90	20.76	0.90	81.7	1.6	31.4	81.0	45.7	136.4	131.7
Work	9.56	17.36	16.22	4.85	82.4	1.9	30.4	80.4	47.4	135.8	132.8
Δ	+0.64	-4.54	-4.54	+3.95	+0.7	+0.3	-1.0	-0.6	+1.7	-0.6	+1.1
J. H. T. Rest	9.34	20.82	19.68	1.30	81.1	1.4	31.2	81.7	45.8	134.7	132.5
Work	9.86	20.33	19.19	1.74	80.6	1.6	32.2	80.3	46.5	135.3	131.8
Δ	+0.52	-0.49	-0.49	+0.44	-0.5	+0.2	+1.0	-1.4	+0.7	+0.7	-0.7
W. C. Rest	9.13	21.54	20.40	1.08	82.1	1.9	32.1	81.6?	41.0	137.6	127.6†
Work	9.29	15.56	14.42	6.04	84.1	2.5	28.2	83.5	42.9	135.3	131.4
Δ	+0.16	-5.98	-5.98	+4.96	+2.0	+0.6	-3.9	+1.9?	+1.9	-2.3	-2.3
O. S. L. Rest	8.63	21.59	20.45	1.12	85.4	1.6	30.6	88.6	39.7	139.2	133.3
Work	9.29	18.36	17.22	3.18	84.6	2.0	29.9	86.3	42.0	136.9	133.3
Δ	+0.66	-3.23	-3.23	+2.06	-0.8	+0.4	-0.7	-2.3	+2.3	-2.3	0.0
J. L. S. Rest	9.79	20.23	19.09	1.08	80.4	1.6	31.6	79.5	48.6	133.8	133.1
Work	10.09	19.56	18.42	1.74	81.9	2.1	32.6	76.6?	49.7	136.8	131.3†
Δ	+0.30	-0.67	-0.67	+0.66	+1.5	+0.5	+1.0	-2.9?	+1.1	+3.0	+3.0
H. T. E. Rest	8.92	21.15	20.01	0.99	82.3	1.7	30.7	84.4	44.3	135.7	133.7
Work	9.41	17.60	16.46	3.13	84.4	2.1	30.6	82.7	47.6	136.7	135.3
Δ	+0.49	-3.55	-3.55	+2.14	+2.1	+0.4	-0.1	-1.7	+3.3	+1.0	+1.6
A. V. B. Rest	8.91	20.94	19.77	0.90	82.9	1.7	30.0	84.1	43.1	135.3	132.2
Work	9.92	18.80	17.66	2.87	79.9	1.9	31.1	77.3	47.3	133.4	129.6
Δ	+1.01	-2.11	-2.11	+1.97	-3.0	+0.2	+1.1	-6.8	+4.2	-1.9	-2.6
W. J. G. Rest	9.47	20.81	19.67	0.95	82.3	1.4	30.6	84.3	42.8	134.9	132.1
Work	10.50	18.70	17.56	2.87	81.4	1.9	31.9	81.7	45.8	135.6	132.5
Δ	+1.03	-2.11	-2.11	+1.92	-0.9	+0.5	+1.3	-2.6	+3.0	+0.7	+0.4
Average, Rest	9.04	21.27	20.13	1.01	82.3	1.6	30.9	84.4	43.6	136.0	132.7
Work	9.63	18.61	17.47	3.10	82.3	2.0	30.9	81.8	46.0	135.8	132.6
Δ	+0.59	-2.66	-2.66	+2.09	0.0	+0.4	0.0	-2.6	+2.4	-0.2	-0.1

* Concentration of calcium plus magnesium in whole blood is assumed to be 5 mEq. per litre in rest and in work.

† Doubtful result. This value is not used in calculating the average.

Interpretation of results.

Concentration changes in protein of serum and hæmoglobin of blood. Zuntz with his associates⁽¹⁴⁾ was perhaps the first to demonstrate clearly that increase in sp. gr. and cell count of blood takes place in exercise. In 28 experiments, marching with a pack of 22–31 kg. over a course of 18–24½ km. caused an increase in sp. gr. of 2 to 4 thousandths and in cell count of about 9 p.c. Later it was shown by Ferrari⁽¹⁵⁾ that the average red cell count of students may increase 10 p.c. during the course of an examination. Since then much more evidence has accumulated that change in degree of physical activity or in emotional state is reflected by hæmoglobin concentration change in the blood.

In the cat suddenly confronted by the barking dog, there is an increase of 20 to 30 p.c. (or, rarely, 40 to 50 p.c.) in red cell count as shown by Lamson⁽¹⁶⁾ and Izquierdo and Cannon⁽¹⁷⁾. The latter authors, having at hand knowledge of the spleen as a reservoir of red cells recently acquired by Barcroft and his associates⁽¹⁸⁾ and many others, demonstrated that when only the liver of the upper abdominal viscera is left innervated, there is no emotional polycythemia. Furthermore:

“After section of the nerves to the spleen, excitement for one minute does not produce polycythemia. . . . Inactivation of the adrenal medulla has no marked influence on emotional polycythemia.”

Aside from contributions of polycythemic blood by the spleen, there may be a change due to salt solution transfer from blood to tissues or interstitial spaces. Imbibition by frog's muscle in strychnine tetanus and simultaneous loss of fluid by the blood was reported by Ranke⁽¹⁹⁾ in 1865. Water content of blood of resting frogs was 88.3 p.c. and of tetanized frogs 87.0 p.c. Corresponding values for muscle were 80.3 and 82.1 respectively. More recently Back, Cogan and Towers⁽²⁰⁾, also working on frog's muscle, found that faradic stimulation caused increases in water content ranging from 0.7 to 7.6 p.c., averaging about 4 p.c.

Increase in hæmoglobin concentration in exercise varies with the species and with the conditions of exercise. For man Bock, van Caulært, Dill, Fölling and Hurxthal⁽²¹⁾ found increases of 5 to 10 p.c. with some difference in individuals, the maximum increase of about 10 p.c. occurring in A. V. B. at a metabolic rate of about 2 litres of oxygen per minute. Increases found by Harrison, Robinson and Syllaba⁽²²⁾ and by Himwich and Loebel⁽²³⁾ were of the same order of magnitude. In contrast with these moderate changes in man are results on the horse reported by Scheunert and Krzywaneck⁽²⁴⁾. During 5 minutes' trot,

six experiments showed increase in cell volume (expressed in p.c. of blood volume) from 30 to 40, 29 to 36, 28.7 to 38, 24 to 35.5, 25 to 37 and 29 to 39.5 p.c. respectively. The average increase was from 27.6 p.c. to 37.6 p.c. or about one-third.

In Scheunert and Krzywanek's experiments increase in plasma protein concentration was determined and associated decrease in plasma volume was estimated. Increase in p.c. cell volume by this water transfer represented but a small part of the total observed increase and it was concluded that the spleen must make a large contribution of cells to the active circulation.

In exercise experiments on man which caused sweating and lasted for 15 to 30 minutes, Cohn⁽²⁵⁾ found a decrease in hæmoglobin concentration. At the same time increase in plasma protein concentration took place. Cohnheim, Kreglinger and Kreglinger⁽²⁶⁾ as well as Gross and Kestner⁽²⁷⁾ found a decrease in red count and p.c. hæmoglobin after prolonged and strenuous mountain climbing. These latter observations we have confirmed in recent experiments but Cohn's result remains unexplained.

It was found by Broun⁽²⁸⁾ that after 10 or 15 minutes' exercise, dogs had an average increase of 3.6 p.c. in total plasma volume and 12.3 p.c. in total cell volume, the range of the latter increment being from 1.5 to 24 p.c. There was thus a distinct increase in circulating blood volume. After several hours' exercise both total cell volume and hæmoglobin content were less than after 10 minutes' exercise, a difference that was much greater in animals which had been confined for several months. The conclusion was reached that blood destruction is a significant phenomenon during prolonged exercise in untrained dogs. Results of a similar character have been obtained by Hastings⁽²⁹⁾.

Barcroft and Florey⁽³⁰⁾ have succeeded in resecting a portion of colon of the dog and sewing it, with blood supply still maintained, into the belly wall. Exercise and emotional disturbance result in a simultaneous decrease in size of the spleen and in the pink colour of the colon. A shutting down of vessels in the splanchnic area is clearly proved by these experiments.

Chiatellino and Margaria⁽³¹⁾ have studied concentration changes in the blood of men during a march of 2 to 6 hours with no water intake. Loss of body weight ranged from 1.6 to 3.5 p.c. Increase was slight for osmotically active substances and marked for serum proteins and red cells. An actual diminution in blood volume was observed.

Finally we come to our own results. We have in Table VIII values

TABLE VIII. Effect on cell volume of concentration changes in serum and cells from rest to work.

Subject	Serum solids		Serum protein		Cell solids		Cell volume		
	Rest (g. per l.)	Work (g. per l.)	Rest (g. per l.)	Work (g. per l.)	Rest (g. per l.)	Work (g. per l.)	Work		
							Rest (p.c.)	(ob- served p.c.)	(calcu- lated p.c.)
D. B. D.	86.5	93.6	70.8	79.9	366	372	42.0	44.1	44.6
P. F. P.	86.9	94.2	—	—	370	374	45.7	47.6	47.4
A. A. McC.	86.4	97.1	—	—	375	378	44.5	47.9	47.2
J. H. T.	84.4	87.0	68.6	71.6	377	380	46.2	47.8	47.1
W. C.	88.4	94.2	72.0	77.7	380	377	44.4	45.8	46.5
O. S. L.	86.2	95.8	71.4	78.0	387	386	41.8	44.9	44.0
J. L. S.	88.1	92.4	69.4	73.9	376	378	48.3	49.4	49.7
H. T. E.	85.2	93.3	69.4	77.0	373	376	44.1	46.7	46.5
A. V. B.	90.8	99.8	65.0	78.8	377	389	43.9	48.8	47.9
W. J. G.	77.8	86.3	62.5	71.2	387	390	44.3	47.4	47.3
Average...	86.1	93.4	68.6	76.0	377	380	44.5	47.0	46.8
B. Subjects after splenectomy.									
W. K.	84.1	90.4	—	—	389	387	48.0	49.4	49.9
„	78.5	89.0	—	—	389	389	43.6	47.0	46.7
„	91.8	91.8	—	—	386	389	48.7	48.3	48.5
E. H.	91.0	100.5	—	—	372	373	48.2	51.4	50.7
Average...	86.4	92.9	—	—	384	385	47.1	49.0	49.0

for serum solids, serum protein, cell solids and p.c. cell volume in rest and work. In addition to the ten subjects already referred to, we were fortunate in securing observations on two young men without spleens. Splenectomy had been performed about two years before our observations on E. H. and five years before in the case of W. K. Recovery was complete in each case.

The last column in this table shows values for p.c. cell volume calculated as follows:

$$V_c' = 100 \left(\frac{V_c P_c}{P_c'} \right) \div \left[\left(\frac{V_c P_c}{P_c'} \right) + \left(\frac{[100 - V_c] P_s}{P_s'} \right) \right],$$

- where V_c' = p.c. cell volume in work;
 V_c = p.c. cell volume in rest;
 P_c = g. of solids per litre of cells in rest;
 P_c' = g. of solids per litre of cells in work;
 P_s = g. of protein per litre of serum in rest;
 P_s' = g. of protein per litre of serum in work.

This formula is a mathematical expression of the hypothesis that all the changes are due simply to loss of water from the blood, during work. The loss of water per unit weight of serum and of cells was determined by analysis but we have no information regarding total blood volume changes.

In most cases determinations of serum solids and of serum protein were made. The values for protein furnish the more suitable basis for recalculation and these values were used when available. Otherwise values for serum solids were employed. The result is essentially the same; the average calculated p.c. cell volume for normal men comes out 46.8 on the basis of serum protein concentration change, and 46.6 on the basis of serum solids change. This fact is expressed in another form in Fig. 1

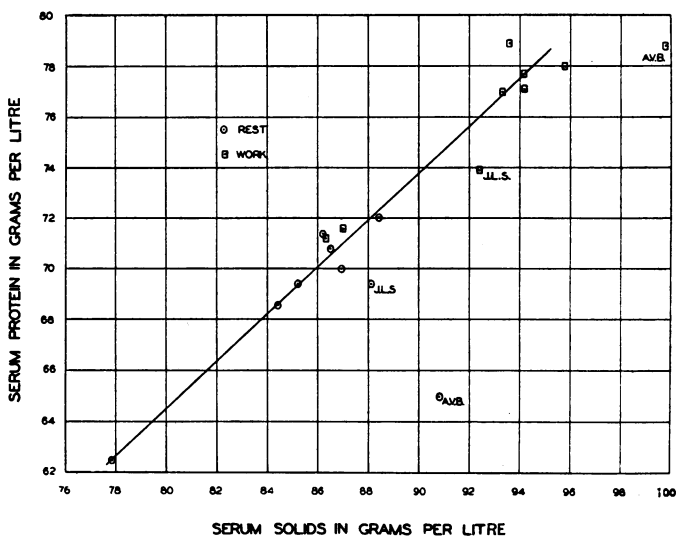


Fig. 1. Relation of serum solids to serum protein in rest and work.

which shows that in most subjects the value for serum solids is merely a linear function of that for serum protein in rest and work. Also it is evident that increase in serum solids is nearly equal to increase in serum protein. Evidently in most subjects concentration of serum fat and other similar substances does not change much in exercise of this character.

The results speak for themselves. It is obvious that in normal man increase in p.c. cell volume during exercise of the sort studied is accompanied by a corresponding increase in serum protein concentration, and the phenomenon is not different in men after splenectomy. Thus the average increase in normal men was 5.6 p.c. and after splenectomy 4 p.c. Clearly the spleen is not essential to this aspect of the phenomenon and seems to play a subordinate rôle under the circumstances of our experiments¹.

¹ Posture effect upon composition of the blood has been studied by W. O. Thompson, P. K. Thompson and M. E. Dailey, *J. Clin. Inv.* 5, 573 (1928). They found changes in

The question as to what changes may have taken place in total blood volume during the course of work cannot be answered. Broun's results (28) on the dog cannot be applied without reservation to our experiments, both because of the difference in species, and because in his experiments at least 4 minutes elapsed after cessation of exercise before blood samples were withdrawn. The marching experiments of Chiatellino and Margaria⁽³¹⁾ were of long duration and direct comparison cannot be made, but their findings make it appear that decrease in blood volume is not incompatible with maintenance of a high metabolic rate in man. The best we can do is to make use of our data on p.c. cell volume and plasma protein concentration, with certain assumptions with regard to total blood volume, in a calculation of probable range in amount and character of new blood.

Such calculations have been made and are shown in Table IX. On

TABLE IX. Outcome of certain assumptions with regard to blood volume changes in exercise*.

	Rest	Work					Assuming blood vol. increase = 5 p.c. and cell vol. of new blood = 70 p.c.
		Assuming total serum proteins constant	Assuming blood vol. decrease = 5 p.c.	Assuming blood vol. constant	Assuming blood vol. increase = 5 p.c.	Assuming blood vol. increase = 10 p.c.	
Blood vol. (litres)	5.0	4.7	4.75	5.0	5.25	5.50	5.25
Cell vol. (p.c.)	44.5†	46.8	47.0†	47.0†	47.0†	47.0†	48.0
Total cell vol. (litres)	2.23	2.20	2.23	2.35	2.47	2.59	2.52
Total serum vol. (litres)	2.77	2.50	2.52	2.65	2.78	2.91	2.73
Serum protein (g. per litre serum)	68.6†	76.0†	76.0†	76.0†	76.0†	76.0†	76.0†
Total serum protein (g.)	190	190	192	201	211	221	208
New blood (litres)	—	None	0.05	0.30	0.55	0.80	0.55
New cells (litres)	—	None	0.03	0.15	0.28	0.40	0.34

* Serum protein concentration in new blood is assumed to be the same as the observed value in our blood specimens. Serum protein concentration change indicates a transfer to tissues of 0.3 litre of salt solution and this transfer is implicit in all our assumptions. Cell volume of new blood is assumed to be 50 p.c. in every case but the last.

† Observed value.

the assumption that total serum protein and total hæmoglobin in the circulation remain constant, while in fact serum protein concentration increases from 68.6 to 76.0 g. per litre, it follows that blood volume decreases 6 p.c. Now in order to restore the original volume, 0.3 litre of blood must be added, and in order to increase p.c. cell volume from 46.6 serum protein concentration and in p.c. cell volume from a reclining to an erect posture, with a minimum of muscular movement, of the same order of magnitude as we have found in exercise. Total serum volume decreased in a reciprocal manner with serum protein concentration and total cell volume remained constant.

to 47.0 the added blood must contain 52 p.c. cells. When blood volume increases 5 p.c., 0.55 litre of new blood is added. The fact that observed p.c. cell volume exceeds calculated cell volume by only 0.2 p.c. thus implies that added blood contains only about 5 p.c. more cells than circulating blood. The experimental evidence on this point is, however, quite inconclusive in any case and wholly without meaning if the volume of added blood is small.

It was found by Bock, van Caulært, Dill, Fölling and Hurxthal⁽²¹⁾ that increase in oxygen capacity is a function of metabolic rate. The present experiments involve increases in metabolic rate of eight to twelve times the resting level. In other running experiments at faster rates, increases in p.c. cell volume are sometimes, but not invariably, greater. Such experiments are for the most part unpublished, but one may be referred to. Hochrein, Dill and Henderson⁽³²⁾ found in an experiment on M. H., running at a rate of 11.3 km. per hour for 15 minutes, an increase in metabolic rate of fifteen times and an increase in p.c. cell volume of one-ninth, a change greater than any and twice as large as the average observed in the present experiments.

The physical condition of the subject may be a factor in increase in p.c. cell volume. In our experiments no well-defined relation was found

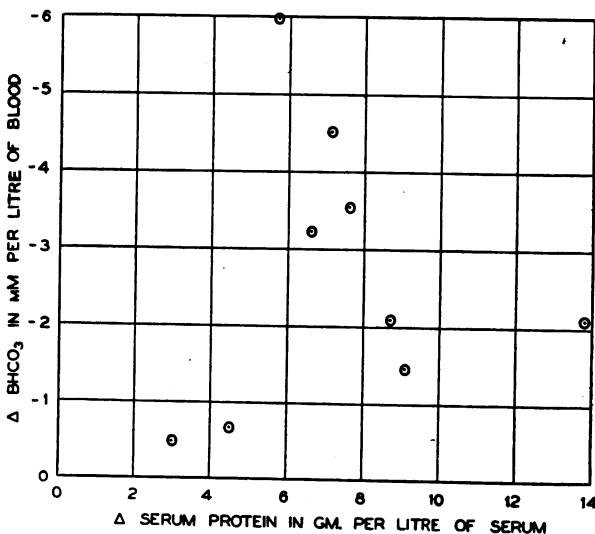


Fig. 2. Serum protein change in relation to change in bicarbonate capacity of whole blood.

between decrease in level of the carbon dioxide dissociation curves and serum protein increments (see Fig. 2). Since the first variable furnishes an

index to physical condition and the second to increase in p.c. cell volume, no relation between physical condition and increase in p.c. cell volume is revealed by the present experiments. Furthermore Bock, van Caulaert, Dill, Fölling, and Hurxthal(21) found about the same increase in oxygen capacity in De Mar, a successful Marathon runner for 20 years, as in untrained subjects.

The time factor must also be considered. The above-mentioned authors found in one experiment that while most of the increase in oxygen capacity had taken place at the end of 6 minutes, there was a further increase of about 0.5 volume p.c. between 6 and 16 minutes after work began. In long-continued work concentration of cells in blood may be appreciably influenced by water loss from the body as a whole or by increased rate of destruction of cells or by both factors combined. In Fig. 3 are plotted results obtained by Talbott, Fölling, Henderson,

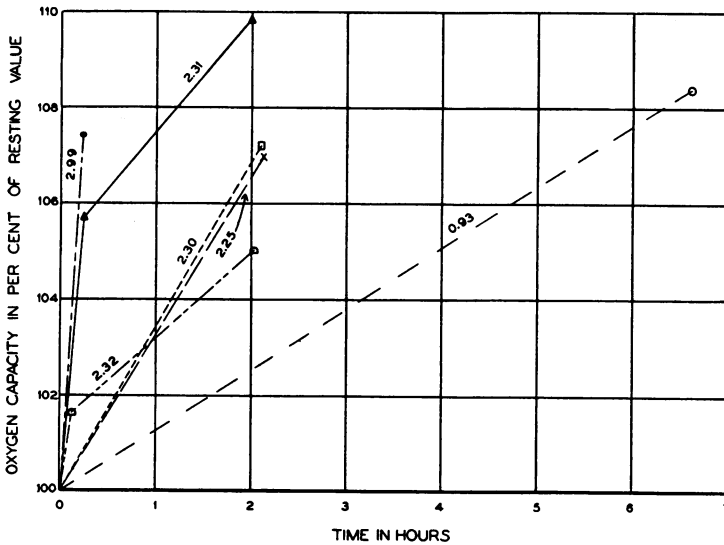


Fig. 3. Change in oxygen capacity during work of different intensities. Oxygen consumption in litres per minute is indicated.

Dill, Edwards and Berggren(33) on the subject J. H. T. It is interesting to note that oxygen capacity increase was greater after a 6-hour walking experiment with an oxygen consumption of 0.93 litre per minute than after three out of four running experiments lasting about 2 hours with an oxygen consumption of about 2.3 litres per minute. J. H. T. drank no water during these experiments so that appreciable cell de-

struction may have taken place while its effect may have been masked by body water loss.

Concentration changes in hæmoglobin of cells. In the above discussion the terms oxygen capacity and cell volume have been used interchangeably, thus implying a constant ratio between these variables in rest and work. The fact that the average increase in cell solids from rest to work is less than 1 p.c., as shown in Table VIII, implies that ratio of oxygen capacity to cell volume does not change notably. Further evidence that such is the case is found in Table X. Hæmoglobin concentrations are

TABLE X. Hæmoglobin concentration at $pH_s = 7.4$.

Subject	Rest (mEq. per l. cells)	Work (mEq. per l. cells)	Δ	Rest (mEq. per kg. cell solids)	Work (mEq. per kg. cell solids)	Δ
D. B. D.	19.84	19.95	+0.11	53.78	53.36	-0.42
P. F. P.	19.48	20.08	+0.60	52.70	53.65	+0.95
A. A. McC.	18.14	19.00	+0.86	48.38	50.26	+1.88
J. H. T.	20.26	20.67	+0.41	53.52	54.30	+0.78
W. C.	20.61	20.42	-0.19	54.20	53.76	-0.44
O. S. L.	20.70	20.69	-0.01	53.42	53.73	+0.31
J. L. S.	20.31	20.43	+0.12	53.94	53.98	+0.04
H. T. E.	20.27	20.28	+0.01	54.20	53.61	-0.59
A. V. B.	20.25	20.37	+0.12	53.95	52.28	-1.67
W. J. G.	21.47	22.25	+0.78	55.26	56.78	+1.52
Average ...	20.13	20.41	+0.28	53.34	53.57	+0.24
Minimum ...	18.14	19.00	-0.19	48.38	50.26	-1.67
Maximum...	21.47	22.25	+0.86	55.26	56.78	+1.88

calculated to the basis of (a) mEq. oxygen combining capacity per litre of cells at pH_s , 7.4, and (b) mEq. per kg. of cell solids. The first calculation is made as follows:

$$\text{mEq. Hb per litre cells} = \frac{(\text{total Hb})_b}{V_c - \frac{7.40 - pH_s}{30}},$$

where $(\text{total Hb})_b$ = mEq. oxygen combining capacity per litre of blood,

V_c = c.c. of cells per c.c. of blood as equilibrated,

pH_s = pH of serum as equilibrated,

and $\frac{7.40 - pH_s}{30}$ is an empirical factor dependent upon the rate of change of cell volume with pH_s . The correction in no case exceeds 0.003 in V_c and is thus nearly but not quite negligible. The second calculation is made by dividing the values for oxygen combining capacity per litre of cells, Table X, by corresponding values for solids per litre of cells given in Table VIII.

The first three columns in Table X suggest that the slight increase in

cell solids from rest to work shown in Table VIII is a reality, for there is a similar increase in oxygen combining capacity. The increase in the first case is 0.8 p.c. and in the other, 1.4 p.c.

The values for Δ in the last column of Table X probably can be taken as a measure of the accuracy of the six determinations involved in this calculation, viz. oxygen capacity, cell solids, and cell volume both in rest and work.

Aside from the evidence that rest to work change in hæmoglobin concentration per litre of cells is small and that change in the ratio hæmoglobin \div cell solids is probably negligible, Table X is interesting in showing the normal range of individual variation. Values for hæmoglobin concentration per litre of cells are already on record for four individuals of this group⁽³⁴⁾. These observations were made a year earlier by the same method, and it is of interest to compare the results, shown in Table XI.

TABLE XI. Cellular hæmoglobin concentration in rest.
Concentrations in mEq. per litre of cells.

Subject	1928	1929
D. B. D.	19.7	19.8
J. H. T.	20.4	20.2
H. T. E.	21.0	20.2
A. V. B.	20.2	20.2

In three cases the results are practically identical. Only in one case is the difference nearly, if not quite, outside the probable limit of error, and in this case evidence exists that the condition of the subject changed during the period in question. Certainly concentration of hæmoglobin in cells is a variable that fluctuates within narrow limits in normal man, whether at rest or at work.

Acid-base equilibrium in serum. Concentrations of individual anions and of Σ cations in true plasma at a carbonic acid pressure of 40 mm. Hg are shown in Table VI. Values for total CO_2 , serum volume, chloride, and phosphate were determined directly and, where the equilibration CO_2 pressure differed appreciably from 40 mm., correction was made to this value. Phosphate corrections are not required and all others can be made by reference to a nomogram of blood of normal man in rest and work, e.g. that of M. H. (32).

Values for $p\text{H}$ are calculated from the equation

$$p\text{H}_s = p\text{K}_s + \log (\text{BHC}\text{O}_3)_s - \log (\text{H}_2\text{C}\text{O}_3)_s,$$

where

$$p\text{K}_s = 6.10,$$

$$\text{mEq. } (\text{H}_2\text{C}\text{O}_3)_s = 0.0329 (\text{H}_2\text{O})_s (p\text{C}\text{O}_2),$$

and

$$(\text{BHC}\text{O}_3)_s = (\text{total CO}_2)_s - (\text{H}_2\text{C}\text{O}_3)_s,$$

accepting the recent determinations of Van Slyke, Sendroy, Hastings and Neill(35) for the solubility of CO₂ in plasma at 38° and correcting it to 37·5°, the temperature we have employed for equilibration. The value used for *pK*_s is that recently established by Hastings, Sendroy and Van Slyke(36).

Lactate in serum is calculated from its determination in whole blood, observation of serum volume and the distribution ratio between serum and cells reported by Edwards, Hochrein, Dill and Henderson(37).

Proteinate is calculated according to Van Slyke, Hastings, Hiller and Sendroy(38).

$$\text{mEq. } (BP)_s = 0\cdot104 (P)_s (pH_s - 5\cdot08),$$

where $(P)_s = \text{g. of protein per litre of serum.}$

The expression Σ anions represents the sum of these determined and calculated anions, while Σ cations represents the sum of determined values for calcium, sodium, and potassium, as given in Table III, and the value of 2·0 assumed as representing concentration of magnesium in normal serum.

The results are too involved to yield to simple treatment and hence

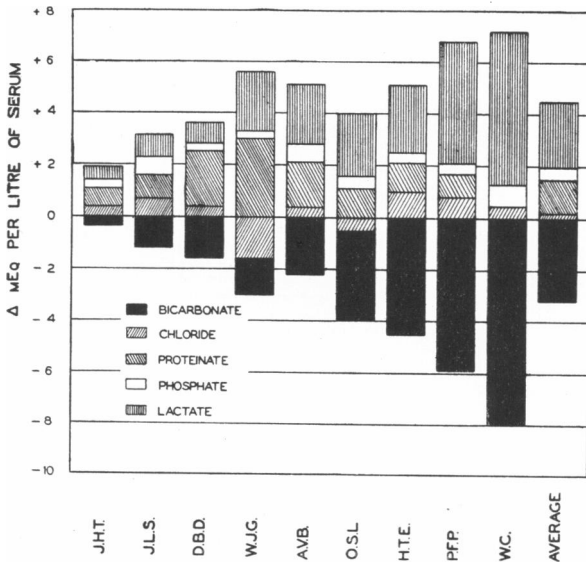


Fig. 4. Increments in principal anions of serum from rest to work.

have been presented graphically in two forms. Fig. 4 shows changes per litre of serum from rest to work. Fig. 5 shows concentration of base and

each principal anion in rest and also the consequences of (a) work without exhaustion with lactic acid accumulation small or negligible but with salt

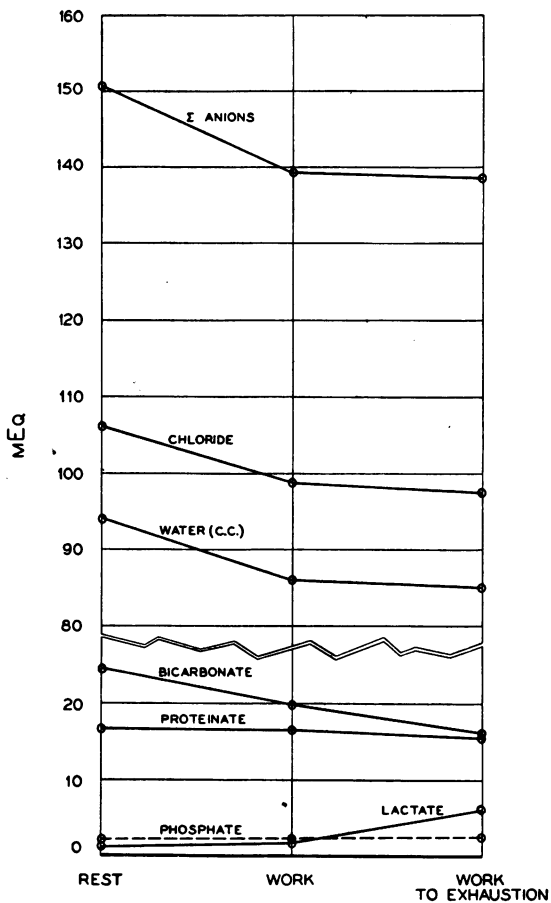


Fig. 5. Effect of work with moderate fatigue and of work to exhaustion on constituents of serum. Calculated on the assumption that total protein of serum remains constant, viz. observed concentrations in work are multiplied by

$$\frac{\text{Protein per litre rest serum}}{\text{Protein per litre work serum}}$$

solution transfer, and (b) work to exhaustion with slightly greater salt solution transfer to tissues and large lactic acid accumulation.

In some particulars, the results are easily understood. Thus there is the reciprocal relation of bicarbonate and lactate already known to occur in whole blood from the work of Bock, van Caulært, Dill, Fölling,

and Hurxthal⁽²¹⁾. Also increase in phosphate has already been described by Havard and Reay⁽³⁹⁾.

On the other hand, there are certain questions heretofore unanswered to which answers can now be given. Thus, on the average, increase in lactate is actually only three-fourths or four-fifths of the decrease in bicarbonate. Taking the subjects individually, Δ lactate as compared with $-\Delta$ bicarbonate is distinctly smaller in five cases, larger in one case and about the same in three cases. Chloride shows a slight increase in seven out of nine subjects with an average increase of 0.2 mEq. or less than 0.2 p.c., thus indicating that the fluid leaving the blood during exercise carries a concentration of chloride equal to that of the blood.

Base bound by protein increases on the average just one-half as much as lactate but there are large individual differences. As shown in Fig. 4, there is a fairly uniform increase in serum protein concentration in most of the subjects, even including those most fatigued, P. F. P. and W. C. Consequently when there is little lactic acid accumulation ΔBP_s is large, since ΔP_s increases and ($pH_s - 5.08$) remains constant or nearly so. But the latter factor decreases with increasing lactic acid accumulation and in the most fatigued subject, W. C., $\Delta BP_s = 0$.

It is interesting and probably significant that for the series $\Delta\Sigma$ anions = $\Delta(BP)_s$, *i.e.* net increase in anions equals increase in non-diffusible anions. Finally, $\Delta\Sigma$ anions = $\Delta\Sigma$ cations from rest to work, approximately.

In short, nothing takes place in the serum which does not have a fairly simple interpretation. In the well-trained subject there is transfer from blood to tissues of a fluid carrying practically unchanged concentrations of diffusible ions. Non-diffusible proteinate with an equivalent amount of base is left behind and there is a higher concentration of phosphate than corresponds to salt solution transfer. This latter change is probably a reflection of increased inorganic phosphate concentration in tissues. In the poorly-trained subject, entrance of lactate decreases bicarbonate and increases acidity.

Values for calcium, sodium, and potassium as given in Table III show no other change worthy of note except that there is a greater relative increase of calcium than of other cations.

Acid-base equilibrium in whole blood. Table VII and Fig. 6 give data for whole blood corresponding to those for true plasma already described. Changes in blood are due not only to changes in plasma and cells but also to change in relative proportion of the two phases. It has already been shown that there is almost no change in concentration of non-diffusible

constituents of cells and it is also true that there is but a slight change in chloride, sodium, and potassium, all of which were determined directly.

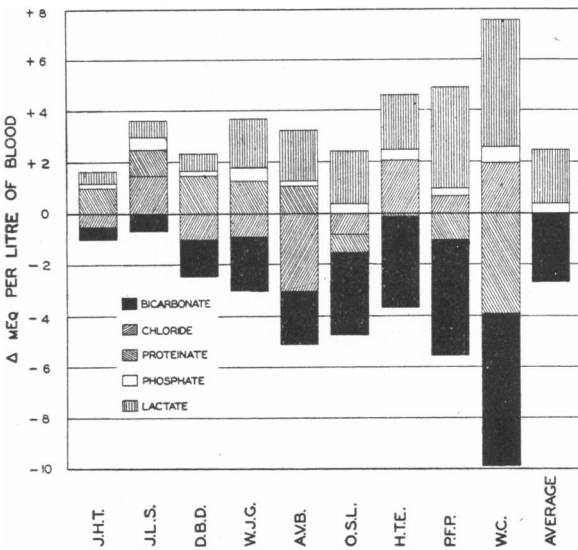


Fig. 6. Increments in principal anions of blood from rest to work.

The components which do change, therefore, are those subject to change with acidosis, viz. $(BP)_c$, lactate, and bicarbonate. The composite picture of blood happens to be simple when the average of the group is considered. Chloride and proteinate are unchanged, ratio of lactate change to bicarbonate change is essentially the same as in plasma, and $\Delta\Sigma$ cations = $\Delta\Sigma$ anions = 0, approximately.

It must be emphasized, however, that blood changes in non-fatigued subjects vary in many respects from those of nearly exhausted subjects. The manner in which $\Delta(BP)_b$ changes with acidosis is shown in Fig. 7. When acidosis is no more than moderate there is an increase in $(BP)_b$ of about 1 mEq. The reason for this is that there is, per litre of blood, not much change in serum protein but a large increase in cell protein. With increasing acidosis there is little if any further increase in blood protein but decreasing amount of base found by protein.

The data given in the above tables may be used for calculating concentration ratios of bicarbonate and chloride ions in cells and plasma. A series of preliminary experiments has already been reported by Edwards, Hochrein, Dill and Henderson⁽³⁷⁾. Their findings have been confirmed in the present experiments, as shown in Table XII.

TABLE XII. Average values for r_{Cl} and r_{HCO_3} at $pH_s=7.45$.

Remarks	r_{Cl}			r_{HCO_3}		
	Rest	Work	Δ	Rest	Work	Δ
12 subjects, 1928	0.640	0.655	+0.015	0.743	0.784	+0.041
10 subjects, 1929	0.633	0.645	+0.012	0.757	0.768	+0.011
2 subjects with maximum fatigue, 1929	0.655	0.665	+0.010	0.775	0.815	+0.040

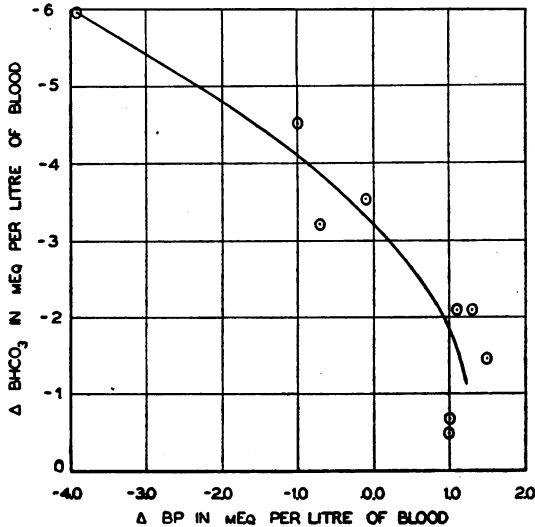


Fig. 7. Base bound by blood proteins in relation to change in bicarbonate capacity of whole blood.

Further, it appears that r_{HCO_3} increases with acidosis, since the most fatigued subject in 1927 and the two most fatigued subjects in 1928 had the greatest average increase in this variable.

Lactic acid accumulation and physical performance. The relation of lactate to bicarbonate change in exercise of this character has been observed on a total of 19 individuals with two or more experiments on five individuals. All these observations are collected in Table XIII and shown graphically in Fig. 8. Subjects are arranged in order of increasing lactic acid concentration, and it will be noted that this is approximately the order of decreasing bicarbonate concentration. This type of experiment furnishes an excellent guide to capacity of individuals for great and sustained physical activity. De Mar, with no appreciable change in lactic acid, is a Marathon runner of 20 years' experience. T. K. was a first-class half-miler 4 years ago and has kept in good condition since then. Probably neither of these men was more fatigued by exercise of this nature than an average person would be by a 20-minute walk.

TABLE XIII. Lactate and bicarbonate changes from rest to work.
 Concentrations are expressed in mEq. per litre of blood at $p\text{CO}_2=40$ mm.

Subject	Lactate increase	Bicarbonate decrease	Bicarbonate minus lactate
C. De M.	0.01	0.00	- 0.01
T. K.	0.24	0.00	- 0.24
J. H. T., March 1929	0.43	0.49	+ 0.06
D. B. D., 1928	0.44	1.93	+ 1.49
W. K.*	0.50	0.45	- 0.05
B. F. J.	0.63	0.63	0.00
J. H. T., Sept. 1929	0.66	0.60	- 0.06
J. L. S.	0.67	0.67	0.00
D. B. D., 1929	0.67	1.44	+ 0.77
A. A. McC.	0.93	1.62	+ 0.69
H. T. E., 1928	1.25	2.74	+ 1.49
G. D.	1.40	2.16	+ 0.76
E. H.*	1.49	2.20	+ 0.71
C. H.	1.67	2.70	+ 1.03
A. V. B., 1928	1.68	2.97	+ 1.29
W. C., Oct. 1929	1.68	2.72	+ 1.04
W. J. G.	1.92	2.11	+ 0.19
A. V. B., 1929	1.97	2.11	+ 0.14
H. T. E., Sept. 1929	1.97	2.20	+ 0.23
O. S. L.	2.06	3.23	+ 1.17
H. T. E., April 1929	2.14	3.55	+ 1.41
H. W.	2.20	2.34	+ 0.14
E. F. W.	3.84	3.33	- 0.51
P. F. P.	3.94	4.54	+ 0.60
W. C., March 1929	4.97	5.98	+ 1.01
Average...	1.57	2.11	+ 0.54

* After splenectomy.

At the other end of the series stands W. C., a young man of 18. A twentieth subject had to quit from exhaustion in 6 minutes. His record is not shown in the figure, for his lactic acid determination was lost, but bicarbonate decrease was 5.2 mEq. per litre. The fact that there is such a wide range in performance is all the more interesting when one bears in mind that these individuals would be rated as normal by an examining physician. It is another illustration of the old principle that the performance of a machine can be judged best, not when idling, but when running under a heavy load.

One variable in performance can be easily evaluated. It is well known that skill in performance of any physical task varies widely. Running calls for skill of a high order, and it has already been shown by Furusawa, Hill, Long and Lupton⁽¹⁾ that oxygen consumption of different individuals varies considerably while running at a given rate. In Fig. 9 comparison has been made of skill in running of 17 individuals. Variation of net oxygen consumption per kg. of body weight ranges from 26 to 40 c.c., the least skilful subject using one-half more fuel than the most skilful. The data upon which this figure is based together with physical

measurements of some of the subjects are given in Table XIV. While there is a fair correlation between skill and lactic acid accumulation,

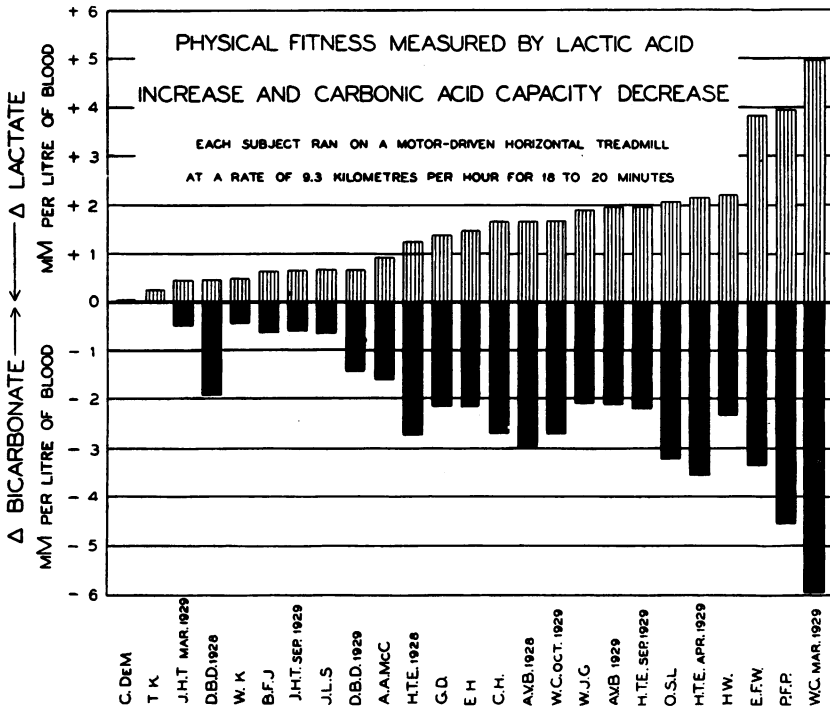


Fig. 8. Increments in blood lactate and in bicarbonate capacity at 40 mm. Hg from rest to work.

TABLE XIV. Physical characteristics and skill index.

Subject	Age (years)	Height (cm.)	Weight (kg.)	Vital capacity standing (c.c.)	Net oxygen used in work (l. per min.)	Skill index
D. B. D.	37	180	72.5	4400	1.91	26.3
P. F. P.	33	173.5	67.6	4550	2.19	32.3
A. A. McC.	23	177.0	74.0	5900	2.70	36.5
J. H. T.	26	171.0	70.4	4000	1.85	26.3
W. C.	18	171.0	62.0	4500	2.49	40.2
O. S. L.	27	188.0	67.2	5950	2.31	34.3
J. L. S.	41	183.2	65.3	5400	2.20	33.7
H. T. E.	32	166.0	67.7	3940	2.04	30.1
A. V. B.	40	173.4	74.2	4000	2.13	28.7
W. J. G.	26	171.0	63.3	4550	2.11	33.2

A. A. McC. is a striking exception. He is one of the most inexpert of runners and at the same time one of the least fatigued subjects. It is not

improbable that of the entire group he would show greatest improvement in training, for he is already well equipped for oxygen transport.

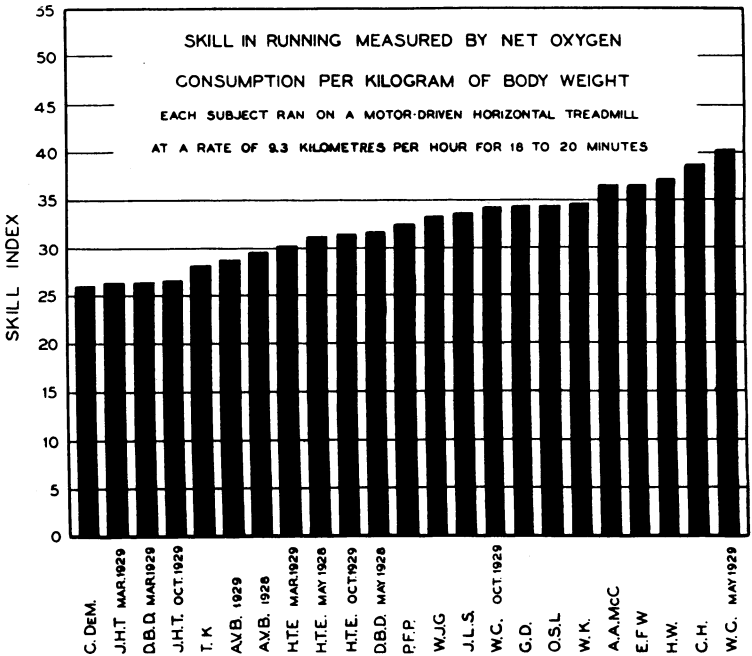


Fig. 9. Skill index expressed as net oxygen consumption per kg. of body weight.

Two or more sets of observations on lactic acid and carbonic acid capacity have been made in the case of five individuals performing the same task at different times. J. H. T., D. B. D., and A. V. B. had about the same lactic acid concentration in 1929 as in 1928. H. T. E. showed only small variation while W. C. in his second experiment showed great improvement. W. C. was the only one of these subjects to show much change in oxygen consumption, using in the second experiment about 2.4 litres of oxygen per minute as compared with 2.8 in the first experiment.

Total ventilation. It is possible from these experiments to study ventilation in relation to time, fatigue, and reaction of arterial blood. The ten subjects may be divided into three groups on the basis of degrees of fatigue. Group I, with less than 1 mEq. lactic acid increase, contains J. H. T., J. L. S., D. B. D., and A. A. McC. The second, with increases of about 1 to 2 mEq., includes W. J. G., A. V. B., O. S. L., and H. T. E.

The last group consists of P. F. P. and W. C. with increases of 3.95 and 4.96 mEq. respectively. Average values for surface area, body weight and for the six observations on ventilation throughout the 20-minute experiment are given in Table XV. Groups I and II show no significant

TABLE XV. Ventilation during work in relation to time and lactic acid accumulation.

Average values by groups.

	Minimum lactic acid; 4 subjects	Medium lactic acid; 4 subjects	Maximum lactic acid; 2 subjects
Surface area (sq. m.)	1.87	1.87	1.77
Weight (kg.)	70.5	68.1	64.8
Ventilation, 3rd min. (l. per min.)	52.3	45.3	54.0
Ventilation, 5th min. (l. per min.)	53.0	50.3	61.5
Ventilation, 7th min. (l. per min.)	53.3	49.5	61.5
Ventilation, 13th min. (l. per min.)	54.3	52.5	70.5
Ventilation, 15th min. (l. per min.)	52.3	51.8	71.0
Ventilation, 17th min. (l. per min.)	53.0	51.3	72.0
Ventilation, average (l. per min.)...	53.0	50.1	65.1

difference except that average weight of the second group is about 3 p.c. less, and average ventilation is about 5 p.c. less. Group III, however, as compared with Group I has an average weight 8 p.c. less and an average ventilation 34 p.c. greater. It is also clear that a steady state was not reached by these two most fatigued subjects until after the seventh minute of the experiment. These observations are fully borne out by unpublished running experiments made in this laboratory on the subjects J. H. T., M. H., and D. B. D. As long as little lactic acid accumulates ventilation reaches a steady state within 3 or 4 minutes. When work is increased enough to cause large lactic acid accumulation, there is a disproportionate increase in ventilation, and instead of early attainment of a constant value the rate continues to accelerate, either until a steady state at a high level of lactic acid is reached, or until the subject stops from exhaustion.

The relation between reaction of the blood and increase in ventilation in exercise is a familiar subject of discussion. Values for pH_s in rest and work¹ have already been given in Table IV. In Fig. 10 we have shown pH of arterial serum in rest and at the end of work as a function of total ventilation. Fig. 11 shows pH_s as a function of change in ventilation

¹ A systematic error is involved in these calculations of pH_s in rest and work for the assumption of a temperature of 37.5° is made. Temperature in rest is somewhat below this and in work of this intensity possibly somewhat higher. Since we did not observe body temperature in these experiments no attempt has been made to correct for the small error involved in the assumption of a constant body temperature.

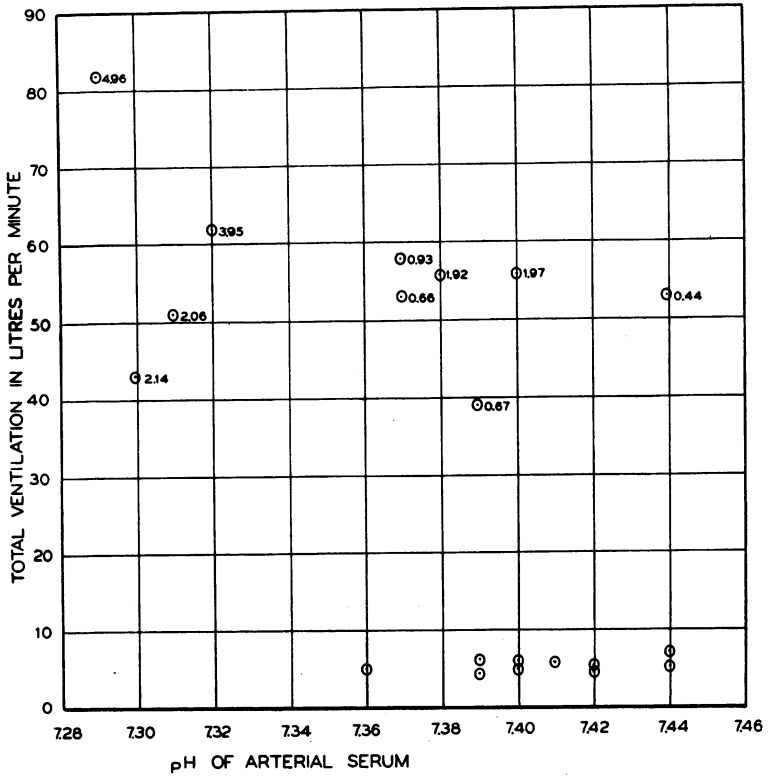


Fig. 10. pH of arterial serum as a function of total ventilation in rest and work. Increase in lactic acid concentration in mEq. per litre of blood is indicated.

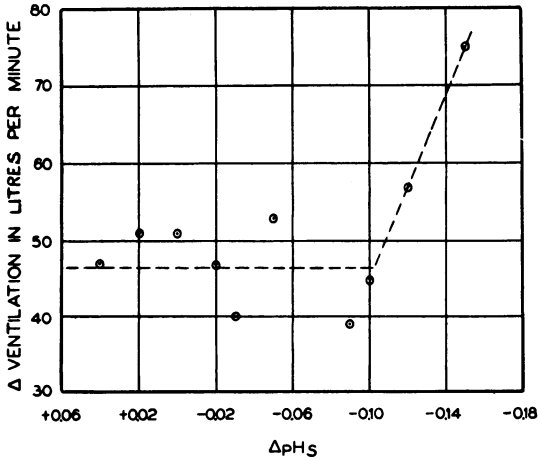


Fig. 11. Change in pH_s as a function of change in ventilation from rest to work.

from rest to work. It is clear that individual variation, both in rest and work, is considerable and that many subjects have a reaction in work well within normal limits for rest. Values in Fig. 10 indicate blood lactate concentration and illustrate again the relation between ventilation increase and lactate concentration. The two subjects with greatest lactate concentration had also greatest ventilation increase.

Increase in ventilation is of course a function of body weight. This latter variable has been eliminated in Table IV which gives values for pH_s and ventilation per kg. body weight. Here again there are large individual variations. Nevertheless it is quite clear that the relation between decrease in pH_s and increase in ventilation is not linear. As has been pointed out by L. J. Henderson⁽¹²⁾, it is clearly impossible to select one variable, such as the hydrogen-ion concentration of arterial blood, and assign to it a unique influence upon the respiratory centre.

Respiratory quotient. This is not a suitable occasion for reviewing the extensive literature upon the R.Q. in exercise, particularly in view of the recent review by Richardson⁽⁴⁰⁾. Values have been reported ranging from well below the usual resting value to unity and above. For example, there are the experiments on college oarsmen of Henderson and Haggard⁽⁴¹⁾ which led them to the conclusion that fat and sugar are burned in the same ratio in rest and work, provided one takes into account the recovery process. The results of Hill and his associates⁽¹⁾ point to an R.Q. of unity for severe exercise of short duration plus recovery. In more moderate exercise involving small oxygen debt their R.Q.s are well below unity. Experiments of particular interest from our point of view are those of Benedict and Cathcart⁽⁴²⁾, who carried out a long series of bicycle ergometer experiments on M. A. M., a professional cyclist. We have collected their values for M.R. and R.Q. in exercise from their Tables Nos. 36-52, 59-62, 68, and 70-90, not including experiments with special diets. Results for each table were averaged except where it was possible to group observations into two or more distinct metabolic levels. Sixty-eight pairs of such observations are shown in Fig. 12. The best fitting straight line for these points¹ corresponds to the equation

¹ The straight line shown on Fig. 12 was derived according to the formula

$$y = Rx - Rx_m + y_m,$$

where

$$x_m = \text{mean value of } x,$$

$$y_m = \text{mean value of } y,$$

$$n = \text{number of observations,}$$

and

$$R = \frac{n \sum xy - \sum x \sum y}{n \sum x^2 - (\sum x)^2}.$$

R.Q. = 0.04 (M.R.) + 0.817, where M.R. is expressed in litres of oxygen used per minute. The results leave no doubt that in these experiments

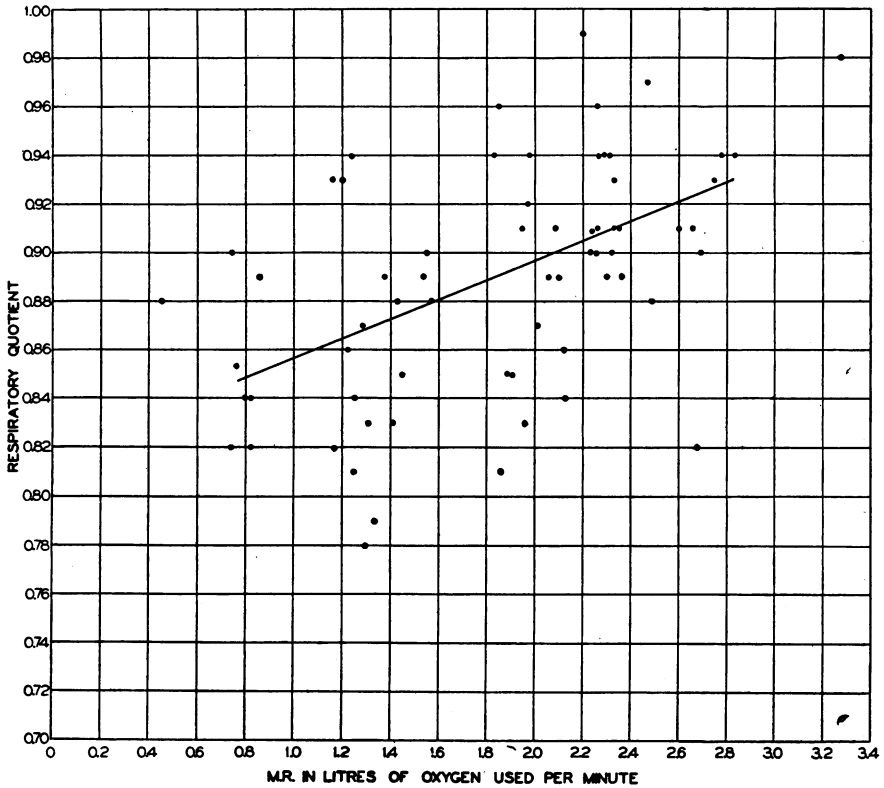


Fig. 12. Change in R.Q. with M.R. Calculated from Benedict and Cathcart(42).

there was a well-defined increase in R.Q. with M.R. This was noted by Benedict and Cathcart(42), who remarked:

“Apparently in the later experiments there was an increase in the respiratory quotients during the working period which was not observed in the earlier experiments, this probably being due to the fact that the excessive muscular work was performed in the last part of the research.”

Bock, van Caulært, Dill, Fölling and Hurxthal(21) also found values increasing with metabolic rate. De Mar, a trained athlete, had the lowest values of the group of four men studied. Talbott, Fölling, Henderson, Dill, Edwards and Berggren(33) in 2-hour experiments on J. H. T. found R.Q.s of about 0.88 at a metabolic rate of about 2.3 litres of oxygen per minute. Unpublished observations on J. H. T.

using about 2.3 litres of oxygen per minute on the bicycle ergometer give values for R.Q. above 0.9 and similar observations have been made on other individuals.

The values given for respiratory quotient in rest in Table II range from 0.72 to 0.88 and average 0.80. Recent observations of Benedict (43) on variation in the R.Q. in rest when a mouthpiece is employed, and its constancy when a suitable mask is used, leave little doubt that our three quotients in rest which depart widely from the average value give a misleading impression of the resting metabolic processes going on in those subjects.

Our evidence, however, that the R.Q.s reported for work indicate approximately what ratio of fat and carbohydrate is being used is as follows:

Carbon dioxide is being produced at about ten times the resting rate. Since the total carbonic acid content of the body is of the same order of magnitude in rest and work, ten times as much would have to be blown off or held back in a given time in order to produce a given change in R.Q. Our observations on alveolar air and on the level of the carbonic acid dissociation curve in rest and work tell us to what extent such a blowing off or retention of carbonic acid has taken place. On the average the change in alveolar carbonic acid pressure is small, as has been pointed out already. Accordingly we have again segregated the ten subjects into groups according to lactic acid accumulation. The R.Q.s thus summarized are presented in Table XVI.

TABLE XVI. Respiratory quotients during work in relation to time and lactic acid accumulation.

	Average values by groups.		
	Minimum lactic acid; 4 subjects	Medium lactic acid; 4 subjects	Maximum lactic acid; 2 subjects
3rd min.	0.90	0.90	1.00
5th min.	0.92	0.94	1.03
7th min.	0.91	0.92	0.98
13th min.	0.90	0.92	1.00
15th min.	0.89	0.92	1.00
17th min.	0.90	0.89	0.98
Average...	0.903	0.915	1.00

Groups I and II, with little or moderate lactic acid concentration, and hence small blowing off of CO₂, again show only slight difference in values for R.Q., the averages being 0.903 and 0.915, respectively. There does appear to be a slight falling off in R.Q. as work continues. Group III,

with maximum fatigue, has quotients of unity. P. F. P. showed a distinct falling off towards the close of the experiment, while W. C. evidently continued to blow off carbon dioxide to the end. We are inclined to accept the quotient 0.91 as a true indication of what materials were being oxidized in Groups I and II. The average M.R. for these groups was 2.41 litres of oxygen per minute and it is interesting that the line indicating the trend of the experiments of Benedict and Cathcart passes through the point (M.R. = 2.41, R.Q. = 0.91). Not much can be said as to fuels used by the third group. A more satisfactory procedure when exhaustion and blowing off of CO_2 occur is that of Hill, Long and Lupton⁽⁴⁴⁾, who followed oxygen consumption and carbon dioxide production through work and complete recovery. Such experiments gave quotients of about unity. Even in such experiments there is the possibility that the recovery process may involve a different proportion of fuels than that of work.

Certain facts seem to be well established and are worthy of emphasis:

(a) Exercise requiring no more than 1.5 litres of oxygen per minute is often carried on with little or no change in R.Q. The extensive experiments of Benedict and Cathcart⁽⁴²⁾ prove this.

(b) Respiratory quotient increases with metabolic rate. This is proved by the work of Benedict and Cathcart⁽⁴²⁾, and again by Bock and his associates.

(c) It is possible to carry on long-continued experiments on the ergometer at a metabolic rate of about 2 litres of oxygen per minute, with high but constant lactic acid and no blowing off of CO_2 . Under such conditions the R.Q. may average 0.94 with a net R.Q. for work of 0.96. This was shown by Henderson, Dill, van Caulært, Fölling and Coolidge⁽⁴⁵⁾.

(d) In view of the increase in R.Q. with M.R. clearly established by the work of Benedict and Cathcart, our results do not conflict with those of Krogh and Lindhard⁽⁴⁶⁾, for their oxygen consumptions were below 1.5 litres per minute.

Pulse and respiratory rates. These observations are particularly interesting in showing to what extent these rates vary among individuals. Respiratory rate in work ranged from 16 in the case of O. S. L. to 44 in the case of W. C. There is a closer relation between pulse rate and performance. Athletes have notoriously slow pulse rates as compared with non-athletes at the same metabolic level. To what extent their increased stroke volume is due to training is quite unknown.

Oxygen and carbon dioxide transport. The composition of alveolar air and of "virtual venous" air as defined by Henderson and Prince⁽³⁾,

with derived calculations, are shown in Table II. Individual determinations are given for alveolar air. Four samples were collected throughout the experiment, and in general the range from rest to work and during the course of work is not very great. This has already been referred to in Table V, and the relative constancy of alveolar carbon pressure has been used as a basis for recalculation to a common basis for all.

Alveolar oxygen pressure in work fluctuated from 87 to 116 mm. although most values were between 100 and 112 mm. Oxygen saturation of arterial blood was probably about 95 p.c. except in the cases of P. F. P. and W. C. where, on account of lactic acid accumulation and shift of the oxygen dissociation curve, it may have been as low as 92 p.c. Our basis for this conclusion consists of the arterial punctures in exercise reported by Dill, Laurence, Hurxthal and Bock⁽¹³⁾, supplemented by two unpublished experiments on the ergometer with lactic acid accumulation somewhat greater than that observed in the cases of P. F. P. and W. C. and with arterial saturations of 91.2 and 91.4 p.c. and with oxygen pressure heads of 35 and 15 mm. respectively.

With these assumptions as to saturation of arterial blood, with the established rate of carbon dioxide production and the calculated values for carbon dioxide and oxygen transport, we have calculated values shown in Table II for venous saturation and rate of blood flow. The eight subjects with least fatigue had venous saturations ranging from 41 to 50, average 44 p.c., while P. F. P. had a value of 39 and W. C. 34. In general those who had higher saturations of venous blood in rest had high values in work also. Differences between venous saturation in rest and work ranged from 31 to 38, and averaged 35 p.c. for all subjects.

Values for venous saturation are more interesting than rate of blood flow for many purposes since the variable of body weight is eliminated, and with a knowledge of the position of the oxygen dissociation curve one can derive the oxygen pressure in blood leaving tissue capillaries. By the methods described by Dill, Talbott, Edwards and Oberg⁽¹⁰⁾, we have estimated pH_c values for mixed venous blood in rest and work. The effect on position of oxygen dissociation curves of changes in pH_c , due to lactic and carbonic acids, has been found to be linear near the physiological range⁽⁴⁷⁾, and hence it is simple to interpolate on a family of oxygen dissociation curves and to estimate value for oxygen pressure in each case. The resulting estimates are shown in Table XVII.

The results in work may be considered a striking confirmation of the estimates of L. J. Henderson⁽¹²⁾ for four subjects near maximum work

TABLE XVII. Pressure of oxygen in mixed venous blood.

Subject	Rest (mm. Hg)	Work (mm. Hg)	Δ (mm. Hg)
D. B. D.	41	25	-16
P. F. P.	40	26	-14
A. A. McC.	38	25	-13
J. H. T.	46	27	-19
W. C.	39	26	-13
O. S. L.	45	30	-15
J. L. S.	45	27	-18
H. T. E.	44	27	-17
A. V. B.	42	27	-15
W. J. G.	49	27	-22
Average...	43	27	-16

on the ergometer. He has fully discussed the significance of this observation, and has estimated that blood leaving the capillary of an active muscle contains oxygen at a nearly constant partial pressure in the neighbourhood of 20 mm.

SUMMARY.

A study has been made of simultaneous changes in several important physiological variables during performance of a fixed task by ten individuals. Supplementary observations have been made on nine other subjects, including two young men after splenectomy. The task consisted in running at 9.3 km. per hour for 20 minutes with an increase in metabolism of eight to twelve times the resting rate.

Concentration of the blood in exercise by transfer of salt solution to the tissues does not commonly exceed 10 p.c. in man and in these experiments averaged about 6 p.c. in normal man and 4 p.c. in two splenectomized subjects. Changes in serum protein concentration corresponded to changes in red cell concentration. The possibility that the spleen may function in such exercise by increasing blood volume is not involved in these observations and deductions. There is no well-defined connection between physical condition and blood concentration change in exercise.

Concentration of hæmoglobin in cells is remarkably constant in normal man and increases only about 1 p.c. in work of this character.

The effect of exercise on concentration of the principal ions in serum and in cells is as follows:

(a) In non-fatigued subjects changes consist chiefly of those related to transfer of fluid carrying diffusible ions from blood to tissues, the exception being a disproportionate increase in inorganic phosphate and calcium of serum.

(b) In exhaustion there is but little greater transfer of fluid from blood to tissues, and consequently only slightly greater increase in serum protein

and in blood hæmoglobin concentrations. Lactate increase in blood is approximately balanced by decrease in other ions, notably bicarbonate and proteinate.

(c) In general, there is an increase of about 2 mEq. of anions and cations per litre of serum but, on account of the decreased proportion of serum in blood during work, there is on the average practically no change in anions and cations per litre of blood.

The principle that a machine can be judged best when running under a heavy load has been exemplified by comparing blood lactate and bicarbonate changes from rest to work. Subjects who, at rest, would be placed in the same category were differentiated precisely by our observations.

Total ventilation in work of this character reaches a steady state in 3 or 4 minutes if lactic acid is not accumulating rapidly. Even when the lactic acid increase is 4 or 5 mEq. per litre, ventilation rate may become nearly constant in from 7 to 15 minutes. The level reached in such a case may be one-third higher than in non-fatigued subjects. In these experiments there was no evidence of a linear relation between decrease in pH_s and increase in ventilation. When lactic acid does not accumulate, the subject may maintain the resting reaction in arterial plasma despite an eight or tenfold increase in metabolic rate.

Work of this level, when there is not excessive exhaustion, is associated with a change in fuel from the resting ratio of one-third carbohydrate and one-half fat to a ratio of two-thirds carbohydrate and one-third fat.

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