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ALTERATIONS IN THE LACTIC ACID CONTENT OF THE BLOOD AS A RESULT OF LIGHT EXERCISE, AND ASSOCIATED CHANGES IN THE CO_2-COMBINING POWER OF THE BLOOD AND IN THE ALVEOLAR CO_2 PRESSURE.

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I. Introduction.

Many workers have estimated the lactic acid content of the blood of man under different conditions of rest and exercise, and a very brief summary of the main results may first be given.

Lactic acid is now generally accepted as a constant constituent of the blood during rest, but the values given for its concentration by different workers vary greatly. This is probably due to the large variety of methods used for the analysis of the lactic acid, and to the fact that insufficient attention has been paid to the glycolysis in shed blood described by C. Bernard which Evans(1) showed (1922) was associated with a fall in capacity for CO_2. Hill, Long and Lupton(2), using the Clausen technique, and with full precautions against glycolysis, etc., obtained resting values which varied between 10 and 25 mg. lactic acid per 100 c.c. blood. Of this Long(3) concludes, as a result of a comparison between values given by the Clausen method and his own thiophene method, that only one-half to three-quarters represents true lactic acid, the rest being due to other substances erroneously estimated as lactic acid by the Clausen method.

In severe and in moderately severe exercise many have been able to demonstrate the existence of an increased concentration of lactic acid in the blood, including Ryffel(4); Fries(5); Lichtwitz(6); Himwich, Loebel, Barr and Green(7); Hill, Long and Lupton(2); Long(2a); Mendel, Engel, Goldschneider and Bauch(8); Schenk(9); Jervell(10); etc. The associated fall in the CO_2-combining power of the blood (Christiansen, Douglas and Haldane(11); Barr, Himwich and Green(7); Bock, Vancaulaert, etc.(12)), the expulsion of CO_2 from the body during exercise, and its retention again during recovery (Douglas, Haldane, Henderson and Schneider(13); Cook and Pembrey(14); Campbell, Douglas and Hobson(15); MacKeith, Pembrey, etc.(16); Hill, etc.(2)), and the fall in alveolar CO_2 tension (Douglas and Haldane(17)) have all been clearly demonstrated under these conditions.

In the case of moderately severe exercise, which can, however, be maintained for a considerable time, it was evident from the early work on the respiratory exchange and blood bicarbonate, referred to above, that an equilibrium must be attained at an early stage of the exercise between the processes of lactic acid production and removal. This has been verified directly by Hill, Long and Lupton, in their experiments on "lactic acid and muscular exercise"(2). Long(2a) found that for a given degree of exertion the blood lactate increased up to a level which it maintained throughout the exercise, this level being higher the more severe the exercise (see also Jervell(10)). Long found also that the rate of lactic acid oxidation, as measured approximately by the total oxygen uptake of the body at the time, varied as the square of the concentration of lactic acid found in the blood, and this agreed with the work of Hartree and Hill(18) on isolated muscle tissue, in which it was found that the maximal rate of recovery heat production varied as the square of the total initial heat liberated in contraction.

The facts may therefore be accepted as well established for the above conditions, but in marked contrast with this abundance of research carried out on the more severe types of exercise is the scarcity of work performed upon exercise such as walking, which is sufficiently gentle and natural to be considered as normal to everyday life. The only systematic work is that of Long who extended the work mentioned above to cover this type of exercise also. He found that, as is generally assumed, the blood changes differed only quantitatively from the changes in moderate exercise. A lactate increase was still found, and it still agreed roughly with the relation: O_2 uptake α (blood lactate concentration^2). This would

imply that even in very light exercise, for which the body is presumably as fully adapted as possible, a generalized increase in lactate occurs in the body, and the task of lactate oxidation and resynthesis is distributed throughout the entire body and not confined to the active tissues alone. The resting lactate concentration would thus probably correspond to the metabolism of the heart and respiratory muscles which occurs in rest.

The following results are collected from the papers of Hill, Long and Lupton, and Long, and are given for comparison with results obtained in the present research. They are corrected where necessary to bring them all to terms of lactate in whole blood:

TABLE I.

Subject	Rate of walk (m.p.h.)	Duration of exercise (min.)	Lactic acid (mg.) per 100 c.c. blood		
			Before walk	After walk*	Increase
J. C. H.	3·3	20	21·5	30·1	8·6
J. C. H.	3·3	30	13·6	31·3	17·7
J. C. H.	3·3	25	21·0	27·1	6·1
C. N. H. L.	3·5	28	13·9	24·4	10·5
C. N. H. L.	3·5	30	12·2	28·1	15·9
C. N. H. L.	3·5	30	14·0	29·6	15·6
S. S.	3·5	30	15·7	31·5	15·8
K. F.	3·7	30	11·6	28·3	16·7
C. N. H. L.	4·1	33	14·3	39·3	25·0
C. N. H. L.	4·1	30	10·1	31·3	21·2
C. N. H. L.	4·1	30	14·3	52·0	37·7
P. E.	4·5	25	12·2	30·1	17·9

* The sample after the walk was taken 1 min. from cessation of the exercise.

In the above experiments no determinations were made of the CO_2-combining power of the blood, nor of the alveolar air changes.

In their early work on similar light exercise Douglas, Haldane and Priestley(17, 19) considered the increase found in the alveolar CO_2 tension to be adequate to account for the increase in respiration which occurred at the same time, and this does not agree with the above results. There is, however, a possibility that the error, which must be introduced into such determinations as a result of the increased importance of the delay involved in making a forced expiration when the breathing is augmented by exercise (Krogh(20)), was sufficient to mask the real state of affairs. Dr Douglas and the writer(21) therefore attempted to demonstrate, following walking at 3 m.p.h. for an hour, the fall of CO_2-combining power of the blood which would be expected to accompany changes of blood lactate of the magnitude of those found by Long. In two experiments no success was obtained, there seeming to be a tendency for the bicarbonate to increase rather than fall.

More striking, however, is the experiment of Bock, Vancaulaert,

etc. (12), on de Mar, a Marathon runner of unusual ability and training. This subject was found to show as a result of a 15 mile run a rise of only about 10 mg. p.c. lactate in the blood, and this was controlled by estimations of the CO_2-combining power of the blood. Towards the end of the run the total pulmonary ventilation was measured as 90·7 l. per min. and the oxygen uptake as 3·5 l. per min., these values being the mean of two separate determinations. Bearing in mind that this is a metabolic level which many would find beyond their powers to maintain at all, this would seem to differ fundamentally from the results of Hill, who looks upon the generalized lactate increase in the body as part of the normal mechanism of increased removal.

In view of these and other scattered observations it seemed necessary to obtain further data upon the reaction of the body to light exercise, such as walking, and it was in the hope of obtaining these that the present research was undertaken.

II. Experimental methods.

Blood samples were in all cases taken without stasis from convenient veins of the forearm, through a hollow needle into a 20 c.c. syringe, a known amount of potassium oxalate having been first placed in the latter. The syringe was inverted several times, until the oxalate was carried into the blood, and the latter was then expelled into a Pyrex-glass tube, containing a known amount of sodium fluoride. The blood was well mixed, and the tube placed on ice, and only removed when some of the blood was needed for analysis. The volume of blood removed from a vein in one sample was kept as near 15 c.c. as possible. In the earlier experiments 0·06 g. oxalate and 0·015 g. fluoride were used, but in the later experiments these amounts were reduced to 0·03 g. and 0·005 g. respectively, the latter corresponding to 0·2 p.c. oxalate and 0·03 p.c. fluoride approximately.

Bicarbonate analyses were performed by the latest form of the Haldane ferricyanide method (22), and the apparatus was completely sunk in an electrically controlled thermostat, at 20° C. All the specimens of sodium fluoride available in the laboratory proved to be sufficiently acid in solution to cause serious errors in the bicarbonate analyses. This acidity was presumably due to the presence of a certain amount of the double salt NaF.HF, and was overcome by heating the salt to red heat, when the HF would be driven off. A few grams of fluoride were treated in this way at the beginning of the research, and after grinding as finely as possible were stored in a well-stoppered bottle for use throughout the

research. Repeated tests showed no deterioration of this sample. This is mentioned, since it is possible that significant errors may be introduced into similar work unless this factor be carefully controlled. The heated fluoride was very slightly alkaline in solution, but much too slightly to cause any error, granted that moderately even solution were obtained in the blood. It was found necessary to shake up the blood very thoroughly before putting it on ice so as to get all the fluoride and oxalate into solution, as otherwise much of the solid would tend to be taken up in the pipette while removing blood from the main tube to perform one bicarbonate analysis. If this occurred the analysis gave a higher value for the CO_2-combining power than subsequent duplicates which agreed together, and controls seemed to show a bigger effect than would be expected from the alkalinity of the fluoride alone. Possibly some other salt action occurs. This error was eliminated by reducing the amounts of oxalate and fluoride used to the lower limits given, and by thorough shaking of the tube as described, but it is another possible source of error which must always be kept in mind, especially if duplicates are not performed. In the present work duplicates were always performed, and at sufficient time apart to show up any progressive change which might be occurring in the blood.

Lactate analyses. The method of Friedemann, Cotonio and Shaffer(23) was used, without modification from the published procedure, except that in order to obtain the accuracy required it was found necessary to use glass-blown apparatus, so as to eliminate the rubber bung from the reaction vessel. All analyses were carried out in duplicate on two sets of apparatus, and the duplicates normally agreed to within 0·02 c.c. $N/100$ iodine, and always to within 0·04 c.c. Protein precipitation was performed by trichloracetic acid. The sample of this used at first gave no blank, but later samples all gave a small blank (about 0·1 c.c. $N/100$ iodine) which was quite constant for a given solution of acid. Unfortunately this was not noticed for some little time, and therefore the lactate values of the preliminary experiments are not accurate to a milligram or two per 100 c.c. blood, though relatively in any experiment they are accurate. The copper-lime method of van Slyke(24) was used for sugar removal. The actual procedure was as follows—5 c.c. blood were run slowly into 25 c.c. 7 p.c. CCl_3COOH in a centrifuge tube. The latter was closed by a rubber bung, and the contents well shaken. After standing an hour or so the mixture was centrifuged, and 25 c.c. of clear fluid obtained. To this 5 c.c. 10 p.c. $CuSO_4$ solution, followed by 20 c.c. 5 p.c. lime suspension, were added, and the mixture

shaken mechanically for ½ to 1½ hours, when it was centrifuged. Enough clear fluid was obtained to perform two analyses on 20 c.c. each. Full blanks were performed in all later experiments.

Phosphate analyses. The method of Fiske and Subbarow was used (25).

Hæmoglobin values were obtained by means of the Gowers-Haldane hæmoglobinometer.

III. Control experiments.

Since the research depended upon the accuracy of the lactate analyses a considerable number of control experiments were performed, from which the following are taken at random:

Table II. Analyses of pure zinc lactate solutions.

Lactate analysed— in lactic acid (mg.)	Lactic acid found (mg.)	Recovery (p.c.)
0·286	0·284	99
0·572	0·579	101
0·858	0·855	100
0·509	0·550	108
0·467	0·490	105
0·934	0·980	105
0·464	0·475	102
0·928	0·933	101
0·464	0·460	99
0·940	0·928	99
0·940	0·911	98
0·962	0·942	97

The lactate used in the above gave 99·7 p.c., the theoretical weight of ash, on heating.

Table III. Recovery from blood of added lactate.

	Lactate added, as lactic acid (mg. p.c.)	Lactic acid found (mg. p.c.)	Lactic acid increase (mg. p.c.)	Recovery (p.c.)
(*a*)	0·0	14·7	—	—
	7·6	22·7	8·0	105
	15·1	30·5	15·8	105
(*b*)	0·0	38·9	—	—
	19·1	57·5	18·6	97
(*c*)	0·0	46·6	—	—
	10·1	55·6	9·0	89
	15·1	61·1	14·5	96
	20·1	65·8	19·2	96

It may be pointed out that in the above, since slaughter-house blood was used, the total amounts analysed were greater than in the actual experiments, where the average was about 12 mg. lactic acid p.c., and this would increase the errors. In spite of this there is a general accuracy well within 1 mg. p.c. The comparative accuracy of the method is

better shown by the results of duplicate extractions upon fresh human blood. The following are all the cases in which this double extraction was performed in the normal course of experiments, and the absolute agreement shows that there was a relative accuracy to within the limits of the titration, *i.e.* one drop of iodine, or about 0·5 mg. lactic acid p.c.:

TABLE IV. Duplicate extractions and analyses on blood lactate.

Lactic acid of blood (mg. p.c.)	
A	*B*
14·7	14·9
9·8	9·8
12·3	12·3
14·9	14·9
14·7	14·7

Controls were also carried out, in which 5 c.c. of diluted blood as well as 5 c.c. of undiluted blood were extracted, and—as the values obtained agreed well—this controlled the accuracy of the blank values obtained, and the efficiency of the methods of extraction.

In performing the phosphate analyses the standard time of 10 min. between mixing the reagents and colour comparison was often extended to some hours. The following controls show the general accuracy of the method, and the fact that the above delay had no significant effect on relative values:

TABLE V. Control experiments for analyses of inorganic phosphate.

Phosphate analysed, as phosphorus (mg.)	Phosphorus found (mg.), with colour comparison	
	At 15 min.	At 12 hours
0·160	0·160	0·160
0·160	—	0·160
0·200	0·200	0·195
0·180	—	0·178
Blood (*a*)	2·92 p.c.	3·10 p.c.
„ +0·4 p.c.	3·32 p.c. (+0·39)	3·51 p.c. (+0·41)
Blood (*b*)	3·38 p.c.	3·45 p.c.
„ +added phosphate	3·62 p.c. (+0·24)	3·67 p.c. (+0·22)

IV. EXPERIMENTAL RESULTS.

The greater number of experiments were performed on the following general plan. The experiment was carried out between about 9 a.m. and 11.30 a.m., and the subject had then had no food since the previous evening. He first rested for an hour in a deck-chair in the laboratory, and at the end of this period—with as little disturbance as possible—one arm was immersed in some hot water for a few minutes and a blood sample collected from a convenient vein. The object of the hot water

was to increase the blood flow through the arm, and so to render the blood obtained more arterial in character. The subject next walked round a track measured out outside the laboratory (about seven laps to a mile) for about 30 min., this being considered long enough to permit of the establishment of fairly complete equilibrium throughout the body.

If an alteration in the lactate concentration occurred of the order of that found by Long, and if equilibrium had been established throughout the body, it was not considered likely that all this lactate could be removed very rapidly after the exercise, so that time was allowed in the earlier experiments to immerse the arm for a short time in hot water before taking the second sample. This therefore was not obtained for 3 to 5 min. after cessation of the walk.

The results of the preliminary experiments are given below:

TABLE VI. Preliminary experiments.

Subject	Rate of walk and duration	Blood lactate found (mg. p.c.)		Combined CO_2 in c.c. p.c. at S.T.P. and CO_2 pressure in saturator
W. H. O.	4 m.p.h. for 38 min.	After 1 hr. rest	14·5	48·7 (at 41·0 mm. Hg)
		4½ min. after walk	13·5	48·7 (at 40·7 „)
W. H. O.	4 m.p.h. for 45 min.	After 1 hr. rest	20·5	— —
		4½ min. after walk	21·3	— —
W. H. O.	4·2 m.p.h. for 47 min.	After 1 hr. rest	11·5	48·2 (at 41·9 „)
		4 min. after walk	11·8	49·9 (at 41·8 „)
W. H. O.	4·5 m.p.h. for 30 min.	After 1 hr. rest	—	45·5 (at 39·7 „)
		After 1 hr. rest	14·5*	44·6 (at 39·5 „)
		5 min. after walk	16·4*	45·4 (at 39·7 „)
C. G. D.	4·0 m.p.h. for 60 min.	After 1 hr. rest	14·5	46·1 (at 38·9 „)
		3 min. after walk	13·9	46·6 (at 39·2 „)
C. G. D.	4·9 m.p.h.	After 1 hr. rest	16·0	46·5 (at 44·3 „)
		5 min. after walk	15·3	46·7 (at 44·3 „)

* Poor lactate analyses in this case.

Since the above six experiments were performed at an early stage of the research, in which CCl_3COOH blanks were not done, these values may be 1 or 2 mg. p.c. too high, but are relatively correct.

Since these experiments showed no increase in blood lactate, nor any fall of CO_2-combining power of the blood after exercise, it was desirable to obtain blood samples from the subjects actually during the course of the exercise. No mechanical platform being available this proved impracticable for walking exercise, and it was necessary to compromise, obtaining blood samples as soon as possible after the cessation of a walk, and in parallel experiments obtaining blood samples actually during the course of light exercise on a cycle ergometer.

Taking first the walk experiments, it was impossible, if the sample were

to be obtained rapidly after cessation of exercise, to submerge the arm in hot water before taking this sample. It is not thought that this can make any real difference to the results, since the exercise itself almost always sufficed to put up the circulation rate in the arms considerably, especially if the hands were kept covered during the walk. On cold days, however, this increase in local circulation rate did not occur, with the result that the attempt to obtain the blood sample rapidly after cessation of exercise failed. This fact is really fortunate in that it provides a control on the experiments—if the blood flow in the arm were not increased as a result of the exercise, and the conditions before exercise and using hot water, and after exercise without the use of hot water, were not strictly comparable the experiment was automatically eliminated. The prominence of the arm veins may be taken as a rough criterion of the local blood flow, and it was found that they normally appeared of similar sizes in the

TABLE VII. Experiments on walking exercise, subject W. H. O.

	Rate of walk and duration	Blood lactate found (mg. p.c.)		Combined CO_2 in c.c. p.c. at S.T.P. and CO_2 pressure in saturator
1.	3·9 m.p.h. for 30 min.	After 1 hr. rest	14·9	— —
		20–80 sec. after walk	14·7	— —
2.	4·0 m.p.h. for 30 min.	After 1 hr. rest	10·0	48·5 (at 39·8 mm. Hg)
		25–60 sec. after walk	7·5	48·5 (at 40·5 ,,)
		Do. (repeat at 24 hrs.)	9·3	— —
3.	4·2 m.p.h. for 28 min.*	After 1 hr. rest	10·6	47·7 (at 40·0 ,,)
		20–70 sec. after walk	11·1	48·6 (at 40·3 ,,)
4.	4·5 m.p.h. for 32 min.†	After 1 hr. rest	8·4	48·6 (at 45·1 ,,)
		30–90 sec. after walk	13·1	47·2 (at 45·2 ,,)
5.	4·5 m.p.h. for 27 min.	After 1 hr. rest	14·8	— —
		27–? sec. after walk	14·8	— —
6.	4·5 m.p.h. for 25 min.	After 1 hr. rest	12·2	47·3 (at 42·3 ,,)
		25–55 sec. after walk	12·0	46·4 (at 42·5 ,,)
7.	4·5 m.p.h. for 27 and 26 min., 5 min. rest between	After 1 hr. rest	11·2	48·4 (at 42·3 ,,)
		35–75 sec. after walk	11·2	48·0 (at 42·4 ,,)
8.	4·7 m.p.h. for 25 min.	After 1 hr. rest	11·4	47·0 (at 40·9 ,,)
		30–68 sec. after walk	19·3	44·7 (at 42·0 ,,)
9.	4·8 m.p.h. for 26 min.	After 1 hr. rest	12·0	47·1 (at 41·1 ,,)
		25–55 sec. after walk	24·7	44·0 (at 41·6 ,,)
10.	5·0 m.p.h. for 40 min.	After 1 hr. rest	10·4	— —
		c. 30 sec. after walk	50·4	— —
11.	5·4 m.p.h. for 14 min.	After 1 hr. rest	7·3	46·2 (at 40·4 ,,)
		20–80 sec. after walk	53·1	38·0 (at 40·1 ,,)

* The walk was carried out in this experiment before the rest period.
† No CCl_3COOH blanks were done in this experiment.

Walking at 4·0 m.p.h.: O_2 consumption = 1·41 l. per min. at S.T.P.
,, 4·3 ,, ,, = 1·50 ,, ,,
,, 4·8 ,, ,, = 1·92 ,, ,,
,, 4·9 ,, ,, = 1·95 ,, ,,

above two conditions. Light pressure was applied to the veins by the subject until the needle had been introduced into the vein, but none during the taking of the sample. The actual procedure was that during the last moments of the walk the subject removed his jacket, and bared the arm from which the sample was to be taken. He then sat down on a stool and at the same time started a stop watch. The sample of blood was taken as quickly as possible, and the time limits noted on the watch. Usually the sample was obtained between about 20 sec. and 1 min. after cessation of the walk. The results are given in Tables VII and VIII,

TABLE VIII. Experiments on walking exercise, subject C. G. D.

	Rate of walk and duration	Blood lactate found (mg. p.c.)		Combined CO_2 in c.c. p.c. at S.T.P. and CO_2 pressure in saturator
1.	4·0 m.p.h. for 31 min.*	After 1 hr. rest 15–60 sec. after walk	10·6 18·9	47·4 (at 40·5 mm. Hg) 46·5 (at 39·3 „)
2.	4·0 m.p.h. for 30 min.*	After 1 hr. rest 15–60 sec. after walk	13·1 8·0	45·0 (at 39·9 „) 46·3 (at 39·0 „)
3.	4·0 m.p.h. for 30 min.	After 1 hr. rest 25–60 sec. after walk	8·0 7·1	— — — —
4.	4·5 m.p.h. for 26 min.	After 1 hr. rest 20–50 sec. after walk	9·9 10·7	47·3 (at 42·4 „) 47·2 (at 41·6 „)
5.	4·5 m.p.h. for 28 and 15 min., 3 min. between	After 1 hr. rest 25–55 sec. after walk	10·6 10·3	49·2 (at 40·6 „) 48·1 (at 41·2 „)
6.	4·7 m.p.h. for 30 min.	After 1 hr. rest 20–60 sec. after walk	9·8 12·3	47·5 (at 39·2 „) 47·5 (at 40·1 „)
7.	4·9 m.p.h. for 31 min.†	After 1 hr. rest 15–60 sec. after walk	9·1 13·7	46·6 (at 41·0 „) 47·1 (at 40·5 „)
8.	4·9 m.p.h. for 28 and 15 min., 4 min. between	After 1 hr. rest 15–47 sec. after walk	8·7 12·6	47·5 (at 40·8 „) 48·7 (at 41·2 „)
9.	4·9 m.p.h. for 33 min.	After 1 hr. rest 20–50 sec. after walk	17·6 21·0	46·9 (at 42·3 „) 47·2 (at 41·4 „)

* The walk was carried out in this experiment before the rest period.
† No CCl_3COOH blanks were done in this experiment.

Walking at 4·0 m.p.h.: O_2 consumption = 1·36 l. per min. at S.T.P.
„ 4·5 „ „ = 1·85 „ „
„ 5·0 „ „ = 2·28 „ „

which also contain the values for O_2 consumption obtained in parallel experiments on the same subject.

The ergometer experiments were undertaken since this was the only type of exercise available during which it was possible to take blood samples without any interruption of the exercise. A Krogh electric brake ergometer was used, and in all the experiments the same rate of work was adopted, *i.e.* 525 kg. m. per min., with a rate of rotation of the pedals of 50 per min. This level of exercise was chosen as giving an oxygen

consumption comparable to that during walking exercise at 4·0 m.p.h. (*c.* 1·4 l. O_2 per min.).

The procedure was similar to that in the walk experiments. The subject, who was always in the post-absorptive state at the time, rested in a deck-chair for an hour as before. At the end of the hour a blood sample was collected, the arm having been warmed up first in hot water. The subject then commenced work on the ergometer, and after a convenient tim a second blood sample was collected without interruption of the work. In this case also it was possible to warm up the arm first, by placing it in a bucket supported at the side of the ergometer. Thus the work sample was in every way comparable to the rest sample. About 5 min. after the second sample had been taken the subject ceased work, and at once got off the ergometer and sat down again in the chair, at the same time starting a stop watch. A third blood sample was then collected, without the use of hot water, the time limits being again noted on the watch.

The results are given in Table IX:

TABLE IX. Ergometer experiments at 525 kg. m. per. min.

	Subject	Blood lactate found (mg. p.c.)		Combined CO_2 in c.c. p.c. at S.T.P. and CO_2 pressure in saturator
1.	W. H. O.	After 1 hr. rest	10·3	48·0 (at 41·6 mm. Hg)
		During work (at 40 min.)	13·4	46·4 (at 42·3 ,,)
		1½–3½ min. after work	11·8	47·3 (at 41·9 ,,)
2.	W. H. O.	After 1 hr. rest	8·2	— —
		During work (at 55 min.)	8·2	— —
		During work (at 68 min.)	12·7	— —
		3–4 min. after work	11·9	— —
3.	W. H. O.	After 1 hr. rest	12·3	46·0 (at 42·9 ,,)
		During work (at 25 min.)	11·1	47·0 (at 42·1 ,,)
		4½–5¾ min. after work	10·5	47·0 (at 42·1 ,,)
4.	C. G. D.	After 1 hr. rest	11·0	47·5 (at 40·8 ,,)
		During work (at 28 min.)	25·7	45·4 (at 41·6 ,,)
5.	C. G. D.	After 1 hr. rest	16·0	42·2 (at 40·8 ,,)
		During work (at 30 min.)	25·5	41·4 (at 40·8 ,,)
		2¾–4 min. after work	23·9	40·9 (at 41·0 ,,)
6.	C. G. D.	After 1 hr. rest	11·1	46·5 (at 42·4 ,,)
		During work (at 44 min.)	16·7	45·9 (at 42·0 ,,)
		6–6½ min. after work	13·6	46·1 (at 42·0 ,,)
7.	C. G. D.	After 1 hr. rest	11·6	48·8 (at 42·4 ,,)
		During work (at 32 min.)	19·3	47·1 (at 41·6 ,,)
		5½–6¾ min. after work	18·6	47·4 (at 41·8 ,,)

W. H. O. working as above: O_2 consumption = 1·40 l. per min. at S.T.P.
,, ,, ,, ,, = 1·32 ,,
C. G. D. ,, ,, ,, = 1·43 ,,
,, ,, ,, ,, = 1·40 ,,

Since the CO_2-combining power of the blood might be affected by changes in dilution, or in the inorganic phosphate content during exercise, the hæmoglobin values of the blood samples were taken in all cases, and the inorganic phosphate content estimated in the earlier experiments. The hæmoglobin values showed no constant or significant alterations, and need not be given here. The phosphate values obtained are given in Table X:

TABLE X. Inorganic blood phosphate changes during exercise.

Subject	Exercise	Inorganic phosphorus (mg. p.c.) Before	After	Change	Lactate change (mg. p.c.)
W. H. O.	Walk at 4·0 m.p.h. for 38 min.	2·86	3·02	+0·16	− 1·0
,,	,, 4·2 ,, 47 ,,	3·24	3·51	+0·27	0
,,	,, 4·5 ,, 30 ,,	3·72	3·75	+0·03	0
,,	,, 4·5 ,, 30 ,,	3·70	3·98	+0·28	0
,,	,, 4·5 ,, 32 ,,	3·68	3·87	+0·19	+ 4·7
C. G. D.	,, 4·0 ,, 61 ,,	3·44	4·00	+0·56	—
,,	,, 4·0 ,, 60 ,,	3·38	3·62	+0·24	+ 0·6
,,	,, 4·9 ,, 32 ,,	3·67	3·90	+0·23	+ 0·7
W. H. O.	Ergometer work for 45 ,,	3·98	4·57	+0·59	+ 3·1
C. G. D.	,, ,, 30 ,,	4·02	4·24*	+0·22	+14·7
,,	,, ,, 30 ,,	4·20*	3·99	+0·21	+ 1·6

The after-work samples were in most cases obtained about 45 sec. after the end of the walk, 2 min. after the end of the ergometer work.

Ergometer work was 525 kg. m. per min. on Krogh electric cycle ergometer.

* Sample taken during work.

Some determinations were made in the usual manner of the oxygen debts incurred in exercise such as studied in the foregoing experiments. The results need not be given in full, but the estimated O_2 debts were as follows:

TABLE XI. Oxygen debts following exercise.

Subject	Exercise	O_2 debt, in l. at S.T.P.
W. H. O.	Walk at 4·0 m.p.h. for 30 min.	1·09
,,	,, 4·5 ,, 30 ,,	0·99
,,	Ergometer work for 30 ,,	0·97
C. G. D.	Walk at 4·0 m.p.h. for 30 ,,	1·07
,,	,, 4·5 ,, 30 ,,	1·49
,,	Ergometer work for 30 ,,	1·62

Ergometer work was 525 kg. m. per min. on Krogh electric ergometer.

A certain number of determinations were made of the alveolar CO_2 pressure changes before and after exercise of the type studied throughout this work. The results obtained are given graphically, as they are most intelligible in this form.

A comparison has been made between the lactate values given by the Clausen(26) and Friedemann(23) methods of analysis, and the results are given in Tables XII and XIII.

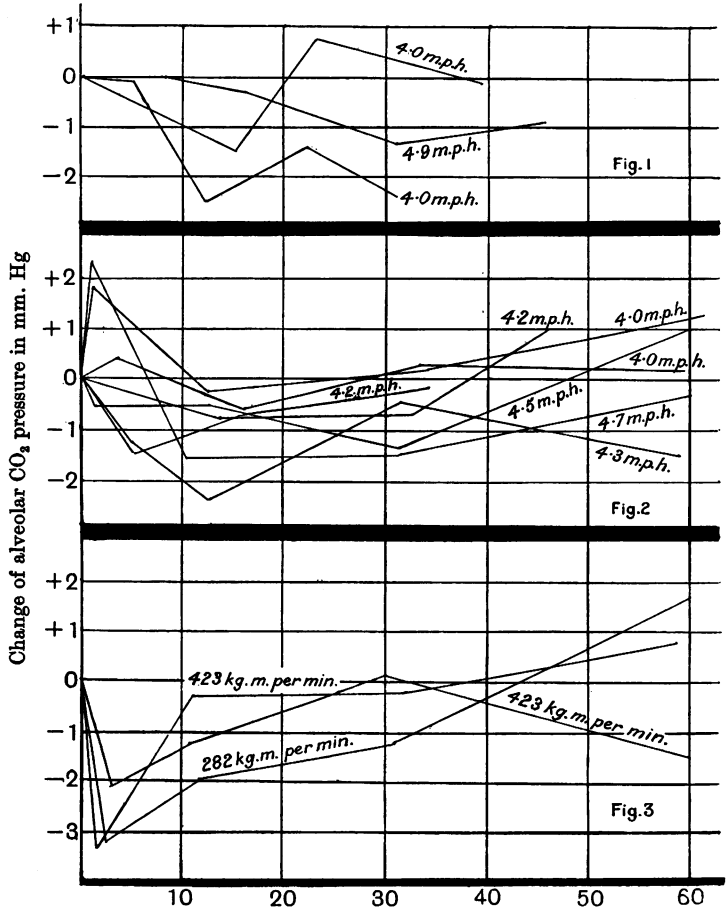

Fig. 1. Subject C. G. D., walking exercise.

Fig. 2. Subject W. H. O., walking exercise.

Fig. 3. Subject W. H. O., ergometer exercise.

It is customary to multiply the value obtained by the Clausen technique by some factor, in order to allow for the low recovery in analyses of pure lactate solutions. The factor adopted in the third column below (*i.e.* × 100/90) is as low as any used in the published work,

and seems near enough for the present purposes, judging from the three analyses given in Table XII, without further justification.

TABLE XII. Comparison of Clausen and Friedemann methods of lactate analysis applied to pure lactate solutions.

Lactate analysed as lactic acid (mg.)	Friedemann value. Lactic acid (mg.)	Clausen value. Lactic acid (mg.)
0·572	0·579	0·545 (95 p.c.)
0·858	0·855	0·727 (85 p.c.)
0·464	0·460	—
0·928 (same sample as next above)		0·853 (92 p.c.)

TABLE XIII. Comparison of Clausen and Friedemann methods of lactate analysis applied to blood extracts.

	Friedemann value (mg.)	Clausen value (mg.)	Clausen value × 100/90 (mg.)
Slaughter-house blood	28·1	36·0	40·0
W. H. O. casual sample	14·8	19·2	21·3
Do. veins compressed	15·2	28·0	31·1
C. G. D. resting sample	9·0	7·7	8·6
Slaughter-house blood	15·5	18·1	20·1
Do. extracting less blood	15·9	18·7	20·7
Slaughter-house blood	38·9	43·0	47·9
Do. + 19·1 mg. p.c.	57·5	59·3	65·9
C. G. D. resting sample*	9·8	10·9	12·2
Do. after walk at 4·7 m.p.h.*	12·3	15·7	17·5
W. H. O. resting sample*	14·9	14·7	16·3
Do. after walk at 3·9 m.p.h.*	14·7	14·5	16·1

* Values of this experiment are the means of duplicate extractions and analyses, which agreed well together.

V. DISCUSSION OF RESULTS.

Before discussing the actual results obtained it must be pointed out that the experiments were performed throughout on the same two subjects, C. G. D. and W. H. O. These subjects differ markedly both in age and in build, so that it is considered as improbable that any results obtained on both can have been due to individual idiosyncracies. Both subjects were fit, but in no sense in athletic training, most of their time being spent in ordinary laboratory work, with occasional games of golf and tennis. Thus they may be taken as corresponding physically to average active adults.

Resting blood lactate concentrations. The values obtained for the samples of blood taken at the end of 1 hr. rest are given below, being retabulated from the tables already given. Only those values are included which are considered to be correct absolutely (*i.e.* when full blanks were performed):

TABLE XIV. Lactic acid of blood during rest.

	Subject W. H. O. Lactic acid (mg. p.c.)	Subject C. G. D. Lactic acid (mg. p.c.)
	10·3	11·0
	8·2	16·0
	12·3	11·1
	14·8	11·6
	12·2	9·9
	7·3	8·7
	11·2	10·6
	10·8	17·6
	11·9	10·6
	11·4	13·1
	10·6	8·0
	10·0	9·8
	14·9	—
Average	11·2	11·5

The resting lactate values obtained seem to be lower and somewhat less variable than most in the literature (*v.* Table I for values obtained by Hill, Long and Lupton). The most probable explanation of this fact would be that the Friedemann method here used gives lower values on blood extracts than the various methods used by former workers. The best of earlier methods was probably the so-called Clausen method (26), and this was used by Hill, etc., in their work. In Tables XII and XIII have been given the results of experiments in which the Clausen and Friedemann methods have been compared, when applied to solutions of pure lactate and also to blood extracts. From these it is clear that the Clausen method must estimate as lactic acid other substances present in the blood, since the Friedemann method gives higher values on pure lactate solutions, and gives an almost 100 p.c. recovery of added lactate in blood, but none the less gives lower absolute values on blood extracts. It is of course impossible to say how far the Friedemann values represent true lactic acid, but they would seem certainly to be nearer to the truth than those given by the Clausen method.

Lactate changes during light exercise. It can be seen from the tables of results given that in most cases parallel analyses were performed on the lactate content and CO_2-combining power of the blood samples obtained. The object of the latter was to provide a control on the lactate changes, if any, found by the direct analyses, but for this control to have any value it was necessary to be reasonably certain that no significant alteration occurred in the CO_2-combining power of the blood from other causes than lactic acid changes. Dodds (27) has shown that the secretion of the digestive juices during digestion is accompanied by marked altera-

tions in the acid-base equilibrium of the body, so that in order to avoid this the subjects were always in the post-absorptive state at the time of an experiment. Even with this precaution it is possible that if an experiment be allowed to overlap, or even approach, the normal meal times some error may arise from the same cause, so that experiments were performed as far as possible at periods intermediate between meal hours. Thus if the experiment commenced at 9 a.m. the rest period ended at about 10 a.m. and the blood samples were collected between 10 a.m. and 11.30 a.m. In this way it is hoped that this error was eliminated. Again, changes in dilution of the blood were controlled by means of the hæmoglobin values of the blood samples, and as already stated no significant alterations found. Changes in the complicated buffer substances of the blood could not be fully controlled, but the inorganic phosphate content of the blood was determined in several early experiments (Table X), and no changes of importance from this point of view were found. Changes in acetone bodies were not properly controlled, but no investigators have found any important changes following ordinary light exercise, nor was any increase found in acetoacetic acid or free acetone in a few cases tested in the present work (these observations were made by placing bisulphite in the receiving vessels of the Friedemann apparatus during the preliminary boiling period, before addition of $KMnO_4$, when any acetone—either preformed or produced by hydrolysis of acetoacetic acid in the acid contents of the reaction vessel—should be trapped, and capable of estimation in the usual manner). In view of all this it seems justifiable to correlate the lactate and bicarbonate changes found.

Turning then to the actual results obtained, it is clear from Table VI that the preliminary experiments gave evidence neither of an increase in blood lactate following exercise, nor of a fall in the CO_2-combining power of the blood. The rates of walk varied between 4 and 4·5 m.p.h. for W. H. O. and 4 and 4·9 m.p.h. for C. G. D., and the after-work samples were obtained between 3 and 5 min. from cessation of the exercise. The duration of the walk varied between half and one hour, and must have been sufficient to allow of the establishment of equilibrium throughout the body, and it was considered unlikely therefore that if a generalized lactate increase had occurred of the order of that found by Hill, etc., it could have been completely masked within so short a time. This assumption has since been verified during the course of the ergometer experiments, to be discussed later. From the present point of view the following results may be quoted from the latter experiments

(Table IX): on W. H. O. (Exp. 2), an increase of 4·5 mg. p.c. lactate during work had only decreased to 3·7 mg. p.c. 3½ min. later; on C. G. D. (Exp. 5), an increase of 9·5 mg. p.c. during work had fallen to one of 7·9 mg. p.c. 3½ min. later; on C. G. D. (Exp. 6), an increase of 5·6 mg. p.c. had fallen to one of 2·5 mg. p.c. 6¼ min. later; on C. G. D. (Exp. 7), an increase of 7·7 mg. p.c. had fallen to 7·0 mg. p.c. 6 min. later; and against this there were no experiments in which an appreciable lactate increase had been masked within 5 min. from cessation of exercise.

In view of the later experiments (Tables VII and VIII) in which the after-walk sample was obtained between the limits of about 20 sec. and 60 sec. after exercise, these early experiments need not be discussed further now, for in so short a time it is almost inconceivable that a significant lactate alteration in the blood could have been masked, granted that approximate equilibrium had been established in the body generally. Hill, Long and Lupton state that the work samples in their experiments were taken 1 min. after cessation of the walk, but do not specify if this was the time of the beginning or end of the sample, or the mean time of these two, but in any case the samples in the present work must have been obtained at least as rapidly.

In spite of the speed with which the after-work samples were obtained, there is only one experiment on either subject (C. G. D., Table VIII, Exp. 1) in which any increase in lactate concentration was found in the blood at rates of walking below 4·5 m.p.h., and at 4·0 m.p.h. there seems some tendency towards an actual fall in blood lactate.

Of the four experiments on W. H. O. at 4·5 m.p.h., and of the two on C. G. D. at the same rate of walking, only the first on W. H. O. showed any increase in the lactate concentration in the blood, and the increase there was only 4·7 mg. p.c. In this one case showing a rise it is probably significant that the subject was feeling rather unwell at the time, and was quite fatigued at the end of half an hour's walk, even at the easy pace studied. Between 4·5 m.p.h. and 4·7 m.p.h. there seems to be, for both subjects, some critical rate of walk, above which only did an increase in blood lactate follow the exercise. In the case of W. H. O., who is of smaller build than C. G. D., the effort of walking at rates above 4·75 m.p.h. is greater than it is for C. G. D., and it also increases more rapidly as the rate is put up. Probably C. G. D. walks normally at a rate slightly above that adopted by W. H. O. In accordance with these facts the lactate increase found in the blood at rates over the critical speed rises more rapidly in W. H. O. than in C. G. D.

The reason for the one discordant result on C. G. D. already mentioned, where an increase of 8·3 mg. p.c. lactic acid was found following a walk at 4·0 m.p.h., is quite unknown, as the experiment seemed in every detail identical with the others. It may be of some significance that this was the next experiment on C. G. D., though at an interval of 14 days, to that in which he gave the highest resting lactic acid level, 17·6 mg. p.c.

The bicarbonate analyses control the results obtained by the direct lactate analyses very well. Thus for W. H. O. in Exps. 2, 3, 6, 7, no increase was found in the blood lactate, and for these experiments the average of the bicarbonate analyses gives:

Before walk: 48·0 c.c. p.c. CO_2 at 41·1 mm. Hg CO_2 pressure in saturator.
After „ 47·9 „ 41·4 „ „

In all the other experiments on W. H. O. an increase was found in the blood lactate, and this was in every case accompanied by a fall in the CO_2-combining power of the blood, which corresponded in magnitude to the lactate rise, and was very evident with any appreciable lactate alteration.

In the case of C. G. D. none of the experiments were at fast enough rates to give, in this subject, a marked alteration of blood lactate, and in accordance with this there was in no case found a significant fall of CO_2-combining power of the blood. In Table VIII, Exps. 7, 8 and 9, the changes are not in agreement, but as they are small this is of no real importance, and on the whole the lactate and bicarbonate changes agree together extremely well in both subjects.

Lactate changes in light ergometer exercise. The results of the ergometer experiments are interesting from several points of view, especially since in them the blood samples were taken actually during the course of the exercise. In the case of C. G. D., who had not done any bicycling for several years, the contrast between the effects of this type of exercise, and those of walking exercise, is very striking. Thus in the first experiment of this type on C. G. D. the blood lactate increased from a normal rest value of 11·0 mg. p.c. to 25·7 mg. p.c. during exercise, although the severity of the exercise, as measured by O_2 uptake, only corresponded to that of a 4 m.p.h. walk. In successive experiments the lactate rise found tended to diminish, and was in order—14·7 mg. p.c., 9·5 mg. p.c., 5·6 mg. p.c., and 7·7 mg. p.c. This was clearly an example of the effect of training, or adaptation of the body to the particular exercise. W. H. O., in contrast to C. G. D., had carried through the experiments on alveolar CO_2 changes

which involved the use of the ergometer, and had in the interval between then and the present experiments done some cycling, and in his case the lactate rise found was always small or zero. In successive cases it was 3·1 mg. p.c., 0 mg. p.c. at 55 min. work, and 4·5 mg. p.c. at 68 min. work, and finally a fall of 1·2 mg. p.c. In the second case on W. H. O. in which a small increase was found in the second work sample, but not in the first, the subject who was still quite comfortable after 55 min. had by the time of the second sample commenced to find the work irksome, and both subjects had the impression that the lactate rise found corresponded roughly to the feeling of discomfort due to the saddle. It would be interesting to compare similar degrees of exercise, using different saddles and cycle frames.

In all these experiments, again, the changes of CO_2-combining power found agree with those of lactate, and adequately control the latter.

The value of these results, as showing the persistence after cessation of exercise of small lactate changes, has already been mentioned.

Alveolar CO_2 *changes following light exercise.* The accumulation, and subsequent removal, of lactic acid in the blood and tissues are accompanied by definite changes in the alveolar CO_2 pressure of the individual, changes which—as mentioned in the Introduction—have been clearly demonstrated in the case of severe exercise. An attempt was therefore made to follow the alveolar CO_2 changes in the case of the types of exercise studied throughout the present research, the object being to provide a control of yet another type on the direct lactate analyses. The alterations which occur are small, and to provide any really adequate investigation would require a separate research. Looking at the graphs (p. 226), which give separately the results on W. H. O. walking and performing ergometer work, and on C. G. D. walking, it is evident that in every case there was a fall of the alveolar CO_2 pressure, soon after cessation of work, to a level below the resting value found in the same experiment. In the walk experiments performed on both subjects this fall seems greatest at a period 10 to 15 min. from the end of the walk, and if it were due to a lactic acid increase in the body there would seem no reason for the delay. It would appear rather more likely that the fall was due to some other factor, such as a temperature change in the body as a result of the exercise, though to be sure of any effect of this nature would need a much fuller investigation than possible in conjunction with the present research. In the three ergometer experiments on W. H. O. the fall seems to have reached its lowest point within the first few minutes from the cessation of exercise, and in contrast to the above

is just such as might be expected to follow an increase of lactic acid in the body.

In the walk experiments on both subjects in analogous conditions no lactate rise was found, so that the alveolar CO_2 results agree with this, but in the ergometer experiments on W. H. O. little or no lactate rise was found. The conditions in these two sets of experiments were, however, not really comparable, since those experiments performed for the investigation of alveolar air changes were carried through at an early stage of the research, when the subject had done no cycling for a year, and were performed on a Martin ergometer which was very uncomfortable for him, whereas the lactate experiments were done late in the research, after the subject had done a fair amount of cycling, and on the far more comfortable Krogh ergometer. It is quite possible, therefore, that a lactate increase did occur, such as would be expected from the alveolar changes found. With so few experiments, however, it is only permissible to say that the two sets are more in agreement than opposition.

Changes of inorganic phosphate in the blood following light exercise. The results given in Table X have already been discussed with regard to their bearing on changes in CO_2-combining power of the blood. The only systematic work published on inorganic phosphate changes in the blood during exercise is that of Havard and Reay(28), who found that immediately after short severe exercise there is a rise in concentration of the blood phosphate, followed at once by a fall to below the resting level. This fall was less in trained than in untrained individuals. The usual maximum for the rise was about 10 p.c. If the work were less severe, but longer continued (*e.g.* up to 15 min. running) the rise tended to be greater, reaching a maximum of about 25 p.c. No relation could be found between phosphate and lactate changes. In none of these experiments was the exercise really light (though Dr Havard has kindly told me that in two unpublished experiments no phosphate increase in the blood was found to follow walking exercise), and the present results are mainly of interest as supplying data for such light exercise. An increase was regularly found to follow the walking exercise, and was usually between 5 and 8 p.c. of the resting values obtained. The samples were taken at an average time of about 45 sec. after the end of the walk, but no attempt was made to obtain samples at later periods to see if any fall subsequently occurred.

Oxygen debts following light exercise. In the case of severe exercise it seems clear that the bulk of the oxygen debt must be incurred in the removal of excess lactic acid which has accumulated throughout the

tissues of the body. If we regard the absence of an increase in the lactic acid in the venous blood from inactive muscles during light exercise as evidence that no generalized increase in the lactic acid in inactive tissues has occurred, and probably no increase in active muscles, a different explanation of the oxygen debt must be found in such circumstances. No investigation of this point has been carried out, but for reference the oxygen debts were measured in the case of the exercise studied in the present work, and for both subjects came to about 1 l. of oxygen (Table XI).

VI. Conclusions.

For the purposes of making any comparison between the results obtained by different workers on a given subject a knowledge of the experimental conditions in each case is essential. These may therefore be now repeated for the present work. The experiments were performed throughout on the same two subjects, who differ markedly in age, build, etc. The subjects were in every case in the post-absorptive state, and the experiments were carried through as far as possible away from normal meal hours. The blood samples were taken from veins of the forearm, and thus represent venous blood from an inactive limb, in which a free circulation had been established, either by submerging the arm in hot water for a few minutes before taking the sample, or as a result of the general increase of blood flow following the exercise. Care was always taken to avoid any constriction of the blood vessels during the taking of the samples, and light pressure was applied to the arm during the introduction of the needle into the vein only.

Working on blood samples obtained in this manner it was found that there was no lactate increase as a result of exercise up to a certain critical level. This critical level varied in one individual for different types of exercise, and with training, and differed in different individuals. For both the present subjects, and for walking exercise, this critical level corresponded to an oxygen utilization of about 1·8 l. per min.

These results obtained from lactate analyses have been confirmed by a parallel study of changes in CO_2-combining power of the blood, and a few observations on alveolar air changes seem also to fall in line with what would be expected from the foregoing.

It is obvious that these results differ fundamentally from those obtained by Hill, Long and Lupton, and by Long (Table I of the Introduction), which showed a lactate increase in the blood even following

very slow walks. There seems no important difference between the conditions of the two sets of experiments, and no suggestion can be offered to account for the discrepancy. The various steps of the analytical procedure have been checked as far as possible, wherever it was considered that they could affect the results, but with no success in showing up any relevant factor. Thus, since the Clausen method gave higher values on blood than the Friedemann method used here, it was thought possible that it would also show some difference in the blood lactate as a result of exercise in cases where the present method did not do so, and controls were performed to test this. Two experiments of this type are given in Table XIII, and are clearly negative. Also we have the fact that bicarbonate analyses have controlled the lactate analyses in the present work. In view of these results it is possible that the explanation of the discrepancy between the two series of experiments is to be found in differences of response of individual subjects under apparently similar experimental conditions.

Accepting the results here obtained it is not easy to give a definite interpretation. In the first place it is possible that there was actually an increase in the lactate concentration of the venous blood passing to the general circulation from the active muscles, but that this had become masked before the blood reached the venous side of the circulation in the inactive arm muscles. If this were the case, since adequate time must have been allowed for the establishment in the experiments of approximate equilibrium, this removal of lactate could scarcely be a mere storage of lactate, but must have been an active process of oxidation and resynthesis. From this it would seem to follow at least that in the inactive tissues in light exercise the lactate concentration is maintained at resting level.

The writer tends to accept a second explanation, that in such light and normal exercise as walking there is no output of lactic acid from the active muscles so long as the oxygen supply can be maintained adequate to all the active tissues. This does not mean that the maximal oxygen uptake of the whole body be not exceeded, but rather that there exist no local areas of anoxæmia, a matter which will depend largely on the development and responsive activity of the capillaries and arterioles in the active muscles. It is quite possible that there might be a large blood flow to a tissue, but if the capillaries were widely spaced there could still exist between them areas of relative anoxæmia during activity of the tissue, and the critical level of exercise at which the lactate began to increase in the blood would depend upon the point at which this

anoxæmia commenced to make itself felt in the particular set of muscles used in the given exercise. Once the critical level were exceeded it would be necessary for the active fibres to hand on to others, more favourably situated, part of their lactic acid to be oxidized or resynthesized, but up to that time there would seem no *a priori* reason why any should be allowed to escape from the fibre in which it was produced.

The results of Hartree and Hill(18) on the relation between recovery rate and lactate concentration, obtained from a study of heat production in muscle tissue, do not disagree with these results, as they are concerned only with the conditions within the fibres.

On such a theory as that supported here the differences between the effects of different types of exercise are easily understood, since the more normal the exercise the more adequate is the circulatory system likely to be to supply oxygen to all the active tissues. Training will also have the effect of improving the local conditions, with the result that for the exercise in question the critical level is raised, as was shown most strikingly in the experiments on de Mar already discussed, which also seem much more readily explicable in the light of the present results than those of Hill, Long and Lupton.

VII. Summary.

1. Changes in the blood as a result of light exercise, especially walking, have been studied on two subjects. The subjects were always in the post-absorptive state at the time of the experiment, and the results apply in every case to venous blood from an inactive limb, through which there was a free circulation.

2. A critical metabolic level was found below which there was no increase in blood lactate as a result of the exercise, although above this level such an increase did occur.

3. The critical level varies for different subjects, and for the same subject for different types of exercise. For the present subjects and for walking exercise it corresponded to an oxygen consumption of about 1·8 l. per min.

4. There is a fall of CO_2-combining power of the blood above the same critical level, but not below it.

5. There was found in every case studied a slight increase in the inorganic phosphate of the blood, following exercise, even when no lactate change occurred.

6. A few observations have been made on alveolar CO_2 pressure changes in similar light exercise.

7. The oxygen debt in very light exercise has little relation to a lactic acid accumulation in the blood, and probably none to the concentration of lactic acid in the tissues at large in the body.

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