ON THE ESTIMATION OF METABOLISM FROM DETERMINATIONS OF CARBON DIOXIDE PRODUCTION AND ON THE ESTIMATION OF EXTERNAL WORK FROM THE RESPIRATORY METABOLISM.

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TOWARDS the close of the Great War, when economy of food consumption was an urgent necessity, considerable attention was paid to the determination of the energetic needs of various kinds of muscular work. The majority of scientific papers then published dealt with the problem *ex post facto*, by a statistical analysis of food budgets in various classes, *e.g.* Dunluce and Greenwood (1918), Greenwood and Thompson (1918). A few, of which the most important was that of Cathcart and Orr (1919), described the results of precise experiments upon subjects carrying out specified tasks. Cathcart and Orr, as also Rosenheim (1919), and Greenwood, Hodson and Tebb (1919), employed the Haldane-Douglas technique, which involves the determination of the respiratory quotient in each experiment. Contemporaneously, Waller advocated the employment of a simplified method involving the sole determination of the volume of CO_2 expired under various conditions and published the results of a large number of experiments upon professional men, dock labourers and other industrially employed persons. Waller's method was subjected to criticism by a number of physiologists (Hill and Campbell (1921), Orr and Kinloch (1921), Gairns and O'Brien (1922)), and a consensus of scientific opinion, based upon theoretical and direct experimental grounds, has decided against his contention. The object of this paper is not merely to add another to the unfavourable criticisms of a process advocated, for what appeared to him urgent practical reasons, by a great physiologist who is no longer with us, but to express in arithmetical form some of the difficulties which this, and other methods, encounter and further to show that one of the ultimate ends Professor Waller had in mind cannot, in the writers' opinion, be attained either by his, or by any other, direct experimental method.

Our investigation which, as premised, is an arithmetical or biometric investigation, falls into two parts. In the first we shall consider the question of how far the respiratory metabolism can be rightly estimated from a knowledge of the CO_2 output alone. In the second we shall discuss the problem of estimating the external work performance of a subject from a knowledge of his respiratory metabolism, and conversely of estimating the respiratory metabolism from a knowledge of the external work performed.

The basis of our work is provided by the long series of observations contained in Benedict and Cathcart's monograph (1913), viz. those relating to

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the trained subject M. A. M. No other data have been used, and there is no question of individual heterogeneity, as when observations upon several different subjects are pooled. Assuming, as we are entitled to assume, that the experimental accuracy of the whole series of observations reached the highest possible standard, we are testing the methods by the most lenient standard; the range of error discerned here must be far less than would exist in the pooled observations of less skilled observers working under less favourable environmental conditions.

PART I.

Waller assumed that the respiratory quotient might be regarded as constant and that the range of error involved (what he meant by this phrase is not quite certain) was only ± 5 per cent. A more elastic assumption might have been made, still without doing violence to his principle that CO_2 determinations alone need be used, if, on examining a series of observations, an approximately linear relation between the value of the output of CO_2 and the respiratory quotient, *or* the intake of oxygen (*both* relations could not be linear), could be discerned. This having been done, the resulting error of prediction could be measured.

The technique of the experiments and the results of the observations used by us are given in detail in Benedict and Cathcart's published work.

The 483 observations used included those taken on the subject lying, sitting at rest, and working; these were first treated as a whole, and the results are shown in Table I.

Table I.

All observations together (rest, sitting and working).

	Mean	Standard deviation	Coefficient of variation	No. of observations
Carbon dioxide in c.c. per min.	719	739	103	483
Oxygen „ „	827	813	98	483
Respiratory quotient	·842	·0696	8	483

Correlation coefficient and ratio.

	r	η	$\eta^2 - r^2$
Carbon dioxide and oxygen	·992 ± ·0006	·994 ± ·0004	·003 ± ·0032

Regression equations.

	Equation	Partial S. D.	Partial coeff. of variation	χ^2	P
Oxygen from carbon dioxide (both in c.c.) per min.	$O = 1{\cdot}0949\,C + 40{\cdot}2438$	116	14	107	Very small

The correlation between CO_2 production and oxygen used is very high, and the relation linear, but the prediction value is very small owing to the large variation of oxygen, which is only reduced to 14 per cent. for a constant value of CO_2, thus giving a probable maximum range of ± 42 per cent. in a single subject. The mean of the respiratory quotient is very close to that given by Waller, but the variation about the mean is approximately 8 per cent., thus giving a probable maximum range of ± 25 per cent. The distribution of carbon dioxide and of oxygen are both so clearly unhomogeneous that no further analysis of the data as a whole was made but two parts were separately treated, namely—

(A) 281 observations taken when the subject was lying at rest on a couch either before or after work.

(B) 163 observations taken during work on the ergometer against varying currents.

In the remaining 39 observations, the subject was sitting on the bicycle with his feet on the pedals, either motionless or with the pedals revolved either by an electric motor, or by the subject with no braking current against the rotation. These could not be included in either A or B, as they involved more external work than those made on the recumbent subject, and no measure of it was obtained.

(A) *Rest.* Table II shows the results of the observations taken when the subject was lying down. The mean respiratory quotient is now less than Waller's

Table II.

(A) *Rest.* Subject lying on a couch, either before or after work.

	Mean c.c. per min.	Standard deviation c.c. per min.	Coefficient of variation	β_1	β_2	No. of observations
Carbon dioxide	213± ·737	18	9	4·210	10·623	281
Oxygen	262±1·17	29	11	2·074	6·907	281
Respiratory quotient	·819± ·0027	·0643	8	·00548	2·75±·14	281

Correlation coefficients and ratios.

	r	η	$\eta^2 - r^2$
Oxygen and carbon dioxide	·672±·022	·714±·020	·057±·019
Respiratory quotient and carbon dioxide	·132±·040	·320±·036	·085±·023

Regression equations.

	Equation	Partial S. D.	Partial coeff. of var.	χ^2	P
Oxygen from carbon dioxide (both in c.c.)	O=1·0649 C+35·4985	21	8·2	7·637	·572
Respiratory quotient from carbon dioxide (in c.c.)	Q=·0004623 C+·7209	·0638	7·8	7·569	·478

value, and the variation about the mean is still approximately 8 per cent. and remains approximately 8 per cent. when carbon dioxide is kept constant, giving a probable maximum range of ± 23 per cent. The total variation of oxygen is larger, but it becomes approximately the same as that of the respiratory quotient when CO_2 is kept constant, although the relation between oxygen and carbon dioxide is more nearly linear than that between CO_2 and the respiratory quotient. By the goodness of fit test the fit of either regression line is not bad, but their value for prediction purposes is better measured by the partial coefficient of variation and this, we see, is too large for the equations to be of serious value for individual predictions.

(B) *Work.* In estimating the errors involved in the prediction from CO_2 in the work observations a quantitative analysis has been made of the effect on the relation and variation of CO_2, oxygen and the respiratory quotient of

(i) The external muscular work being done at the time of taking the observation.

(ii) The total external muscular work done up to that time from the beginning of that day's experiment.

(iii) The speed of revolution of the pedals.

The measure taken for the work was the number of calories per minute for the different speeds and currents obtained graphically from the calibration curves given for the two ergometers used[1]. Each observation covered a period of from 10–16 minutes, and to get the total previous work done, half of that done in the current period was added to the sum of that done in previous periods and intervals of the same day. The previous work was practically continuous in all but a few cases where resting periods intervened, but it was not uniform in either speed or intensity. This fact probably lessens its value as a contributing factor, and may in part account for the relatively small influence it shows here. The results of the work observations are shown in Tables III, IV, V, and VI. Table III shows that while the initial coefficients of variation of CO_2 and oxygen are naturally much larger than in the rest experiments, that of the respiratory quotient is slightly smaller. The mean of the respiratory quotients is now above Waller's value.

Table III.

(B) *Work.* Subject working on an ergometer against an electric current.

	Mean c.c. per min.	Standard deviation c.c. per min.	Coefficient of variation	No. of observations
Carbon dioxide	1659±27	516	31	163
Oxygen	1876±29	543	29	163
Respiratory quotient	·8854±·0032	·0607	7	163
	Rev. per min.	Rev. per min.		
Speed	90±·902	17	19	163
	Cal. per min.	Cal. per min.		
Work per minute	1·580±·029	·554	35	163
	Calories	Calories		
Total previous work done	106±3·9	74	70	163

Total correlation coefficients and ratios.

	r	η	$\eta^2 - r^2$
Oxygen and carbon dioxide	·970±·003	·971±·003	·0025±·005
Respiratory quotient and carbon dioxide	·495±·040	·581±·035	·093 ±·032
Respiratory quotient and oxygen	·307±·048	·471±·041	·127 ±·038
Carbon dioxide and work per min.	·914±·009	·938±·006	·045 ±·022
Carbon dioxide and speed	·791±·020	·835±·016	·072 ±·028
Carbon dioxide and total previous work	·158±·052	·406±·044	·140 ±·040
Oxygen and work per min.	·906±·009	·939±·006	·060 ±·026
Oxygen and speed	·767±·022	·825±·017	·092 ±·032
Oxygen and total work	·111±·052	·377±·045	·130 ±·038
Respiratory quotient and work per min.	·393±·045	·597±·034	·202 ±·047
Respiratory quotient and speed	·385±·045	·585±·035	·194 ±·046
Respiratory quotient and total work	·232±·050	·401±·044	·107 ±·035
Speed and work per min.	·582±·035	·677±·029	·120 ±·037

The least linear of all the relations are those involving the respiratory quotient, though that between CO_2 and the respiratory quotient is just within the range of possible linearity. The total previous work done also shows non-

[1] P. 27 of Publication of No. 187 and pp. 18–28 of Publication 123 of the Carnegie Institute of Technology.

linear relations. In spite of this want of strict linearity the partial correlations and standard deviations were calculated. The former are shown in Table IV. Oxygen and carbon dioxide have a final correlation of ·6 and carbon dioxide and the respiratory quotient of ·3, oxygen and the respiratory quotient of − ·3. The work per minute still has a correlation of approximately ·9 with both CO_2 and oxygen, when the other variables are kept constant. The effect

Table IV.

(B) *Work.* Total and partial correlation coefficients.

Variables kept constant	Oxygen and carbon dioxide	Respiratory quotient and carbon dioxide	Oxygen and respiratory quotient	Carbon dioxide and work per minute	Carbon dioxide and speed	Carbon dioxide and total previous work
None	·970 ± ·003	·495 ± ·040	·307 ± ·048	·914 ± ·009	·791 ± ·020	·158 ± ·052
Work per minute	·825 ± ·017	·363 ± ·046	− ·125 ± ·052	—	·786 ± ·020	·054 ± ·053
Speed	·925 ± ·008	·337 ± ·047	·021 ± ·053	·912 ± ·009	—	·092 ± ·052
Total previous work	·970 ± ·003	·477 ± ·041	·291 ± ·048	·912 ± ·009	·787 ± ·020	—
Work per min. and speed	·627 ± ·032	·328 ± ·047	− ·386 ± ·045	—	—	·019 ± ·053
Work per min. and total previous work	·831 ± ·016	·360 ± ·046	− ·117 ± ·052	—	·785 ± ·020	—
Speed and total previous work	·927 ± ·007	·327 ± ·047	·017 ± ·053	·911 ± ·009	—	—
Work per min., speed and total previous work	·635 ± ·032	·330 ± ·046	− ·371 ± ·046	—	—	—
Carbon dioxide	—	—	—	—	—	—
Oxygen	—	—	—	·339 ± ·047	·302 ± ·048	—
Oxygen and speed	—	—	—	·537 ± ·037	—	—
Carbon dioxide and speed	—	—	—	—	—	—

Variables kept constant	Oxygen and work per minute	Oxygen and speed	Oxygen and total previous work	Respiratory quotient and work per minute	Respiratory quotient and speed	Respiratory quotient and total previous work
None	·906 ± ·009	·767 ± ·022	·111 ± ·052	·393 ± ·045	·385 ± ·045	·232 ± ·050
Work per minute	—	·697 ± ·027	− ·058 ± ·053	—	·209 ± ·051	·190 ± ·051
Speed	·882 ± ·012	—	·018 ± ·053	·226 ± ·051	—	·199 ± ·051
Total previous work	·906 ± ·010	·764 ± ·022	—	·373 ± ·045	·368 ± ·046	—
Work per min. and speed	—	—	− ·133 ± ·052	—	—	·184 ± ·051
Work per min. and total previous work	—	·702 ± ·027	—	—	·203 ± ·051	—
Speed and total previous work	·884 ± ·012	—	—	·212 ± ·050	—	—
Work per min., speed and total previous work	—	—	—	—	—	—
Carbon dioxide	·202 ± ·051	—	—	− ·167 ± ·051	—	—
Oxygen	—	—	—	—	—	—
Oxygen and speed	—	—	—	—	—	—
Carbon dioxide and speed	·245 ± ·050	—	—	—	—	—

of speed apart from that of work is also brought out. Speed of work has a correlation of approximately ·8 with CO_2 and ·7 with oxygen, when the work is kept constant. The total previous work done has negligible correlation with both CO_2 and oxygen; but as pointed out before this may be due to the conditions of the experiments. The final correlations of work done, total previous work, and speed with the respiratory quotient are small but of more equal value, being approximately ·2 in each case.

Variation in oxygen and respiratory quotient for given values of CO_2.

Table V shows the limits of accuracy of the determination of oxygen and the respiratory quotient from the carbon dioxide output.

Considering oxygen first, the total variation of oxygen consumption is about 29 per cent., and when CO_2 is kept constant becomes 7 per cent., thus giving a probable maximum range of ± 21 per cent., and this is not appreciably

Table V.

(B) *Work.* Variation of oxygen and respiratory quotient.

	Oxygen		Respiratory quotient		
	Standard deviation c.c. per min.	Coefficient of variation	Standard deviation	Coefficient of variation	
Total	543	28·97	·0607	6·86	
Partial, keeping constant					
Carbon dioxide	133	7·06	·0528	5·96	1st order
Work per minute	230	12·24	·0558	6·31	1st order
Speed	349	18·60	·0561	6·33	1st order
Total previous work	540	28·79	·0591	6·67	1st order
Carbon dioxide and work per min.	130	6·92	·0520	5·88	2nd order
Carbon dioxide and total previous work	130	6·96	·0519	5·87	2nd order
Carbon dioxide and speed	133	7·06	·0528	5·96	2nd order
Work per min. and speed	165	8·77	·0546	6·17	2nd order
Work per min. and total previous work	229	12·22	·0548	6·19	2nd order
Speed and total previous work	349	18·59	·0549	6·21	2nd order
Work per min., carbon dioxide and total previous work	128	6·80	·0512	5·78	3rd order
Carbon dioxide, work per min. and speed	128	6·85	·0516	5·83	3rd order
Carbon dioxide, speed and total previous work	130	6·96	·0519	5·87	3rd order
Work per min., speed and total previous work	163	8·70	·0537	6·06	3rd order
Carbon dioxide, work per min., speed and total previous work	126	6·73	·0499	5·63	4th order

(B) *Work.* Carbon dioxide.

	Standard deviation c.c. per min.	Coefficient of variation
Total	515·7	31·1
Partial, keeping constant		
Work per minute	209·3	12·6
Speed	315·5	19·0
Oxygen	125·7	7·6
Work per min. and speed	129·5	7·8
Oxygen and work per min.	118·3	7·1
Oxygen and speed	119·9	7·2
Oxygen, work per min. and speed	101·1	6·1

lessened by keeping constant also the work per minute, total previous work and speed of work.

In the case of the respiratory quotient the total variation is approximately 7 per cent., reducing to 6 per cent. (*i.e.* a probable maximum range of ± 18 per cent.) when CO_2 is kept constant, and, as in the case of oxygen, this is very little further reduced by keeping constant the work per minute, total work done, and speed.

We may conclude, therefore, that as far as regards the determination of oxygen consumption or the respiratory quotient from CO_2, either by Waller's assumption of a constant respiratory quotient, or by the slightly more elastic method of treating rest and work observations separately, and assuming a linear relation between CO_2 and either oxygen or the respiratory quotient, the results obtained are not suitable for very accurate measurement even in the case of a single subject working under homogeneous conditions, and would therefore be still more inaccurate if applied generally.

Part II.

We think the results described in the first part are sufficient to prove that no estimate of the respiratory metabolism based upon a measurement of the CO_2 output alone, is of much use in assessing individual cases. When the average of a large number of like observations is in question, the method has (and has long been known to have) value, but for the purpose for which it was re-introduced by Waller, the quantitative assessment of the expenditure of energy by individuals, or very small groups of individuals, observed through a short interval of time, it cannot be approved. This conclusion is reached after analysing observations of a high order of experimental precision made upon a single subject; it clearly follows that the rough and ready exploitation of the method in ordinary clinical work is not a scientific procedure at all.

Something more remains to be said on the general question. In the classical memoir of Lavoisier and Seguin, the proposition was first maintained that given a knowledge of the oxygen consumption and the pulse rate, the mechanical equivalent of any human effort could be found. It was recognised that age, sex, etc. must introduce variations, but, in the words of the authors, "ces lois sont même assez constantes, pour qu'en appliquant un homme à un exercice pénible, et en observant l'accélération qui résulte dans le cours de la circulation, on puisse en conclure à quel poids, élevé à une hauteur déterminée, répond la somme des efforts qu'il a faits pendant le temps de l'expérience" (collected edition of Lavoisier's *Works*, vol. II. p. 697, Paris 1862). The question is, can, under the improved technical conditions of modern experimental science, Lavoisier's prophecy be made good? Given, for instance, oxygen consumption, respiratory quotient, and speed of work performance, with what accuracy can we determine the amount of external work done? Conversely, given a knowledge of the external work, with what exactitude is the respiratory metabolism assigned?

Table VI shows in the last column the reduction of variability of work performance when different combinations of the other variables are made constant. The values of the partial coefficients of variation must be considered not alone, but in relation to the range of work covered by the experiments, which is measured by the total coefficient of variation given at the head of the column, and is, of course, arbitrarily fixed by the conditions of the experiment.

Thus an original variation of 35·1 per cent. in the work is reduced to 14·2 per cent. when the carbon dioxide output alone is known, or 14·8 per cent. when the oxygen consumption alone is known. When both carbon dioxide and oxygen are known there is very little improvement in the variation, which is still approximately 14 per cent. The respiratory quotient by itself is not of value in estimating the external work, and if both carbon dioxide and oxygen are to be used, the direct linear form with oxygen gives a slightly better result than the relation assumed by using CO_2 and the respiratory quotient linearly. The additional knowledge of speed reduces the variation to 11·7 per cent. when only CO_2 is given, and to 11·4 per cent. when CO_2 and oxygen are both given.

Table VI.

Variations in work per minute.

	Standard deviation	Coefficient of variation	
Total	·554	35·1	
Partial Variables kept constant			
Carbon dioxide	·225	14·2	1st order
Oxygen	·234	14·8	1st order
Speed	·451	28·5	1st order
Respiratory quotient	·510	32·3	1st order
Carbon dioxide and speed	·185	11·7	2nd order
Oxygen and speed	·213	13·5	2nd order
Carbon dioxide and oxygen	·220	13·9	2nd order
Carbon dioxide and respiratory quotient	·222	14·0	2nd order
Carbon dioxide, speed and oxygen	·179	11·4	3rd order

The range of work covered by the experiments used is large, consequently it was thought worth while to see if the above conclusions still hold good when the range of work is reduced. Reducing the range of work to 1·0–2·1 calories per minute instead of 0·4–2·5 calories per minute, we find that an original variation of 22·4 per cent. in the work becomes 12·7 per cent. when CO_2 output is kept constant and 13·4 per cent. when O_2 intake is kept constant, results which are practically of the same order as those quoted above (see Table VIII).

Table VII shows the chief regression equations and compares the above theoretical variations with those actually obtained by substituting a random sample of 50 of the observations in these equations. The results are practically the same. They support Waller's contention to this extent, that they show that, given the CO_2, the additional knowledge of oxygen only increases the accuracy of estimation of external work by 1 per cent. or less of the mean work; this is true whether speed of performance is known or not. But they also bring out the point that even under the most favourable conditions, the knowledge of all three variables—carbon dioxide, oxygen and speed—does not reduce an

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original variation of 35 per cent. to 36 per cent. in the external work below 11 per cent. or 12 per cent. of the mean external work. In other words, roughly one third of the original variation still remains. These results must be con-

Table VII.

(A) Work per minute in terms of carbon dioxide, oxygen and speed.

(B) Carbon dioxide and oxygen in terms of work.

	Regression equations	Standard deviations 163 observations		Root mean square error from a random 50 observations	
		Actual	% of mean	Actual	% of mean
(A)					
Work from carbon dioxide	$W = \cdot0009824\, C - \cdot04996$	·225	14·2	·253	16·1
Work from carbon dioxide and oxygen	$W = \cdot0006312\, C + \cdot00034360\, O - \cdot11168$	·220	14·0	·236	15·0
Work from carbon dioxide and speed	$W = \cdot0013031\, C - \cdot0122472\, S + \cdot52136$	·185	11·7	·218	13·8
Work from carbon dioxide, oxygen and speed	$W = \cdot0009537\, C + \cdot0003417\, O - \cdot0122385\, S + \cdot45944$	·179	11·4	·195	12·4
	Corresponding total standard deviation of work	·554	35·1	·567	36·0
(B)					
Carbon dioxide from work	$C = 850{\cdot}26\, W + 315{\cdot}81$	209·3	12·6	267·5	15·9
	Corresponding total standard deviation of CO_2	515·7	31·1	584·7	34·7
Oxygen from work	$O = 888{\cdot}58\, W + 471{\cdot}57$	229·6	12·2	237·5	12·6
	Corresponding total standard deviation of O_2	543·4	29·0	597·5	31·8

W = Work in calories per minute.
C = Carbon dioxide in c.c. per minute.
O = Oxygen in c.c. per minute.
S = Speed in revolutions per minute.

sidered as showing the *minimum* limits of the accuracy, not only of Waller's method but also of the more complete method of taking oxygen into account.

If we consider the reverse problem, namely to determine the respiratory metabolism from the given external work, we find that the final variation of oxygen or carbon dioxide is still 12 per cent. to 13 per cent. from an original variation of about 30 per cent., and as before the reduced range observations show results of the same order.

The results of this analysis express in a somewhat more precise and detailed form what may be generally inferred from such a table as that on pp. 141–2 of Benedict and Cathcart's monograph. It is seen that the subject's "efficiency" varies in the series from a maximum of 25·2 per cent. to a minimum of 15·5 per cent. With such a range (the mean "efficiency" is 21·6, the standard deviation 2·6, the coefficient of variation 12·2) it is evident that the variability of predicted results must be large.

In this work we have not the complication of numerous subjects, and numerous machines, constructed on different lines, with differing efficiencies. The practical conclusion seems, therefore, to be that, when any experimental

Table VIII.

Range of work reduced to 1·0–2·1 calories per minute.

	Mean c.c.	Standard deviation c.c.	Coefficient of variation	No. of observations
Carbon dioxide	1627·4	392·0	24·1	109
Oxygen	1855·6	396·9	21·4	109
Respiratory quotient	·8774	·0636	7·2	109
	Cal. per min.	Cal. per min.		
Work per minute	1·598	·3578	22·4	109

Coefficients of correlation.

Work and carbon dioxide	·823 ± ·021
Work and oxygen	·801 ± ·023
Work and respiratory quotient	·391 ± ·055

Partial standard deviations.

	Actual calories per minute	% of mean
Work keeping CO_2 constant	·203	12·7
Work keeping O_2 constant	·214	13·4
Work keeping respiratory quotient constant	·329	20·6
	c.c.	
CO_2 keeping work constant	222·7	13·7
O_2 keeping work constant	237·7	12·8
Respiratory quotient keeping work constant	·0584	6·7

calibration of different forms of muscular work is based upon the confrontation of small samples of measurements upon different subjects, only the roughest results are attainable. We think it is certain that the difference in total energy transformation between, say, a needlewoman and a coal hewer, transcends even our very wide margins of variability, but it does not appear to be at all probable that either by Waller's technique, by the complete actual technique of indirect calorimetry or by any at present available method, the physiological calibration of industrial work can usefully be attempted on a grand scale. It seems indeed that in practice the experimental method will be restricted to the purpose of furnishing a control of the ostensibly less scientific data afforded by dietary studies, it being of course understood that the dietary studies are planned and conducted in accordance with biometric requirements.

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