STUDIES IN HUMAN PHYSIOLOGY

IV. Vital Capacity, Respiratory Rate and Volume, and Composition of the Expired Air

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In the previous numbers of this series may be found a record of the intra-individual variations of metabolism (1), cardio-vascular conditions (2), and alveolar air and blood-gas capacities (3) of five normal, adult, human subjects who were under observation during the two-year period, February 1925 to February 1927.

The introductory part of the first paper should be consulted for details as to the general plan and routine of the determinations. It must suffice, here, to recall that two of the subjects, A. B. and C. D., were men and were under observation continuously throughout the entire two-year period. The remaining three subjects were women; two of them, E. F. and G. H., served during the first year, February 1925 to February 1926; the third, K. L., was under observation during the second year, from February 1926 to February 1927.

During the first year determinations were made on each of the four subjects, A. B., C. D., E. F., and G. H., approximately once a week; during the second year, on the other hand, each of the subjects, A. B., C. D., and K. L., reported for observation on an average of twice a week.

This report deals with the volume and rate of respiration and the vital capacity of these subjects. Of these, the data in regard to the respiration pertain to the basal condition. Preliminary to the metabolism determinations the subjects were fitted with a Fitz pneumograph (4) which was connected with a recording tambour. The pneumograph was always carefully adjusted so as to cause no annoyance and in fact was unnoticeable. The recording tambour wrote on a smoked kymograph drum to which was also adjusted a time marker and a signal magnet; the latter was connected with a key which was closed and opened by the operator at the beginning and end of the metabolism period. In this way there was obtained a record of the number of respirations during each ten-minute metabolism period; from June of the first year (1925) until the end these were almost invariably run in duplicate on A. B., C. D., and K. L., and whenever time permitted on E. F. and G. H. When this was the case, in order to tire the subject as little as possible, it was the custom to remove the mouthpiece and nose-clip at the end of the first period so that the breathing might be unobstructed and normal during the ten minutes or so required to make the temperature, barometer and spirometer readings and secure samples of the air in the spirometer. During this intermission the subject remained perfectly quiet and relaxed; and it may be stated that upon resumption of the second determination the same precautions were observed as at the beginning as to rinsing out the spirometer—not merely to remove any traces of atmospheric air that might have entered the connecting tubing but also in order to allow three or four minutes to elapse for the subsidence of any disturbance that might have resulted from the renewed application of the mouthpiece and nose-clip.

During the second year, i.e., from February 1926 to February 1927 and therefore only with subjects A. B., C. D., and K. L., it was customary to secure an additional record of the respiration toward the end of this period of intermission; viz., after the subject had been breathing normally and without any obstruction for several minutes and just before beginning the second metabolism determination. The recording apparatus was situated behind the subject so this record could be obtained without in any way attracting the attention and therefore without any conscious modification of the breathing. The kymograph was speeded up for this record so that the inspiratory and expiratory phases could be accurately measured. For this purpose as many complete respirations were carefully measured as seemed necessary to secure a representative average; ten was the minimum number and then only if the respiration was very regular; if at all irregular, the average was based on twenty-five or more separate measurements.

For both years we have, then, the respiratory rates during the collection of the expired air for the metabolism determinations; and in addition, there is for the second year and for comparison with these, the average inspiration and expiration and rate of the normal respiration, secured under as nearly identical conditions as possible except for the avoidance of any possible modification that might arise from the use of the mouthpiece and nose-clip or other effect that might be caused by breathing into the spirometer.

The tidal and minute volumes are derived from the spirometer readings and the rates of respiration observed during the ten-minute collections of the expired air for the metabolism determinations. In the tables these have been recorded as reduced to standard conditions, 760 mm. and 0°C., and also as recalculated to body temperature, 37°C., and the barometric pressure that prevailed at the time of collection. All of these calculations as well as all those involved in the metabolism determinations were greatly facilitated by the use of Carpenter's tables (5) and it is an inexcusable negligence that our indebtedness to this extremely helpful aid should have remained unacknowledged until now. Both sets of values have been recorded because of the special interest that attaches to each for certain purposes. The actual volumes of air breathed have perhaps the greatest immediate physiological significance so the statistical analysis has been based on these figures.

It remains to mention a matter of considerable interest in itself and which is of importance also because it is responsible for a sharp dichotomy between the results of the two years. During the first year, February 1925 to February 1926, the side-arm of the "T" tube which connected the subject with the Saad valves, together with the stem of the rubber mouthpiece, constituted an additional dead-space of approximately 50 cc. During the second year both of these were shortened so that when the mouthpiece was in place the subject was breathing almost directly into the free space between the valves and therefore with practically no dead-space increment.

This difference in method should be kept in mind as it will have to be referred to later as an explanation of the different results that were obtained in the two years. It may be said in anticipation that the difference occasioned in this way is quantitative rather than one of kind. The data of the second year, with practically no rebreathing, are obviously more nearly normal than the others; and a comparison of the two, especially when it can be made in the same subjects, as in the cases of A. B. and C. D., who served through both years, throws interesting light on the manner in which the respiration is adjusted in response to the amount of rebreathing involved in the technique of the first year.

The methods of sampling and analyzing the expired air have been described in the first paper of this series and need not be repeated here.

Determination of the vital capacity. It may also be recalled from the previous papers of this series that upon completion of the collection of the expired air for the metabolism determinations, and of obtaining alveolar air samples, the subject arose and went through with the performance necessary for the determination of Schneider's cardio-vascular rating At the end of this the vital capacity was determined. This was done by having the subject expire, from the standing position, into the 100 liter spirometer which was previously used for the collection of the expired air during the metabolism determinations. In order to make up for the lack of precision with which such a large spirometer can be read, several expirations, properly spaced, were made in the course of a single determination and the average of the three best checks recorded as the day's value.

The temperature of the spirometer and the barometric pressure were

TABLE 1

Statistical constants

FUNCTION	SUBJECT AND YEAR	NUMBER OF OBSERVATIONS	MAXIMUM AND MINIMUM	MODE	ARITHMETICAL MEAN	STANDARD DEVIATION	COEFFICIENT OF VARIATION
Vital capacity; (cc.) (37°C. and observed barometer	A. B. (both years)	91	2,800–3,300	3,200	3,118± 9	118	3.8
	C. D. (both years)	91	4,200–4,900	4,600	4,556±10	147	3.2
	E. F. (1925)	37	2,900–3,300	3,200	3,165±15	131	4.1
	G. H. (1925)	24	2,800–3,700	3,100	3,200±29	208	6.5
	K. L. (1926)	50	2,500–3,000	2,700	2,748±13	134	4.9
	Average					148	4.5
Normal respiration:							
Rate per minute	A. B. (1926)	88	9–18	14	13.8±0.1	1.43	10.4
	C. D. (1926)	88	12–18	14	14.0±0.1	1.03	7.4
	K. L. (1926)	84	12–19	15	15.1±0.1	1.27	8.4
	Av.				14.3	1.24	8 7
Inspiration (seconds)	A. B. (1926)	88	1.2–2.3	1.5	1.56±0.02	0.23	14.7
	C. D. (1926)	88	1.3–2.3	1.7	1.77±0.02	0.22	12.4
	K. L. (1926)	84	1.1–2.1	1.4	1.40±0.01	0.16	11.5
	Av.				1.58	0.20	12.9
Expiration (seconds)	A. B. (1926)	88	1.9–4.3	2.9	2.85±0.03	0.39	13.5
	C. D. (1926)	88	2.1–3.2	2.5	2.56±0.02	0.24	9.4
	K. L. (1926)	84	1.9–3.1	2.6	2.61±0.02	0.28	10.6
	Av.				2.67	0.30	11.2
Respiration during collection of expired air for the metabolism determinations:							
Rate per minute	A. B. (1925)	79	7–15	13	11.3±0.1	1.68	14.9
	(1926)	181	8–15	13	12.1±0.1	1.22	10.0
	C. D. (1925)	75	11–16	14	14.0±0.1	0.93	6.7
	(1926)	171	11–14	13	12.8±0.0	0.57	4.5
	E. F. (1925)	65	13–22	16	16.0±0.2	1.90	11.9
	G. H. (1925)	55	14.21	15	15.8±0.1	1.27	8.0
	K. L. (1926)	164	13–16	15	14.6±0.0	0.74	5.1
	Av. 1925				14.3	1.45	10.4
	Av. 1926				13.2	0.84	6.5

TABLE 1—*Concluded*

FUNCTION	SUBJECT AND YEAR	NUMBER OF OBSERVATIONS	MAXIMUM AND MINIMUM	MODE	ARITHMETICAL MEAN	STANDARD DEVIATION	COEFFICIENT OF VARIATION
Tidal volume (cc.) (37°C. and observed barometer)	A. B. (1925)	79	320–740	420, 470, 490	487±6	89	18.2
	(1926)	181	330–600	360	401±3	50	12.4
	C. D. (1925)	75	290–490	440	415±4	49	11.9
	(1926)	171	370–470	400	406±1	20	4.9
	E. F. (1925)	65	290–480	410	380±4	49	13.0
	G. H. (1925)	55	300–500	400, 420	404±4	41	10.2
	K. L. (1926)	164	290–380	330	334±1	17	5.2
	Av. 1925				422	57	13.3
	Av. 1926				380	29	5.6
Minute volume (cc.) (37°C. and observed barometer)	A. B. (1925)	79	4,200–6,200	5,500	5,313±30	426	8.0
	(1926)	181	4,300–5,400	4,800	4,755±11	221	4.6
	C. D. (1925)	75	4,300–6,800	6,000, 6,200	5,737±39	531	9.3
	(1926)	171	4,500–5,700	5,200	5,176±13	246	4.7
	E. F. (1925)	65	4,800–7,100	5,600	5,988±46	555	9.3
	G. H. (1925)	55	4,400–8,500	6,300	6,329±62	684	10.8
	K. L. (1926)	164	4,200–5,500	4,700	4,844±15	282	5.8
	Av. 1925				5,842	549	9.4
	Av. 1926				4,925	250	5.0
CO_2 per cent in expired air	A. B. (1925)	79	3.1–4.1	3.6	3.59±0.02	0.22	6.2
	(1926)	181	3.7–4.2	3.8	3.88±0.01	0.11	3.0
	C. D. (1925)	75	3.0–4.5	3.4	3.68±0.03	0.34	9.3
	(1926)	171	3.7–4.4	4.0	3.96±0.01	0.12	2.9
	E. F. (1925)	65	2.7–3.9	3.1	3.25±0.02	0.29	9.0
	G. H. (1925)	55	2.5–4.0	3.0	3.11±0.03	0.33	10.6
	K. L. (1926)	164	3.3–3.9	3.6	3.58±0.01	0.15	4.1
	Av. 1925				3.41	0.32	8.8
	Av. 1926				3.81	0.13	3.3
O_2 per cent in expired air	A. B. (1925)	79	16.1–17.6	17.0	16.91±0.02	0.31	1.8
	(1926)	181	16.1–16.9	16.6	16.53±0.01	0.16	1.0
	C. D. (1925)	75	15.8–17.5	17.0	16.78±0.03	0.39	2.3
	(1926)	171	15.8–16.7	16.4	16.36±0.01	0.20	1.2
	E. F. (1925)	65	16.3–17.8	17.5	17.24±0.03	0.36	1.7
	G. H. (1925)	55	16.1–18.2	17.5, 17.6	17.39±0.04	0.42	2.4
	K. L. (1926)	164	16.0–17.0	16.7	16.56±0.01	0.21	1.3
	Av. 1925				17.08	0.37	2.1
	Av. 1926				16.48	0.19	1.2

noted and from these were calculated the volume of the vital capacity at standard conditions as well as at body temperature and the observed barometric pressure. Both of these sets of values have been recorded because we have never been able to determine from previously published data on the vital capacity to what conditions of temperature and pressure the gas volumes are supposed to apply.

RESULTS. *I. Statistics.* The statistical constants for these data are given in table 1.

1. The effect of rebreathing. The most outstanding feature of table 1 is the marked difference between the statistical values for each of the two years. This can only be attributed to the increased amount of rebreathing which resulted from the enlargement of the dead space during the first year. As might have been expected, the larger the dead space, the greater is the rate and volume of respiration and the oxygen per cent, and the less is the carbon dioxide per cent of the expired air. The only really valid comparisons here are between the mean values for A. B. and C. D. for each of the two years, since they were the only subjects who served under both conditions. Their figures conform to the general averages, however, with the single exception of the respiratory rate of A. B., which is lower during 1925, when the dead space and rebreathing were large, than during 1926 when both were reduced to a minimum.

As a matter of fact it cannot be concluded that the effect of the rebreathing is to increase the respiratory *rate;* for if the rates of A. B., C. D., and K. L. during the collection of the expired air in 1926 are compared with their normal values for the same year it will be seen that in each instance the latter are higher than the former, the averages being 14.3 and 13.2, respectively. This is of interest as indicating that the adjustment to this type of demand for increased respiration is almost entirely effected by variation in the minute and tidal volumes, with compensatory alterations in the composition of the expired air.

Even more striking, however, than the difference in the mean values of the volume and composition of the expired air is the difference in the variability of these functions which results from changes in the volume of the dead space and the amount of rebreathing which it entails. Thus during 1925 when the dead space and rebreathing were relatively large, the standard deviations and the coefficients of variation are, on the average, about twice as great as during the second year when the dead space and rebreathing were reduced to a minimum.

This difference in variability can hardly be attributed to variations in the dead space itself, i.e., within either year, for identically the same apparatus was used throughout each year; and the absolute variations in the size of the dead space were certainly no greater during 1925, when it was large, then during the following year when it was small. Nor can the lower values of these constants for 1926 be explained as due to the greater number of observations per subject for this year as compared with its predecessor. This might, undoubtedly, play a part in causing such a result; but its inadequacy as even a significant partial explanation is apparent from a comparison of these data with those for the total oxygen consumption and carbon dioxid production as given in the first paper of this series (1). These latter were computed from the very determinations that are being presented here; consequently the number of entries from which the measures of dispersion were calculated are the same in each case. What is found, on making the comparison, is that the standard deviations and coefficients of variation for oxygen comsumption and carbon dioxid production are practically the same for C. D. for both years; and they are practically the same for K. L., with 164 observations as for E. F., with 65, or G. H., with 55; only A. B. shows a slightly lower variability during the second year, but with nothing like the same difference that is found for these respiratory functions. This comparison is very instructive also as showing the relative constancy of the metabolism as compared with the respiration; and the lack of effect which different methods of collection of the expired air, with their varying effects upon the external respiration, have upon the computed metabolic rate; even though the calculation is based upon these same variable respiratory data. This has already been referred to in the first paper of this series as something to be developed in full at this time; and as confirming an observation originally made by Carpenter.

The increased variability of the respiration when the dead space and rebreathing are large must indicate, therefore, a *bona fide* variability in the physiological response to this condition. This will be further illustrated in a later section where it will be shown that the magnitude of the seasonal variation for each of the two years provides additional confirmation of this conclusion.

2. The difference between duplicate determinations. One of the most unexpected results to emerge from this work was evidence as to the instability of the respiratory rate and volume as compared with the other functions for which we have similar duplicate determinations. This variability is shown in the following tabulations:

Variations of duplicate observations from their means		Number of observations				
Actual difference	Difference as approximate per cent of the mean*	A. B.	C. D.	K. L.	Total	Per cent of the total observations
Respiratory rate						
Respirations per minute	*per cent*					*per cent*
0.0	0	2	3	11	16	6
±0.10–0.25	±1	26	56	51	143	51
0.26–0.50	3	16	30	15	61	22
0.51–0.75	5	15	7	2	24	10
0.76–1.00	7	12			12	4
1.01–1.25	9	6	1	1	8	3
1.26–1.50	11	2			2	1
1.51–1.75	13	8			8	3
1.76–2.00	15	3			3	1
2.01–2.25	17	1			1	
Total....................		91	107	80	278	
Tidal volume						
cc.	*per cent*					*per cent*
0	0	0	2	7	9	3
±1–5	±1	10	39	38	87	32
6–10	2	9	32	22	63	23
11–15	3	15	14	7	36	13
16–20	4	10	8	3	21	8
21–25	5	10	5	1	16	6
26–30	7	2	3	1	6	2
31–35	8	7			7	3
36–40	10	4			4	1
41–50	11	8			8	3
51–100	19	16			16	6
Total..................		91	103	79	273	
Minute volume						
cc.	*per cent*					*per cent*
0	0	0	0	0	0	0
±1–25	±0.5	8	6	11	25	9
26–50	1.0	12	16	10	38	14
51–75	1.5	18	16	11	45	16
76–100	2.0	14	13	13	40	15
101–125	2.5	11	16	10	37	14
126–150	3.0	9	8	6	23	8
151–175	3.5	7	7	8	22	8
176–200	4.0	5	4	3	12	5
201–225	4.5	1	6	3	10	4
226–250	5.0	3	6	2	11	4
251–300	6.0		3	2	5	2
301–400	7.0	1			1	
401–500	9.0	2	2		4	1
Total...................		91	103	79	273	

* Approximate, because the actual deviations from the means which are grouped in the first column have not been divided in each case by the indivdual mean value; instead, the mid-value of the group has been divided by the average for the three subjects which is, in round numbers, 13, for respiratory rate; 400, for tidal volume; and 5000, for the minute volume. Needless to say, this introduces no appreciable

If these figures are compared with those of a somewhat similar table which has been given in the first paper of this series (1, p. 619) for the total oxygen consumption, it can easily be seen to what degree the respiration is exceptionally variable; thus, 95 per cent of the duplicate oxygen determinations agree within three per cent or less with their means, whereas this limit includes only 79 per cent of the observations on respiratory rate; and 71 to 76 per cent of the observations on tidal and minute volume, respectively.

Again, the most extreme deviation of any pair of oxygen determinations from their mean is 5.3 per cent (1, p. 618) whereas the extreme deviation for the respiratory rate is 17 per cent; for the tidal volume, 19 per cent; and minute volume, 9 per cent.

And, finally, a comparison of the average variations from the means tells the same story; for these respiratory functions the figures, derived from the preceding tabulations, are as follows:

	AVERAGE DEVIATION OF DUPLICATE DETERMINATIONS FROM THEIR MEANS; PERCENT OF THE MEAN
Respiratory rate	2.8
Tidal volume	3.7
Minute volume	2.4

The corresponding value for the oxygen determinations is 1.2 per cent (1, p. 618); and for the basal pulse rate, 1.8 per cent (2, p. 299).

These relatively large differences between duplicate determinations of the respiratory values are spontaneous and cannot be attributed to any systematic error in so far as we know. For a while it was thought that the first value was consistently higher than the second, perhaps due to a failure to attain a strictly basal state at the beginning of the experiment. That this is not so, is apparent from the following tabulation:

	NUMBER OF OBSERVATIONS IN WHICH THE FIRST DETERMINATION IS	
	Greater than the second	Less than the second
Respiratory rate	149	113
Tidal volume	130	134
Minute volume	138	135

So that, with the exception of the respiratory rate, and even here the difference is not significant enough to be attributed to a systematic error, the second value of a pair of determinations is as likely as the first to be the larger of the two.

Although there is no real proof that it is not so, it seems improbable that these differences are psychic or emotional in origin. At least, the subjects have been unable to recall any difference of mental state even at the close of periods between which the respiratory differences were large.

It may be thought that too much is being made of this matter; perhaps those with a larger experience in these affairs will see nothing unexpected in the occurrence of such variations. Our apology is that to us these data have presented evidence of a degree of variability in fundamental processes, under as nearly identical and basal conditions as it seems possible to reproduce, that was entirely unsuspected. The difference between duplicate metabolism determinations has been attributed to errors of technique. And perhaps it is. But our evidence shows that the basal pulse rate and respiration, in the determination of which the experimental error is small or absent altogether, show, when reduced to comparable bases, an even greater variability than the computed metabolism.

Not exactly in this same catagory yet related to it, is the degree of correlation between the respiratory rates during the duplicate collections of the expired air and the normal rate during the period of intermission between them. Just as the two former may differ considerably from each other, so their average for any one set of determinations shows but a small part of the correlation that might be expected with the normal rate. The coefficients of correlation are as follows:

A. B.	+0.38 ±0.06
C. D.	+0.18 ±0.07
K. L.	+0.39 ±0.06
Average	+0.32

3. The correlation between the different respiratory functions and between them and the metabolism. In addition to the above table showing the correlation between the normal respiratory rate and the average of the rates observed during the collection of the expired air, we add the following to show the correlation between the intra-individual, day-to-day variations of the minute volume and the respiratory rate (during collection of the expired air) and tidal volume:

	COEFFICIENTS OF CORRELATION BETWEEN THE MINUTE VOLUME AND:			
	Tidal volume		Rate of respiration	
	1925	1926	1925	1926
A. B.	+0.27 ±0.08	+0.43 ±0.04	+0.12 ±0.07	−0.14 ±0.05
C. D.	+0.83 ±0.02	+0.56 ±0.03	−0.10 ±0.07	+0.44 ±0.04
E. F.	+0.57 ±0.06		+0.26 ±0.08	
G. H.	+0.89 ±0.02		+0.31 ±0.08	
K. L.		+0 68 ±0.03		+0.42 ±0.04
Average	+0.64	+0.56	+0.15	+0.24

The data are presented separately for each of the two years in this and in the following tables on account of the slight difference in the collection of the expired air which has been referred to so often before. This makes no appreciable difference in these figures; and these are of significance as showing that variations in the minute volume are largely due to alterations of like sign in the depth of the tidal respirations. Indeed, in two instances, C. D., 1925, and A. B., 1926, the correlation between the total ventilation and the rate of respiration is negative; the figures are not large enough to be of any great significance in themselves; but they may suggest an explanation of the fact which has been noted on a previous page, that the respiratory rates during collection of the expired air in 1926 are slightly lower than the corresponding normal rates, during the determination of which there was no possibility of rebreathing, with its consequent augmentation of the total ventilation.

To what degree the respiration depends upon the metabolic rate of the body at the time, as measured by its oxygen consumption and carbon dioxid production, is shown by the following correlations between the intra-individual, day-to-day variations of these functions:

Coefficients of correlation

	OXYGEN CONSUMPTION		CARBON DIOXID PRODUCTION	
	1925	1926	1925	1926
Minute volume:				
A. B.	+0.34 ±0.07	+0.51 ±0.04	+0.36 ±0.06	+0.90 ±0.01
C. D.	+0.38 ±0.06	+0.46 ±0.04	+0.35 ±0.07	+0.74 ±0.02
E. F.	+0.11 ±0.08		+0.50 ±0.06	
G. H.	0.00		+0.37 ±0.08	
K. L.		+0.28 ±0.05		+0.85 ±0.01
Average	+0.21	+0.42	+0.40	+0.83
Tidal volume:				
A. B.	−0.04 ±0.07	+0.19 ±0.05	+0.32 ±0.07	+0.50 ±0.04
C. D.	+0.56 ±0.05	+0.36 ±0.05	+0.28 ±0.07	+0.72 ±0.03
E. F.	−0.22 ±0.08		+0.16 ±0.08	
G. H.	−0.12 ±0.09		+0.24 ±0.09	
K. L.		+0.76 ±0.02		+0.89 ±0.01
Average	+0.05	+0.44	+0.25	+0.70
Rate of respiration:				
A. B.	+0.16 ±0.07	−0.04 ±0.05	−0.17 ±0.07	−0.27 ±0.05
C. D.	−0.13 ±0.08	0.00	−0.06 ±0.08	+0.18 ±0.05
E. F.	+0.44 ±0.07		+0.27 ±0.08	
G. H.	+0.25 ±0.09		+0.22 ±0.09	
K. L.		0.00		+0.15 ±0.05
Average	+0.18	−0.01	+0.06	+0.02

These figures are especially interesting. In the first place they show that the rate of respiration is governed in no way by the metabolic rate. The tidal and minute volumes, on the other hand, are very significantly related to the rate of metabolism, particularly during 1926. This would seem to show that the increased dead space and rebreathing during 1925 introduced variations in the pulmonary ventilation which had no connection with, and obscured its relationship to the metabolic rate.

In this connection the correlation between the pulmonary ventilation and the carbon dioxid production deserves particular notice. All references to the disturbing effect of "auspumpung" on the apparent carbon dioxid production have purposely been deferred until this point. In the first paper of this series it was shown that the non-protein respiratory quotient was more variable than the total metabolic rate; and from this it was concluded that the metabolic materials were more variable than the total metabolic level. Such a conclusion is of course unjustified unless it can be made reasonably certain that the carbon dioxid output during the period of the determinations was free from untoward disturbances, of which "auspumpung" is recognizably the most to be suspected.

The evidence which we have here in regard to the correlation between the carbon dioxid output and the tidal and minute volumes of the respiration seems to be particularly significant in regard to this point. It will be seen that the correlations are unusually high for 1926 and are more than twice as high for this year as for 1925. And it will be easily appreciated that it was during 1925, when the correlation is low, that conditions were most favorable for an abnormal carbon dioxid output. If we consider A. B. and C. D., alone, 1925 included the period of their adjustment to the technique of the determinations; a matter which is well known to favor an unduly high carbon dioxid output, unless the subjects are already somewhat used to the process, as indeed these were. Nevertheless their correlations are highest during the second year after a year of practice and habituation to the apparatus. But more important, 1925 was the year of the abnormally large dead space with the augmented pulmonary ventilation which it produced. This condition, more than any other, would seem to have favored an increased output of carbon dioxid associated with the increased breathing. And yet the fact seems to show that the increased respiration, due to this artificial condition, only served to obscure, in this case as with the oxygen consumption, a more fundamental relationship between the carbon dioxid production and the volume of respiration.

The conclusion seems well grounded, therefore, that the high correlation between the carbon dioxid output and the minute and tidal volumes is not due to an artificially stimulated respiration washing out correspondingly increased amounts of carbon dioxid; on the other hand, the figures must be taken to mean that the fundamental factor in regulating the volume of the respiration is the rate of carbon dioxid production; which, of course, is merely confirmation, from a hitherto unused source, of a fact that is already well known. The significance of its substantiation from these data, however, lies chiefly in the fact that it insures confidence in our figures for carbon dioxid production and hence for any conclusions based upon them.

Inter-individual correlation between metabolism and respiration: The number of these subjects is too few to prove anything in regard to inter-individual correlations; but with this understanding, the following figures, derived from the intensive study of these five individuals, are suggestive:

SUBJECT	MEAN OXYGEN CONSUMPTION	MEAN VITAL CAPACITY	MEAN MINUTE VOLUME		MEAN TIDAL VOLUME	
			1925	1926	1925	1926
	cc. per minute	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*
A. B.	177	3,118	5,313	4,755	487	401
K. L.	181	2,748		4,844		334
E. F.	186	3,165	5,988		380	
G. H.	188	3,200	6,329		404	
C. D.	200	4,556	5,737	5,176	415	406

It may be said at once that there is no evidence of any inter-individual correlation between metabolic rate and the tidal volume. The same is true for the minute volume for 1925; even if the two sexes are considered separately the slopes of the lines connecting the homo-sexual points are too dissimilar to have any meaning. Here as in so many instances before, the artificial stimulation of the respiration by the large dead space of 1925 would appear to have obscured a fundamental relationship; at least we may judge so from the evidence for 1926 which shows a direct proportionality between oxygen consumption and minute volume. It is emphasized again, however, that at best this is very meagre evidence which has value only as a suggestion of possible relationships.

The same is true of the data in regard to oxygen consumption and vital capacity. In order to make anything of it at all, it is necessary to consider the sexes separately. When this is done the lines connecting the points for the men and the points for the women are sufficiently similar in slope to give some value to the suggestion which is thus offered of a positive correlation between the metabolic rate and the vital capacity.

4. Sex differences. Again very tentatively and without wishing to seem to do more than merely describe what can be observed in these data, we call attention to the following figures taken from table 1:

FUNCTION	MEANS			
	1925		1926	
	Men	Women	Men	Women*
Respiratory rate:				
1. During collection of the expired air	12.7	15.9	12.5	14.6
2. Normal			13.9	15.1
Composition of expired air:				
1. Per cent carbon dioxid	3.64	3.18	3.92	3.58
2. Per cent oxygen	16.90	17.32	16.45	16.56

* There was only one woman subject, K. L., during 1926.

In these functions which, unlike the vital capacity and volume of respiration, might be supposed to be independent of body size, it can be seen that these data show a consistent sex difference for both years. Whether or not such a difference would be confirmed on a larger number of subjects is a matter that would seem deserving of future attention in the light of this suggestion.

On firmer ground is the following comparison of the variability shown by the two sexes; these figures also are transposed from table 1 to facilitate comparison.

	STANDARD DEVIATION				COEFFICIENT OF VARIATION			
	1925		1926		1925		1926	
	Men	Women	Men	Woman*	Men	Women	Men	Woman*
Respiratory rate:								
During collection of expired air	1.31	1.59	0.90	0.74	10.8	10.0	7.3	5.1
Normal			1.23	1.27			8.9	8.4
Inspiration			0.23	0.16			13.6	11.5
Expiration			0.32	0.28			11.5	10.6
Tidal volume	69.00	45.00	35.00	17.00	15.1	12.6	8.7	5.2
Minute volume	479.00	620.00	234.00	282.00	8.7	10.1	4.7	5.8
Composition of the expired air:								
CO_2 per cent	0.28	0.31	0.12	0.15	7.8	9.8	3.0	4.1
O_2 per cent	0.35	0.39	0.18	0.21	2.1	2.1	1.1	1.3
	BOTH YEARS				BOTH YEARS			
	Men		Women		Men		Women	
Vital capacity	132		158		3.5		5.2	

* Only one woman subject, K. L., during 1926.

The data of the two years show consistent differences in spite of the difference in absolute magnitude of the constants and indicate that there is no sex difference in variability in these functions; the average coefficients of variation for the two years are 7.5 and 7.4 for the men and women, respectively.

In conclusion we should like to summarize the data which have been presented in this and the preceding papers of this series, regarding the variability of the different functions studied. These are arranged in the following table in order of increasing coefficients of variation. For the respiratory functions which are dealt with in this report we have used the average coefficients of variability for 1926, since these values are more nearly normal than those for the preceding year.

FUNCTION	AVERAGE COEFFICIENT OF VARIATION
1. Oral temperature	0.5*
2. Oxygen per cent of expired air	1.2*
3. Alveolar oxygen, per cent	3.3
4. Alveolar oxygen, tension	3.5
5. Carbon dioxid per cent of expired air	3.6*
6. Calories per sq. meter per hour	3.8*
7. Total oxygen consumption, cc. per minute	4.0*
8. Vital capacity	4.4*
9. Basal pulse rate	4.7*
10. Basal systolic blood pressure	4.9
11. Alveolar carbon dioxid per cent	5.1*
12. Alveolar carbon dioxid tension	5.2*
13. Total carbon dioxid production, cc. per minute	5.2*
14. Minute volume	5.3*
15. Non-protein respiratory quotient	5.3
16. Non-protein oxygen, cc. per minute	5.8*
17. Standing systolic blood pressure	6.0*
18. Respiratory rate, collection of expired air	6.2
19. Blood carbon dioxid capacity	6.9
20. Tidal volume	7.0
21. Non-protein carbon dioxid, cc. per minute	7.1*
22. Standing pulse rate	7.4*
23. Pulse rate after exercise	7.8
24. Respiratory rate, normal	8.7
25. Blood oxygen capacity	9.5*
26. Duration of expiration	11.2
27. Duration of inspiration	12.9
28. Protein carbon dioxid, cc. per minute	18.3*
29. Protein oxygen, cc. per minute	18.3*

* Coefficient of variation for the women greater than for the men.

This table will be useful for those who are interested in these matters by making readily available a comparison of the relative variability of these functions. Its pertinence in this connection is the summary which it provides of the relative variability of the men and women. In 18 out of the 29 functions studied, or practically two-thirds of the cases, the women have proven to be more variable than the men. Whether this argues for a disturbing effect of menstruation or whether its cause is to be sought for elsewhere cannot be decided at this time. The fact would seem to be important and to deserve further attention in the future.

II. The effect of sleep on the respiration. As has been mentioned in our first and second reports where its effects on the metabolism and basal pulse rate were described, A. B. and C. D. went to sleep during the first of duplicate determinations 30 and 10 times, respectively. The averages for these periods during the first of which the subject slept and during the second of which he was awake, are given in the following table; and for comparison there are included the averages for the first and second periods of an equal number of duplicate determinations from the same times of the year, during both of which the subjects were awake:

SUBJECT		MINUTE VOLUME			TIDAL VOLUME			RATE OF RESPIRATION		
		First	Second	Diff.	First	Second	Diff.	First	Second	Diff.
		cc.	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*			
A. B.*	(W. 30)	3,887	3,886	1	315	340	25	124	116	8
	(S. 30)	3,838	3,994	156	300	342	42	128	118	10
C. D.*	(W. 10)	4,222	4,250	28	326	333	7	130	128	2
	(S. 10)	4,237	4,398	162	333	339	6	127	130	3

* W, awake during both of two consecutive determinations; S, asleep during the first of two consecutive determinations; the numbers, 30 and 10, are the number of pairs of observations on which the averages are based. By an unfortunate error the number of observations for A. B. has been given in previous reports as 20.

Again we wish to emphasize the caution that these results do not pretend to define the effect of deep sleep. Such dozing as the subjects might do within the ten-minute metabolism period does seem, however, to have had a definite effect in reducing the minute volume; this amounts to 157 and 134 cc., or 4.0 and 3.1 per cent for A. B. and C. D., respectively. This is in line with the reduction in metabolism and pulse rate as described in the first two papers. Whether this reduction in minute volume should be considered as due to reduction in tidal volume, or rate of respiration, or both, is not certain. These data would indicate the possibility of individual differences; both are affected in the case of A. B.; with C. D., on the other hand, the reduction seems to be accomplished entirely by reduced rate of breathing. From the other evidence which has been

TABLE 2

The effect of menstruation; averages of the observations on the women, arranged according to their position in the menstrual cycle

The numbers in parentheses are the number of observations on which each average is based.

FUNCTION	SUBJECT	MENSTRUAL PERIOD	INTERMENSTRUAL PERIOD			
			First week	Second week	Third week	Fourth week and longer
Vital capacity (cc.) (37°C., observed barometer)	E. F.	3,158 (4)	3,185 (13)	3,113 (6)	3,193 (6)	3,282 (8)
	G. H.	2,954 (4)	3,076 (9)	3,013 (5)	3,099 (9)	3,088 (6)
	K. L.	2,733 (4)	2,739 (11)	2,784 (10)	2,712 (10)	2,736 (9)
	Av.	2,949 (12)	3,007 (33)	2,932 (21)	2,967 (25)	2,974 (23)
Respiration during collection of expired air for the metabolism determinations:						
Respiration rate per minute	E. F.	16.7 (9)	16.1 (17)	15.8 (11)	15.7 (13)	15.6 (15)
	G. H.	14.2 (9)	15.4 (14)	15.4 (11)	16.0 (12)	15.9 (9)
	K. L.	14.4 (12)	14.2 (39)	14.7 (36)	14.6 (36)	14.6 (35)
	Av.	15.0 (30)	14.9 (70)	15.0 (58)	15.1 (61)	15.1 (59)
Minute volume (cc.). (37°C., observed barometer)	E. F.	6,083 (9)	5,847 (17)	5,525 (11)	6,032 (13)	6,225 (15)
	G. H.	6,194 (8)	6,117 (15)	6,105 (11)	6,546 (12)	6,784 (9)
	K. L.	4,671 (12)	4,901 (39)	4,715 (36)	5,001 (36)	5,080 (35)
	Av.	5,529 (29)	5,384 (71)	5,132 (58)	5,525 (61)	5,631 (59)
Tidal volume (cc.) (37°C., observed barometer)	E. F.	370 (9)	371 (17)	353 (11)	388 (13)	409 (15)
	G. H.	387 (8)	397 (14)	398 (11)	411 (12)	427 (9)
	K. L.	324 (12)	331 (39)	321 (36)	343 (36)	347 (35)
	Av.	356 (29)	354 (70)	342 (58)	366 (61)	375 (59)
Carbon dioxid per cent of expired air	E. F.	3.21 (9)	3.26 (17)	3.44 (11)	3.27 (13)	3.14 (15)
	G. H.	3.18 (8)	3.15 (15)	3.19 (11)	3.04 (12)	2.93 (9)
	K. L.	3.59 (12)	3.66 (39)	3.65 (35)	3.49 (36)	3.48 (35)
	Av.	3.36 (29)	3.46 (71)	3.52 (57)	3.35 (61)	3.31 (59)
Oxygen, per cent of expired air	E. F.	17.29 (9)	17.20 (17)	16.94 (11)	17.22 (13)	17.36 (15)
	G. H.	17.26 (8)	17.30 (15)	17.31 (11)	17.44 (12)	17.58 (9)
	K. L.	16.57 (12)	16.47 (39)	16.43 (35)	16.64 (36)	16.69 (35)
	Av.	16.98 (29)	16.82 (71)	16.70 (57)	16.92 (61)	16.99 (59)

given in this paper that adjustments of pulmonary ventilation usually involve variations of tidal volume to a greater extent than of rate, this result for C. D. may be considered less typical than the other and due, perhaps, to the smaller number of determinations on which his averages are based.

III. The effect of menstruation. In table 2 the data for the three women are arranged according to their incidence in relation to the menstrual cycle.

It may be said at once that there is no evidence for an effect of menstruation on either the vital capacity or rate of respiration. On the other hand, the minute and tidal volumes and the composition of the expired air do seem to be definitely affected; and the grand averages for these functions, which are shown graphically in figure 1, are based on sufficiently concurrent testimony to have a strong validity. Thus all of the subjects are alike in showing a sharp rise in the tidal and minute volumes, which begins in the middle of the inter-menstrual period and culminates in the week just preceding the onset of menstruation; the oxygen percentage of the expired air follows a similar rise during the same period, while the carbon dioxid percentage falls reciprocally.

So much is very definite; on the other hand, just what values to assign to the menstrual period itself and the week immediately following, in relation to this latter part of the curve, is not so clear. From the confidence which we have in the data for K. L. (1, p. 624) and the fact that in these functions her testimony is corroborated by that of G. H., we are inclined to believe that the average values for the menstrual period and the week following are rendered too high by the aberrant values of E. F. during this time. This is more particularly true of the minute volume; in the cases of the tidal volume there is so little divergence among the three subjects, even in this part of the period, that it is difficult to doubt the substantial accuracy of the average curve throughout; and the same is true for the data in regard to the composition of the expired air.

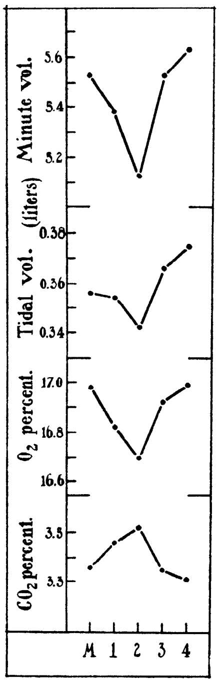

Fig. 1. The effect of menstruation; grand averages from the data of table 2. *M*, *1*, *2*, *3*, and *4* are respectively the menstrual period and the first, second, etc., weeks of the inter-menstrual period.

Our conclusion, then, would be that the tidal and minute volumes are perhaps slightly lower just after menstruation than during the period itself; and that they rise rapidly during the latter part of the inter-menstrual period to their largest values just before the beginning of the next menstruation. The oxygen percentage of the expired air follows a similar course and is followed in an inverse relationship by the percentage of carbon dioxid.

It is worth noting that the curves for minute and tidal volumes, both individually and as grand averages, are markedly similar to those for oxygen consumption and carbon dioxid production, as given in our first report (1, p. 623). This is significant in the light of the rather high correlation which, on a previous page, was shown to exist between these variables for the data as a whole. Thus their correspondence during the menstrual cycle would seem to constitute a strong presumption against the possibility of these variations, either of metabolism or pulmonary ventilation, being the result of chance.

Since we may not have occasion to refer to this matter in detail again it may be permissible to refer here to further consistencies of inter-relationship which give added credence to the possibility of genuine menstrual variation. Thus in addition to the correlation which has just been referred to between the variations of metabolism and pulmonary ventilation throughout the menstrual cycles of these subjects, it may be seen by reference to our second and third papers that further consistent correlations are to be found in the menstrual variations of the basal pulse rate and composition of the alveolar air.

For example, in the light of the rather high correlation which has been shown to exist for the data as a whole between the basal pulse rate and the rate of metabolism (2, p. 302) it could be expected that during the first part of the inter-menstrual period, when the metabolism is low, the pulse rate should also be low; and conversely, during the latter part of the period, when the metabolic rate is highest, the pulse rate should be highest. Such, in fact, proves to be the case.

And finally, as was shown in the third report, the alveolar carbon dioxid is lowest just preceding menstruation and rises to a maximum toward the middle of the inter-menstrual period; in other words, the alveolar carbon dioxid concentration varies inversely with the pulmonary ventilation during the menstrual cycle. At the same time it was shown that the blood carbon dioxid *capacity* varied in the same manner as the alveolar carbon dioxid concentration. This would seem to imply periodic variations in the blood alkali reserve; when this is at its highest value toward the end of the first half of the inter-menstrual period not only would a higher alveolar carbon dioxid concentration be tolerated but it would be necessary in order to provide the usual stimulus to respiration. And when it is remembered that the metabolic rate, i.e., the rate of carbon dioxid production, is lowest at just this time, the decreased pulmonary ventilation follows as a logical consequence. In like manner the reciprocal variations during the latter part of the menstrual cycle may be explained in a similar way.

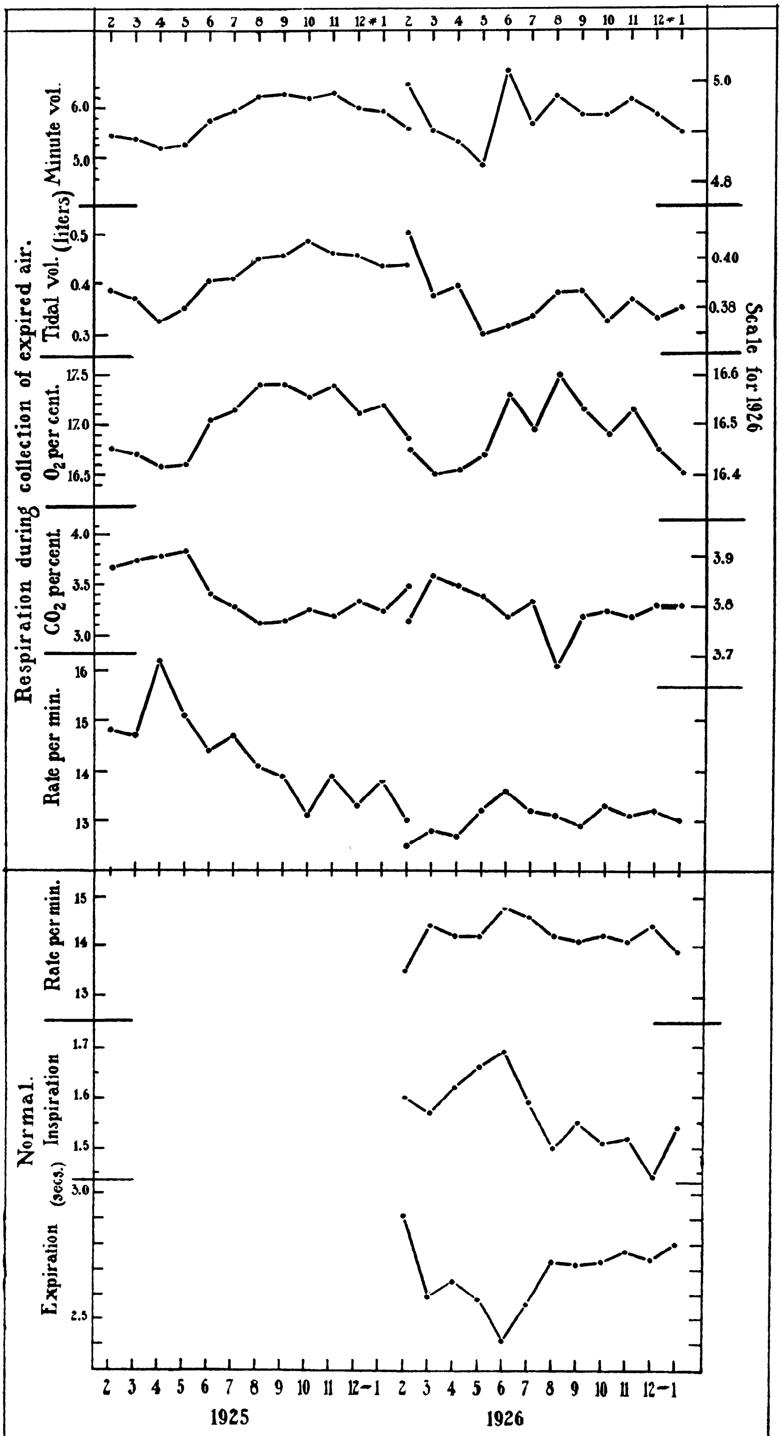

Fig. 2. Seasonal variation; grand averages for each month from the data of table 3. It will be noted that the curves for 1926–7 for the tidal and minute volumes and the composition of the expired air are plotted on a much larger scale than during 1925; for explanation see the text.

It is not intended that this explanation should be accepted as final. All that it is desired to do is to point out the seemingly coördinated variation of these different functions; whatever the final explanation of it may prove to be, the temporal correlation of so many variables would seem to indicate that we are dealing here with a genuine physiological disturbance and not with fortuitous variations.

IV. Seasonal periodicity. The monthly averages upon which the conclusions of this section rest are given in table 3; the grand averages computed therefrom are shown, with the exception of the vital capacity, in figure 2.

Neither the vital capacity nor the rate of respiration appear to us to have any seasonal variation. This does not mean that the vital capacity is invariable; in the case of A. B. it rises gradually to a maximum during the first year and subsides to its original value at the end of the second; with C. D. it rises gradually throughout the two year period; and each of the other subjects shows individual peculiarities which make it impossible to speak of anything like a common seasonal variation for this function.

We do not believe, either, that it is possible to make out a seasonal variation in the case of the respiratory rate; the average curves are reproduced in figure 2 to show the correspondence in the fortuitous fluctuations of the normal rate and the rate during the collection of the expired air during the second year. During this year there does seem to be a maximum during the summer; but the average effect is small and the individuals are not at all concurrent; neither are the curves for the rate during the collection of the expired air at all alike for the two years.

Another reason for producing the curve for normal respiratory rate is for the purpose of contrasting it with the curves for the lengths of the inspiratory and expiratory phases. These components of the respiratory act show a most definite seasonal variation in length; and, curiously enough, in such an exactly reciprocal manner as to leave the total length apparently unaffected, as was remarked above. Unfortunately we have these data for only one year; but they inspire confidence on account of the substantial agreement among the three subjects and the clear-cut nature of the result.

The evidence for seasonal variation of the minute and tidal volumes and the composition of the expired air is the most definite, uniform and conclusive of any that we have for any of the functions that we have studied; the precision with which the observations on the different subjects agree as to the magnitude and time of incidence of the maximum and minimum effects makes the average curves of figure 2 unusually trustworthy. From them it will be seen that the tidal and minute volumes are lowest in the spring and increase uniformly to a maximum in the late summer and fall; the oxygen percentage of the expired air follows an

TABLE 3

Monthly averages

SUBJECT	DATE	VITAL CAPACITY		RESPIRATION										
				Normal			During collection of expired air							
								Minute volume		Tidal volume		Composition of the expired air		
		0°C.—760 mm.	37°C.—observed barometer	Inspiration	Expiration	Rate per minute	Rate per minute	0°C.—760 mm.	37°C.—observed barometer	0°C.—760 mm.	37°C.—observed barometer	Per cent CO_2	Per cent O_2	Number of observations
		cc.	cc.	seconds	seconds			cc.	cc.	cc.	cc.			
E.F.	1925 Feb.	2,634	3,247				18.1	4,449	5,526	246	306	3.57	16.78	4
	Mar.	2,584	3,210				15.7	4,272	5,286	273	337	3.71	16.65	4
	Apr.	2,598	3,222				18.0	4,929	6,111	274	340	3.31	17.22	5
	May	2,621	3,239				17.7	4,405	5,433	249	308	3.68	16.77	3
	June	2,498	3,073				15.8	4,635	5,698	293	360	3.26	17.05	8
	July	2,519	3,108				16.0	4,819	5,952	301	372	3.17	17.23	10
	Aug.	2,600	3,195				16.7	5,498	6,755	329	404	2.93	17.61	5
	Sep.	2,596	3,204				14.9	5,077	6,255	341	420	3.06	17.49	7
	Oct	2,525	3,098				15.2	5,303	6,502	351	430	3.10	17.54	5
	Nov.	2,548	3,152				14.9	5,197	6,434	348	430	3.06	17.58	3
	Dec.	2,591	3,197				13.9	4,711	5,817	341	420	3.29	17.14	5
	1926 Jan.	2,597	3,166				14.1	4,903	6,019	348	427	3.12	17.33	4
	Feb.						14.2	4,791	5,869	340	417	3.25	17.16	2
G. H.	1925 Feb.						16.5	5,180	6,349	316	387	3.24	17.22	2
	Mar.						15.3	4,733	5,797	309	379	3.50	16.84	4
	Apr.						16.5	4,249	5,255	259	318	3.65	16.65	4
	May	2,716	3,334				15.6	4,731	5,824	304	374	3.58	16.89	5
	June	2,573	3,154				15.7	5,009	6,160	319	392	3.08	17.37	7
	July	2,434	3,002				16.9	5,507	6,794	325	401	2.69	17.64	8
	Aug.	2,710	3,343				15.1	5,196	6,409	345	425	2.93	17.59	3
	Sep.	2,509	3,083				15.1	5,544	6,834	366	451	2.85	17.71	4
	Oct.	2,556	3,159				14.8	5,383	6,658	366	452	2.98	17.61	4
	Nov.	2,857	3,483				15.7	5,634	6,873	360	440	2.77	17.79	2
	Dec.	2,706	3,318				15.5	5,495	6,758	354	436	2.91	17.57	4
	1926 Jan.	2,633	3,263				15.3	5,074	6,289	332	412	2.91	17.54	6
	Feb.	2,428	2,994				15.0	5,212	6,434	348	429	2.93	17.44	2
K. L.	1926 Feb.	2,255	2,760	1.50	2.37	15.5	14.9	3,980	4,926	266	330	3.61	16.46	6
	Mar.	2,282	2,839	1.34	2.58	15.2	13.9	3,922	4,848	282	348	3.72	16.32	18
	Apr.	2,326	2,865	1.42	2.43	15.6	14.3	3,941	4,844	276	339	3.70	16.41	18
	May	2,243	2,762	1.42	2.60	15.0	14.8	3,949	4,854	268	329	3.57	16.56	16
	June	2,325	2,868	1.42	2.26	16.5	15.3	4,141	5,114	270	333	3.45	16.77	18
	July	2,216	2,714	1.31	2.43	16.1	14.6	3,910	4,790	268	328	3.58	16.51	12
	Aug.	2,277	2,793	1.37	2.73	14.7	14.8	3,955	4.847	268	328	3.47	16.72	10

TABLE 3—*Continued*

SUBJECT	DATE	Vital capacity: 0°C.—760 mm.	Vital capacity: 37°C.—observed barometer	Respiration, Normal: Inspiration	Respiration, Normal: Expiration	Respiration, Normal: Rate per minute	During collection of expired air: Rate per minute	Minute volume: 0°C.—760 mm.	Minute volume: 37°C.—observed barometer	Tidal volume: 0°C.—760 mm.	Tidal volume: 37°C.—observed barometer	Composition of the expired air: Per cent CO_2	Composition of the expired air: Per cent O_2	Number of observations
		cc.	*cc.*	*seconds*	*seconds*			*cc.*	*cc.*	*cc.*	*cc.*			
K. L.	1926 Sep.	2,196	2,698	1.50	2.77	14.1	14.5	3,852	4,716	266	326	3.49	16.65	16
	Oct.	2,198	2,728	1.39	2.78	14.4	14.9	3,853	4,769	258	319	3.56	16.55	12
	Nov.	2,151	2,641	1.33	2.73	14.8	14.6	3,984	4,893	273	335	3.47	16.72	17
	Dec.	2,135	2,619	1.34	2.81	14.6	13.9	3,915	4,808	282	346	3.60	16.55	13
	1927 Jan.	2,111	2,602	1.51	2.97	13.4	13.7	3,840	4,756	281	348	3.68	16.33	6
A. B.	1925 Feb.	2,384	2,914				9.4	3,911	4,780	419	512	3.84	16.62	3
	Mar.	2,430	2,986				12.5	4,196	5,155	340	417	3.68	16.81	4
	Apr.	2,422	2,963				13.9	3,981	4,869	289	353	3.86	16.53	4
	May	2,432	2,987				13.1	3,974	4,849	304	372	3.82	16.59	4
	June	2,462	3,028				12.3	4,606	5,666	376	462	3.48	17.06	11
	July	2,509	3,097				11.4	4,284	5,288	380	469	3.51	16.96	9
	Aug.	2,632	3,222				10.9	4,632	5,668	435	532	3.29	17.29	6
	Sep.	2,665	3,273				11.3	4,668	5,720	420	515	3.40	17.19	7
	Oct.	2,610	3,209				8.4	4,415	5,430	498	613	3.59	16.98	9
	Nov.	2,641	3,220				11.1	4,594	5,599	428	521	3.53	17.13	9
	Dec.	2,597	3,205				10.0	4,287	5,296	431	532	3.67	16.82	5
	1926 Jan.	2,622	3,225				12.6	4,395	5,408	350	431	3.44	16.95	8
	Feb.	2,574	3,186	1.66	3.52	11.7	10.0	3,779	4,668	386	477	3.86	16.42	11
	Mar.	2,543	3,143	1.63	2.76	13.7	11.6	3,686	4,554	322	398	3.92	16.41	20
	Apr.	2,581	3,185	1.56	3.07	13.2	11.1	3,885	4,782	356	438	3.86	16.48	16
	May	2,550	3,161	1.53	2.80	13.8	12.2	3,753	4,639	308	380	3.86	16.47	17
	June	2,540	3,132	1.66	2.61	14.2	12.4	3,810	4,701	309	381	3.97	16.47	18
	July	2,540	3,123	1.71	2.66	13.8	12.1	3,894	4,786	324	398	3.97	16.54	14
	Aug.	2,511	3,082	1.55	2.81	13.8	11.5	3,902	4,788	343	420	3.75	16.66	11
	Sep.	2,488	3,050	1.42	2.79	14.4	11.7	3,982	4,878	341	422	3.85	16.63	18
	Oct.	2,426	3,007	1.46	2.84	14.0	12.2	3,941	4,872	327	404	3.86	16.55	16
	Nov.	2,531	3,101	1.53	2.85	13.8	12.2	3,937	4,834	329	404	3.87	16.59	18
	Dec.	2,455	3,016	1.39	2.75	14.5	13.0	3,900	4,793	301	370	3.81	16.52	14
	1927 Jan.	2,432	2,996	1.43	2.76	14.3	12.8	3,936	4,843	309	381	3.80	16.58	8
C. D.	1925 Feb.	3,525	4,329				15.1	4,158	5,107	276	339	4.04	16.41	2
	Mar.	3,592	4,385				15.4	4,369	5,334	283	346	4.01	16.52	5
	Apr.	3,623	4,424				14.8	3,748	4,574	253	309	4.32	16.04	4
	May	3,649	4,494				14.1	3,926	4,836	279	344	4.25	16.15	4
	June	3,481	4,286				13.9	4,452	5,481	320	394	3.80	16.69	10

TABLE 3—*Concluded*

SUBJECT	DATE	VITAL CAPACITY: 0°C.—760 mm.	VITAL CAPACITY: 37°C.—observed barometer	RESPIRATION: Normal: Inspiration	RESPIRATION: Normal: Expiration	RESPIRATION: Normal: Rate per minute	During collection of expired air: Rate per minute	Minute volume: 0°C.—760 mm.	Minute volume: 37°C.—observed barometer	Tidal volume: 0°C.—760 mm.	Tidal volume: 37°C.—observed barometer	Composition of the expired air: Per cent CO_2	Composition of the expired air: Per cent O_2	Number of observations
		cc.	*cc.*	*seconds*	*seconds*			*cc.*	*cc.*	*cc.*	*cc.*			
C. D.	1925 July	3,500	4,307				14.5	4,611	5,674	318	391	3.76	16.73	8
	Aug.	3,728	4,573				13.8	4,942	6,065	358	439	3.32	17.13	5
	Sep.	3,785	4,645				14.1	5,096	6,257	361	443	3.29	17.24	9
	Oct.	3,751	4,638				13.9	5,007	6,190	362	448	3.37	17.00	8
	Nov.	3,695	4,577				13.7	5,052	6,235	371	458	3.42	17.10	7
	Dec.	3,678	4,549				13.6	4,927	6,090	362	448	3.50	16.95	7
	1926 Jan.	3,642	4,492				13.2	4,907	6,020	373	460	3.52	16.97	7
	Feb.	3,592	4,417	1.65	2.83	13.4	12.7	4,059	5,387	344	426	3.83	16.46	10
	Mar.	3,659	4,514	1.75	2.43	14.4	13.0	4,298	5,315	332	410	3.94	16.45	18
	Apr.	3,765	4,641	1.89	2.44	13.9	12.8	4,072	5,009	316	389	3.97	16.35	18
	May	3,773	4,633	2.04	2.35	13.7	12.6	4,096	5,034	325	400	4.02	16.29	16
	June	3,732	4,585	1.99	2.36	13.8	13.0	4,256	5,255	328	404	3.93	16.43	17
	July	3,754	4,620	1.74	2.60	14.0	12.8	4,207	5,173	329	404	3.87	16.41	18
	Aug.	3,806	4,666	1.58	2.66	14.2	12.9	4,312	5,284	335	411	3.83	16.41	10
	Sep.	3,866	4,731	1.73	2.59	13.9	12.6	4,267	5,215	337	412	4.00	16.31	14
	Oct.	3,846	4,735	1.69	2.57	14.2	12.9	4,200	5,168	326	401	3.96	16.33	16
	Nov.	3,805	4,691	1.71	2.73	13.6	12.5	4,206	5,171	337	414	4.01	16.29	16
	Dec.	3,798	4,645	1.58	2.66	14.2	12.7	4,271	5,211	337	411	3.99	16.27	14
	1927 Jan.	3,796	4,690	1.68	2.66	13.9	12.4	4,137	5,098	333	411	3.91	16.29	8

exactly parallel course; and the carbon dioxid percentage varies in an exactly inverse relationship to these.

The curves for minute and tidal volumes of figure 2 are plotted from the gas volumes as recalculated to body temperature, 37°C., at the observed barometric pressures; a comparison of the two sets of data as recorded individually in table 3 will show, however, that the same variation is to be observed after they have been reduced to a common basis of comparison, viz., 0°C., and 760 mm. pressure. The variation is therefore of actual physiological significance and cannot be attributed to fortuitous variations in the measurement of the gas volumes.

An insight into the meaning of this variation may be derived from a comparison of the data for each of the two years. It will be noted that the curves for 1926 (fig. 2) are plotted on a much larger scale than those of the first year; had they been plotted on the same scale they would be practically straight lines. This magnification accentuates the irregularities and accounts for the angularities of the curves for 1926 as compared with the smoothness of those of 1925; it is indispensable, however, for revealing the essential similarity in kind of the data for the two years.

This difference in absolute magnitude of the effect in the two years must be due to the relatively large dead space and rebreathing which resulted from the apparatus used during 1925 and which has had to be referred to so often before as imposing peculiarities of degree upon the data for this year. From this it may be inferred that normal, natural breathing, with no artificial augmentation of the dead space, which we closely approximated but did not completely achieve during 1926, would probably show very little or no seasonal variation in the volume of the pulmonary ventilation. We are therefore indebted to what we long considered an unhappy technical blunder for revealing a factor which without it might easily have remained unrecognized. For it was only in consequence of the very apparent results of the first year that we were led to inspect the data of the second under sufficient magnification to discover its similar seasonal variation in miniature.

The conclusion from this must be that the sensitivity of the respiratory center changes with the time of year, being least in the spring and greatest in the late summer and early fall. The variations in the pulmonary ventilation which have been observed are therefore measures of the response of the center at different times to a constant stimulus; this stimulus, during these determinations, being the amount of carbon dioxid in the inspired air; which, in turn, was determined by the size of the dead space in the apparatus used for collection of the expired air. Since this was large in 1925 the response of the center was large, a fact which was referred to earlier as evident in the mean values and degree of dispersion of the data for this year; being small in 1926, the response was also smaller, as was again corroborated by the statistical analysis of the previous section.

In the main, this corroborates the conclusion arrived at by Lindhard in the painstaking work (6) to which reference has already been so often made. Although we have been unable to confirm his findings in regard to the seasonal variations of metabolism (1), alveolar carbon dioxid (3), or respiratory rate (below, this paper), we are in agreement as to an increased sensitivity of the respiratory center during the warmer parts of the year, as evidenced by maximal pulmonary ventilation at this time. Lindhard makes no mention, however, of the marked spring depression which is so pronounced in our records.

Again attention may be called to the fact that these variations in pulmonary ventilation seem to be effected entirely by variations in depth rather than in rate of respiration. Thus the latter not only fails to show any corresponding seasonal variation, but if we refer back to table 1 it can be seen that there is less difference between the statistical values for respiratory rate for the two years than there is for the other components of the respiration. Not only that, but the measures of dispersion and, more particularly, the maxima and minima, the modes and the arithmetical means are of the same order of magnitude for the normal rate as for the rates during collection of the expired air, either for 1925, with the large dead space and augmented ventilation, or for 1926 when these were more nearly normal. The same thing has also been noticed in connection with menstruation where we were unable to find any consistent variation in rate although the volumes and composition of the expired air were quite evidently affected. The only exception to the rule was in the case of the effect of sleep on the respiration of C. D; here the decreased minute volume could only be attributed to change in rate. But this, as already pointed out, may easily be in error on account of the small number of observations involved; and particularly so, since with A. B. the effect was, again, due largely to variation in tidal volume. Thus although the respiratory rate has been shown to be quite unstable, the average deviation of duplicate determinations from their means and the coefficients of variation both being large, this variability would seem to be spontaneous and fortuitous; and, at least under these basal conditions, quite unrelated to the adaptive alterations in pulmonary ventilation which we have been considering.

In conclusion it may be mentioned that the seasonal variation in composition of the expired air seems to be such as to prevent the variation in pulmonary ventilation from obscuring the true gaseous exchange. Reference to our first paper will show that the metabolic rate, whether measured by oxygen consumption or carbon dioxid production, varied within almost exactly the same limits during each of the two years of this study. This, we may suppose with good reason, is quite as it should be. Such a result could not have been derived from these respiratory data, however, unless the variations in pulmonary ventilation, which were roughly twice as great in 1925 as in 1926, had been very accurately compensated for by changes in the composition of the expired air. The consistent interrelationship of all of these variables would seem, therefore, to justify a high degree of confidence in these results for the data as a whole.

By contrast, however, it must be remarked as a seeming defect in the evidence for *seasonal* variation that there is lacking, here, the precise correlation of all the functions which appear to be involved, such as made the picture of menstrual variation so clear-cut and decisive. The most unequivocal examples of seasonal variation from among all of our data are provided by the basal pulse rate which was described in our second report and the pulmonary ventilation given here. These are both very little liable to falsification through errors of technique; and for both of them there is unanimous agreement among the subjects of this group. But we find that the basal pulse rate is lowest during the summer; whereas the minute and tidal volumes are just as definitely lowest in the spring. The significance of this disagreement becomes apparent when it is attempted to reconcile each of these with the metabolic rate. This has been shown in these papers to have about the same degree of high correlation with both the basal pulse rate and the minute volume for the data as a whole. But insofar as the average effect is concerned the metabolic rate is definitely lowest in the summer, i.e., in its seasonal variation it satisfies the expected correlation with the pulse rate, while violating the other.

It is true that the evidence for a summer depression of the metabolic rate was not unanimous; with C. D., the rate was definitely lowest in the spring; and with A. B., there was in both years a pronounced spring depression. But these individual differences hold no solution of the problem for there were no exceptions to the variations in pulse rate and pulmonary ventilation; and therefore neither individually nor as averages can the expected correlations all be satisfied.

This may mean that what we have called seasonal variations are merely coincident, chance fluctuations; this is all but impossible to believe of evidence as little subject to experimental error, as definite, and as consistently shown by all of the subjects as the variations in pulse rate and minute volume; and while it would not be so difficult to suspect the metabolism data, the mere fact that such definite variations are observable in such fundamental processes as the pulse rate and pulmonary ventilation would make a variation in metabolism seem very reasonble. It may be suggested that the failure to obtain as consistent correlations among the functions seeming to show a seasonal variation as was obtained, for example, in the menstrual cycle, is due to the temporal dispersion of the data which gives opportunity for the play of disturbing factors that do not have time to make themselves felt in periods of shorter duration.

Such a conclusion is altogether too vague to be regarded as a happy ending to this subject. It will serve, however, to give point to our hope that no one will ever accuse us of having pretended to have settled the possibility or exact nature of seasonal variation. Our work was done as carefully as it seemed possible to do it; and our main purpose has been to describe as accurately and with as little bias as possible such results as the data show. But it is thoroughly realized that in the case of a subject as large as that of seasonal periodicity, where an entire year is required for the completion of a single experiment, not only time but even more rigorously controlled determinations will be required to secure enough and adequate data for finally settling this question.

SUMMARY

This is the fourth of a series of reports in which we have described the intra-individual variations of weight, temperature and metabolism (1), pulse rate and systolic blood pressure (2), and the composition of the alveolar air and blood gas capacity (3) of five normal, adult human subjects who were under observation from February 1925 to February 1927.

This paper deals with the variations in vital capacity, the rate and volume of the respiration and the composition of the expired air.

For each of these functions are given the statistical constants defining the modes and means and the extent and degree of variability. In addition we have calculated the degree of correlation between the rate and minute and tidal volumes of the respiration; and between these and the oxygen consumption and carbon dioxid production.

There is an unusually high correlation between the volume of pulmonary ventilation and the carbon dioxid output; reasons are given for believing that this is not due to increased breathing washing out increased amounts of carbon dioxid, but is an expression of the fundamental control of pulmonary ventilation by the rate of carbon dioxid production.

A sharp dichotomy separates the results of the two years as regards the minute and tidal volumes and the composition of the expired air; this was due to the dead space in the apparatus for collecting the expired air being large (about 50 cc.) during the first year and small or practically negligible during the second. The large dead space was associated not only with large absolute values for these functions, but occasioned, also, a much greater degree of variability.

Going to sleep (dozing) during the collection of the expired air definitely decreases the minute volume 3 to 4 per cent; it is not clear to what extent this is due to variations of rate or of tidal volume; though other evidence would seem to indicate that the latter is probably most involved.

Menstruation cannot be seen to have any effect on the vital capacity nor the rate of respiration; on the other hand the volume of pulmonary ventilation and the composition of the expired air are definitely affected. These variations are so concisely illustrated in figure 1 that they need not be repeated here. In addition it is shown that the menstrual variations in metabolism, pulse rate, composition of the alveolar air and blood gas capacity which have been described in the previous reports may be consistently correlated with the changes described here.

Neither the vital capacity nor the respiratory rate can be seen to have a seasonal variation; the tidal and minute volumes and the composition of the expired air, however, show the most definite and uniform variation of any of the functions we have studied except the basal pulse rate; these are so clearly shown in figure 2 that they need not be described again. In addition, attention is called to the difficulty of correlating the seasonal

variations of metabolism, pulse rate and the ventilation which these data seem to show as indicating the need for much further work before this matter can be considered settled.

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