THE VOLUME OF THE "DEAD SPACE" IN BREATHING. By A. KROGH and J. LINDHARD.

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In a recent paper Douglas and Haldane[1] have published a series of experiments to show that the "dead space" may be increased during muscular work to several times the resting volume. They observed a very regular increase from 160 c.c. during rest in bed to 622 c.c. while the subject walked at the rate of five miles an hour, with a corresponding increase in metabolism from 237 c.c. to 2573 c.c. oxygen per minute. When this paper appeared we were preparing for publication a series of experiments on the regulation of respiration and circulation during the initial stages of muscular work. We had assumed a constant dead space, and if Douglas and Haldane were right we would have to recalculate all our experiments and reconsider several portions of our argument. We could not, for reasons to be stated presently, accept the results of Douglas and Haldane as binding, but on the other hand we could not disregard them, as they might very well be correct—at least qualitatively—and it became necessary therefore that we should attempt also a determination of the dead space under the conditions of rest and work.

Douglas and Haldane have calculated the dead space from (1) the CO_2 percentage of the expired air, (2) the average CO_2 percentage of the alveolar air and (3) the average volume of one breath. The average volume of one breath and the CO_2 percentage of the expired air were determined from respiration experiments made by means of the Douglas respiration apparatus, and we have no doubt that the accuracy was ample for the purpose. The average composition of the alveolar air was determined by the method of Haldane and Priestley[2] as the average of samples taken by a sharp expiration at the end of a normal inspiration and at the end of a normal expiration. This method will give fairly consistent results, and when the mean is taken of a number of determinations the accidental error may become very small, but there

[1] This *Journal*, XLV. p. 235. 1912.

[2] *Ibid.* XXXII. p. 240. 1905.

is no guarantee that the result corresponds really to the average composition of the alveolar air, and in our opinion several reasons point *a priori* to the conclusion that it does not.

1. While the minimum CO_2 percentage in the alveolar air corresponds exactly in point of time to the end of inspiration, the maximum will normally occur a certain time after the end of expiration and the beginning of the next inspiration, even if there is a pause. The CO_2 percentage will go on increasing while the alveolar air, standing after expiration in the air passages, is being rebreathed, and it is only when pure outside air begins to enter the alveoli that the CO_2 percentage begins to fall. This time, from the end of expiration to the moment when fresh air begins to enter the alveoli, amounts in some of our respiration experiments during rest to $\frac{1}{3}$ or even $\frac{1}{2}$ of the total period of inspiration.

2. Even if samples of alveolar air were drawn representing exactly the maximum and minimum CO_2 percentages occurring, it would not follow that their arithmetic mean would correspond exactly to the average CO_2 percentage in the alveoli, and it could not be expected to correspond to the average composition of the air expired from the alveoli, which portion alone goes with the air from the dead space to make up the total expired air[1]. It is a well-known fact that the exhalation of CO_2 from the blood depends very largely on the percentage of the gas in the alveolar air, being diminished by a high percentage and increased by a low (washing out of CO_2). This fact holds good also for every single breath. The rise of CO_2 tension in the alveoli after inspiration will not simply be proportional to the time but will take place at a decreasing rate[2]. It is for this reason that the alveolar respiratory quotient is often considerably lower than that found for expired air, when the alveolar sample has been taken at the end of expiration.

The above criticisms do not detract in any way from the value of the Haldane-Priestley method of taking alveolar samples. The results obtained by this method during ordinary respiration are undoubtedly accurate enough for most purposes, and even if small systematic errors are present, they cannot affect the comparisons between different individuals or between different conditions of altitude above sea-level, diet or season in the same individual. When, however, the alveolar

[1] This point will be treated more fully in a paper by one of us which is being published in the *Skand. Arch. Physiol.*

[2] The oxygen intake will not be affected in this way, but variations in the rate of blood flow will have a most powerful influence on it.

CO_2 percentage is used together with the corresponding percentage in the expired air for calculating the dead space of the subject, even small deviations from the true composition of the air expired from the alveoli may have a very considerable effect upon the reliability of the result as pointed out by one of us[1].

3. The sharp expiration by which the alveolar sample is procured takes a certain time. Though this may vary in different individuals and depend further on the mental effort of the subject, it cannot possibly be shortened beyond $\frac{1}{3}$ second, and according to our experience it is never less than about $\frac{1}{2}$ second. During rest the carbon dioxide produced in this interval is insignificant and cannot raise the percentage of CO_2 in the alveolar air to any appreciable extent. When the CO_2 production is 240 c.c. per minute it will be 2 c.c. in $\frac{1}{2}$ second, and if we take the volume of air present in the lungs as 3 l. the rise in CO_2 percentage during the sharp expiration will probably be about 0·1 % and perhaps less. During muscular work, however, the influence of the unavoidable delay in getting the sample may become very great; 40 c.c. CO_2 produced per second must raise the CO_2 percentage to a very appreciable extent during even the sharpest possible expiration.

We must therefore consider the alveolar samples obtained by the direct method during muscular work as untrustworthy in so far as they do not represent the real average composition of the alveolar air, and we cannot accept the calculations of the dead space based upon them without further investigation.

Of the methods applied or proposed for determinations of the dead space in breathing that devised by Siebeck[2] appeared to us to be the most rational in principle, and the tests carried out by him seemed to demonstrate its reliability. It consists in taking one breath of hydrogen from a small spirometer and thereupon to expire once into the same. A sample of alveolar air from the end of expiration is taken and analysed for hydrogen, and the total amount of H_2 expired is calculated from an analysis of the contents of the spirometer.

In this method also the difficulty and possible uncertainty lie in the alveolar sample. It must be an essential condition that the hydrogen inspired into the alveoli should be uniformly mixed up in the alveolar air during the very short time it is retained in the lungs. Our own experience with regard to nitrous oxide[3] pointed decidedly against this

[1] I. Lindhard. *Skand. Arch. Physiol.* xxvi. p. 273. 1912.

[2] *Skand. Arch. Physiol.* xxv. p. 87. 1911.

[3] Krogh and Lindhard. *Skand. Arch. Physiol.* xxvii. p. 110. 1912.

possibility, since we found that not less than three respirations were necessary to produce a uniform mixture of this gas in the alveoli, but Siebeck had carried out test experiments which seemed to be conclusive.

Siebeck[1] compared a number of experiments in all of which he had taken a constant inspiration of 500 c.c. hydrogen, while the expirations were varied from 92 c.c. to 1690 c.c. The hydrogen percentage in the expired volume of air decreased regularly with increasing expirations, and, when the H_2 in successive 100 c.c. portions of one deep expiration was calculated, it was found, that while the first 400 c.c. showed H_2 percentages decreasing from 88·5 to 12·9 %, the composition of the rest showed small and irregular variations only. We have repeated Siebeck's test in practically the same manner and obtained an identical result.

We made the following experiments in the order indicated.

I. L. Inspiration 0·50 litre hydrogen.

No.	Expiration l.	Hydrogen in expired air, %	No.	Expiration l.	Hydrogen in expired air, %
1	0·30	41·0	5	1·11	20·6
2	0·35	37·9	6	1·37	18·45
7	0·47	37·1	12	1·53	19·35
3	0·52	29·4	9	1·54	18·7
4	0·83	23·4	10	1·85	17·4
8	0·98	20·7	11	1·98	16·8

From these experiments the curve shown in Fig. 1 was constructed. The following table, showing the average hydrogen percentages in increasing expirations from 300 c.c. to 2 litres and in successive portions of 300 c.c. alveolar air, has been interpolated from the curve.

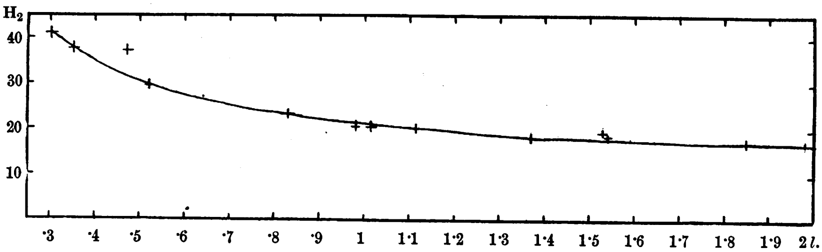

Fig. 1.

The variations in composition of the alveolar air amount to 2 % hydrogen (11·8–13·7). They are not larger than we must expect from the unavoidable experimental errors, and there is nothing like a regular

[1] Siebeck. *Ztschr. f. Biol.* LV. p. 278. 1910.

Expiration l.	Hydrogen %	Hydrogen c.c.	H_2 in alv. air c.c.	H_2 in alv. air %
0·3	41·0	123		
			27·5	13·8
0·5	30·1	150·5		
			38	12·7
0·8	23·55	188·5		
			37	12·3
1·1	20·5	225·5		
			35	11·8
1·4	18·65	261		
			38	12·7
1·7	17·6	299		
			41	13·7
2·0	17·0	340		
			Average (0·5 to 2·0 l.)	12·24

decrease in hydrogen percentage. The test carried out by us would therefore appear to confirm Siebeck's conclusion. In spite of this the alveolar air after a single inspiration of hydrogen can be shown to be incompletely mixed and to contain more hydrogen in the portions expired earlier than in the later.

When we began to make the determinations of the dead space we employed a mixture containing 15 to 20 % hydrogen because that would be most convenient to analyse and the accuracy ought to be quite sufficient. The results were very unsatisfactory. The dead space as determined varied quite irregularly and was generally much larger than we thought at all likely. We then tested every detail of the method and found that the only possible source of the irregularities must be the alveolar samples. We arranged therefore to take two samples of alveolar air from different depths during one and the same expiration. The subject expired through a four way tap and a rubber tube of suitable dimensions into a recording spirometer, and the samples were taken into vacuous sampling vessels connected with the tubing just in front of the mouth. In this way we obtained practically instantaneous sampling. In the first five of the determinations given below various hydrogen mixtures were inspired from the recording spirometer and expired back into it. In Exps. 6, 7, 8 and 10 pure hydrogen was inspired from a bell jar immersed under water (see Fig. 2). In Exp. 9 a hydrogen mixture was inspired from a bag and the volume could not be accurately measured. The points on the expiration curves at which the alveolar samples of 20 c.c. were drawn were in most cases visible on the records as momentary stops in the rise of the spirometer, but the location is not always certain.

Among the ten determinations made there is only one exception (No. 5) to the rule that the last portion of the expiration will contain

	Inspired l.	Expired l.	Alveolar samples at l.	Hydrogen %	Difference %	
1	1·1	2·3	1·7 2·3	3·33 2·97	12	
2	1·1	2·7	1·3 2·7	3·04 2·57	18	
3	1·35	3·25	1·35 3·25	4·43 3·82	16	
4	3·3	3·3	1·2 3·3	12·51 12·15	3	
5	1·2	2·1	0·8 2·1	6·90 6·95	−1	
6	0·5	2·1	1·0 2·1	14·00 13·02	7	
7	0·5	1·6	0·9 1·6	17·33 16·09	8	Inspirations after deep expirations.
8	0·5	1·4	0·9 1·4	17·86 16·66	7	
9	>3	3·0	0·8 2·5	11·63 11·43	2	Inspiration from residual air.
10	1·3	2·2	1·0 2·2	32·43 30·97	4·5	

less of the inspired gas than the earlier. As might be expected a very deep inspiration will diminish the differences between different portions of the expired air.

In these circumstances it would appear to be an almost hopeless task to make determinations of the dead space, but as Siebeck had obtained results which were fairly consistent and on the whole probable we could not give the matter up, without attempting to reduce the errors as far as possible.

The dead space is computed from the equation :

$$Eh_e = (E - D)\, h_a + Dh_i.$$

This equation is transformed to

$$D\,(h_i - h_a) = E\,(h_e - h_a) \text{ or } D = E\,\frac{h_e - h_a}{h_i - h_a},$$

in which E is the volume of the expiration and D the dead space. h_e, h_a and h_i are the percentages of hydrogen in expired air, alveolar air and inspired air respectively. E, h_e and h_i can be determined with great accuracy while h_a is always more or less uncertain. The error on h_a will have influence on the differences $h_e - h_a$ and $h_i - h_a$ and it is obviously of advantage to make these differences as large as possible in order to reduce the influence of the error. This is done by making E small and h_i large, that is by inspiring pure hydrogen and making a small expiration. It is of advantage further to reduce the volume of the inspiration, because that will reduce h_a.

Though a large inspiration of a hydrogen mixture will give the smallest absolute error on h_a it is easy to see that it will be much less favourable for a determination of the dead space than a small inspiration of pure hydrogen. A few concrete examples from our determinations will serve to make this clear.

1. Inspired 1·1 l. air with 13·70 % H_2; expired 2·34 l. with 4·69 % H_2.
Alveolar sample I after 1·75 l. expiration 3·33 % H_2.
Alveolar sample II after 2·34 l. expiration 2·97 % H_2.

$$\text{I.}\quad D=2{\cdot}34\,\frac{4{\cdot}69-3{\cdot}33}{13{\cdot}7-3{\cdot}33}=\mathit{307}\text{ c.c.}$$

$$\text{II.}\quad D=2{\cdot}34\,\frac{4{\cdot}69-2{\cdot}97}{13{\cdot}7-2{\cdot}97}=\mathit{374}\text{ c.c.}$$

2. Inspired 1·3 l. hydrogen; expired 2·22 l. air with 36·26 % H_2.
Alveolar sample I after 1·2 l. expiration 32·43 % H_2.
Alveolar sample II after 2·22 l. expiration 30·97 % H_2.

$$\text{I.}\quad D=2{\cdot}22\,\frac{36{\cdot}26-32{\cdot}43}{99{\cdot}67-32{\cdot}43}=\mathit{122}\text{ c.c.}$$

$$\text{II.}\quad D=2{\cdot}22\,\frac{36{\cdot}26-30{\cdot}97}{99{\cdot}67-30{\cdot}97}=\mathit{171}\text{ c.c.}$$

3. Inspired 0·5 l. hydrogen; expired 1·07 l. air with 24·97 % H_2.
Alveolar sample I 16·90 % H_2.
Alveolar sample II 16·00 % H_2. Assumed in accordance with Exp. 6, p. 4.
Alveolar sample III 15·00 % H_2.

$$\text{I.}\quad D=1{\cdot}07\,\frac{24{\cdot}97-16{\cdot}90}{99{\cdot}67-16{\cdot}90}=1{\cdot}07\,\frac{8{\cdot}07}{82{\cdot}77}=\mathit{104}\text{ c.c.}$$

$$\text{II.}\quad D=1{\cdot}07\,\frac{24{\cdot}97-16{\cdot}00}{99{\cdot}67-16{\cdot}00}=1{\cdot}07\,\frac{8{\cdot}97}{83{\cdot}67}=\mathit{115}\text{ c.c.}$$

$$\text{III.}\quad D=1{\cdot}07\,\frac{24{\cdot}97-15{\cdot}00}{99{\cdot}67-15{\cdot}00}=1{\cdot}07\,\frac{9{\cdot}97}{84{\cdot}67}=\mathit{128}\text{ c.c.}$$

It follows from the above considerations and examples that the variations and uncertainties with regard to the composition of the alveolar air will make the results obtained with hydrogen mixtures absolutely unreliable. Large inspirations and expirations of pure hydrogen may give very divergent results, but though results obtained with small inspirations and expirations of the pure gas are still somewhat uncertain, they cannot probably be more than 20 c.c. from the truth. As this degree of accuracy is sufficient for our purposes, and indeed for most purposes with regard to the dead spaces, we have made a number of determinations. It is obvious that neither the inspiration nor the expiration can be reduced indefinitely in volume, because it is essential that they should be sufficient to wash out the dead space completely. We have found that to ensure this a volume of not less than three times the dead space is necessary and sufficient.

The final form which the method has taken in our hands is therefore the following (Fig. 2): the graduated bell-jar 1 and the rubber tube up to the tap 2 is filled, generally with 500 c.c. pure hydrogen (99·67 %), and submerged. A small rubber ball is suspended from the top of the jar to act as a valve and prevent inspiration of water. The subject breathes through a mouthpiece or mask connected with the four way tap at 5, and before the experiment the passage is open to the atmosphere through 4. After an expiration the subject turns the tap and inspires the hydrogen from 1 and thereupon expires through 3 to the recording spirometer 7. At the end of the expiration, which should be 600 to 800 c.c. in volume, the tap is closed and an alveolar sample is taken into the vacuous sampling vessel 6. The contents of the spirometer and the rubber tube connecting it with the tap are thoroughly mixed, and a sample is taken into 8. The dead space of the tubing 3–7 and the

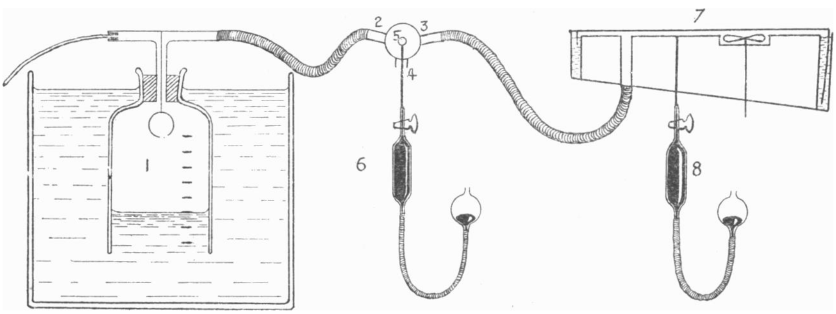

Fig. 2.

spirometer has been accurately determined once for all. We always record the expiration on a revolving drum, and this has helped us in several cases, especially in determinations during muscular work, to avoid gross errors, which may be caused for instance by a small inspiration from the spirometer. We have not in the present series of experiments reduced the volumes to 37° and saturation with moisture but taken them as they were read off from the spirometric record, that is at the barometric pressure obtaining and saturated at a temperature of about 18° C. in almost all our experiments.

If the personal dead space of the subject is required the volume of tubing from the tap to the mouth (generally 12 c.c.) is deducted, and the remaining volume of air must be reduced to 37° and saturation at that temperature. In the tables given below the volume of tubing has been deducted, but the reduction to 37° has been performed only on the final result for each subject.

We have made a number of determinations on four different subjects during rest, that is sitting on a stationary bicycle ergometer with the feet resting on supports.

For I. L. we have utilised the expirations between 0·52 and 1·37 l. of the Siebeck test series, assuming an alveolar H_2 percentage of 12·24, the average found, and compared these with a series of single determinations after the method described and with inspirations of 500 c.c. H_2 throughout.

Siebeck test series		Single determinations		
Expiration l.	Dead space c.c.	Date	Expiration l.	Dead space c.c.
0·52	91	27/12	0·6	96
0·83	93	28/12	0·6	101
0·98	83	31/12	0·8	83
1·10	100	2/1	1·0	94
1·37	85	—	1·0	108
		21/1	0·7	95
		25/1	0·7	96
		18/2	0·6	112
Mean	90 c.c.			98 ± 3 c.c.
		Mean deviation of one determination ...	...	$\mu = \pm 8$ c.c.
		Personal dead space (37°) ...		109 c.c.

On the other subjects we have made the following determinations:

Subject	Date	Inspired H_2 l.	Expired l.	Dead space c.c.	Mean	Personal dead space c.c. (37°)
A. K.	18/2	0·5	0·7	154		
—	—	—	0·65	131		
—	—	—	1·0	150		
—	25/2	—	1·0	150		
—	—	—	1·1	150	143 ± 3	159
—	—	—	0·85	146	$\mu = \pm 11$	
—	4/3	0·75	0·8	156		
—	17/5	0·5	0·6	136		
—	20/5	0·75	0·65	125		
—	—	0·6	0·8	132		
F. N.	15/4	0·75	0·6	157		
—	—	—	0·9	164	155	173
—	—	—	0·8	144		
H. P.	20/5	0·6	0·8	168	162	181
—	—	0·6	0·85	156		

We have subjected the method to a further test by artificially increasing the dead space with a tube of 80 c.c. put in between the mouth of the subject and the tap. We found

I. L.

Date	Inspired H_2 l.	Expired l.	Dead space c.c.
31/12	0·5	0·9	161
21/1	—	0·75	181
	Mean ...	...	171
	Normal dead space		98
	Difference	...	73

A. K.

Date	Inspired H_2 l.	Expired l.	Dead space c.c.
18/2	0·5	0·9	201
—	—	0·8	198
25/2	—	1·1	212
—	—	1·15	203
—	—	1·0	206
	Mean ...	...	204
	Normal dead space		143
	Difference	...	61

In the experiments with I. L. the result is satisfactory but with A. K. it is decidedly too low. We found however that a smaller tube of 40 c.c. capacity could be determined accurately enough in experiments on A. K. We found 45·5 c.c. as the average of two determinations giving 188 and 189 c.c. for the total dead space. The reason why the whole of the large tube could not be found is in our opinion simply that the inspiration of 500 c.c. was not sufficient to wash out completely a dead space of about 230 c.c. When we increased the inspiration to 750 c.c. we found in two experiments with the tube of 80 c.c. values of 200 and 229 c.c. for the total dead space, corresponding to 57 and 86—average 72—for the tube.

In several of the preceding experiments the rate of inspiration and expiration has been varied, but when such variations are kept within ordinary limits we cannot detect any influence. When both the inspiration and the expiration were much prolonged we found slightly higher values for I. L. (113, 126) than the normal 98 c.c. This is a result to be expected from a prolonged expiration because the H_2 percentage in the alveolar air must be lowered during the long expiration and the sample taken at the end must become less representative. A prolonged inspiration alone does not produce any increase in the value found for the dead space viz. I. L. 109 c.c., A. K. 136 c.c.

Concluding from all the preceding tests that the Siebeck method will give fairly reliable determinations of the effective dead space in breathing we have applied it during muscular work on the bicycle ergometer corresponding to 500 to 750 kgm. per minute or a respiratory exchange of 1500 to upwards of 2000 c.c. oxygen per minute. The work was in every case continued for at least two minutes before an experiment was made. To make quite sure that the method would not fail in these circumstances we have repeated the Siebeck test on I. L. while a constant amount of work (500 kgm. per minute) was being performed by the subject.

We made the following single determinations with inspirations of 0·50 l. hydrogen throughout:

No.	Expiration l.	Hydrogen in expired air, %
1	0·25	43·4
2	0·53	26·95
7	0·71	21·95
3	0·82	21·55
8	1·04	18·4
4	1·16	17·7
5	1·55	15·85
6	1·99	14·3

From these results the curve Fig. 3 was constructed which gave by interpolation

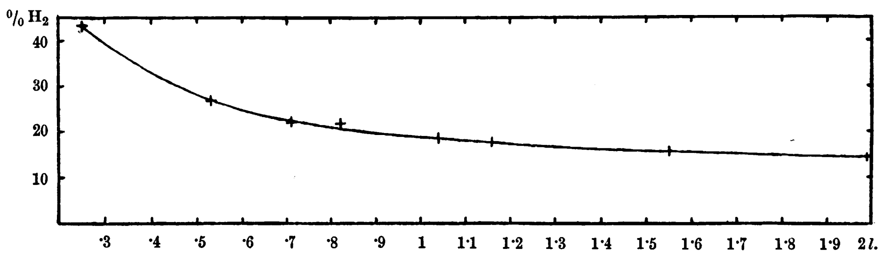

Fig. 3.

Expiration l.	Hydrogen %	Hydrogen c.c.	H_2 in alv. air c.c.	H_2 in alv. air %
0·3	39·5	118		
			22	11
0·5	28·0	140		
			18	9
0·7	22·5	158		
			31	10·3
1·0	18·9	189		
			27·5	9·2
1·3	16·65	216·5		
			33	11
1·6	15·6	249·5		
			25	8·3
1·9	14·5	274·5		
			Average (0·5 to 1·9 l.)	9·3

The observed variations in the composition of the different portions of alveolar air are within the limits of error and no definite tendency can be detected[1]. Variations of this order of magnitude cannot seriously affect the determinations of dead space. When we take the mean of the values below 0·5 l. (9·3 %) as the average alveolar H_2 percentage we can utilise the expirations of suitable size as above for determinations of

[1] The hydrogen percentages are distinctly lower than in the corresponding experiment during rest, owing partly to the rapid absorption of H_2 taking place during work but especially to a larger volume of air being present in the lungs at the end of expiration.

the effective dead space during work and compare them with direct determinations on I. L.[1]

Siebeck test series Work 500 kgm.		Single determinations Work 750 kgm. per min.		
Expiration l.	Dead space c.c.	Date	Expiration l.	Dead space c.c.
0·53	91	18/2	1·1	98
0·71	87	—	1·2	98
0·82	99	4/3	1·1	83
1·04	93			
1·16	95			
Mean ...	93		Mean ...	93
Found during rest	90		Found during rest	98

Determinations made on I. L. when the dead space was increased by a mask of 60 c.c. gave during rest 122, 142 and 159 c.c.—mean 141, and during work 135, 158—mean 146.

In experiments on H.P. and A.K. we experienced serious difficulties in determining the dead space during work, because these subjects were scarcely able to control their breathing with sufficient precision. As a rule, though not always, they inspired and expired more rapidly than during rest, which does not much matter, but usually they could not avoid making a very slight inspiration (50 c.c. or less) after being turned on for expiration into the spirometer. In order to be sure of detecting this inspiration, which will diminish the value found for the dead space by something like the volume inspired, we found it necessary to start with 100 to 200 c.c. air in the spirometer. Any inspiration, however small, then becomes visible on the graphic record.

We did not succeed at all in obtaining reliable figures for H. P. Two determinations gave:

Inspired l. H_2	Expired l.	Dead space c.c.	Inspired from spirometer, c.c.	Dead space corrected, c.c.
0·6	0·96	108	60	168
0·6	0·92	141	40	181
			Found during rest	162

but the quantitative value of the corrections is of course uncertain.

On A. K. we obtained two perfectly reliable determinations

Inspired l. H_2	Expired l.	Dead space c.c.
0·6	0·83	136
0·6	0·81	148
	Mean ...	142
	Found during rest	143

We feel justified in concluding that the effective dead space is not measurably altered during muscular work, and even if this conclusion could be doubted, on the grounds that some—absolutely unknown—

[1] In all the work experiments on I. L. the inspirations were 0·5 l. and the rate of inspiration and expiration was not on the whole greater than during rest.

source of systematic error might be present in the work experiments and absent in the rest experiments, it is evident at all events that the alterations which Haldane and Douglas deduce from their experiments cannot be real. With an increase of the dead space to 600 c.c. the hydrogen from an inspiration of 500 c.c. should not enter the alveoli at all, whereas we find between 300 and 400 c.c. H_2 in the alveolar air after such an inspiration.

Haldane and Douglas lay great stress upon the importance from a teleological point of view of the increase in the dead space. They contend that a dilatation of the small bronchi is necessary to adjust the resistance to the greatly increased ventilation during muscular work. It must be borne in mind, however, that the volume of the small bronchi can only be a fraction of the total dead space—probably between 20 and 40 c.c. and perhaps less, since the mouth, larynx, trachea and large bronchi, which do not dilate appreciably, will normally account for 100 c.c. or more. In the bronchioli of less than 0·2 mm. effective diameter the resistance to the passage of air is inversely proportional, not simply to the sectional area (d^2), but (roughly) to the square of it (d^4). A doubling of the volume, that is an increase in the total dead space probably between 20 and 40 c.c., would therefore reduce the resistance to $\frac{1}{4}$, or perhaps further if the bronchioli are at all shortened by the dilatation. A comparatively slight increase in volume would therefore in any case suffice to adjust the resistance to the increase in ventilation during severe work, and increases of 400 c.c. or more are from the teleological point of view improbable in the extreme, because they would diminish the resistance in the small bronchi out of all proportion to the needs and render the ventilation of the alveoli much less effective. If we take for instance a total ventilation of 40 l. per minute with a frequency of 20 (corresponding to work of about 650 kgm.) a dead space of 150 c.c. will give an alveolar ventilation of 37 l., but if the dead space is 500 c.c. the alveolar ventilation is reduced to 30 l.

Our subjective experience leads us to believe that the resistance of the air passages is not diminished at all during muscular work. We find that the exertion necessary to make a single voluntary forced breath does not differ perceptibly from that experienced when the breathing is violent just after a short term of severe muscular work—during the work it cannot be estimated. In the latter case the dilatation should be in force according to Haldane and Douglas, while in the former it cannot probably come into play. We find further that during prolonged forced breathing a decrease in resistance is not at all noticeable.

It is not proved and in our opinion not very likely that the bronchioli are the seat of the principal resistance against the ventilating currents of air. In many persons the nose is undoubtedly the narrowest portion of the air passages, where even a slight diminution of the sectional area produces a distinct increase in resistance even during rest. In not a few cases active dilatation of the nostrils is observed when the breathing is increased. That would not have any meaning if the principal resistance was met with in the bronchioli.

When the dead space is not materially increased during muscular work it must follow that in these circumstances the Haldane-Priestley samples of alveolar air give values for the average CO_2 tension which are much above the real, and it becomes doubtful whether the alveolar CO_2 tension is at all increased during work. This consequence of our results may seem startling. We hope shortly to publish experiments which will show, independently of any assumption regarding the dead space, that the increase in alveolar CO_2 tension during work—if any—is very slight only.

With regard to the Siebeck method employed by us we conclude from all the experiments and tests that the effective dead space can be fairly accurately determined by its means when all the precautions referred to above are observed. The mean error of a single determination is however rather large (about 10 $^0/_0$) and there may easily, in spite of the precautions, be some systematic error besides. The tests carried out, and especially the double determinations on the alveolar air, go to show however that such an error—if it exists—is not likely to exceed 20 c.c.

SUMMARY.

1. The distribution of a gas in the alveolar air after one inspiration of it is not uniform. The last portions of an expiration will contain less of the gas than the earlier.

2. When certain precautions are observed the Siebeck method of determining the effective dead space in breathing will give results which are sufficiently reliable for most purposes, although probably not quite free from systematic error.

3. The effective dead space in breathing is not appreciably altered during heavy muscular work.

4. The direct method of determining the composition of the alveolar air from samples taken at the end of inspiration and expiration becomes untrustworthy during muscular work.