A Clinical Review of the Single Breath Method of Measuring the Diffusing Capacity of the Lungs*

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Over the past ten years, tests of pulmonary diffusing capacity have become increasingly popular in the evaluation of lung disease. This era might be said to have begun with the work of Lilienthal, Riley, Proemmel and Franke1 in 1946. These investigators measured the diffusing capacity for oxygen by a method which required considerable time and skilled personnel, and for this reason the test, as a routine measure of lung function, was not widespread. The re-introduction of carbon monoxide (CO) into the field of pulmonary physiology resulted in the development of several different methods of measuring diffusing capacity for CO. Although Krogh and Krogh2 had used this gas to measure diffusion in man as early as 1910, it was not until 1954 that its value for measuring diffusing capacity was fully appreciated. In that year, Filley, McIntosh and Wright3 described a steady state method which required an arterial puncture and an accurate measure of the partial pressure of carbon dioxide in the arterial blood, in order to estimate the mean alveolar concentration of carbon monoxide. This procedure unfortunately limited the routine use of the test. Since then, three general methods of measuring diffusing capacity with CO have been developed. All of these avoid the necessity of an arterial puncture and blood analysis by replacing the indirect method of obtaining the alveolar concentration of CO (of Filley, et al.) by a direct sampling of alveolar gas. By doing so, certain inaccuracies were introduced and this has led to considerable discussion as to which of these is the best method. The simplification and standardization of the procedure has also led to the widespread use of the tests.

The three practical methods for measuring pulmonary diffusing capacity for CO are the steady state,4,5 the rebreathing6,7 and the single breath8 techniques. The rebreathing method has not been used widely, but both single breath and steady state methods are now used routinely in many laboratories. A considerable amount of literature has been devoted to a comparison of the three.8,9,10 The advantage of one over the others has not been completely settled, but generally it can be said that the rebreathing technique has not become as popular as the other two methods, there is a close correlation between the steady state and single breath methods in patients with uniform ventilation and blood flow, but no relation when there is inequality between ventilation and blood flow. Bates et al.11 believed the single breath is inferior to the steady state method, firstly since the former gives normal results in patients with emphysema who by any steady state technique would have a much reduced diffusing capacity, and secondly, since it is technically more difficult to perform.

The first of these criticisms cannot be answered at the present. It was thought, however, that since this laboratory has been performing the single breath method for the past eight years, it might be useful to review our results over a portion of this period in an attempt to answer the second criticism. It should be emphasized that the tests were performed routinely in a service laboratory and not under the careful control expected in a research laboratory.

It is the purpose of this paper, then, to review all cases on whom this test was routinely performed, in addition to other parameters, over the past two years, with emphasis on the theoretical and technical errors inherent upon the measurement of al-

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veolar volume, breath-holding time and adequate dead space washout, and the consequent effect on diffusing capacity.

Materials and Methods

The results of lung function tests on all patients studied routinely in this laboratory over the past two years were reviewed, the only selection being that vital capacity, residual volume, expiratory flow rate, alveolar gas uniformity and diffusing capacity had been performed on all.

Vital capacity was measured in a 10 L. Osborn-Blodgett spiromyograph, and residual volume by a modified closed circuit helium dilution method using a Cambridge catharometer. The expiratory flow rate was measured between 200 - 1,200 ml. on the Osborn-Blodgett spiromyograph at a speed of 2.67 cm./sec. by the method described by Cander and Comroe, and the alveolar gas uniformity test by the method of Comroe and Fowler.

The single breath diffusing capacity was that of Ogilvie, Forster, Blakemore and Morton, the volume tracing being recorded on the Osborn-Blodgett spirometer at a speed of 5.34 cm./min. CO was analyzed in a Liston-Becker Model 15A infra-red analyzer after the expired gas had been passed over a drying agent (calcium chloride). Helium was analyzed in a Cambridge catharometer after absorption of carbon dioxide. To correct for loss of volume caused by absorption of this carbon dioxide, expired gas was also analyzed for carbon dioxide, with a Liston-Becker Model 16 infra-red analyzer, and the appropriate correction made.

Since it was felt that the evenness of alveolar gas distribution would on theoretical grounds, significantly affect the single breath measurement of diffusing capacity, patients were divided into two groups: Group I was composed of 38 patients who had an alveolar gas uniformity test of 2.0 per cent or less; Group II was composed of 43 patients who had an alveolar gas uniformity test greater than 2.0 per cent. The mean vital capacities, residual volumes and expiratory flow rates for these two groups, together with their standard deviations, are shown in Table 1.

Results and Discussion

In calculating the diffusing capacity it is essential to know the total alveolar volume at full inspiration. This is composed of the inspired volume, recorded during the test, and the residual volume, measured separately, usually by the helium dilution or nitrogen washout methods. These volumes are shown graphically in Fig. 1, together with the breath holding time and dead space washout. Our results, means and standard deviations of which are shown in Table 2, will be discussed under these headings.

Alveolar Volume

There is some disagreement in regard to whether or not alveolar volume affects diffusing capacity. Krogh stated that as alveolar volume increased above mid-capacity, diffusing capacity increased proportionately. Ogilvie et al. measuring diffusing capacity on five subjects on whom alveolar volume was purposely kept low and again
when alveolar volume was high, found that when alveolar volume increased on the average by 56 per cent, diffusing capacity increased by only 9 per cent. Marshall, on the other hand, showed that when alveolar volume increased 56 per cent, diffusing capacity increased 24 per cent. This author also demonstrated that diffusing capacity, as measured by the single breath and steady state methods, was the same in normal subjects when allowance was made for the different lung volumes at which the measurements were made. Similar suggestions have been made by others.

There is a strong suggestion, then, that diffusing capacity is affected by alveolar volume. This volume, as previously stated, is composed of the inspired volume and the residual volume. These will be discussed separately in an attempt to show whether or not, in a routine lung function laboratory, the alveolar volume has been compromised in any way.

**The Lung Volume, Breath-Holding Time, and Dead Space Washout in the Single Breath Diffusing Capacity.**

**Inspired Volume**

This volume, measured from the recording obtained while performing the single breath test, might be considered to be an inspiratory vital capacity. It is usually greater than the standard expiratory vital capacity especially in subjects in whom there is bronchial obstruction. In spite of this, the average inspired volumes in both groups were found to be lower than the standard expiratory vital capacity. The 38 patients of Group I (those with an alveolar gas uniformity of 2.0 per cent or less) had a mean inspired volume which was 398 ml. less than the expiratory vital capacity. In the 43 patients of Group II (those with an alveolar gas uniformity of greater than 2.0 per cent) the mean inspired volume was 177 ml. less than the expiratory vital capacity. Although these are small reductions, they are more significant when one consid-

**FIGURE 1**

**FIGURE 2**
ers that the inspired volume was less than the exhalatory vital capacity even in Group II in which bronchial obstruction was generally present (Table 1). This can be considered a technical error; the patient was not instructed to expire and inspire fully.

The importance of this error may be estimated by comparing the alveolar volume calculated by assuming the patient was capable of inspiring a volume equal to the standard exhalatory vital capacity, with the alveolar volume calculated on a basis of inspired volume. In Group I the mean alveolar volume based on the exhalatory vital capacity was 5.6 per cent greater than that based on the inspired volume while in Group II the former was 2.7 per cent greater than the latter.

One might conclude then, that the importance of the alveolar volume is still debatable. If, however, we accept the statement of Marshall that when the alveolar volume is increased by 56 per cent, the diffusing capacity increases 24 per cent, or that of Cadigan et al. that when this volume is increased 92 per cent the diffusing capacity increases 47 to 60 per cent, it is unlikely that our small mean reduction in alveolar volume of 5.6 per cent and 2.7 per cent caused by failure to inspire and expire fully, will affect the diffusing capacity to any significant degree. Larger reductions, such as that found in one patient whose potential alveolar volume was reduced by 20 per cent might be more important.

**Residual Volume**

Perhaps one of the more attractive features of the single breath method is its brevity. Ogilvie et al. estimate a test in duplicate can be done in five to ten minutes, not including the time to perform the residual volume. The helium dilution method of measuring residual volume will at least triple this time and the nitrogen washout method will increase it even further. This measurement, then, detracts considerably from the single breath method as a brief test of measuring diffusing capacity in a lung function laboratory, unless this volume is also measured routinely. Ogilvie et al attempted to obviate this difficulty by calculating the residual volume from the inspired volume and the dilution of helium in the expired alveolar sample obtained while measuring the single breath diffusing capacity. They found the resulting volumes "to be useless in all but extreme circumstances," due to uneven distribution of inspired gases, the inference being that the residual volume so obtained, did not compare favorably with the helium dilution or nitrogen washout methods.

To investigate this matter further, residual volume was re-calculated on our 81 subjects using the inspired volume and the dilution of helium in the expired alveolar sample obtained while performing the single breath diffusing capacity. Since this is the volume believed to be effective in regard to diffusion, it will be termed effective.

<table>
<thead>
<tr>
<th>Table 2—Summary of Results on 81 Patients</th>
</tr>
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<tbody>
<tr>
<td>Group I</td>
</tr>
<tr>
<td>-------------------------------------------</td>
</tr>
<tr>
<td>Alveolar gas uniformity per cent</td>
</tr>
<tr>
<td>Number of patients</td>
</tr>
<tr>
<td>Difference between V.C. and I.V. ml.</td>
</tr>
<tr>
<td>Per cent difference of A.V. based on V.C.</td>
</tr>
<tr>
<td>from A.V. based on I.V. per cent</td>
</tr>
<tr>
<td>Difference between true R.V. and effective R.V. ml.</td>
</tr>
<tr>
<td>Per cent difference of D, (true R.V.) from D, (effective R.V.) per cent</td>
</tr>
<tr>
<td>Breath holding time sec.</td>
</tr>
<tr>
<td>Per cent error in D, assuming a 10 sec. breath holding period per cent</td>
</tr>
<tr>
<td>Dead space washout ml.</td>
</tr>
</tbody>
</table>

residual volume. This was compared with the residual volume obtained by the closed circuit helium dilution method. It will be termed true residual volume. In Group I, the mean effective residual volume was 154 ml. higher than the true residual volume while in Group II, the mean effective residual was 819 ml. less than the true residual volume. The reason for some effective residual volumes being higher than the true residual volumes is no doubt the fact that the patient did not expire fully during the single breath test, thus giving a falsely high effective residual volume.

Since the disparity between these two residual volumes is believed to be a function of the uneven distribution of inspired gas, the differences between the two were plotted against the alveolar gas uniformity test of Comroc and Fowler. This relationship is shown in Fig. 2. A low correlation exists (r=0.59). It should be pointed out, however, that in three patients of Group I and 19 patients of Group II, dead space was not washed out adequately while performing the single breath diffusing capacity. Inadequate dead space washout lowers effective residual volume. The difference between the two residual volumes is thus increased. The circled points on Fig. 2, representing those patients in whom there was inadequate dead space washout, are erroneously low. Adequate dead space washout would move these circled points upward and a better correlation would be expected.

From Fig. 2, however, it can be said that there is a tendency for the effective residual volume to become lower in respect to true residual volume, as the inspired gases become more unevenly distributed. This infers that effective residual volume represents the volume of areas relatively well ventilated while true residual volume represents areas relatively well and poorly ventilated.

It can be concluded then, that measuring residual volume by the dilution of a single breath of helium, is not a valid measure or even a fair approximation of that found with the closed circuit helium dilution technique. Indeed, it becomes more invalid as the alveolar gases become more unevenly distributed. Nevertheless, if one accepts the thesis that the dilution factor obtained in the single breath test for diffusing

<table>
<thead>
<tr>
<th>Subject</th>
<th>Test</th>
<th>Dead Space Washout</th>
<th>Final CO</th>
<th>Initial CO</th>
<th>Per cent Increase of III</th>
<th>Final CO</th>
<th>Per cent Increase of III</th>
<th>Diffusing Capacity ml CO/mm. mm Hg</th>
<th>Alveolar Gas Uniformity</th>
<th>Per cent</th>
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<tbody>
<tr>
<td>I</td>
<td></td>
<td></td>
<td>0.349</td>
<td>0.107</td>
<td>32</td>
<td>24.9</td>
<td>35.6</td>
<td>2.2</td>
<td>6.5</td>
<td>8.7</td>
</tr>
<tr>
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<td></td>
<td></td>
<td>0.352</td>
<td>0.155</td>
<td>24</td>
<td>24.9</td>
<td>30.5</td>
<td>1.7</td>
<td>0.9</td>
<td>2.6</td>
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<tr>
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<td></td>
<td>0.379</td>
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<td></td>
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<tr>
<td>I</td>
<td></td>
<td></td>
<td>0.267</td>
<td>0.135</td>
<td>21</td>
<td>34.3</td>
<td>32.6</td>
<td>1.4</td>
<td>6.1</td>
<td>7.5</td>
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<tr>
<td>II</td>
<td></td>
<td></td>
<td>0.261</td>
<td>0.139</td>
<td>17</td>
<td>34.0</td>
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<td>I</td>
<td></td>
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<td>0.257</td>
<td>0.115</td>
<td>43</td>
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<td>I</td>
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<td></td>
<td>0.256</td>
<td>0.103</td>
<td>20</td>
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<td>1.4</td>
<td>3.6</td>
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<tr>
<td>II</td>
<td></td>
<td></td>
<td>0.243</td>
<td>0.100</td>
<td>24</td>
<td>28.7</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>III</td>
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<td></td>
<td>0.276</td>
<td>0.124</td>
<td>26.5</td>
<td></td>
<td></td>
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</tbody>
</table>

Mean 7 27 1.6 5.5 6.0
capacity is not a measure of the true residual volume especially in those patients with uneven distribution of inspired gas, it is obvious that the true residual volume, as measured by the closed circuit helium dilution method (steady state) is not the volume to which CO is exposed while measuring the single breath diffusing capacity. The volume of lung to which the CO is exposed is represented by the volume measured by the single breath helium dilution factor i.e., the effective residual volume. It might be said that when calculating single breath diffusing capacity, one should use single breath residual volume.

For this reason, diffusing capacities were recalculated using effective residual volume rather than true residual volume to determine alveolar volume. In the 38 patients in Group I, the mean diffusing capacity was 4 per cent higher than that in which the true residual volume was used. In the 43 patients in Group II, the mean diffusing capacity using effective residual volume was 11 per cent less than that using true residual volume.

It seems reasonable to conclude that the effective residual volume should be used to calculate alveolar volume, since this is the volume to which CO is exposed in the single breath test. In patients with uneven alveolar gas distribution, this will usually lower diffusing capacity, though according to A thromp and Marshall, this does not correct for the low correlation between the steady state and single breath methods in such patients.

**Breath Holding Time**

A standardized breath holding time is essential to this test, since diffusing capacity becomes progressively lower as time increases. Ten seconds has been chosen as a suitable period for breath holding.

This is measured from the start of inspiration to the point at which the alveolar gas is sampled. A stop watch is used for this purpose. In practice the exact point at which inspiration begins can be observed accurately from the volume tracing. The end point cannot be so accurately observed, since the patient must be asked to expire at approximately nine seconds, he must respond quickly, dead space without washout must occur promptly and the gas sample should be accepted at ten seconds. A

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**TABLE 4—Effect of No Dead Space Washout on Five Patients with Uneven Distribution**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Test</th>
<th>Dead Space Washout</th>
<th>Final helium</th>
<th>Initial CO</th>
<th>Final CO</th>
<th>Diffusing Capacity ml CO/min./mm Hg</th>
<th>Alveolar Gas Uniformity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ml</td>
<td>Per cent</td>
<td>Per cent</td>
<td>Per cent</td>
<td>Per cent</td>
<td>Pred. Obs. I II I III III III Per cent</td>
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<tr>
<td>I</td>
<td>725</td>
<td>5.21</td>
<td>0.187</td>
<td>21</td>
<td>0.124</td>
<td>23 25.8 21.6 3.1 2.0 5.1 6.1</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>789</td>
<td>5.50</td>
<td>0.197</td>
<td>15</td>
<td>0.119</td>
<td>29 24.7</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>0</td>
<td>6.32</td>
<td>0.226</td>
<td>1.53</td>
<td>19.6</td>
<td></td>
<td></td>
</tr>
<tr>
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<td>786</td>
<td>4.16</td>
<td>0.149</td>
<td>29</td>
<td>0.103</td>
<td>44 26.2 19.8 0.5 5.4 4.9 4.8</td>
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</tr>
<tr>
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<td>867</td>
<td>4.68</td>
<td>0.168</td>
<td>14</td>
<td>0.117</td>
<td>26 19.3</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>0</td>
<td>5.86</td>
<td>0.182</td>
<td>1.148</td>
<td>14.4</td>
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</tr>
<tr>
<td>I</td>
<td>808</td>
<td>4.37</td>
<td>0.156</td>
<td>26</td>
<td>0.079</td>
<td>82 26.0 31.7 2.6 16.8 19.4 4.3</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>800</td>
<td>4.37</td>
<td>0.156</td>
<td>26</td>
<td>0.076</td>
<td>89 34.3</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>0</td>
<td>4.49</td>
<td>0.197</td>
<td>1.144</td>
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</tr>
<tr>
<td>I</td>
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<td>5.07</td>
<td>0.187</td>
<td>17</td>
<td>0.090</td>
<td>60 20.3 35.2 3.0 19.0 16.0 7.7</td>
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<td>89 32.2</td>
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<td>5.93</td>
<td>0.218</td>
<td>1.144</td>
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<td>35 22.6 13.1 0.2 3.1 3.3 6.3</td>
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</tr>
<tr>
<td>II</td>
<td>1107</td>
<td>4.86</td>
<td>0.179</td>
<td>21</td>
<td>0.136</td>
<td>29 13.3</td>
<td></td>
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<tr>
<td>III</td>
<td>0</td>
<td>5.86</td>
<td>0.216</td>
<td>0.176</td>
<td>10.0</td>
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</table>

Mean 22 51 1.9 9.3 9.7
certain degree of inaccuracy, then, is bound to occur.

In the 81 patients studied, diffusing capacity was calculated first on the assumption that breath holding time was ten seconds. The actual breath holding time was then measured from the volume tracing, as accurately as possible with a chart speed of 5.34 cm./min., and diffusing capacity was then recalculated using the correct timing.

In Group I, average breath holding time was 9.9 sec., an acceptable error of 1 per cent. These times, however, ranged from 8.8 sec. (12 per cent error) to 12.4 sec. (24 per cent error). The assumption that breath holding time was 10 sec. then, produced an error of 4 per cent in diffusing capacity, the range being from 19 per cent less to 14 per cent more than the correct 10 sec. value.

In Group II, average breath holding time was 10.0 sec. with a range of 8.1 sec. (19 per cent error) to 11.5 sec. (15 per cent error). This resulted in an average error in diffusing capacity of 6 per cent, the range being from 22 per cent less than the correct 10 sec. value to 23 per cent more.

It can be seen then, that though the mean error in timing was only 1 per cent in Group I and 0 per cent in Group II, and though the average error in diffusing capacity was low in both groups, individual errors, as indicated by the range, were quite marked. This is a difficult problem to overcome since it is caused by inability of the patient to expire promptly and rapidly and inability of the technician to judge how promptly and rapidly the patient will expire. The solution to the problem lies in preparing the patient with careful instructions, greater care in timing by the technician and finally a measurement of the breath holding time with the appropriate correction in the calculation of the diffusing capacity. As suggested previously, the time correction is not a completely accurate one since diffusing capacity drops as breath holding time increases. This reduction in diffusing capacity, however, is not a serious one. Ogilvie et al. showed that at nine seconds of breath holding, diffusing capacity was only 1.6 per cent more and at 11 seconds was only 1.6 per cent less than its interpolated value at the standard time of ten seconds.

**Dead Space Washout**

One of the major problems in both the steady state and single breath methods of measuring diffusing capacity is the matter of obtaining a suitable sample of alveolar gas. In the single breath method there are two problems involved. The first of these is that after the patient has held his breath for ten seconds, the technician must allow him to expire sufficient gas to wash out his dead space before accepting the sample. The second problem is that, after dead space washout is complete, the sample accepted must be large enough to allow for analysis of CO, helium and carbon dioxide.

The volume of gas required for dead space washout is 750 ml. This figure is obtained from the work of Fowler who showed that washout volume during maximal inspiration and expiration was 526 ml. (S. D. ± 118 ml.). The minimum volume of sampled alveolar gas sufficient for analysis was found by Ogilvie et al. to be 300 ml. According to these authors, then, a patient must be able to expire a minimum of 1,050 ml. after breath holding. In our experience, a satisfactory analysis for CO, helium and carbon dioxide could not be made on a sample of 300 ml.; a volume of 900 ml. was necessary, requiring the patient to expire approximately 1,700 ml. after breath holding period.

This presents a considerable problem in patients who have a vital capacity of approximately 2,000 ml. The technician must observe the volume tracing on the kymograph, and, as the patient expires, he must rapidly approximate 750 ml. on the tracing to allow for dead space washout. At this point, he must accept the sample, collecting, in our laboratory, 900 ml. for analysis. Acceptance of the sample, before washout of 750 ml. is complete will theoretically result in an error in diffusing capacity, while
acceptance of the sample after more than 750 ml. is discarded for washout, will leave an insufficient volume for analysis.

The dead space washout in Group I was 1157 ml. All but three of the 38 patients in this group had a dead space washout in excess of 750 ml. In these three, washouts were 521, 526, 560 ml., some 200 ml. less were required. Since the inspired volume in all was approximately 2,000 ml. the error is purely technical though a difficult one to overcome, since it was presumably obvious to the technician that little more than the minimum volume of 1,700 ml. was available for dead space washout and alveolar sample.

As will be shown later, lack of dead space washout lowers diffusing capacity. Of the three patients in Group I who had a low washout, two had diffusing capacities slightly in excess of the average predicted values, based on the regression equation of Ogilvie et al., suggesting dead space had actually been washed out. The third patient had a diffusing capacity of 5.1 ml. CO/min./mm.Hg less than the average predicted value, but within the normal range.

In Group II, the situation was quite different. The mean dead space washout was 775 ml., 19 of the 43 patients having a dead space washout of less than 750 ml. All these patients were able to inspire a volume of more than 1,000 ml.; five, however, inspired less than 1,700 ml. and the remainder were in general not in excess of this. Nine of the 19 patients had a diffusing capacity below the range of normal. Adequate washout may or may not have increased these to within the range of normal. Such an error must be considered to be a technical one, though it is quite possible that air trapping with the rapid forceful expiration necessary in the test might have reduced the expired volume to less than the inspired volume. The fact that lung function generally, in Group II was much more reduced in comparison with Group I, (Table 1) no doubt lead to this error.

It can be concluded, then, that dead space washout generally was adequate in Group I, but in almost half the patients of Group II, dead space washout was inadequate. The technical error in the latter group was no doubt the result of poorer function in those patients.

The effect of inadequate dead space washout may be estimated by examining the formula used for the calculation of diffusing capacity. This is as follows:

\[
\text{Diffusing capacity equals} \\
(\text{ml.CO/min./mm.Hg}) \\
\text{Alveolar volume times 60} \\
\text{Time in sec. times (B.P.-47)} \\
\text{Natural Log. Initial CO concentration in} \\
\text{expired alveolar gas} \\
\text{Final CO concentration in} \\
\text{expired alveolar gas.}
\]

Both the initial and the final CO concentrations are affected by dead space washout. Initial CO is determined by the dilution of helium. If the dead space is not washed out, the final concentration of helium in the expired sample will be abnormally high and this in turn will result in an abnormally high initial CO. The numerator of the above equation, then, will be increased and this will tend to increase the diffusing capacity. The final concentration of CO is determined by direct analysis of the expired sample. Again if the dead space washout is inadequate, this concentration will be abnormally high, the denominator of the above equation will be increased and this will tend to reduce the calculated diffusing capacity. The total effect on the diffusing capacity of the increases in both initial and final CO concentrations will depend on the degree of change of each factor. It might be surmised that, since the final concentration is always lower than the initial concentration, the per cent increase in the former will be greater than that of the latter when dead space washout is inadequate, and therefore, the total effect on diffusing capacity will be to lower it.

To illustrate this, five subjects with normal alveolar gas distribution and five patients with uneven alveolar gas distribution were examined. On each, diffusing capacity
was measured twice with adequate dead space washout and once with no dead space washout. The results are shown on Tables 3 and 4.

In the absence of dead space washout, helium concentration and both initial and final CO concentrations were always higher than the previous two tests with adequate washout. In those with even gas distribution, however, lack of washout resulted in a mean increase in initial CO concentration of 7 per cent but a mean increase of 27 per cent in final CO concentration. This caused a mean reduction in diffusing capacity of 5.5 and 6.0 ml. CO/min./mm.Hg when compared with the two diffusing capacities obtained when washout was adequate, both figures being in excess of the 1.6 ml. CO/min./mm.Hg check in the first two tests.

In the five patients with uneven alveolar gas distribution, the mean increase in initial and final concentrations of CO were greater, the former being 22 per cent and the latter 51 per cent. Again, although the first two diffusing capacities checked within 1.9 ml. CO/min./mm.Hg, lack of dead space washout caused a decrease in diffusing capacity of 9.3 and 9.7 ml. CO/min./mm.Hg.

It is obvious from Table 3 and 4 that in those with uneven alveolar gas distribution, both the initial and final concentrations of CO increased on the average more than in those subjects with even alveolar gas distribution, when dead space was not washed out. The reason for this no doubt lies in the volume of expired gas collected. The helium and CO lying in the dead space after inspiration will be diluted more if it is expired into, for example, a volume of 4,000 ml. than it would if expired into a volume of 2,000 ml. The inspired volumes in the five subjects with even gas distribution averaged 3,720 ml. while this volume in the five patients with uneven gas distribution averaged 2,520 ml. It can be assumed that there was a similar discrepancy in the expired volumes, thus resulting in less dilution of dead space helium and CO when no dead space was washed out in those with uneven distribution. The size of the expired sample was probably further reduced by air trapping, since all these patients had marked obstructive disease.

It should be emphasized that this is a situation in which expired volume is important rather than the evenness of alveolar gas distribution. A patient with restrictive disease, as is found in the various forms of "pulmonary fibrosis," will have a low inspired volume and probably even alveolar gas distribution. If this dead space is not adequately washed out, the helium and CO lying in that dead space will not be diluted as much as, for example, an emphysematous patient who has a normal inspired volume and uneven gas distribution, since presumably the volume of expired gas sampled will be less in the restrictive condition than in the obstructive one.

It can be concluded, then, that adequate dead space washout is an important item when performing the single breath diffusing capacity. In patients with a low inspired volume, and presumably a low expired volume it is of even greater importance, and it is in these patients that there is a greater tendency to compromise dead space washout in order to obtain a sufficient volume of gas for analysis.

**Summary and Conclusions**

1. A critical review of the single breath method of measuring diffusing capacity has been made on 81 patients studied routinely over a two year period.

2. Failure of the patient to inspire and expire fully while performing the test was not a serious source of error.

3. It is suggested that the residual volume calculated from the helium dilution obtained while performing the single breath diffusing capacity (effective residual volume), is the correct volume to use, rather than the residual volume calculated by the closed circuit helium dilution method (true residual volume), since this is the volume to which CO is exposed during the test.

4. Differences between effective and true residual volume correlate roughly with the
evenness of alveolar gas distribution.

5. Breath holding times on the average were measured with an acceptable error, though occasional unavoidable inaccuracies suggest that time corrections should be made.

6. Inadequate dead space washout was shown to be the most serious source of error in this series. This was especially so in those with reduced lung function since they had a smaller volume to expire after breath-holding, the alveolar sample was smaller, and any contaminating dead space gas in the sample was relatively undiluted, resulting in an erroneously low diffusing capacity.

7. There are several potential areas in which technical error may occur in the single breath diffusing capacity performed in a routine service laboratory. These can be overcome by proper patient instruction, care in timing, and correction in timing, with special attention being paid to the adequacy of dead space washout.

Résumé

1. L'auteur a fait une revue critique de la méthode de respiration simple pour mesurer la capacité de diffusion sur 81 malades étudiés en pratique courante pendant une période de deux ans.

2. Le fait que le malade n'inspirait et n'expirait pas complètement pendant la pratique du test ne fut pas une source grave d'erreur.

3. L'auteur suggère que le volume résiduel, calculé d'après la dilution d'hélium obtenue pendant que se pratiquait le test de respiration simple pour la mesure de la capacité de diffusion (volume résiduel effectif) est le volume correct à utiliser, plutôt que le volume résiduel calculé par la méthode de dilution de l'hélium en circuit fermé (forme résiduel vrai) puisque c'est le volume avec lequel l'oxyde de carbone est en rapport pendant le test.

4. Les différences entre volume résiduel effectif et vrai correspondent en gros à la régularité de la distribution du gaz alvéolaire.

5. Les températures inspiratoires en apnée furent mesurées en moyenne avec un pourcentage d'erreur acceptable, bien que d'éventuelles imprécisions inévitables amènent à penser que l'on devrait faire des corrections de temps.

6. Un "rinçage" insuffisant de l'espace mort se révéla être la source d'erreur la plus sérieuse dans ce groupe. Il en fut ainsi parfois chez ceux atteints de réduction de la fonction pulmonaire, puisqu'ils avaient un plus petit volume à expirer après prise de souffle, l'échantillon d'air alvéolaire était plus petit, et une certaine contamination du gaz de l'espace mort dans cet échantillon n'était relativement pas dilué, d'où il résulte une capacité de diffusion faussement basse.

7. Il existe plusieurs zones potentielles dans lesquelles une erreur technique peut survenir dans la méthode de respiration simple pour étudier la capacité de diffusion, pratiquée au laboratoire de façon courante. Elles peuvent être surmontées par l'instruction convenable du malade, par le soin apporté au chronométrage et sa correction, et par l'attention spéciale que l'on doit apporter à la juste valeur du "rinçage" de l'espace mort.

Zusammenfassung

1. Es wurde bei 81 routinemäßig über eine Zweijahresperiode beobachteten Patienten eine kritische Übersicht der Einzelatmenmethode vorgenommen für die Messung der Diffusionskapazität.

2. Ein Versagen der Patienten bei der vollen Einatmung und Ausatmung während der Vor- nahme des Testes war keine ernsthafte Fehlerquelle.

3. Es wird angenommen, daß das Residualvolumen, wie es aus der Heliumlösung kalkuliert ist, die man erzielt bei der Durchführung der Einzelatmen-Diffusionskapazität (effektives Residualvolumen), das korrekt zugrunde zu legende Volumen darstellt und zwar eher als dasjenige Residualvolumen, das man kalkuliert aus dem geschlossenen Kreislaufsystem, das der Heliumlösungs- methode zugrundelieg (echtes Residualvolumen), da dies das Volumen ist, dem CO während des Testes ausgesetzt ist.


5. Atemanhaltezeiten wurden durchschnittlich gemessen mit einem erträglichen Fehlerbereich, obgleich gelegentliche unvermeidbare Ungenaugkeiten es nahelegen, daß hier Zeitkorrekturen gemacht werden müssen.

6. Inadäquater Tetraustausch ließ sich als die erheblichste Fehlerquelle in dieser Reihe nachweisen. Dies war besonders dann der Fall, wenn die Lungenfunktion reduziert war, da dabei kleinere Volumen nach dem Atemstillstand auszuatmen waren, ferner die alveoläre sample klein war und jede vermengende Totaumgasmenge in der sample relativ ungelöst war, so daß irrtümlich ein niedriger Diffusionsvermögen resultierte.
7. Es bestehen mehrere potentielle Bereiche, bei denen technische Irrtümer bei der Einzel-tem-Diffusionskapazität vorkommen, wenn die Durchführung in einem Routine-Laboratoriums-dienst erfolgt. Dies läßt sich beheben durch entsprechenende Belehrung des Patienten, sorgfältige Zeitbestimmung und Korrektur dieser Zeitbe-stimmung, wobei besonders der Adäquatheit des To-trau sem washout geeignet werden müßt.

References

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PRIMARY MYOCARDIAL DISEASE

Fifty cases of heart failure not attributable to the common etiologic factors are described under the name, "Primary myocardial disease." Attention has been called to the predominance of alcoholism and malnutrition as possible agents. Extensive graphic and hemodynamic studies have been employed to understand the genesis of the physical findings better and to characterize the typical right-sided events that occur early and prominently in this disease.

It is suggested that diagnosis of primary myocardial disease be based on positive evidence rather than a mere exclusion of all known causes. In this respect, history of excessive alcoholic intake and poor nutrition, and physical findings indicative of early right heart involvement have been of the greatest value. Biopsy and postmortem examinations of the myocardium have revealed nonspecific features of muscle fiber hypertrophy and fibrosis.