II. THE CARBON DIOXIDE ABSORPTION CURVE AND CARBON DIOXIDE TENSION OF THE BLOOD IN CARDIAC DYSPNEA.

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INTRODUCTION.

In cardiac dyspnea the carbon dioxide tension of the alveolar air as determined by the Haldane method is lower than normal in comparison with the plasma bicarbonate as measured by means of the Van Slyke pipette (1, 2). The ratio between these two in health and in most pathological conditions has been shown by Van Slyke, Stillman, and Cullen (3), Walker and Frothingham (4), and Peters (1, 5) to be very close, varying from the mean by only 10 per cent. The existence of such a close relation might well be expected in the light of current theories with regard to the physicochemical control of the respiratory mechanism. That this relation should be disturbed in cardiac dyspnea is hardly extraordinary.

In the average normal person at rest carbon dioxide content, carbon dioxide tension, and hydrogen ion concentration of arterial and of venous blood all vary within comparatively narrow limits both individually and in relation to one another. Furthermore, the physicochemical regulatory mechanism is so delicately adjusted that changes in any of these factors are reflected in an immediate response on the part of the respiratory mechanism, which produces a compensatory alteration of the alveolar CO₂. As long as the sensibility of the respiratory center and the mechanical facilities for the exchange of gases between the blood and the air in the lungs remain unaffected, changes in any of these factors are instantly compensated by changes in one or all of the others. If either the
sensibility of the respiratory center or the mechanical facilities for the elimination of CO₂ in the lungs are impaired, one or all of the normal interrelations must be disturbed.

In cardiac decompensation, with dyspnea, there is evidence that the efficiency of the lungs as a means for the oxygenation of the blood and the elimination of CO₂ is greatly reduced (2, 6). There is also a possibility that the circulation is retarded.

In an attempt to throw some light on the exact cause of the discrepancy between alveolar and plasma values we first devoted our attention to a study of those factors of the respiratory system that may be termed mechanical: the function of the lungs and the upper respiratory tract. The results of this study have been published. It was found that air obtained by the Haldane method from patients with cardiac dyspnea was comparable in a functional sense to that obtained from trained normal subjects (2). That is, the air so obtained was the air employed for the exchange of gases between the blood and the outside air and was the only air available for this purpose. Realizing the objections that might be raised to the use of the term "alveolar" air in this sense, we suggested the terms "effective" or "exchange" air. By this means we evaded the criticisms which had been advanced by Siebeck (6). The latter, in the course of some studies of the lung volume in cardiac decompensation, came to the conclusion that the lungs in this condition failed to function efficiently as a tonometer. He decided that the mixing of gases in the lungs was imperfect and that methods for obtaining alveolar air were inapplicable. However, he considered the alveolar air only as a means of ascertaining the carbon dioxide tension of the arterial blood. Although our findings were not entirely in accord with Siebeck's, no attempt to controvert his statement was made. The question of the relation of alveolar CO₂ to arterial tension was entirely ignored, although its importance was fully recognized. Further studies convinced us that the effective lung volume was diminished (7) and the effective ventilation increased (8) in cardiac decompensation. Pearce (9) had proposed as an explanation of the disturbance of the alveolar: plasma ratio a retarded circulation. In view of the changes in the lung volume and the findings of Siebeck, however, this could not be definitely proved by the ordinary respiratory methods. Pearce assumed what Siebeck denied,
the applicability of alveolar methods as a means of determining arterial CO₂ tension. Even in normal subjects such an assumption seemed to be open to some criticism. The only direct evidence of a definite relation between alveolar and arterial CO₂ tension was given by Krogh and Krogh (10) in some tonometric experiments on animals. There was no evidence of any kind that a similar relation existed in diseases involving disturbances of the respiratory mechanism. Obviously it was necessary to find a means to measure the arterial CO₂ tension and to compare this with the alveolar CO₂ tension. For this reason the method described in the first paper was employed in the study of patients with cardiac decompensation. The CO₂ absorption curves of seven patients were obtained one or more times. Complete experiments were made on four cases out of seven. The results of these experiments are collected in Table III, arranged as were those of the normal subjects in Table VI of Paper I. Detailed protocols of all seven cases are presented at the end of this paper.

**Level of the Absorption Curve in Cardiac Dyspnea.**

The absorption curves of normal individuals fall within certain definite limits and are constant and characteristic for any given individual. This is far from the case in pathological subjects. The variations in both group and individual are considerable. The limits of normal variations in height are about 43 to 56 volumes per cent. The limits of variation of twenty-two patients with various pathological conditions were 32.4 to 70.2 volumes per cent, about three times as great. It is probable that a study of more patients with a greater variety of pathological conditions would show a still greater range of variation. In relatively few cases has more than one observation been made; but in these few the changes in height at different times are also quite striking. The maximum change observed was in Case 11, whose curve rose from 36.2 to 51.1 in the course of 4 days. Such fluctuations are not restricted to conditions of recognized acidosis, such as is found in diabetes mellitus or in nephritis. They occur also in cardiac valvular disease and in severe anemia.

The height of the absorption curves of seven decompensated cardiac patients, on whom eleven observations were made, varied from 32.4 to 52.0 volumes per cent, with an average value of 44.7
### TABLE I.

**Absorption Curve at 40 Mm. CO₂ Tension in Seven Patients with Cardiac Decompensation and Dyspnea.**

<table>
<thead>
<tr>
<th>Case.</th>
<th>Diagnosis.</th>
<th>CO₂ content. vol. per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. G. B.</td>
<td>Paroxysmal tachycardia. Some dyspnea; considerable cyanosis; fluid in right pleural cavity and in abdomen; edema of both ankles; temperature 103°.</td>
<td>45.4</td>
</tr>
<tr>
<td>7. J. D. B.</td>
<td>Aortic regurgitation. Mar. 19. Able to be up and about ward, but showed moderate dyspnea and orthopnea, with faint cyanosis of lips and finger-tips even while at rest. Apr. 30. Condition practically unchanged.</td>
<td>45.0 47.5</td>
</tr>
<tr>
<td>8. F. H.</td>
<td>Mitral stenosis; auricular fibrillation. Marked dyspnea and orthopnea; considerable cyanosis; general edema; hydrothorax and ascites.</td>
<td>47.5</td>
</tr>
<tr>
<td>11. J. K.</td>
<td>Mitral stenosis; auricular fibrillation. Apr. 16. Extreme cyanosis; moderate hyperpnea and edema. Apr. 20. Cyanosis and hyperpnea improved.</td>
<td>36.2 51.1</td>
</tr>
<tr>
<td>10. J. M.</td>
<td>Mitral stenosis; auricular fibrillation. Apr. 9. Extreme cyanosis; moderate dyspnea and edema. Apr. 23. Cyanosis continues; dyspnea and edema gone; still some hyperpnea.</td>
<td>38.7 48.1</td>
</tr>
<tr>
<td>12. C. C.</td>
<td>Mitral stenosis. Marked cyanosis; moderate hyperpnea.</td>
<td>32.4</td>
</tr>
</tbody>
</table>

Maximum. ................................................... 52.0
Minimum. ................................................... 32.4
Average. ................................................... 44.7
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volumes per cent (see Table I and Fig. A). Of the seven patients three showed a definite reduction of the alkali reserve of the blood during the stage of most severe decompensation. Later observations on two of these, at the time when compensation was becoming reestablished, gave normal values. The other four cases showed no departure from the normal as regards the height of their curves.

![Graph](http://www.jbc.org/)

**Fig. A.** A comparison of limits of absorption curves of normal and cardiac subjects.

- Limits of cardiac curves.
- Limits of normal curves.

A low absorption curve is not a characteristic of the condition of cardiac decompensation. What factors determine the presence of such a curve in certain cases is not clear. As we shall show later, there is a relative retention of carbon dioxide in the arterial and venous blood of the cases with acidosis. This, in itself, should tend to produce an increase rather than a reduction of the alkali reserve, according to Henderson and Haggard (11).
It has been demonstrated by several observers, using various methods, that reduction of the partial pressure of oxygen in the blood produces a reduction of carbon dioxide tension and carbon dioxide content of the blood (12-15). However, in these studies the reduction of oxygen tension was produced in such a way that CO₂ was not allowed to accumulate in the blood. Whether a similar reduction in the level of the absorption curve will be produced by low oxygen in the presence of CO₂ accumulation has not been determined. That there is a certain amount of oxygen unsaturation in the arterial blood and a very marked degree of oxygen unsaturation in the venous blood of some patients with cardiac decompensation has been shown by Harrop (16). As the most notable feature of the three patients with low absorption curves was a degree of cyanosis out of all proportion to the degree of dyspnea and hyperpnea, it seemed possible that the height of the absorption curve might bear some relation to the degree of oxygen unsaturation of the arterial and the venous blood.

That no such relation can be clearly established in our cases is evident from Table II, in which are shown the height of the carbon

<table>
<thead>
<tr>
<th>Subject and diagnosis</th>
<th>Date</th>
<th>CO₂ capacity of blood</th>
<th>Oxygen capacity of blood</th>
<th>Oxygen content</th>
<th>Oxygen saturation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>vol. per cent</td>
<td>vol. per cent</td>
<td>vol. per cent</td>
<td>vol. per cent</td>
</tr>
<tr>
<td>1. J. P. Normal</td>
<td>Mar. 12</td>
<td>55.9</td>
<td>22.5</td>
<td>19.8</td>
<td>88.0</td>
</tr>
<tr>
<td>2. D. P. B. &quot;</td>
<td>May 14</td>
<td>43.6</td>
<td>21.4</td>
<td>19.3</td>
<td>6.9</td>
</tr>
<tr>
<td>3. W. S. M. &quot;</td>
<td></td>
<td>48.2</td>
<td>24.9</td>
<td>21.9</td>
<td>5.8</td>
</tr>
<tr>
<td>4. M. C. Asthma and emphysema &quot;</td>
<td></td>
<td>12 49.0</td>
<td>21.3</td>
<td>17.2</td>
<td>11.0</td>
</tr>
<tr>
<td>5. H. R. Polycythemia</td>
<td>Apr. 28</td>
<td>47.9</td>
<td>23.9</td>
<td>22.6</td>
<td>9.0</td>
</tr>
<tr>
<td>6. J. K. Cardiac</td>
<td>&quot;</td>
<td>51.1</td>
<td>26.5</td>
<td>25.0</td>
<td>22.5</td>
</tr>
<tr>
<td>7. J. M. &quot;</td>
<td>&quot;</td>
<td>48.1</td>
<td>20.8</td>
<td>22.0</td>
<td>11.0</td>
</tr>
<tr>
<td>8. J. D. B. &quot;</td>
<td>&quot;</td>
<td>47.5</td>
<td>13.9</td>
<td>14.3</td>
<td>3.7</td>
</tr>
<tr>
<td>9. G. B. &quot;</td>
<td>Mar. 24</td>
<td>45.4</td>
<td>21.7</td>
<td>5.0</td>
<td></td>
</tr>
<tr>
<td>10. J. M. &quot;</td>
<td>Apr. 9</td>
<td>38.7</td>
<td>20.2</td>
<td>16.7</td>
<td>8.5</td>
</tr>
<tr>
<td>11. J. K. &quot;</td>
<td>Mar. 16</td>
<td>36.2</td>
<td>26.5</td>
<td>24.2</td>
<td>9.9</td>
</tr>
<tr>
<td>12. C. C. &quot;</td>
<td>Apr. 9</td>
<td>32.4</td>
<td>18.3</td>
<td>18.0</td>
<td>8.2</td>
</tr>
</tbody>
</table>
dioxide absorption curve, and the oxygen content and saturation of both arterial and venous blood. At least, if the low curve is due to oxygen unsaturation, this is not the only active factor.

Although the restoration of compensation was associated with a return of the absorption curve to its normal level in Cases 10 and 11, the height of the absorption curve is no indication of the severity of the cardiac decompensation. The three cases with low curves were discharged from the hospital improved, while Cases 6, 8, and 9 with normal curves, failed to improve and died shortly after the observations reported.

There was nothing in the clinical picture to suggest a nephritic acidosis in any of these cases as the cause of the low absorption curves. Rather complete renal functional studies were made in Case 10. His blood non-protein nitrogen was only 43 mg. per 100 cc. and his phenolsulfonephthalein excretion 60 per cent in 2 hours.

We are then left to the conclusion that cardiac decompensation is sometimes associated with a real reduction of the alkali reserve of the blood, which disappears when compensation is reestablished. Why this should occur in some instances and not in others is not explained.

Arterial and Venous Carbon Dioxide Tension and Hydrogen Ion Concentration and Alveolar Carbon Dioxide Tension in Cardiac Dyspnea.

Complete experiments were made on four out of the seven cases with cardiac decompensation. The results of these experiments appear in Table III (arranged as were those of the normal subjects in Table VI, Paper I), and in Charts 7, 10, 11, and 12 inclusive. If the general averages in Table III are compared with those in Table VI, Paper I, the following points of distinction appear:

1. Although there is little difference in the range of variation of arterial CO$_2$ tension in the two tables, the CO$_2$ tension during cardiac dyspnea is high in relation to the level of the absorption curve because the absorption curves are low in three of the four subjects.

2. The consequence is that the arterial pH values in cardiac dyspnea are on the average lower than normal, indicating a carbon dioxide retention in the arterial blood.
### Table III

**Results of the Study of Seven Cardiac Patients with Dyspnea.**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Date</th>
<th>Alveolar CO$_2$ tension</th>
<th>Arterial CO$_2$ tension</th>
<th>Arterial CO$_2$ reaction</th>
<th>Venous CO$_2$ tension</th>
<th>Venous CO$_2$ reaction</th>
<th>Difference between arterial and venous CO$_2$ tension</th>
<th>Difference between alveolar and arterial CO$_2$ tension</th>
<th>Difference between venous and arterial CO$_2$ tension</th>
<th>Difference between venous and arterial CO$_2$ reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. G.B.</td>
<td>Mar. 24</td>
<td>25.2</td>
<td>7.42</td>
<td>49.1</td>
<td>42.5</td>
<td>7.30</td>
<td>7.25</td>
<td>54.8</td>
<td>61.0</td>
<td>47.2</td>
</tr>
<tr>
<td>7. J.D.B.</td>
<td>Apr. 30</td>
<td>27.6</td>
<td>7.42</td>
<td>52.2</td>
<td>52.2</td>
<td>7.26</td>
<td>7.26</td>
<td>63.4</td>
<td>75.0</td>
<td>55.2</td>
</tr>
<tr>
<td>8. E.H.</td>
<td>Mar. 10</td>
<td>26.0</td>
<td>7.34</td>
<td>53.9</td>
<td>39.6</td>
<td>7.20</td>
<td>7.20</td>
<td>48.8</td>
<td>50.5</td>
<td>42.5</td>
</tr>
<tr>
<td>9. P.O.S.</td>
<td>Apr. 20</td>
<td>22.0</td>
<td>7.32</td>
<td>52.4</td>
<td>39.7</td>
<td>7.13</td>
<td>7.13</td>
<td>47.1</td>
<td>50.0</td>
<td>42.9</td>
</tr>
<tr>
<td>10. J.M.</td>
<td>Ap. 9</td>
<td>26.0</td>
<td>7.34</td>
<td>53.9</td>
<td>39.6</td>
<td>7.20</td>
<td>7.20</td>
<td>48.8</td>
<td>50.5</td>
<td>42.5</td>
</tr>
<tr>
<td>11. J.K.</td>
<td>Apr. 20</td>
<td>22.0</td>
<td>7.32</td>
<td>54.2</td>
<td>42.5</td>
<td>7.13</td>
<td>7.13</td>
<td>47.1</td>
<td>50.0</td>
<td>42.9</td>
</tr>
<tr>
<td>12. C.C.</td>
<td></td>
<td>27.4</td>
<td>7.22</td>
<td>53.5</td>
<td>42.5</td>
<td>7.13</td>
<td>7.13</td>
<td>47.1</td>
<td>50.0</td>
<td>42.9</td>
</tr>
<tr>
<td>Maximum</td>
<td></td>
<td>33.0</td>
<td>7.42</td>
<td>54.2</td>
<td>42.5</td>
<td>7.30</td>
<td>7.30</td>
<td>48.8</td>
<td>50.5</td>
<td>42.5</td>
</tr>
<tr>
<td>Minimum</td>
<td></td>
<td>22.0</td>
<td>7.22</td>
<td>39.7</td>
<td>39.7</td>
<td>7.13</td>
<td>7.13</td>
<td>42.9</td>
<td>46.5</td>
<td>46.5</td>
</tr>
</tbody>
</table>

*Note: The values for Apr. 20 on J.K. have been omitted. The sum of the maximum and minimum values has been computed.*
3. The alveolar CO₂ tension is, as has been previously pointed out, lower than normal. It is variable in relation to the absorption curve and may be, as in Case 12 (Chart 12), comparatively high, giving an alveolar pH far below the normal limits.

4. The difference between alveolar and arterial CO₂ tension is consistently increased. In five experiments on dyspneic cardiac patients this difference never fell below 13 mm. and in one case it reached the astonishing figure of 19 mm.

5. The venous CO₂ tension falls within normal limits, but, like the arterial, is high in relation to the level of the absorption curve.

6. There is no consistent increase in the difference between arterial and venous CO₂ content or tension, although in one or two instances both were slightly above the normal limits.

When each of these factors is studied in relation to the individual subjects of these experiments, it is apparent that only one is definitely and consistently present in every instance of cardiac dyspnea: this is the increase in the difference between alveolar and arterial CO₂ tension.

Although the average arterial CO₂ tension is relatively high and the arterial pH, in consequence, lower than normal, in Cases 7 (Chart 7) and 10 (Chart 10) the pH of the arterial blood is quite within normal limits. Can one say, then, that a carbon dioxide retention is characteristic of cardiac dyspnea, or does it occur only in certain cases, possibly those who show a considerable reduction in the height of the absorption curve, as do Cases 11 and 12? Unfortunately the range of variation in the normal arterial pH makes this question hard to answer. Absolute values are of little assistance in judging relative factors. Our results suggest that different normal subjects maintain the pH of their arterial blood at different levels. Furthermore the resting arterial pH level seems to be characteristic and constant for a given individual, as is the level of the absorption curve itself. In this case an arterial pH which is normal for one individual might mean a considerable retention of carbon dioxide in the case of another.

The statement was made above that there was nothing characteristic about the height of the absorption curve of the blood of patients with cardiac dyspnea, but that in certain cases low curves were found, indicating a diminution of the available alkali of the blood. We were then considering the absolute level of the
absorption curve. Again attention must be called to the fact that we are dealing in relative values only and that absolute levels, although satisfactory for purposes of clinical study, give little information with regard to functional changes in physiology or pathology. In order to ascertain whether a given pathological condition has changed the level of either the absorption curve or the arterial pH of an individual, it is not enough to know the limits of variation of normal individuals as a group. It is necessary to know the normal resting absorption curve and arterial pH of the given subject under investigation. In clinical investigations this is not always possible. Patients with severe cardiac dyspnea do not invariably recover. Of our seven cases three died without any intervals of improvement (Cases 6, 8, and 9); one (Case 7) had a chronic cardiac decompensation which resisted treatment, increasing gradually but steadily. Cases 10 and 11 improved. The former never completely recovered compensation; the latter made a very rapid recovery and was discharged without dyspnea or hyperpnea. Two determinations of the absorption curve were made on the blood of four of the seven patients: Cases 7, 9, 10, and 11.

In Case 9 the second observation, made 2 weeks after the first, revealed a drop of 4 volumes per cent in the height of the absorption curve. During this time the condition of the patient had continuously grown worse. The two observations on Case 7, at an interval of almost 6 weeks, were only about 2 volumes per cent apart. The second was the higher. There was little change in Case 7's condition on these two occasions. Possibly his dyspnea was a little more severe in the earlier experiment; his general condition seemed a trifle less favorable at the time of the second observation. The changes in absorption curve and in condition are, in any event, of no significance.

The rise in level of the absorption curves that occurred during the clinical improvement of Cases 10 and 11 is very striking. Although it is impossible, then, to say that cardiac dyspnea is always attended by a lowering of the absorption curve, there is a suggestion that such an association is not uncommon.

For the arterial pH our data are much more meager. This was determined in only four cases and in only two of these were two determinations obtained. In one of these, Case 10, the pH
remained unchanged in spite of a rise in the level of the absorption curve; in the other, Case 11, both pH and absorption curve rose. The latter regained compensation more completely than did the former in the interval between observations. The second experiment on Case 11 gives normal results in all essentials. Even the difference between alveolar and arterial CO₂ tension has returned to normal limits. It is quite conceivable that the picture presented by Case 10 on April 23 represents a preliminary step on the way to compensation and that, with complete recovery, which never occurred, the arterial pH would also have risen. There is no doubt that Case 12 had an uncompensated acidosis because his arterial pH lay below the normal limits. A definite carbon dioxide retention or uncompensated acidosis occurred in two subjects, then. In the others a similar condition cannot be excluded as the result of our experiments although the arterial pH lay within normal limits.

There is nothing questionable about the increased difference between arterial and alveolar CO₂ tension. It occurred consistently in the presence of dyspnea and returned to normal in the one instance in which compensation was definitely reestablished. It is inconceivable that such a difference is due merely to errors in analytical methods or in calculation. It has been shown that the assumption that the alveolar air is in carbon dioxide equilibrium with the arterial blood is not always in keeping with the facts. That such differences as occurred in normal resting subjects might be only temporary was pointed out. But in cardiac dyspnea the differences are far greater and are invariably present.

Such a difference in itself might be produced by a diminution of the rate of the circulation. The venous blood might return to the lungs with an accumulation of carbon dioxide too great to permit complete removal in the lungs. The CO₂ remaining would pass on into the arteries and produce an increase in ventilation by its action on the respiratory center. In this case the difference between arterial and venous CO₂ tension and arterial and venous CO₂ content should be increased. Such an increase

1 By a carbon dioxide retention or uncompensated acidosis we mean an accumulation of carbon dioxide sufficient to produce a real change in the pH of the blood.
is sometimes found, but it is not consistent and bears no relation
to the arterial-alveolar discrepancy. The differences between
arterial and venous CO\textsubscript{2} tension and arterial and venous CO\textsubscript{2}
content in Case 7, for instance, are only 4.0 mm. and 3.6 volumes
per cent respectively, while the arterial-alveolar difference is
14.9 mm. In addition to our own experiments we have calcu-
lated the differences between arterial and venous CO\textsubscript{2} content
and CO\textsubscript{2} tension in ten of Harrop's (16) cardiac cases who showed
definite evidences of decompensation. The calculations were
made by the same formula employed in the normal cases (see
Paper I). The results appear in Table IV and can be compared
with Harrop's normal cases in Table VIII, Paper I. In his cases,
as in ours, there is little evidence of a diminished circulation rate.
A retarded circulation would seem to be, therefore, at the most
only an occasional minor cause of the difference between arterial
and alveolar CO\textsubscript{2} tension.

The predominant cause must lie in the lungs themselves.
There must be an interference with the escape of CO\textsubscript{2} from the
blood in the pulmonary circulation. This seems the more prob-
able because of the known changes in the effective lung volume
(7, 17). There may be portions of the lungs in which the circu-
lation is more or less intact, but which contain no air. Or there
may be portions of the lungs which are air-containing, but immo-
bile and not adequately ventilated by the respirations. The
latter is the view of Siebeck (6). Present methods of measuring
lung volume have failed to settle the question because they are
capable of measuring only the portions of the lungs that contain
air available for respiratory purposes. Whether or not there is
a true carbon dioxide retention in all cases of cardiac dyspnea,
there is always an interference with the elimination of CO\textsubscript{2} from
the blood and, therefore, a compensated or potential acidosis.

If the alveolar air is considered from the standpoint of respira-
tory mechanics, as a measure of the effective ventilation, a greater
effective ventilation is necessary in order to maintain a given
arterial carbon dioxide tension in the case of the patient with
cardiac dyspnea than is necessary in the case of the normal
person. To what extent does this account for the increase in
the hydrogen ion concentration of the arterial blood? Docs the
alveolar carbon dioxide tension always indicate a ventilation in
excess of the normal in relation to the height of the absorption curve? If this were true the alveolar pH should always be considerably above 7.30. This is not true in Case 10, April 9, Case 11, April 16, and Case 12. In these instances the alveolar carbon dioxide is at or below the normal limit in relation to the height of

TABLE IV.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Arterial CO₂ content</th>
<th>Arterial oxygen content</th>
<th>Venous CO₂ content</th>
<th>Venous oxygen content</th>
<th>Difference between arterial and venous CO₂ content</th>
<th>Difference between arterial and venous CO₂ tension</th>
<th>Oxygen capacity</th>
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<tr>
<td></td>
<td>vol. per cent</td>
<td>vol. per cent</td>
<td>vol. per cent</td>
<td>vol. per cent</td>
<td>mm. Hg</td>
<td>vol. per cent</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>46.4</td>
<td>17.2</td>
<td>54.0</td>
<td>6.9</td>
<td>7.6</td>
<td>15.4</td>
<td>20.3</td>
</tr>
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<td></td>
<td>46.3</td>
<td>19.6</td>
<td>48.7</td>
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<td>2.4</td>
<td>4.9</td>
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<td></td>
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<td>15.5</td>
<td>11.8</td>
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</tr>
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</table>

the corresponding absorption curves. Although these three patients showed some dyspnea the ventilation was insufficient to compensate for the low absorption curves they presented. Nor was this due to the fact that they had passed the limits of compensation and were unable to increase their ventilation.
further. In none of these cases was dyspnea a prominent feature. The actual minute volume of respiration of Case 10 was only 8,650 cc. with a respiratory rate of 18 per minute. This suggests that the uncompensated acidosis found in these cases was not due entirely to an inability of the injured respiratory mechanism to effect the proper carbon dioxide elimination, but to the fact that the respiratory center was not so sensitive as normal to its natural stimulus, the hydrogen ion concentration of the blood. As the comparative lack of dyspnea shown by these patients is not at all typical of cardiac decompensation, this insensibility of the respiratory center to the natural acid stimulus is not necessarily a characteristic of cardiac dyspnea per se.

In the normal subjects the pH of the arterial and venous blood was found to be almost identical in spite of a considerable difference in CO₂ content. This was possible because of the effect of oxygen on the absorption curve. The same holds true of the cardiac cases, in some of whom even larger differences of CO₂ content occur. The difference in pH of arterial and venous blood never exceeds 0.04 and is, therefore, within the limits of error of the method.

One may pause for a moment to consider what bearing the presence of a carbon dioxide retention in association with a low absorption curve may have on the work of Henderson and Haggard (11). They claim that any damming back of carbon dioxide causes the blood to abstract alkali from the tissues and produces a rise in the level of the absorption curve. The facts here established for cardiac dyspnea are quite at variance with such a theory unless one argue from a teleological standpoint that the damming back of carbon dioxide is produced in an attempt to withdraw alkali from the tissues and thus restore the alkali of the blood to its normal level. Aside from the fact that this ascribes to the blood a purposeful effort at compensation, this is not the usual reaction to a reduction in the level of the absorption curve as is evidenced by the curves of nephritis patients (see Case 5, Paper I, and Case 16, Paper III).

It is interesting to compare the relations that obtain in cardiaics with those found by Means, Bock, and Woodwell (18) in pneumonia and with those found by us in one case of severe asthma and emphysema with extreme cyanosis (Case 13, Chart 13).
These investigators found a carbon dioxide acidosis in three pneumonia patients, without any reduction in the level of the absorption curve. They, however, accept Henderson's view that oxygen does not affect the absorption curve of blood. Fortunately they have published figures which allow us to make corrections by our formula. As we have calculated their results the arterial pH values in their three cases are: for E. D., 7.23 uncorrected, 7.28 corrected; for G. A., 7.30 uncorrected, 7.35 corrected; for N. D., 7.27 uncorrected, 7.30 corrected. Because of the degree of oxygen unsaturation in the arterial blood of pneumonia patients these corrections are much larger than the corresponding corrections in cardiac dyspnea, where the oxygen unsaturation of the arterial blood is usually comparatively slight.

If oxygen does affect the CO₂-combining capacity of blood there is little evidence of a carbon dioxide acidosis in these figures alone.

Case 13 had an asthmatic condition of long standing with an extreme emphysema and the most extraordinary cyanosis. His face and extremities were at all times a deep purple and during his acute attacks were almost black. The experiment was performed during one of these attacks. His absorption curve lies at a normal level. His arterial tension is quite high in proportion and about 18 mm. higher than the alveolar tension, which lies at a pH of 7.33. The corrected arterial pH is 7.22. The most striking thing about his chart is the enormous venous carbon dioxide tension. Although the difference between the arterial and venous carbon dioxide content is only 5.7 volumes per cent, the portion of the absorption curve on which the arterial and venous points lie is so flat that this represents a change of CO₂ tension of about 40 mm. uncorrected, as far as we can tell by extrapolating the venous point. The compensating effect of oxygen is, however, also increased by the flatness of the curve sufficiently to reduce the venous tension about 35 mm. (In calculating the effect of oxygen on the venous point in this case we were unable to use our formula because the CO₂ tension was above 70 mm. A value for K of 0.414 was used instead of the usual 0.34. This is the average value of K between 70 and 90 mm. From Table I it appears that there is a considerable variation in the value of K above 70 mm. and there may be a large error in this correction.) In spite of this there is still a very
considerable difference in pH between the arterial and venous blood. This difference is, however, much less than would occur if the arterial tension were lower on a curve of the same level, because of the difference in the slope of the pH lines. In a study of these factors may lie an explanation of the relatively great tolerance for carbon dioxide found by Scott (19) in emphysema patients. No general conclusions can be drawn from this one patient as to the respiratory mechanism in emphysema or asthma. The picture is similar to that of cardiac dyspnea in the fact that there is a marked difference between the alveolar and the arterial CO₂ tension, suggesting again a functional impairment of the ventilating power of the lungs. Furthermore, there is a carbon dioxide retention, as evidenced by the low arterial pH.

**Plasma Bicarbonate as a Measure of the Alkali Reserve.**

As a result of a large series of observations of the carbon dioxide-combining capacity of the venous plasma of decompensated cardiac patients made in 1916 and subsequently, we were led to conclude that the alkali reserve of the blood of these patients, although quite variable, lay for the most part within normal limits. The same thing is true of the present cases, if we consider the carbon dioxide capacity of the plasma. Six determinations in this series vary from 55.0 to 75.7 volumes per cent. Among these is a determination made on Case 11 from the same specimen of blood that showed such a marked reduction in the height of the absorption curve.

The contradictory results obtained from whole blood and from venous plasma may be explained by variations in the carbon dioxide content of the venous blood. As the tension of carbon dioxide in blood is increased the bicarbonate of the blood also increases. This is evidenced by the fact that the slope of the absorption curve is greater than that of the curve which represents the solubility of carbon dioxide in the blood. The increase in the bicarbonate of blood in response to increases of CO₂ tension is associated with a transfer of base from cells to plasma. Joffe and Poulton (20) have demonstrated that the change in bicarbonate content of whole blood is reflected in the plasma. This had already been clearly demonstrated by Van Slyke and Cullen (21). Van Slyke and Cullen, Straub and Meier (22), and
others have shown that the CO₂ absorption curve of plasma is much flatter than that of whole blood, approaching more nearly the curve of a simple bicarbonate solution.

In this case the carbon dioxide-combining capacity of the venous plasma must be dependent, to some extent at least, upon the carbon dioxide tension or content of the venous blood at the time that it is withdrawn. Table V shows this relation clearly. In this table are represented the carbon dioxide content of venous blood, drawn directly, without stasis, beneath albolene; the

<table>
<thead>
<tr>
<th>Subject</th>
<th>CO₂ capacity of whole blood.</th>
<th>CO₂ content of venous blood.</th>
<th>CO₂ capacity of venous plasma.</th>
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<td>69.1</td>
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carbon dioxide capacity of whole blood at 40 mm. of CO₂ tension and 37.5°C.; and the carbon dioxide capacity of venous plasma determined according to the technique of Van Slyke (23). (For the last, venous blood was withdrawn under albolene, centrifuged in this condition, and the plasma removed to a separatory funnel and saturated with alveolar CO₂.) The observations are arranged according to the magnitude of the CO₂ content. The plasma capacity parallels the CO₂ content rather more closely than it does the CO₂ capacity of whole blood. But, if the CO₂ capacity
of the plasma is to be used as a measure of the bicarbonate content of the blood, it should vary directly as the CO₂ capacity of the whole blood.

The cardiac cases are not the only ones in which the plasma method fails to agree with the whole blood method. H. G. shows a slight acidosis on the basis of his plasma figures, although the whole blood CO₂ capacity is normal. In this case the venous carbon dioxide content is very low. The discrepancy is slight, but is quite striking in comparison with J. D. B., a cardiac patient with an absorption curve at the same level as that of H. G. Even in normal subjects estimations of the bicarbonates of whole blood from those of plasma may prove inaccurate. This is well illustrated in the case of D. P. B., who on several occasions showed a CO₂ capacity relatively higher in the plasma than in the whole blood.

In severe anemia the use of plasma may lead to misinterpretations. In this condition, as we shall show, the whole blood curve becomes relatively flat, approaching that of plasma. Changes in CO₂ tension, therefore, produce relatively small alterations in CO₂ content. The consequence is that the values obtained from whole blood are high in comparison with those obtained from plasma. This is especially noticeable in Cases A. B. and E. S. (The corresponding hemoglobin values were 32 and 35 per cent respectively.) This may explain the fact that Kahn and Barsky (24), studying the plasma in pernicious anemia, found a reduction of the alkali reserve in three cases, while the four cases in our series gave consistently high values for the CO₂-combining capacity of whole blood.

Finally, a further source of error lies in the fact that the absorption curves of plasma from different specimens of blood may differ. This has been demonstrated by Straub and Meier (22).

The use of the CO₂-combining power of the plasma as a measure of the alkali reserve will cause little or no error in most cases if it is employed only in those conditions in which the respiratory and circulatory systems are undisturbed and react in the normal manner to the natural stimuli. It was to subjects of this type that Van Slyke and coworkers (25) first applied it with such success that his method has become the standard method for the measurement of the alkali reserve. Henderson and Haggard
(26) have contended that whole blood is preferable to plasma. The latter, however, was chosen by Van Slyke with full recognition of the error involved, because of technical reasons, especially the fact that whole blood demanded immediate analysis, whereas plasma could be kept for a considerable length of time without deterioration. Furthermore, the coagulum produced by the addition of acid to whole blood rendered the cleansing of his pipette difficult. With the substitution of tartaric acid for sulfuric in the Van Slyke method one of the technical reasons for preferring plasma has been removed. The impossibility of keeping whole blood for any length of time remains an objectionable feature.

If, for this reason, the use of plasma is found necessary, variations in carbon dioxide saturation, the chief cause of error in the use of plasma, must be avoided. This can easily be effected by bringing the whole blood into equilibrium with a standard air-CO₂ mixture, e.g. alveolar air, before removing the plasma. If this were done at least the chief objection to the use of plasma would be removed. However, the air-CO₂ mixture used for saturation of whole blood must be more carefully standardized than is the case when plasma is employed. This is evident from the differences in the absorption curves of whole blood and plasma. Small variations in carbon dioxide tension have a much greater effect on the carbon dioxide content of whole blood. The use of alveolar air, which is the usual procedure with plasma might, with whole blood, introduce a perceptible error. Under resting conditions the alveolar CO₂ tensions of normal individuals should not vary by more than a few millimeters. As the corresponding change in the carbon dioxide content of the blood is only half as great, the use of alveolar air by an operator trained in respiratory methods should produce no serious errors.

Under these conditions plasma should give values that are dependable as far as the ability of the blood to neutralize acids other than carbonic is concerned. For the study of the respiratory function of the blood, on the other hand, whole blood alone can be used. In order to avoid unnecessary complications, the normal limits of variation at room temperatures will have to be more definitely established, as whole blood work up to the present has been confined almost entirely to physiological studies and saturation has been effected at body temperature.
Just as this paper was approaching completion the final report of the work of Joffe and Poulton (20) on the absorption curves of whole blood and plasma appeared. On the basis of their findings they also conclude that the carbon dioxide capacity of plasma separated from venous blood is not a proper measure of the available alkali of the blood. They advise a method identical with that here proposed.

Up to the time that Van Slyke published his method the presence of a carbon dioxide retention had not yet been demonstrated in any pathological condition, and, although the possibility of such an occurrence was clearly recognized by him, it did not seem of sufficient practical importance to outweigh the obvious technical advantages of plasma over whole blood. As applied to the study of diabetes the use of plasma probably introduced no serious error. When we presented our data to Dr. Van Slyke we found that he had come to practically the same conclusion as a result of some studies on anesthesia.

**Carbon Dioxide Content of the Venous Blood in Cardiac Dyspnea.**

It is clear that a discrepancy between the CO₂ capacity of whole blood and that of venous plasma may be produced by at least three factors: (1) An abnormal venous carbon dioxide tension; (2) a disturbance of the normal proportion of cells to plasma; (3) an abnormality in the carbon dioxide absorption curve of the plasma itself. The second of these we may assume to be unimportant in cardiac dyspnea, although we have not investigated the matter carefully. In the majority of cases hemoglobin determinations were made by means of the oxygen capacity and revealed no striking changes. The plasma absorption curve has not been determined. We have, however, studied the venous carbon dioxide content of a number of subjects.

The determination of the presence or absence of carbon dioxide retention in the venous blood is not so simple a matter as it may appear. The results obtained by previous observers are not at all consistent. Harrop (16) found that the difference between arterial and venous carbon dioxide content was sometimes increased in cardiac dyspnea, indicating a relative retention of carbon dioxide in the venous blood. Table IV gives a summary of Harrop's findings. The results obtained from the five cases
in our series appear in Table III. The two sets of observations are in essential agreement. The difference between arterial and venous blood was much more variable in decompensated cardiac cases than in normal subjects, and in some of the former was relatively increased. Scott (27) has recently reported the CO₂ content of the plasma of both arterial and venous blood lower than normal in cardiac decompensation. A few unpublished determinations made by one of us on venous plasma in 1916 were not in agreement with his findings. The values obtained were more variable than those obtained from normal subjects, but the variations were not predominantly low. In some cases they were quite high. The same is true of the values obtained from whole blood. Their only characteristic is a great range of variation (see Tables I and III). By comparison with Table V it will be seen that these variations bear a rough relation to the height of the absorption curves.

Neither Harrop's nor Scott's method can throw much light on the question of the presence or absence of a carbon dioxide retention. The absolute value for carbon dioxide content of either whole blood or plasma, whether arterial or venous, although of interest, cannot be accepted as a satisfactory criterion. The CO₂ content which is normal for a blood with a high absorption curve is excessive for a blood with a low absorption curve, if the reaction of the blood is to be maintained constant. The locus of points of equal pH is represented by straight lines passing through the origin. As the curves become lower, therefore, equal amounts of CO₂ have a greater effect in changing the pH. The presence of a carbon dioxide retention can only be determined, then, by a comparison of the carbon dioxide content of the blood with the height of the absorption curve. Such a comparison appears in the venous pH values in Table III. In the case of the three cardiac patients with low absorption curves (Cases 10, 11, and 12) there is a definite carbon dioxide retention which explains the falsely high values for bicarbonate obtained by the plasma CO₂ capacity method of Van Slyke (23).

SUMMARY AND CONCLUSIONS.

1. A study has been made of the carbon dioxide absorption curve of the blood of seven patients with cardiac decompensation
and dyspnea. In three out of the seven low curves were found. In two of these cases the curves returned to the normal level when compensation was reestablished. Clinically these patients were distinguished by the presence of an extreme degree of cyanosis with little dyspnea. No relation could be established between the reduction of the absorption curve and the oxygen unsaturation of the arterial or venous blood. A low absorption curve was not an indication of the severity of the condition. No signs of renal involvement were discovered in any of these cases.

2. The reduction of the alkali reserve indicated by these low absorption curves was not reflected in the plasma. The CO₂ capacity of the venous plasma is determined by the carbon dioxide tension at which it existed in the body rather than by the carbon dioxide-combining capacity of the blood. For this reason the determination of the plasma bicarbonates by the technique originally proposed is not applicable as a measure of the alkali reserve in conditions associated with CO₂ accumulation in the venous blood. A true measure of the bicarbonate content of blood is obtained from the carbon dioxide capacity of whole blood. As whole blood deteriorates when kept, while plasma does not, it may still be necessary to employ plasma for purposes of routine procedure. In this case errors due to variations in carbon dioxide saturation may be avoided by saturating the whole blood with a standard air-CO₂ mixture before separating the plasma. With this modification the method may be rendered applicable to the determination of the alkali reserve of the blood. For the study of the respiratory function of the blood, however, only whole blood should be used.

3. (a) In four cases arterial and venous carbon dioxide tension were determined. The alveolar carbon dioxide tension was also determined. The only consistent and characteristic finding was an increase in the difference between alveolar and arterial CO₂ tension. This difference varied from 13 to 19 mm.

(b) In two cases there was a definite CO₂ retention in the arterial and venous blood with a consequent lowering of the pH.

(c) No consistent increase in the difference between arterial and venous CO₂ content or tension could be demonstrated, although in one or two instances it was slightly greater than normal.
4. The causes of the discrepancy between the alveolar carbon dioxide tension and the carbon dioxide-combining capacity of the venous plasma in cardiac dyspnea are:

(a) The fact that the carbon dioxide capacity of the plasma gives values that are too high in the presence of carbon dioxide retention such as is sometimes found in cardiac dyspnea.

(b) The alveolar carbon dioxide is very low in proportion to the carbon dioxide content of the venous blood and does not bear a definite relation to the height of the absorption curve.

5. The causes of cardiac dyspnea seem to be: The fact that a greater ventilation is necessary to effect the normal carbon dioxide elimination. This is largely brought about by an impairment of the efficiency of the pulmonary mechanism for the exchange of gases between the blood and the outside air. This necessitates the maintenance of a greater difference in carbon dioxide pressure between the blood in the pulmonary circulation and the alveolar air in order to effect the normal carbon dioxide output. To maintain the carbon dioxide tension and the hydrogen ion concentration at the proper level the alveolar carbon dioxide tension must be abnormally low. In some cases a diminution of the circulation rate may be an additional factor in the production of a carbon dioxide acidosis. Finally in a certain proportion of the cases, at least, there is a real reduction of the available alkali of the blood. In at least two cases with a reduction of the available alkali of the blood were found indications of a comparative insensibility of the respiratory center to its natural physicochemical stimulus, the hydrogen ion concentration of the blood.

BIBLIOGRAPHY.


**EXPLANATION OF CHARTS.**

**Chart 7.**


Looks chronically ill. Moderate dyspnea even while at rest, but able to walk around ward. Faint cyanosis of lips and finger-tips. Lungs clear.

Heart very much enlarged, with loud systolic and diastolic murmurs, maximum over the aortic area. X-ray revealed aneurysmal dilatation of the ascending aorta.

Wassermann ++ + + .

Patient improved but slightly and is still in the hospital at the time of publication.


<table>
<thead>
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<th>Alveolar CO₂ before venous puncture, mm</th>
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<tr>
<th>CO₂ absorption curve:</th>
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<tr>
<td>CO₂ tension, mm Hg</td>
</tr>
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<td>CO₂, vol. per cent.</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

| CO₂ content of venous blood, vol. per cent. | 49.8 |
| CO₂ capacity of venous plasma (41.7 mm. Hg) vol. per cent. | 60.7 |
| O₂ capacity of blood, vol. per cent.        | 16.4 |
Experiment 2. Apr. 30. Condition practically unchanged, although cyanosis may be slightly increased.

Alveolar CO₂ before arterial puncture, mm 27.3
27.1
27.7

"CO₂ after " " " " 27.6

CO₂ absorption curve:

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<th>CO₂ tension, mm Hg</th>
<th>59.8</th>
<th>47.2</th>
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<td>CO₂, vol. per cent</td>
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<td>52.9</td>
<td>39.8</td>
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<tr>
<td></td>
<td>56.1</td>
<td>50.7</td>
<td>40.3</td>
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</table>

CO₂ content of arterial blood, vol. per cent 49.3
48.9

CO₂ " " venous " " " " 52.0
53.4

Difference between arterial and venous CO₂, vol. per cent 3.6
O₂ capacity of blood, vol. per cent 13.9
O₂ content of arterial blood, vol. per cent 14.3
O₂ " " venous " " " " 3.7
O₂ consumption, vol. per cent 10.6
O₂ saturation of arterial blood, per cent 100
O₂ " " venous " " " " 27

Respiratory quotient of blood 0.34

CHART 7. Experiment of Apr. 30. Directions for interpretation of charts are given in Paper I.

Temperature normal. Pulse absolutely irregular; rate 72 to 100. Blood pressure: systolic 138; diastolic 86. Heart moderately enlarged both to the right and left. Loud blowing, systolic murmur at apex, accompanied by rough thrill. No murmurs at base. Electrocardiogram shows auricular fibrillation.

Urine contains considerable albumin, with a few granular and hyaline casts. Specific gravity 1.023 to 1.027. Non-protein nitrogen of blood 43 mg. per 100 cc. Phenolsulfonephthalein excretion 60 per cent in 2 hrs. Discharged from hospital, improved, 1 week after last experiment.

Experiment 1. Apr. 8, 1920.

<table>
<thead>
<tr>
<th>Minute volume of respirations, cc</th>
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<tr>
<td>Respirations per min.</td>
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</tr>
<tr>
<td>CO₂ in expired air 2.40 per cent.</td>
<td>208</td>
</tr>
<tr>
<td>CO₂ output per min., cc.</td>
<td>1,197</td>
</tr>
</tbody>
</table>

Experiment 2. Apr. 9. Condition unchanged.

Alveolar CO₂ before arterial puncture, mm.………. 25.0

CO₂ absorption curve:

<table>
<thead>
<tr>
<th>CO₂ tension, mm. Hg</th>
<th>75.8</th>
<th>54.4</th>
<th>44.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO₂, vol. per cent.</td>
<td>56.6</td>
<td>46.0</td>
<td>41.7</td>
</tr>
<tr>
<td>CO₂ content of arterial blood, vol. per cent</td>
<td>39.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CO₂ " " venous " " " " .................. 49.5

Difference between arterial and venous CO₂, vol. per cent... 10.2

CO₂ capacity of venous plasma (40.9 mm. Hg), vol. per cent, 59.4

O₂ " " " blood, vol. per cent... 20.7

O₂ content of arterial blood, vol. per cent... 16.7

O₂ " " venous " " " " .................. 8.5

O₂ consumption, vol. per cent.................. 8.2

O₂ saturation of arterial blood, per cent... 63

O₂ " " venous " " " " .................. 42

Respiratory quotient of blood....................... 1.24

Experiment 3. Apr. 23. Condition greatly improved. Quite comfortable. No edema. Signs of fluid in chest gone. Cyanosis still well marked. Heart action good, rate about 60, with practically no pulse deficit. Is able to be out of bed and to walk about ward without difficulty or discomfort.

Vital capacity of lungs, cc.................................. 2,463

Minute volume of respirations, cc.......................... 9,854

Tidal air 498 cc. Respirations per min. .................. 19.8
CO₂ in expired air 2.72 per cent. CO₂ output per min., cc. 268
Alveolar CO₂ before arterial puncture, mm.......................... 34.2
  " CO₂ after " " " ........................................ 31.2
CO₂ absorption curve:
  CO₂ tension, mm. Hg........................................ 80.4  26.6
  CO₂ vol. per cent........................................... 64.6  38.0
  63.9  40.5
CO₂ content of arterial blood, vol. per cent............................. 53.8
CO₂ " " venous " " " ........................................ 54.2
  63.0
Difference between arterial and venous CO₂, vol. per cent.... 9.3
CO₂ capacity of venous plasma (52.0 mm. Hg), vol. per cent. 75.7
O₂ " " blood, vol. per cent..................................... 22.0
O₂ " " venous " " " .......................................... 11.1
  11.0
O₂ consumption, vol. per cent........................................ 10.9 or 9.7
O₂ saturation of arterial blood, per cent............................ 100
O₂ " " venous " " " .......................................... 53
Respiratory quotient of blood........................................ 0.85 or 0.96

CHART 10. 1. Experiment of Apr. 9.
2. Experiment of Apr. 23.

Urine shows cloud of albumin, no casts. Specific gravity 1.018.

Discharged from hospital improved, 9 days after last experiment.

Experiment 1. Apr. 16, 1920.

**Alveolar CO₂ before arterial puncture, mm.**
- 23.0
- 22.1

**CO₂ after arterial puncture, mm.**
- 21.4

**CO₂ absorption curve:**

<table>
<thead>
<tr>
<th>CO₂ tension, mm. Hg</th>
<th>68.0</th>
<th>47.1</th>
<th>36.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO₂, vol. per cent.</td>
<td>47.7</td>
<td>38.3</td>
<td>35.8</td>
</tr>
<tr>
<td></td>
<td>47.4</td>
<td>39.4</td>
<td></td>
</tr>
</tbody>
</table>

**CO₂ content of arterial blood, vol. per cent.**
- 36.8
- 35.0

**CO₂ venous blood, vol. per cent.**
- 44.8
- 46.1

**Difference between arterial and venous CO₂, vol. per cent.**
- 9.6

**CO₂ capacity of venous plasma (37.8 mm. Hg), vol. per cent.**
- 55.0

**O₂ content of arterial blood, vol. per cent.**
- 26.3
- 26.7

**O₂ venous blood, vol. per cent.**
- 9.9

**O₂ consumption of arterial blood, per cent.**
- 14.3

**O₂ saturation of arterial blood, per cent.**
- 91

**Respiratory quotient of blood.**
- 0.67


**Vital capacity of the lungs, cc.**
- 1,800

**Alveolar CO₂ before arterial puncture, mm.**
- 30.2
- 34.7

**CO₂ after arterial puncture.**
- 32.5
CO₂ absorption curve:

<table>
<thead>
<tr>
<th>CO₂ tension, mm. Hg</th>
<th>CO₂, vol. per cent.</th>
</tr>
</thead>
<tbody>
<tr>
<td>37.8</td>
<td>49.1</td>
</tr>
</tbody>
</table>

CO₂ content of arterial blood, vol. per cent. 53.7

O₂ tension, vol. per cent. 25.0

O₂ venous tension, vol. per cent. 22.5

O₂ consumption, vol. per cent. 2.5

O₂ saturation of arterial blood, per cent. 94

O₂ venous saturation, per cent. 85

(O₂ capacity of Apr. 16 used for calculations.)

**Chart 11.**

1. Experiment of Apr. 16.
2. Experiment of Apr. 20.
Case 12. C. C. Mitral stenosis. Looks chronically ill. Lies quietly in bed, with only slight dyspnea and no orthopnea. Very marked cyanosis of head and extremities. Somewhat irrational.

Experiment 1.

Alveolar CO₂ before arterial puncture, mm. 23.0
26.1
27.8

CO₂ absorption curve:

<table>
<thead>
<tr>
<th>CO₂ tension, mm. Hg</th>
<th>CO₂, vol. per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>66.2</td>
<td>43.7</td>
</tr>
<tr>
<td>47.6</td>
<td>34.3</td>
</tr>
<tr>
<td>39.0</td>
<td>33.0</td>
</tr>
<tr>
<td>45.3</td>
<td>35.9</td>
</tr>
<tr>
<td>33.0</td>
<td></td>
</tr>
</tbody>
</table>

CO₂ content of arterial blood, vol. per cent 33.4
33.6
33.4

CO₂ venous " " " 43.1
42.6

Difference between arterial and venous CO₂, vol. per cent 9.4
9.3

O₂ capacity of blood, vol. per cent 18.3
18.3

O₂ content of arterial blood, vol. per cent 18.0
18.0

O₂ venous " " " 3.2
3.2

O₂ consumption, vol. per cent 14.8
14.8

O₂ saturation of arterial blood, per cent 98
98

O₂ venous " " " 18
18

Respiratory quotient of blood 0.64
Case 13. M. C. Bronchial asthma with severe emphysema. Male, age 40 years, single, hospital orderly.

Complains of severe dyspnea and cough. Has been admitted to the hospital several times. Looks acutely distressed. Is sitting up in bed. Respirations are rapid and labored, with prolonged, wheezing expiration. Most intense cyanosis of head and extremities, which are a deep purple. Veins of neck engorged. Lungs show boardy resonance everywhere. Expiratory breath sounds prolonged, high pitched, and wheezing. Rhonchi and rales of all kinds heard all over chest. Heart: apex and borders of dulness not made out. Sounds distant. No murmurs made out. Pulse about 100.

Experiment 1. May 12, 1920.

<table>
<thead>
<tr>
<th>Experiment 1</th>
<th>May 12, 1920</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alveolar CO₂ before arterial puncture, mm.</td>
<td>39.8</td>
</tr>
<tr>
<td>CO₂ after puncture, mm.</td>
<td>44.1</td>
</tr>
<tr>
<td>CO₂ after puncture, mm.</td>
<td>41.2</td>
</tr>
<tr>
<td>CO₂ after puncture, mm.</td>
<td>40.9</td>
</tr>
</tbody>
</table>

CO₂ absorption curve:

| CO₂ tension, mm. Hg | 61.9 | 15.1 | 75.1 | 39.6 |
| CO₂ vol. per cent. | 57.0 | 32.2 | 56.9 | 48.7 |
| CO₂ vol. per cent. | 56.3 | 31.0 | 58.2 | 50.1 |

CO₂ content of arterial blood, vol. per cent. 58.4

| CO₂ vol. per cent. | 56.7 |
| CO₂ vol. per cent. | 62.5 |

Difference between arterial and venous CO₂, vol. per cent. 5.7

CO₂ capacity of venous plasma (51.2 mm. Hg), vol. per cent. 74.5

| O₂ blood, vol. per cent. | 21.3 |
| O₂ blood, vol. per cent. | 17.2 |
| O₂ blood, vol. per cent. | 11.0 |
| O₂ blood, vol. per cent. | 6.2 |
| O₂ blood, vol. per cent. | 81 |
| O₂ blood, vol. per cent. | 52 |
| Respiratory quotient of blood | 0.92 |
Additional Protocols.


Condition did not respond to treatment and patient died suddenly 6 days after the experiment here reported.


$CO_2$ absorption curve:

$CO_2$ tension, mm. Hg. ................. 78.7 47.2 11.6
$CO_2$, vol. per cent. .................. 61.1 49.1 27.4 26.4

$CO_2$ content of venous blood, vol. per cent. ................. 54.8
$O_2$ capacity of blood, vol. per cent. ................. 21.7
$O_2$ content of venous blood, vol. per cent. ................. 5.0
$O_2$ saturation of venous blood, per cent. ................. 23

Temperature about 100. Pulse absolutely irregular, rate slow as the result of digitalis therapy.

Heart enlarged to the right and left, with systolic and diastolic thrill and shock, maximum over the midcardiac area. Auricular fibrillation.

Patient died 2 days after the experiment here reported.


<table>
<thead>
<tr>
<th>CO₂ tension, mm. Hg</th>
<th>CO₂, vol. per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.0</td>
<td>34.8</td>
</tr>
<tr>
<td>34.8</td>
<td>69.5</td>
</tr>
</tbody>
</table>

CO₂ content of venous blood, vol. per cent. 51.1
CO₂ capacity of plasma (44.0 mm. Hg), vol. per cent.. 64.0


Wassermann ++++.

Patient died 3 weeks after the last experiment without having left the hospital.

Experiment 1. Mar. 9, 1920.

<table>
<thead>
<tr>
<th>CO₂ tension, mm. Hg</th>
<th>CO₂, vol. per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>66.8</td>
<td>59.9</td>
</tr>
<tr>
<td>59.9</td>
<td>20.6</td>
</tr>
</tbody>
</table>

CO₂ content of venous blood, vol. per cent. 62.1
CO₂ capacity of venous plasma (51.1 mm. Hg), vol. per cent.. 74.2


<table>
<thead>
<tr>
<th>CO₂ tension, mm. Hg</th>
<th>CO₂, vol. per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>(26.4)</td>
<td>93.7</td>
</tr>
<tr>
<td>93.7</td>
<td>51.8</td>
</tr>
</tbody>
</table>

CO₂ content of venous blood, vol. per cent. 56.9
O₂ capacity of blood, vol. per cent.. 22.3
II. THE CARBON DIOXIDE ABSORPTION CURVE AND CARBON DIOXIDE TENSION OF THE BLOOD IN CARDIAC DYSPNEA
John P. Peters, Jr. and David P. Barr

J. Biol. Chem. 1921, 45:537-570.

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