INFLUENCE OF GASEOUS TRANSFER BETWEEN THE COLON AND BLOOD STREAM ON PERCENTAGE GAS COMPOSITIONS OF INTESTINAL FLATUS IN MAN

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The behavior of gases in the gastro-intestinal tract has been the subject of several studies, and it is generally concluded that the atmospheric air entering the stomach during swallowing and the gases arising in the intestinal tract by fermentation are modified by interchange with the gases of the blood stream. This exchange of gas between the lumen of the intestine and the blood circulating in its wall is expected to be the same response occurring between gases contained in any body cavity and the blood stream. Campbell (1), Henderson (2) and Seevers (3) are in agreement that any gas introduced into the pleural cavity, the peritoneal cavity, the bladder or subcutaneous tissues approaches equilibrium with the partial pressures of that gas in the venous blood and tissue fluids. These investigators found equilibrium values for oxygen ranging from about 20 to 30 mm. Hg (2.63% to 3.95%) and for carbon dioxide averaging 50 mm. Hg (6.58%).

In view of the supposition that the behavior of gases in the gastro-intestinal tract is the same as in any body cavity, with the possible exception of the influence of gases produced by bacteria in the colon, the present investigation was undertaken for a more satisfactory explanation of some obvious discrepancies reported pertaining to the normal gas compositions of the intestinal tract.

In an analysis of gas as discharged via the anus, Fries (4) found the following percentage volume compositions: 10.3% carbon dioxide, 0.7% oxygen, 29.6% methane and 59.4% nitrogen. In the case of the stomach, Planer (5) reported 23 to 33% carbon dioxide, 0.8 to 6.1% oxygen and 66 to 68% nitrogen in the dog, while Kantor (6) determined the gases in man as 4.16% carbon dioxide, 17.08% oxygen and 78.82% nitrogen. From his analytical data Ruge (7) concluded that when food is present in the alimentary canal, the oxygen tension is practically nil while carbon dioxide may exist at very high tensions (50% of one atmosphere) in the large intestine. Hibbard (8) studied the gas which forms above obstructions in the small bowel and found that it consisted generally of about 70% nitrogen, 6 to 9% carbon dioxide (a concentration approaching that in the blood) and 10 to 12% oxygen.

McIver and coworkers (9) have stressed the importance of the physical process of diffusion as being the determining factor governing the rate of gas absorptions. They found that the quantity of a given gas which will diffuse across a membrane in unit time depends directly upon the differences in partial pressure of the gas on either side of the membrane, the extent of its surface, and inversely upon its thickness. The absolute value of the rate of diffusion when these conditions are defined is determined by the characteristic of the gas and by the nature of the membrane through which it passes.

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2 Abridgment of portion of thesis submitted to the faculty of the Graduate School of the University of Illinois in partial fulfillment of the requirements for the degree of Ph.D. in Physiology.
is diffusing. These investigators derived equations predicting the absorption coefficients of various gases, on the basis of the observation that an equilibrium is reached when the partial pressure of the gas in the lumen is equal to the mean tension of the gas dissolved in the circulating blood. This condition of equilibrium should be the same, regardless of the direction from which it is approached. It is interesting to note that in every case they found that carbon dioxide diffuses rapidly, oxygen more slowly and nitrogen hardly at all.

In the experimental work that follows, comparison is made between the absorption coefficient of gases determined on the basis of McIver's equation and the absorption coefficients calculated on the basis of the experimental data reported.

EXPERIMENTAL

The experimental work involved three parts: a) the absorption of oxygen as contained in room air, b) the absorption of carbon dioxide as contained in a mixture of 25 per cent carbon dioxide and 75 per cent nitrogen, and c) the absorption of nitrogen. The behavior of these gases was studied by introducing 500-cc. volumes into the colons of normal healthy male adult subjects by way of an open-tipped rubber tube inserted into the rectum for a distance of about 10 cm. This type of experimentation was always done on individuals who had recently defecated. The subjects were instructed to rest comfortably in a hospital bed in any position desired, since position was not found to influence the results. Gas samples of 30 cc., sufficient for duplicate analyses, were withdrawn into a 50-cc. syringe at periodic intervals of time, the gas being stored over saturated sodium chloride solution contained in a series of burettes. The gas samples were analyzed for oxygen, carbon dioxide, methane and hydrogen. Nitrogen was considered for all practical purposes as the residual gas and was estimated by difference. The analyses were carried out in an apparatus designed for rapid manipulation and utilizing the usual principles of analysis, oxygen being absorbed by alkaline pyrogallol, carbon dioxide by concentrated potassium hydroxide and methane and hydrogen determined by slow combustion.

Gas tensions in mixed venous blood were determined by a breathing technique, which is a composite of the Plesch procedure as described by Peters and Van Slyke (10), the Henderson and Prince method (11) and the method of Burwell and Robinson (12). The method used was designed to eliminate some of the causes for criticism and include the advantages for each of the techniques. The procedure was carried out as follows:

A rubber bag (fig. 1, c) of about 1500 cc. capacity was filled with about 1000 cc. of nitrogen. The nose of the subject was closed with a clip and he applied his mouth to the breathing tube at A, the stopcock B being turned so that he was connected with the outside air. The subject breathed normally for a short period, after which he emptied his lungs as deeply as possible by a forced expiration into the out-
side air and then quickly inhaled the entire content of the bag by adjusting the three-
way stopcock. He then rebreathed deeply the mixture in the bag for 25 seconds,
five respirations usually sufficing. At the end of the last expiration into the bag, the
stopcock was again turned, shutting off the bag, and the subject removed his mouth
from the breathing tube and breathed outside air. The procedure was repeated a
sufficient number of times (with 3-minute intervals to allow for return of normal
conditions of respiration and circulation) until constancy of composition was found
in successive analyses. The gas samples for the analyses were removed at D.
When the subject was at rest, constancy of composition was attained usually after
about the fifth inhalation and exhalation procedure. Thus gas tensions in mixed ve-
nous blood were determined indirectly by analyzing carbon dioxide and oxygen ten-
sions in alveolar air which has been retained in the lungs until equilibrated with those
tensions in the mixed venous blood coming from the right ventricle of the heart. A
more direct method would obviously be to analyze blood from a superficial vein, but

\[
\begin{array}{|c|c|c|c|c|}
\hline
\text{SAMPLE} & P \text{ OBSERVED} & t & P \text{ CALCULATED} & \Delta \text{ DEV.} \\
\hline
1 & 20.93 & 0 & 20.59 & -0.34 \\
2 & 17.98 & 10 & 18.03 & +0.05 \\
3 & 14.78 & 25 & 14.93 & +0.15 \\
4 & 12.00 & 40 & 12.48 & +0.48 \\
5 & 9.87 & 65 & 9.46 & -0.41 \\
6 & 7.25 & 95 & 7.10 & -0.15 \\
7 & 5.39 & 125 & 5.61 & +0.22 \\
8 & 4.72 & 155 & 4.68 & -0.04 \\
9 & 3.39 & 185 & 3.10 & -0.29 \\
\hline
\end{array}
\]

\[\text{Equation: } P \text{ calc.} = 17.43 e^{-0.0155 t} + 3.11\]

\(\Sigma \).................

-0.55

-0.09

this would be impractical for human subjects, while the method described is suffi-
ciently approximate to direct blood analysis to warrant its more practical usage. The
described technique is not to be confused with the more commonly used method of
determining carbon dioxide and oxygen tensions of quickly expelled alveolar air in
equilibrium with the arterial blood.

RESULTS

Absorption of oxygen. According to the diffusion theory, the rate at which a gas
flows across a membrane is directly proportional to the difference in pressures on the
two sides of the membrane, so that when oxygen, as contained in room air, is intro-
duced into the colon, a pressure gradient exists between that oxygen in the colon
and the oxygen tension in venous blood. Therefore, absorption of the oxygen will
take place into the blood stream until this gradient approaches zero.

A typical set of data is shown in table 1, demonstrating a progressive decrease
in the percentage of oxygen of one atmosphere during the designated intervals of
time, while figure 2 pictures a graph of these results in which the changes in composition of the gas samples were plotted as points describing a curve with the percentage of gas on the vertical axis against time on the horizontal axis.

The type of progressive absorption observed here appears to follow an exponential curve, and therefore, any equation to fit such a curve would have to be of the type $P = a e^{-kt} + c$, where $P$ is the pressure in percentage of one atmosphere, $a$ is the effective initial pressure gradient, $e$ indicates natural logs, $k$ is the absorption coefficient, $t$ is time in minutes and $c$ is a constant determining the limits of the curve and is assumed to be the gas tension in the venous blood. The equation, as calculated on the basis of that specific set of data shown in table 1 and figure 2, is observed to be $P = 17.43 e^{-0.01358 t} + 3.11$, while the closeness of fit is indicated by a comparison of the observed $P$ with calculated $P$ values.

In figure 2 it is observed that the percentage of oxygen approaches and reaches equilibrium with the venous oxygen tension in a period of 185 minutes. The graph also shows the counterprocess of diffusion, that of entrance of carbon dioxide into the lumen of the colon from the blood stream, and indicates the relatively short time in which the tension of carbon dioxide in the colon reaches the venous tension of 6.73 percent in this specific experiment, as indicated by the straight solid line. The higher tension of carbon dioxide in the colon can logically be accounted for by that amount produced by the intestinal flora.

Table 2 summarizes the results of ten experiments, indicating the equations for the absorption curves, the absorption coefficients as the $k$ value in these equations, the statistical significance of the data, and a comparison of these $k$ values and those calculated by McIver on the basis of an equation derived on theoretical considerations already mentioned. His equation for calculating the $k$ value is as follows: $k = \frac{1}{t} \left[ -\log e (a - x) \right]$, where $(a - x)$ is the pressure gradient.

The average equation is $P = 17.13 e^{-0.01638 t} + 3.52$, while the average $k$ value
is \(-0.01658 \pm 0.0006\), this average comparing favorably with the average \(k\) value of \(-0.01638\) calculated from McIver’s equation. The statistical analyses show a high degree of significance for the results.

**Absorption of carbon dioxide.** Table 3 and figure 3 indicate the very rapid absorption of carbon dioxide, the greatest volume of the gas being absorbed in the first twenty minutes and attaining a final equilibrium of 7.89 per cent in ninety minutes in this particular experiment. This equilibrium value compares favorably

<table>
<thead>
<tr>
<th>EXP. NO.</th>
<th>EQUATION</th>
<th>(-k) VALUE + SE</th>
<th>PROBABILITY</th>
<th>MC IVER’S (-k) VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(P = 17.386^{-0.0171} + 3.67)</td>
<td>(0.01971 \pm 0.00017)</td>
<td>.01</td>
<td>.01838</td>
</tr>
<tr>
<td>2</td>
<td>(P = 19.41e^{-0.0350} + 4.25)</td>
<td>(0.01280 \pm 0.00007)</td>
<td>.01</td>
<td>.01309</td>
</tr>
<tr>
<td>3</td>
<td>(P = 14.05e^{-0.0230} + 3.22)</td>
<td>(0.01632 \pm 0.0001)</td>
<td>.01</td>
<td>.01354</td>
</tr>
<tr>
<td>4</td>
<td>(P' = 13.94e^{-0.0180} + 4.13)</td>
<td>(0.01858 \pm 0.00015)</td>
<td>.0001</td>
<td>.01881</td>
</tr>
<tr>
<td>5</td>
<td>(P = 17.43e^{-0.0163} + 3.11)</td>
<td>(0.01553 \pm 0.001)</td>
<td>.0001</td>
<td>.01557</td>
</tr>
<tr>
<td>6</td>
<td>(P = 17.58e^{-0.0176} + 3.46)</td>
<td>(0.01766 \pm 0.00014)</td>
<td>.0001</td>
<td>.01683</td>
</tr>
<tr>
<td>7</td>
<td>(P = 17.64e^{-0.0161} + 3.40)</td>
<td>(0.01611 \pm 0.001)</td>
<td>.0001</td>
<td>.01685</td>
</tr>
<tr>
<td>8</td>
<td>(P = 18.30e^{-0.0197} + 3.33)</td>
<td>(0.01607 \pm 0.001)</td>
<td>.0001</td>
<td>.01603</td>
</tr>
<tr>
<td>9</td>
<td>(P = 17.64e^{-0.0160} + 3.21)</td>
<td>(0.01669 \pm 0.001)</td>
<td>.0001</td>
<td>.01643</td>
</tr>
<tr>
<td>10</td>
<td>(P = 17.93e^{-0.0173} + 3.41)</td>
<td>(0.01573 \pm 0.000)</td>
<td>.0001</td>
<td>.01501</td>
</tr>
</tbody>
</table>

\[ P = 17.13e^{-0.0080} + 3.52 \]

<table>
<thead>
<tr>
<th>SAMPLE</th>
<th>(P) OBSERVED</th>
<th>(t)</th>
<th>(P) CALCULATED</th>
<th>(\Delta) DEV.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25.89</td>
<td>0</td>
<td>19.73</td>
<td>-6.16</td>
</tr>
<tr>
<td>2</td>
<td>20.00</td>
<td>5</td>
<td>18.07</td>
<td>-1.93</td>
</tr>
<tr>
<td>3</td>
<td>15.91</td>
<td>10</td>
<td>16.62</td>
<td>+0.71</td>
</tr>
<tr>
<td>4</td>
<td>12.56</td>
<td>20</td>
<td>14.27</td>
<td>+1.71</td>
</tr>
<tr>
<td>5</td>
<td>10.60</td>
<td>35</td>
<td>11.78</td>
<td>+1.18</td>
</tr>
<tr>
<td>6</td>
<td>9.68</td>
<td>50</td>
<td>10.14</td>
<td>+0.46</td>
</tr>
<tr>
<td>7</td>
<td>8.64</td>
<td>70</td>
<td>8.79</td>
<td>+0.15</td>
</tr>
<tr>
<td>8</td>
<td>8.26</td>
<td>90</td>
<td>8.03</td>
<td>-0.23</td>
</tr>
<tr>
<td>9</td>
<td>7.89</td>
<td>95</td>
<td>7.90</td>
<td>+0.01</td>
</tr>
</tbody>
</table>

\[ \Sigma \]  

\[ \text{Equation: } P \text{ calc. } = 12.72e^{-0.0086t} + 7.01 \]

with the venous blood carbon dioxide tension of 7.01 per cent. The equation describing the curve for this experiment is \(P = 32.72e^{-0.0086t} + 7.01\). It will be observed from the calculated pressure percentages of carbon dioxide that the derived equation fits the curve of absorption less accurately than for the absorption of oxygen. Figure 2 also shows the inward diffusion of oxygen from the blood stream, and again is seen to approach the venous blood tension of 3.75 per cent, the actual value being somewhat lower than this venous tension for the same reason that carbon dioxide remains
at equilibrium above the venous tension, namely, the utilization of oxygen and the production of carbon dioxide by the metabolic processes of the intestinal flora.

Table 4 summarizes the results of ten experiments, indicating the equations for the absorption curves, the absorption coefficients, the statistical significance of these data and a comparison of the $k$ values and those calculated by McIver's equation.

The average equation is $P = 13.89 e^{-0.02884 t} + 6.86$, while the average $k$ value is $-0.02884 \pm 0.0006$, this value comparing less favorably with the average $k$ value

<table>
<thead>
<tr>
<th>EXPT. NO.</th>
<th>EQUATION</th>
<th>$-k$ VALUE $\pm$ SE</th>
<th>PROBABILITY</th>
<th>MCIVER'S $k$ VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$P = 9.70e^{-0.03771} + 8.05$</td>
<td>$0.023577 \pm 0.0003$</td>
<td>0.01</td>
<td>0.02772</td>
</tr>
<tr>
<td>2</td>
<td>$P = 15.84e^{-0.03497} + 6.39$</td>
<td>$0.020945 \pm 0.0004$</td>
<td>0.001</td>
<td>0.03143</td>
</tr>
<tr>
<td>3</td>
<td>$P = 12.72e^{-0.03580} + 7.01$</td>
<td>$0.028505 \pm 0.0003$</td>
<td>0.001</td>
<td>0.03094</td>
</tr>
<tr>
<td>4</td>
<td>$P = 15.22e^{-0.03974} + 6.02$</td>
<td>$0.028004 \pm 0.0004$</td>
<td>0.001</td>
<td>0.03120</td>
</tr>
<tr>
<td>5</td>
<td>$P = 13.35e^{-0.03000} + 7.93$</td>
<td>$0.030000 \pm 0.0004$</td>
<td>0.001</td>
<td>0.03097</td>
</tr>
<tr>
<td>6</td>
<td>$P = 14.51e^{-0.03044} + 6.25$</td>
<td>$0.028944 \pm 0.0004$</td>
<td>0.001</td>
<td>0.03154</td>
</tr>
<tr>
<td>7</td>
<td>$P = 14.34e^{-0.03969} + 6.89$</td>
<td>$0.028922 \pm 0.0004$</td>
<td>0.001</td>
<td>0.03133</td>
</tr>
<tr>
<td>8</td>
<td>$P = 13.41e^{-0.03596} + 7.42$</td>
<td>$0.028550 \pm 0.0004$</td>
<td>0.001</td>
<td>0.03102</td>
</tr>
<tr>
<td>9</td>
<td>$P = 15.53e^{-0.03944} + 6.05$</td>
<td>$0.026414 \pm 0.0014$</td>
<td>0.05</td>
<td>0.03277</td>
</tr>
<tr>
<td>10</td>
<td>$P = 14.26e^{-0.03911} + 6.56$</td>
<td>$0.032221 \pm 0.0043$</td>
<td>0.0001</td>
<td>0.03446</td>
</tr>
</tbody>
</table>

$P = 13.89e^{-0.02884 t} + 6.86$ | $0.02884 \pm 0.0006$ | 0.03040

Fig. 4. ABSORPTION OF NITROGEN in the colon, showing the inward diffusions of both carbon dioxide and oxygen.
tion taking place beyond this value. The graph also shows the inward diffusions of both oxygen and carbon dioxide into the intestinal lumen from the blood stream until they reach their respective venous blood concentrations.

**DISCUSSION**

Throughout this work, the importance of the venous blood gas tensions has been stressed in limiting the extent of absorption of gases from the colon. Oxygen, carbon dioxide and nitrogen transfer between the colon and blood stream occur at a rate commensurate with physical principles described by McIver. This absorption rate of gas has been found to depend on the partial pressure gradient existing between the lumen of the colon and the venous blood. The results imply that the percentage volumes of gas compositions in intestinal flatus as discharged via the anus approximate the tensions of these gases in venous blood once an equilibrium has been established, with possible variations due to the presence of different types of intestinal flora. As one would expect, the predominant gas in such flatus is nitrogen. Once nitrogen has gained entrance into the intestinal tract, either from swallowed air or by diffusion from the blood stream, it is not significantly reabsorbed, not only because of its low diffusion constant and low solubility in blood, but also because the blood and tissues are already saturated with this gas existing there under a partial pressure of about four-fifths of an atmosphere and because this entire amount is held only in the form of a physical solution in the blood plasma. This is not the case with oxygen and carbon dioxide, which exist only to a small degree in physical solution, but are present almost wholly in chemical combination in the blood. In connection with this, the very rapid absorption of carbon dioxide during the first 20-minute period, as seen in figure 3, is interpreted as not being strictly a diffusion process but a chemical effect; that is, the formation of bicarbonate in the blood catalyzed by the enzyme carbonic anhydrase. This could well account for the rather poor fit of the exponential equation to the experimental data.

On the basis of averages obtained from numerous analyses of normal flatus, as expelled by the way of the anus, and the experimental data already reported, such gas discharges are composed of 3.0\% oxygen, 7.5\% carbon dioxide and 80.0\% nitrogen, the remaining 9.5\% being divided between methane, hydrogen and other residual gases. These figures take into account the influence of the intestinal flora and indicate the deviation that could occur from the average venous gas tensions of 3.52\% oxygen, 6.86\% carbon dioxide and 80.0\% nitrogen.

In the light of the experimental results obtained, the lack of uniformity in agreement between previous investigators on the analyses of gastro-intestinal gases may be due, in part, to the interval of time elapsing between the introduction of the gas studied and the final analysis. It would appear that Fries' analysis of methane is considerably higher than one would expect, while Planer's analysis of carbon dioxide is in great excess of what would be expected on the basis of experiments reported here, owing to the rapid diffusion rate of this gas. Both of these high percentages would produce a nitrogen value somewhat lower than might be anticipated, since such nitrogen percentages are calculated by difference.
SUMMARY

The absorption rate of gas in the colon of man depends on the partial pressure gradient existing between the lumen and the venous blood. The average venous blood tension of oxygen was 3.52 volume per cent (27 mm. Hg), proving to be the limiting factor in the extent of absorption of this gas from the colon. The same has been found to be true for carbon dioxide in which the average venous tension of 6.86 volume per cent (52 mm. Hg) limits the extent of absorption for this gas. The high blood tension of nitrogen of about 80.0 volume per cent (608 mm. Hg) retards the absorption of this gas from the colon, thus explaining the predominance of this gas in intestinal flatus.

The authors are indebted to Dr. Kenneth L. Blaxter for advice on the statistical handling of the data.

REFERENCES