THE DETERMINATION OF CARBON MONOXIDE IN BLOOD.

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(Received for publication, September 15, 1919.)

The determination of carbon monoxide in blood may be performed by gasometric, colorimetric, or spectrophotometric methods.

Previous gasometric methods have been laborious and most of them required special apparatus (as those of Gréhant, de Saint Martin, Nicloux, and others). The method employed by Zuntz and Plesch (1) seems to be the easiest. They determine the carbon monoxide in 1 cc. of blood, using ferricyanide to set the gases free (CO and O₂) and burn the CO to CO₂, which is absorbed by KOH. They calculate the amount of CO by the difference in pressure as in Haldane and Barcroft's method for blood gas analysis. According to the authors, the expulsion of the blood gases is finished after 1 hour.

The calorimetric method of Haldane (2) is based upon the fact that dilute carmine solutions have nearly the same color as dilute solutions of carbon monoxide hemoglobin. If it is known how much carmine has to be added to normal blood in order to give it the same color as blood completely saturated with carbon monoxide, and it is determined how much of the carmine must be added to normal blood to give it the color of the blood with the unknown content of CO, a simple calculation by proportion will give the degree of saturation with carbon monoxide.

This method seems to be very accurate in Haldane's hands, while others, like Krogh (3), and Zuntz and Plesch (1), have been unable to obtain good results with it. Plesch (4) has modified it, using a hemoglobin solution saturated with carbon monoxide instead of carmine for the titration.
Spectroscopic methods have been used by Hüfner and later by Hartridge (5). Krogh (6) has recently modified the method of the latter and used it for the determination of the oxygen capacity of very small amounts of blood; his method is still rather rough, but he hopes to make it more accurate with finer instruments.

An easy gasometric method seems still to be needed and we have worked out one which permits the determination of the carbon monoxide gasometrically in 2 cc. of blood in the course of 10 to 15 minutes. We have employed this method for the determination of the blood volume and for the study of the action of carbon monoxide on blood.

The Method.

The principle of our method is to set free the oxygen and carbon monoxide from their combination with hemoglobin in the blood by addition of ferricyanide and then to remove both gases with the help of a Torricellian vacuum in the Van Slyke apparatus for blood gas analysis. The oxygen is absorbed in the apparatus by alkaline pyrogallate and the volume of residual carbon monoxide is measured directly at atmospheric pressure, a correction being made for the small and constant amount of nitrogen gas physically dissolved by blood.

The procedure is, up to the time when the expelled gas is measured, exactly the same as that for the oxygen method described by Van Slyke (7), and it is therefore unnecessary to repeat it here; the same amount of blood and the same solutions are used, and only the shaking has to be continued a little longer before a constant reading is obtained. This takes about 2 to 3 minutes and is a little different for different species of blood; it probably depends upon the facility with which the blood is laked.

When the reading of the volume of the gas mixture, consisting of oxygen, carbon monoxide, and a little nitrogen, is constant, a solution of alkaline pyrogallate1 is introduced into the cup of the apparatus, is covered by a thin layer of paraffin oil, and is allowed to flow slowly down the inner wall of the graduated part of the apparatus.

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1 Prepared by dissolving 10 gm. of pyrogallic acid in 200 cc. of strong potassium hydroxide (160 gm. of KOH dissolved in 130 cc. of water).
apparatus. A little suction is produced during this part of the procedure by lowering the leveling bulb slightly.

The absorption of the oxygen is very rapid and is completed in less than 1 minute; the reading is taken and the pyrogallate solution introduced once more until a constant reading is obtained. The gas is then measured under barometric pressure in the same way as described by Van Slyke for carbon dioxide (8) and oxygen.

As the solution is very dark and it is a little difficult to get good readings of the meniscus, we have produced a new meniscus by letting a little water flow down after the pyrogallate solution; the water floats on the top of the fluid and one can get readings to about 0.002 cc. Instead of water a few drops of octyl alcohol may be used.

The apparatus is washed out twice with dilute ammonia solution after each determination.

Calculation. The gas measured is reduced to standard conditions by multiplying by the factor $(0.999 - 0.0046 t) \times \frac{Barometer}{760}$, $t$ being the temperature in °C. If 2 cc. of blood have been used, the values of this factor in Column 3 of Table I of Van Slyke's paper on oxygen may be used, the result then being expressed in cc. of CO per 100 cc. of blood, when the nitrogen correction, 1.2 cc., is subtracted.  

EXPERIMENTAL.

Air was analyzed in the Van Slyke apparatus in order to find the best way of absorbing the oxygen. When the pyrogallate solution was introduced in the manner described above, the oxygen was absorbed in 30 seconds.

The method was tried in the following way. As the oxygen and the carbon monoxide replace each other in the combination with hemoglobin and the oxygen capacity equals the carbon monoxide capacity, blood with known percentages of carbon monoxide may be obtained by mixing different amounts of blood

2 The nitrogen correction is 1.2 per cent, instead of the calculated value 0.9 per cent, when actually determined by Bohr and by ourselves.
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saturated with carbon monoxide with blood saturated with air. By taking, for instance, one part of CO blood and four parts of O₂ blood, the analysis should give 20 per cent CO and 80 per cent O₂.

Table I shows the amounts of oxygen and carbon monoxide found by analysis and the amount calculated.

<table>
<thead>
<tr>
<th>No.</th>
<th>Blood used</th>
<th>Found.</th>
<th>Calculated.</th>
<th>Kind of blood</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Oxygen</td>
<td>CO</td>
<td>Proportion of hemo-globin saturated with CO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>cc.</td>
<td>cc.</td>
<td>per cent</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>0.212</td>
<td>0.206</td>
<td>50.7</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>0.208</td>
<td>0.210</td>
<td>49.8</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>0.118</td>
<td>0.240</td>
<td>32.9</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>0.170</td>
<td>0.238</td>
<td>31.1</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>0.088</td>
<td>0.250</td>
<td>26.0</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>0.128</td>
<td>0.390</td>
<td>24.5</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>0.068</td>
<td>0.240</td>
<td>22.1</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>0.054</td>
<td>0.224</td>
<td>19.43</td>
</tr>
<tr>
<td>9</td>
<td>4</td>
<td>0.091</td>
<td>0.434</td>
<td>17.3</td>
</tr>
</tbody>
</table>

It is seen from Table I how closely the found values agree with those calculated, except in No. 8, where the discrepancy is 2.7 volumes per cent. By taking 4 cc. of the same blood instead of 2 cc., this error is brought down to 0.6 volume per cent. We therefore recommend the use of a little more blood, 3 or 4 cc. (and the correspondingly increased amount of ammonia), for analysis, if the percentage saturation of CO is very small and the actual amount of CO found in 2 cc. of blood is 0.05 cc. or less.

In two rather rough experiments, two guinea pigs were given illuminating gas under a bell jar until they fell unconscious. They were then taken out and blood was drawn by heart puncture for analysis. One of them died while the blood was being taken; the other recovered and behaved normally an hour afterwards.

Table II shows that a guinea pig can recover after carbon monoxide poisoning, even when the blood is 76.3 per cent saturated with carbon monoxide.
TABLE II.

<table>
<thead>
<tr>
<th>Remarks.</th>
<th>O₂</th>
<th>CO</th>
<th>Satur-</th>
<th>per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guinea Pig 1.</td>
<td>0.115</td>
<td>0.333</td>
<td>75.4</td>
<td>Died during bleeding.</td>
</tr>
<tr>
<td>&quot;     2.</td>
<td>0.080</td>
<td>0.258</td>
<td>76.3</td>
<td>Recovered.</td>
</tr>
</tbody>
</table>

SUMMARY.

A method is described for the determination of carbon monoxide in blood, the technique of which is exactly the same as that previously described by Van Slyke for the determination of oxygen, except that after the gases are extracted the oxygen is absorbed in the apparatus by introducing alkaline pyrogallate solution. The carbon monoxide remains and is measured directly at atmospheric pressure.

BIBLIOGRAPHY.

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