A METHOD FOR THE DETERMINATION OF CYCLOPROPANE, ETHYLENE, AND NITROUS OXIDE IN BLOOD WITH THE VAN SLYKE-NEILL MANOMETRIC APPARATUS*

BY F. S. ORCUTT AND R. M. WATERS

(From the Departments of Anesthesia and Pharmacology, University of Wisconsin School of Medicine, Madison)

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The determination of anesthetic gases in blood taken from patients during anesthesia has been reported in several instances (1-3). In each case, however, reservation has been made as to the accuracy of the results because of errors in the vacuum extraction method. The principal source of error has been that the volume of gas determined was not corrected for unextracted gas. This technical difficulty was recognized by the authors cited and the error which was introduced was probably of insufficient magnitude to alter the interpretation of their results significantly. It is felt by the authors of this paper, however, that there is a need for a method by which anesthetic gases can be accurately determined on a single sample without detracting from the accuracy of analysis for carbon dioxide and oxygen.

The determination of blood gases by the Van Slyke-Neill manometric method (4) is based on the principle of extracting the gases from the blood and reagent in a partial vacuum. The gases are separated by absorption with specific reagents, and the volume per cent of the gas in the original blood sample is calculated from the resulting differences in pressures read on the manometer at constant volume.

A correction must be made, however, for the unextracted gas in the liquid. This is accomplished by the factor $1 + (\alpha'(A - S))$ where $A - S$ is the volume at which extraction takes place, and $S$ the volume of the liquid. The $\alpha'$ is equivalent to $\lambda$, or the Ost-

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wald solubility expression which may be obtained from the Bunsen absorption coefficient $\alpha$ by multiplying by $(1 + 0.003671t)$.

At the present time it is necessary to make this calculation for each gas from the value of $\alpha$ for water found in the literature. This procedure is open to two objections. The values found in the literature are not always in close agreement. Secondly, these constants are for pure water, whereas the constants desired are for the acid and alkaline reagents containing blood. For gases with fairly high solubilities, such as the anesthetic gases, there may be considerable variation between the values for pure water and those for aqueous solutions.

By a method recently proposed by one of the authors (5), it is possible to determine accurately the solubility of various gases not only in pure liquids but in solutions as well. The determination is made on the Van Slyke-Neill manometric apparatus, so that the solubility constant for the correction is determined on the same piece of apparatus and under the same condition as is the actual determination of gas in the blood.

Using this method, the authors have determined the solubilities of cyclopropane, ethylene, and nitrous oxide in the various reagents used, and constructed tables of factors for each gas by which the observed pressure is multiplied to give either mM per liter of blood, or volumes per cent in the blood.

**General Procedure for Analysis of Blood Containing Anesthetic Gases**

The general procedure for combined carbon dioxide and oxygen in blood (4) is used with a few modifications. After $p_1$ is read on the manometer and 1 cc. of deaerated alkali run in to absorb carbon dioxide, the solution is again evacuated at the 50 cc. level for 2 or 3 minutes to liberate that part of the anesthetic gas absorbed by the alkali. The level of the liquid is brought to the 2 cc. mark as carefully as before the $p_1$ reading (40 seconds), so that a standard amount is reabsorbed as Van Slyke and Neill (4) point out with carbon dioxide. The $p_2$ is then taken and the oxygen absorbent added as usual. The solution is then shaken for 2 to 3 minutes at 50 cc. to liberate the anesthetic gas absorbed by the hydrosulfite reagent. The level is carefully raised to the 2 cc. mark again in 40 seconds and the $p_1$ reading taken. The anesthetic gas is then determined by difference as in the carbon monoxide determina-
tion (4); viz., the gas is forced out through the cock without loss of liquid and the liquid level brought back to 2 cc. for the $p_4$ reading. The concentration of gas in the blood is calculated by $(p_1 - p_4)$ times the factor given in Table III.

To determine whether or not the anesthetic gas is liberated to approximately the same extent after addition of the alkaline reagents, parallel determinations were made—one where the deaerated reagents were saturated with cyclopropane and one with no cyclopropane. The results, in mm. of Hg, are as follows:

<table>
<thead>
<tr>
<th>Pressure differences</th>
<th>Deaerated reagents with CnHs</th>
<th>Deaerated reagents</th>
</tr>
</thead>
<tbody>
<tr>
<td>$p_1 - p_2$</td>
<td>1.9</td>
<td>1.9</td>
</tr>
<tr>
<td>$p_2 - p_3$</td>
<td>1.0</td>
<td>0.9</td>
</tr>
</tbody>
</table>

**Error Due to Nitrogen**

If the anesthetic gas diluted with oxygen is administered by the open technique, it is not necessary to correct for nitrogen in the blood if a half hour or more of anesthesia has elapsed. The original level of nitrogen in the blood is 1.2 or 1.3 volumes per cent with an inspired atmosphere of 79 per cent nitrogen. When this high concentration is reduced, the level in the blood must also fall. Although nitrogen continues to enter the blood from the tissues, it is not likely that after half an hour of a nitrogen-deficient atmosphere in the lung that the concentration in the blood will exceed 0.2 or 0.3 of a volume per cent. This being the limit of accuracy of the apparatus with a 1 cc. sample, no correction for nitrogen need be made.

If a closed system with carbon dioxide absorption is used, a careful flushing of the system with oxygen and the anesthetic gas from time to time suffices to reduce the nitrogen content of the blood. If it is desired to take a blood sample shortly after induction, the nitrogen in the blood is probably reduced at least one-half, so that the error would not exceed 0.5 volume per cent.

**Influence of Presence of Cyclopropane, Ethylene, and Nitrous Oxide on Accuracy of CO₂ and O₂ Measurements**

The solubility of the three anesthetic gases was determined for each of the three solutions which are used during the course of the
blood gas determination; viz., Solution 1, 2.5 cc. of acid ferrocyanide reagent plus 1 cc. of blood; Solution 2, the same as Solution 1 plus 1 cc. of 1 N alkali; Solution 3, the same as Solution 2 plus 1 cc. of alkaline hydrosulfite reagent. The solubility was determined by the method referred to above (5). The calculation was made by the formula

\[
\frac{(A - S)p}{(B - W_s)S - Sp} \times \frac{273.1 + t_s}{273.1 + t_e} = \lambda = \alpha'
\]

where 
- \(A\) = chamber capacity
- \(S\) = sample size
- \((A - S)\) = volume during extraction
- \(p\) = pressure due to the liberated gas
- \(B\) = barometric pressure
- \(W_s\) = vapor pressure of solvent at temperature of saturation
- \((B - W_s)\) = partial pressure of gas during saturation
- \(t_s\) = temperature of saturation
- \(t_e\) = "" "" extraction
- \(\lambda\) = Ostwald solubility expression, equivalent to \(\alpha'\)
- \(\alpha'\) = Van Slyke and Neill expression

The correction factor by which the pressure of liberated gas is corrected for unextracted gas is obtained from the following formula (4).

\[
1 + \frac{S\alpha'}{A - S} = J
\]

In Table I are given the values of \(\alpha'\) and \(1 + (S\alpha'/(A - S))\) for each of the three solutions referred to above. It will be noted that for each gas the solubility (\(\alpha'\)) decreases as the pH is increased from Solutions 1 to 2 to 3. The decrease in solubility is compensated in each case by the increase in amount of solution, so that the correction factors lie in the same range.

To determine the effect of the slight variation in these factors, the corrections in mm. of mercury may be obtained by assuming a pressure for each gas which is in the range of pressure usually determined: for cyclopropane and ethylene, 25 mm.; for nitrous oxide, 60 mm. When these pressures are divided by the solubility correction factor for each solution, the theoretically observed pressure may be obtained. These figures are given in Table II. The only significant difference is with nitrous oxide between Solutions 1 and 2. This difference of 0.5 mm., however, is equivalent to 0.1
volume per cent, which is within the accuracy of the CO₂ and O₂ determinations.

From this evidence it may be concluded that under these conditions, CO₂ and O₂ may be absorbed in the presence of cyclopropane, ethylene, and nitrous oxide, so that the differences in

**TABLE I**

*Constants for Anesthetic Gases in Reagent-Blood Mixtures*

<table>
<thead>
<tr>
<th>Solution No.</th>
<th>Reagent-blood mixture</th>
<th>Cyclopropane</th>
<th>Ethylene</th>
<th>Nitrous oxide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>α'</td>
<td>1 + $\frac{Sa'}{A-S}$</td>
<td>α'</td>
</tr>
<tr>
<td>1</td>
<td>2.5 cc. acid ferricyanide + 1 cc. blood at 25° (A - S = 3.5)</td>
<td>0.408</td>
<td>1.031</td>
<td>0.118</td>
</tr>
<tr>
<td>2</td>
<td>Same as Solution 1 + 1 cc. 1 N alkali at 25° (A - S = 4.5)</td>
<td>0.354</td>
<td>1.035</td>
<td>0.110</td>
</tr>
<tr>
<td>3</td>
<td>Same as Solution 2 + 1 cc. alkaline hydrosulfite at 25° (A - S = 5.5)</td>
<td>0.296</td>
<td>1.037</td>
<td>0.093</td>
</tr>
</tbody>
</table>

**TABLE II**

*Observed Pressures of Anesthetic Gases over Reagent-Blood Mixtures*

<table>
<thead>
<tr>
<th>Solution No.*</th>
<th>Cyclopropane (25 mm. present)</th>
<th>Ethylene (25 mm. present)</th>
<th>Nitrous oxide (60 mm. present)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24.2 mm. Hg</td>
<td>24.8 mm. Hg</td>
<td>57.3 mm. Hg</td>
</tr>
<tr>
<td>2</td>
<td>24.2 mm. Hg</td>
<td>24.8 mm. Hg</td>
<td>56.8 mm. Hg</td>
</tr>
<tr>
<td>3</td>
<td>24.1 mm. Hg</td>
<td>24.8 mm. Hg</td>
<td>56.8 mm. Hg</td>
</tr>
</tbody>
</table>

* For the composition of the solutions see Table I.

the observed pressures may represent the true pressures of CO₂ and O₂ present within the usual limits of accuracy of the manometric determination.

**Calculation of Factors for Cyclopropane, Ethylene, and Nitrous Oxide**

The calculation of factors for the three anesthetic gases by which the observed pressure ($p_3 - p_4$) is multiplied to give concentrations in the blood was made by the formula given by Van Slyke and
Neil (4). The other variable factor given in this formula (beside the solubility correction factor) is the amount of gas reabsorbed when the solution is brought up to the 2 cc. level after extraction, in the arbitrary time of 40 seconds. This factor \( i \) for cyclopropane was found to be 1.01, for ethylene 1.08, and for nitrous oxide 1.03. This indicates that 1, 8, and 3 per cent of the liberated gases, respectively, were reabsorbed when the volume was reduced to 2 cc.

It is interesting to note that ethylene has such a high reabsorption rate compared with carbon dioxide (1.7 per cent), cyclopropane, and nitrous oxide, although its solubility is lower than any of these gases.

With the values of \( 1 + (S \alpha'/(A - S)) \) for 25° given in Table I for Solution 3, and similar values determined for other temperatures, and the values of \( i \) given above, the factors in Table III were compiled. The observed partial pressure of any of these three anesthetic gases may be converted to concentration in the blood by the formula,

\[
(p_a - p_s) \times f = \text{concentration in blood}
\]

where \( f \) is the suitable factor at the temperature of measurement.

TABLE III
Factors for Calculation of \( C_3H_6 \), \( C_3H_4 \), or \( N_2O \) Content of Blood

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Factors by which mm. of ( p_{C_3H_6} ), ( p_{C_3H_4} ), or ( p_{N_2O} ) are multiplied to give mm ( \text{Ca}_3H_6 ), ( \text{Ca}_3H_4 ), or ( \text{Ca}N_2O ) per liter of blood</th>
<th>Volume per cent ( \text{Ca}_3H_6 ), ( \text{Ca}_3H_4 ), or ( \text{Ca}N_2O ) in blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>( a = 2.5 ) ( i = 1.01 )</td>
<td>( a = 2.5 ) ( i = 1.08 )</td>
</tr>
<tr>
<td>21</td>
<td>( a = 2.5 ) ( i = 1.01 )</td>
<td>( a = 2.5 ) ( i = 1.08 )</td>
</tr>
<tr>
<td>22</td>
<td>( a = 2.5 ) ( i = 1.01 )</td>
<td>( a = 2.5 ) ( i = 1.08 )</td>
</tr>
<tr>
<td>23</td>
<td>( a = 2.5 ) ( i = 1.01 )</td>
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</tr>
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<td>24</td>
<td>( a = 2.5 ) ( i = 1.01 )</td>
<td>( a = 2.5 ) ( i = 1.08 )</td>
</tr>
<tr>
<td>25</td>
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<td>( a = 2.5 ) ( i = 1.08 )</td>
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<tr>
<td>26</td>
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<td>27</td>
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<tr>
<td>29</td>
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<td>( a = 2.5 ) ( i = 1.08 )</td>
</tr>
<tr>
<td>30</td>
<td>( a = 2.5 ) ( i = 1.01 )</td>
<td>( a = 2.5 ) ( i = 1.08 )</td>
</tr>
</tbody>
</table>
A method is proposed for determining cyclopropane, ethylene, and nitrous oxide in blood, as well as CO₂ and O₂ in the presence of these gases.

Suitable factors for each gas have been compiled and tabulated by which the observed partial pressure may be converted to concentration in the blood.

Corrections have been made for unextracted portions of the gases in the solutions from which they are extracted by direct solubility measurements in these solutions.

It is of interest that the rate of reabsorption in water of ethylene, nitrous oxide, carbon dioxide, and cyclopropane is in the ratio, roughly, of 8, 3, 1.7, and 1, respectively, whereas the ratio of solubilities for the same gases, respectively, is 1, 5, 8, and 2.

**BIBLIOGRAPHY**

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