OXYGEN TURNOVER RATE IN THE VENOUS RESERVOIR

BY

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SUMMARY

In a study of the oxygen stores of the body anaesthetized paralyzed dogs were hyperventilated \((P_aO_2 = 15 \text{ mm Hg})\) for 2 hours. During the final 30 minutes the inspired mixture was altered from oxygen to air. The rates at which alveolar and arterial oxygen concentrations approached their new steady-state values were represented by the half-times \((t_1/2)\) 0.17 and 0.23 minutes respectively. The turnover rate in venous blood oxygen content proceeded at a considerably slower rate, \(t_1/2 = 0.75\) minutes. The data presented here will be useful in constructing models to predict changes in body oxygen content during anaesthesia with controlled breathing and hyperventilation.

Body oxygen stores are located almost exclusively in alveolar gas and in the circulating blood. These reservoirs turn over rapidly in response to alterations in inspired oxygen concentration, alveolar ventilation and cardiac output. The rate at which alveolar and arterial oxygen concentrations are altered by new conditions can be reliably estimated from the magnitude of alveolar ventilation. During air breathing, the venous blood volume (Farhi, 1964) is the single largest reservoir of oxygen in the body. Although it is well recognized that the turnover rate of oxygen in the venous reservoir is blood flow dependent, there are no studies in which this rate of adjustment is explicitly stated.

During steady hyperventilation when the inspired oxygen concentration is abruptly changed from pure oxygen to air, alveolar and arterial oxygen concentrations will turn over rapidly and the turnover rate of oxygen in mixed venous blood will be related to the magnitude of blood flow and the size of the venous pool. The purpose of this study then is to measure the rate at which oxygen concentration in venous blood approaches its new equilibrium value when, during steady hyperventilation, the inspired mixture is altered from 100 per cent oxygen to air.

METHODS

Adult mongrel dogs were anaesthetized with pentobarbitone, 30 mg/kg given intravenously. An endotracheal airway was used and cuff inflated to ensure a leakproof system. Mechanical ventilation was accomplished with a Palmer pump. To produce skeletal muscle paralysis, a 0.1 per cent solution of suxamethonium chloride in 5 per cent dextrose in water was given intravenously at a rate of 0.5 mg/min. Ventilation was measured with a 13.5-l. spirometer. A catheter was placed in a femoral artery. Using the technique of Rahn and Lategola (1953), a catheter was placed in the right ventricle or pulmonary artery via the external jugular vein. In each case the tip of the catheter for sampling mixed venous blood was 1–2 cm proximal or distal to the pulmonary valve. A thermistor was used to measure retrocardiac oesophageal temperature.

Each study was 2 hours in duration with constant hyperventilation throughout. After ventilation with air for 60 minutes the animal breathed oxygen for 30 minutes. At the end of this half-hour arterial and mixed venous blood samples were obtained in syringes whose deadspace was filled with heparin solution. The samples were immediately immersed in an ice bath.

Blood pH, \(P_CO_2\) and \(P_O_2\) were measured at 37°C with electrodes maintained at that temperature in a constant-temperature water bath. Blood pH was measured with a modified capillary glass electrode, \(P_CO_2\) and \(P_O_2\) with carbon dioxide (Severinghaus and Bradley, 1958) and oxygen electrodes (Clark, 1956) respectively. A polypropylene-covered oxygen electrode was used. The coefficients of variation for replicates of blood oxygen tension were 0.6 per cent (air) and 1.7 per cent (100 per cent oxygen).
Blood Po₂ was corrected for the membrane electrode blood-gas difference by tonometry at 37°C using a sample of the animal's blood (Finley et al., 1960). In these studies the relationship of electrode response to gas and blood of the same Po₂ was relatively constant. In this study mixed venous oxygen tension varied from 33 to 46 mm Hg and in this range of blood Po₂, gas/blood = 1.025 ± 0.003 (mean ± SE).

Blood haemoglobin oxygen saturation was derived from measured Po₂ and pH using the nomogram of Rossing and Cain (1966). The reliability of the measurements of blood oxygen tension will determine the accuracy of this approach, particularly to the measurement of venous blood oxygen saturation. Ninety-five per cent of all observed values of PVO₂ in the range 33-46 mm Hg will be expected to be less than 1.2 per cent different from the actual mean values (coefficient of variation is 0.6 per cent). In terms of oxygen tension this amounts to a variation of 0.4-0.6 mm (from low to high venous oxygen tensions) and for all values the oxygen saturation will be in error by less than 1 per cent saturation. Blood oxygen capacity was estimated using the measured haemoglobin concentration. Blood oxygen content (CO₂) = (oxygen saturation x oxygen capacity) + (amount oxygen dissolved). Dissolved oxygen in vol. per cent = Po₂ x 0.023/760 x 100; where 0.023 = solubility coefficient of oxygen in whole blood in ml oxygen per ml blood at 37°C.

At the end of the period of oxygen breathing, the inspired mixture was abruptly changed to air. End-tidal nitrogen concentration was measured during this initial period of oxygen washout, using a rapidly responding nitrogen meter. Arterial and mixed venous blood samples were obtained at 0.5, 1, 2, 3, 10 and 30 minutes.

PAN₂ (alveolar nitrogen tension) was assumed to be approximately equal to the end-tidal N₂ concentration measured during the change from oxygen to air breathing. The value of PAN₂ was used in the estimate of PAO₂ (alveolar oxygen tension) during this adjustment.

\[ P_{AO_2} = P_{Fi_2} - P_{ACO_2} - P_{AN_2}. \]

The value of PAO₂ is an approximation during this unsteady state. PACO₂ was assumed equal to PACO₂.

At the end of the final 30 minutes of air breathing mixed expired oxygen and carbon dioxide concentrations were measured using the method of Scholander (1947). Oxygen consumption (VO₂), carbon dioxide production (VCO₂), and the respiratory exchange ratio (R) were computed from the following expressions:

\[ VO_{2\,SM} = VE_{STPD} \left[ \frac{Fi_{O_2} - CO_{2} - FO_{2}}{1 - Fi_{O_2}} \right] - FE_{O_2} \]
\[ VCO_{2\,SM} = VE_{STPD} \cdot FO_{2} \]

\[ R = \frac{VCO_{2}}{VO_{2}} \]

The final equilibrium value for alveolar oxygen concentration (FAO₂) was solved graphically with the oxygen-carbon dioxide diagram (Rahn and Fenn, 1955), using the measured values of R and PACO₂. Cardiac output (Q) was calculated from VO₂ and the A-V oxygen difference.

\[ Q = \frac{VO_{2}}{(CA_{O_2} - CV_{O_2})}. \]

During the period of oxygen washout, the changes in FAO₂, CAO₂ and CVO₂ were analyzed in terms of the rate at which each approaches its new equilibrium value. A means of expressing the rate of change is use of the half-time. Half-time is the time for the variable in question to change 50 per cent of the overall change, and in this study is expressed in minutes.

**RESULTS**

Seven dogs averaging 11.0 kg were studied. Blood haemoglobin concentration averaged 14.0 g/100 ml with no measurable change through the study. The total volume of blood sampled was less than 5 per cent of the estimated total circulating blood volume (Reeve et al., 1953). Oesophageal temperature averaged 37.5°C and blood gas tensions were not corrected for this 0.5°C blood-to-electrode temperature difference. Arterial carbon dioxide tension averaged 15.6 and 15.1 mm Hg at the end of oxygen and air breathing respectively.

Table I lists the average values for P AO₂ (arterial oxygen tension), CAO₂ (arterial oxygen content), PVO₂ (mixed venous oxygen tension) and CVO₂ (mixed venous oxygen content) during the adjustment from oxygen to air breathing. The average values for FAO₂ were 0.45, 0.29, 0.23 and 0.20 at ½, ¼, 1 and 1 minute respectively. At 30 minutes FAO₂ averaged 0.186, VO₂ averaged 53.3 ml/min, R averaged 0.92, and Q averaged 0.85 l./min.
TABLE I
Arterial and mixed venous blood oxygen concentrations following step decrease in \( F_{O_2} \), from 1.00 to 0.209. Ventilation constant.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>( P_{O_2} ) (mm Hg)</th>
<th>( C_{A O_2} ) (vol. %)</th>
<th>( P_{V O_2} ) (mm Hg)</th>
<th>( C_{V O_2} ) (vol. %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>592.1 ± 7.5</td>
<td>20.54 ± 0.85</td>
<td>45.6 ± 4.2</td>
<td>15.12 ± 0.81</td>
</tr>
<tr>
<td>0.5</td>
<td>169.1 ± 12.7</td>
<td>19.12 ± 0.84</td>
<td>42.1 ± 8.8</td>
<td>14.52 ± 0.92</td>
</tr>
<tr>
<td>1</td>
<td>125.1 ± 5.6</td>
<td>18.89 ± 0.85</td>
<td>38.9 ± 3.9</td>
<td>13.74 ± 1.11</td>
</tr>
<tr>
<td>2</td>
<td>114.4 ± 2.3</td>
<td>18.84 ± 0.84</td>
<td>34.9 ± 3.0</td>
<td>12.79 ± 1.02</td>
</tr>
<tr>
<td>3</td>
<td>111.2 ± 2.1</td>
<td>18.79 ± 0.84</td>
<td>33.7 ± 3.1</td>
<td>12.38 ± 1.11</td>
</tr>
<tr>
<td>10</td>
<td>112.2 ± 2.0</td>
<td>18.85 ± 0.84</td>
<td>33.2 ± 2.8</td>
<td>12.49 ± 1.12</td>
</tr>
<tr>
<td>30</td>
<td>109.1 ± 2.4</td>
<td>18.78 ± 0.84</td>
<td>33.7 ± 2.4</td>
<td>12.38 ± 0.91</td>
</tr>
</tbody>
</table>

Values represent mean and SE (7 studies).

CAO2 are represented by the half-times 0.17 and 0.23 minutes respectively, while the change in CV02 proceeds more slowly with a half-time of 0.75 minutes.

**FIG. 1**

In figure 1 are plotted the average values of \( F_{A O_2} \), \( C_{A O_2} \) and \( C_{V O_2} \) during the adjustment from oxygen to air breathing. After 3 minutes, the washout process is essentially near completion. Analysis of this data was made in terms of the rate at which each variable approaches its asymptote and is seen in figure 2. The change in \( F_{A O_2} \) and \( C_{A O_2} \) are represented by the half-times 0.17 and 0.23 minutes respectively, while the change in \( C_{V O_2} \) proceeds more slowly with a half-time of 0.75 minutes.

**FIG. 2**
Oxygen washout. Changes in \( F_{A O_2} \), \( C_{A O_2} \) and \( C_{V O_2} \) plotted semilogarithmically versus time.

**DISCUSSION**

**Alveolar ventilation.**
Hyperventilation results in a rapid turnover of oxygen in alveolar gas and aids in distinguishing the venous from the alveolar and arterial changes. The animal was hyperventilated for a total duration of 2 hours in each study.

**Alveolar oxygen stores.**
During oxygen breathing the increase in the total oxygen content of the body is considerable. In the dog the resting lung volume is 30 ml/kg body weight (Simmons and Hemingway, 1955). The increase from air to oxygen breathing represents at least a six-fold increase in the alveolar
oxygen stores or an increase of approximately 24 ml oxygen per kg body weight.

**Arterial oxygen stores.**

During high oxygen breathing the arterial oxygen tension will equal the alveolar oxygen tension, if no shunting is present. In the present study, average alveolar oxygen tension is 697 mm compared to an average arterial tension of 592 mm. On the average, the fraction of cardiac output passing through shunts is equal to 5.5 per cent. Shunting of this magnitude is responsible for an arterial blood oxygen content 1–2 per cent lower than that obtained with no shunting whatsoever.

**Venous oxygen stores.**

During the adjustment from oxygen to air breathing, mixed venous oxygen tension decreased an average of 12 mm Hg and represented a change of 2.64 vol. per cent. Previous descriptions of body oxygen stores (Farhi, 1964) have assumed that the venous volume represents 75 per cent of the total blood volume. In the dog with a blood volume equal to 10 per cent of body weight there would be 75 ml of venous blood per kg of body weight. In the present study this would represent a change of 1.98 ml oxygen per kg when changing from oxygen to air breathing.

The total amount of oxygen lost from venous blood, when changing from oxygen to air breathing, can be recovered when cardiac output is increased. For purposes of illustration, the following assumptions will be made: during oxygen breathing arterial and mixed venous oxygen content are 220 and 170 ml oxygen per litre respectively, and during air breathing are 200 and 150 ml oxygen per litre respectively. The loss from venous blood is 20 ml oxygen per litre; with a blood volume 10 per cent of body weight (75 per cent venous) this would represent 1.5 ml oxygen per kg body weight. To recover this 20 ml oxygen per litre of venous blood while continuing to breathe air, arteriovenous oxygen content difference would need to decrease by an equivalent amount and would become 30 ml oxygen per litre (200 ml/l. minus 170 ml/l.). Assuming that oxygen consumption remained constant and equalled 175 ml oxygen/sq.m/min, the two values for cardiac index would be 3.5 (175/50) and 5.8 (175/30) l./sq.m/min. This represents a 65 per cent increase in cardiac output and would be sufficient to restore the oxygen lost from venous blood in the change from oxygen to air breathing.

It is also interesting to note that when the rate of change in venous blood is extrapolated to the initial concentration, the intercept is at zero time plus 20 seconds. This can be interpreted as meaning that on the average the initial change in mixed venous oxygen content requires about ½ minute following the alveolar change and presumably represents the average circulation time.

The splenic blood volume in the dog is significantly altered by pentobarbitone anaesthesia. Several decades ago pentobarbitone was shown to cause dilatation of the spleen, resulting in 18–29 per cent of the total red cells being located in the spleen (Hahn, Bale and Bonner, 1942–43). More recently, pentobarbitone anaesthesia in the dog was demonstrated to decrease the arterial haematocrit by 8 per cent during the first 1–2 hours of anaesthesia. In this later study it was demonstrated that total plasma volume and red cell mass remained unchanged, and also that in previous studies of the effect of pentobarbitone anaesthesia in the dog there was a failure to appreciate the important influence of the duration of anaesthesia. Whether or not the splenic sequestration of red cells causes a redistribution of blood in the total arterial versus total venous volumes is unknown. For the present, the assumption that 75 per cent of the blood volume is venous still appears to be a reasonable one.

**Cardiac output.**

The arteriovenous oxygen content difference had increased at the end of the study, when compared to the value 30 minutes earlier during oxygen breathing. If oxygen consumption during the period of oxygen breathing were equal to that obtained 30 minutes later, then the cardiac output during the oxygen period would be about 16 per cent greater than the later value. This is not consistent with the finding that cardiac output in the anaesthetized dog decreases during oxygen breathing (Murray, 1964). Other studies (Gilmore, 1965) have demonstrated a 25 per cent decrease in cardiac output from the first to second hour of pentobarbitone anaesthesia in the dog breathing air. It appears, then, in the present study in the dog, that the decrease in cardiac output is related
to the duration of pentobarbitone anaesthesia and that this effect far outweighs the effect of altering the breathing mixture from oxygen to air.

Voluntary hyperventilation in man results in an increase in cardiac output (Greisheimer, 1965); however, the conditions in the present study are quite different. Cardiac output in dogs remains unchanged when they are hyperventilated artificially (Brown, 1953; Rowe, Castillo and Crump ton, 1962). The hypocapnia that accompanies hyperventilation will result in a redistribution of cardiac output, such as increasing skeletal muscle blood flow and decreasing blood flow to the skin. However, there is no evidence to suggest that the distribution of arterial versus venous volumes is changed.

Tissue oxygen stores.

The oxygen stores of the body are assumed to be contained essentially in the lung and the circulatory blood volume. There is, however, an additional quantity of oxygen dissolved in tissues throughout the body. During the oxygen washout process in these present studies, $P_{V02}$ decreased 12 mm Hg. The non-vascular water content of the body is approximately 60 per cent of body weight or 600 ml/kg. Assuming that tissue dissolved oxygen in this 600 ml/kg also decreased 12 mm Hg, the quantity of oxygen released would be $12 \times (0.023/760) \times 600 = 0.22$ ml oxygen/kg body weight. During this period, mixed venous oxygen content decreases 2.64 vol. per cent. Assuming total blood volume in the dog equals 10 per cent body weight with three-fourths venous, the quantity of oxygen released from mixed venous blood $(2.64 \times 0.75)$ equals 1.98 ml oxygen per kg body weight. The quantity liberated from tissues is at most 10 per cent of that made available from the venous reservoir and in terms of the total body reservoir is generally considered of minimal importance. Oxygen in muscle myoglobin is considered to be unavailable under the conditions described here (Farhi, 1964).

Rates of oxygen turnover.

Although separation of the oxygen stores of the body into three compartments, alveolar, arterial and venous, allows consideration of the effects of ventilation and cardiac output on the different compartments, the quantitative effects of one upon another is a highly complex relationship. However, we can use an approximation to demonstrate the relation of turnover rates to the volume of oxygen exchanged. When flow through a compartment is constant, and when mixing in the compartment is uniform, then the rate of change of concentration of the substance in question will proceed at a predictable rate when the substance in question in the compartment which had previously been at constant concentration is presented with a step change in the input concentration. The relationship describing rate of change under these conditions is known as the time-constant (TC).

$$TC = \frac{\text{Volume of compartment}}{\text{Flow}}.$$  

For example, in the present study the average volume of the venous compartment was assumed to be equal to 75 per cent of the average blood volume $(0.75 \times 0.10 \times 11 \text{ kg})$ or 0.825 l. Cardiac output averaged 0.85 l./min. Therefore if a step change in concentration were presented

$$TC = 0.825 \frac{l.}{0.85 \text{ l./min}} = 0.97 \text{ min}.$$  

For purposes of illustration the theoretical venous half-time $= \log_{2} \cdot \text{time-constant} = 0.67$ min $(0.693 \cdot 0.97 \text{ min})$. The observed half-time in venous blood was 0.75 min, about 10 per cent greater, and results from the actual conditions present physiologically, namely the fact that although the alveolar and arterial concentrations turn over rapidly, the change is not instantaneous and therefore a step change cannot be presented to the venous compartment.

Implications.

Recognition of the limited and labile nature of the oxygen stores of the body is essential in assessing methods of maintaining patient oxygenation during anaesthesia. In addition, the turnover rates measured here will be useful in developing models to predict changes in body oxygen content during anaesthesia with controlled breathing and hyperventilation.

ACKNOWLEDGEMENTS

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REFERENCES


TURN-OVER D'OXYGENE DANS LE RESERVOIR VEINEUX

Des chiens paralysés anesthésiés ont été hyperventilés (Paco2 = 15 mm Hg) durant deux heures, afin d'étudier les dépôts d'oxygène dans le corps. Au cours des 30 dernières minutes, le mélange respiré a été changé d'oxygène en air. La vitesse à laquelle les concentrations alvéolaires et artérielle d'oxygène atteignaient leur nouveau taux permanent, est représenté par les demi-temps (t½) respectifs de 0,17 et 0,23 minutes. Le turn-over de l'oxygène du sang veineux était considérablement plus lent, t½ = 0,75 minutes. Les données présentées serviront à construire des modèles, servant à prédire les changements des taux d'oxygène dans l'organisme durant l'anesthésie sous respiration contrôlée et hyperventilation.

SAUERSTOFFUMSATZ IM VENENBLUT

ZUSAMMENFASSUNG

Bei einer Untersuchung der Sauerstoffspeicher des Körpers wurden paralysierte Hunde in Narkose zwei Stunden lang hyperventiliert (Paco2 = 15 mm Hg). Während der letzten 30 Minuten enthielt das Atemungsgemisch statt Sauerstoff Luft. Die Geschwindigkeit, mit der sich die Sauerstoffkonzentration im Bereich der Alveolen und Arterien dem neuen Gleichgewichtszustand näherte, betrug, durch die Halbzeit (t½) dargestellt, 0,17 bzw. 0,23 Minuten. Im Venenblut änderte sich der Sauerstoffgehalt mit t½ = 0,75 Minuten beträchtlich langsamer. Die hier gemachten Angaben werden bei der Konstruktion von Modellen zur Vorhersage der Sauerstoffgehaltsänderungen im Körper während der Narkose bei kontrollierter Beatmung und Hyperventilation von Nutzen sein.