Alveolar partial pressures of carbon dioxide and oxygen measured by a heli

J Jordanoglou, G Tatsis, J Danos, S Gougoulakis, D Orfanidou, M Gaga

Abstract
A non-invasive technique was developed for measuring alveolar carbon dioxide and oxygen tension during tidal breathing. This was achieved by solving the Bohr equations for mean alveolar carbon dioxide and oxygen tension (PACO₂, PAO₂) from known values of the deadspace:tidal volume ratio measured by helium washout, and from the mixed expired partial pressure of carbon dioxide and oxygen. The derived values of wPACO₂ and wPAO₂ were compared with PACO₂ obtained from arterial gas analysis and PAO₂ calculated from the ideal air equation. Four normal subjects and 58 patients were studied. Calculated and measured PCO₂ values agreed closely with a difference in mean values (wPACO₂ – PACO₂) of 0.01 kPa; the SD of the differences was 0.7 kPa. The difference in mean values between wPAO₂ and PAO₂ was 0.02 kPa; the SD of the differences was 0.93 kPa. The method is simple and not time consuming, and requires no special cooperation from the patients. It can be applied in the laboratory or at the bedside to any subject breathing tidally. Physiological deadspace:tidal volume ratio, PAO₂ and PACO₂, static lung volumes, respiratory exchange ratio, carbon dioxide production, oxygen uptake, tidal volume, and total ventilation can be measured with acceptable accuracy and reproducibility in one test. An arterial blood sample is needed initially to provide an independent measure of PAO₂ and for measurement of the alveolar-arterial PO₂ difference. Subsequently, PAO₂ can be estimated from wPAO₂ sufficiently well for clinical purposes and PAO₂ or SAO₂ can be monitored by non-invasive methods.

Methods
PROTOCOL
We studied 62 subjects, 52 men and 10 women, aged 30–75 years. The subjects consisted of four normal subjects (doctors working in the unit) and 58 patients with chronic bronchitis and emphysema, asthma, or lung fibrosis of different causes. The patients were investigated as part of their routine assessment before and after treatment. The procedure can be divided into three stages (fig 1).

A Helium equilibration between lungs and spirometer
For helium equilibration between lungs and spirometer1 the subject first rebreathed helium in a closed circuit, as for measurement of functional residual capacity (FRC). Rebreathing was discontinued when the helium fractional concentration measured at the mouth had remained stable in both respiratory phases for about one minute (FeO).

B Helium washout from the lungs
The patient breathed ambient air quietly through the valve system (A and B, fig 1) until the fractional concentration of helium in the last expire (n—that is, Fn) was 1–2%. The mean helium fractional concentration (Fe) in mixed expired air was measured in bag 1.

C Expired helium free air collection
One to two minutes after stage B subjects were asked to breathe quietly through valves A and B as previously but expired air was now collected in bag 2. The mean fractional concentrations of carbon dioxide (FECO₂) and oxygen (FEO₂) were then measured in bag 2. Arterial blood was sampled in the middle of the expired air collection for measurement of PAO₂ and PAO₂.

The method can also be applied with the subject breathing oxygen enriched inspired air, provided that the inspired concentration of oxygen remains stable during the entire procedure.

The test requires the subjects to breathe tidally at their own rate for about 10 minutes through a mouthpiece while in a sitting or semirecumbent posture. The method can be applied by a technician in the laboratory or at the bedside, and in total takes 20–30 minutes.

The following indices were calculated from the results of the helium washout test: functional residual capacity (FRC), the physiological deadspace:tidal volume ratio measured by the classical carbon dioxide method (Vd/Vt) and by the helium washout.
Alveolar partial pressures of carbon dioxide and oxygen measured by a helium washout technique

Figure 1 Diagram of the mechanical system used for the helium washout technique.

 technique (wVD/VT), alveolar carbon dioxide and oxygen tensions measured by the helium washout technique (wPAO2, wPAO2), the respiratory exchange ratio (RE), carbon dioxide production (VCO2), oxygen uptake (VO2), minute ventilation (VE), and tidal volume (VT). Alveolar carbon dioxide and oxygen tensions (wPAO2, wPAO2) were calculated according to equations 1 and 2 (appendix). Alveolar oxygen tension was also calculated from the ideal air equation (PAO2).

Subjects underwent the helium washout test on two consecutive occasions; a mean value of wPAO2 and wPAO2 was then used. PAO2 was measured once.

INSTRUMENTATION
A water spirometer (Mijnhardt Volutest) was used. Valves A, C, and D were two way valves and valve B a one way Rudolph valve (1400) (dead space 50 ml). The total dead space of the system, including mouthpiece, tubing, and valves A and B, was 100 ml. Expired volume was measured by a screen (Fleisch No II) connected to a pneumotachograph (Godart) attached to a pen recorder or oscilloscope. The heli um fractional concentration in the spirometer, bag 1, and each expiration was measured by a helium–carbon dioxide meter (Mijnhardt; linear response up to 90%, response time < 100 ms) connected to a pen recorder. The same instrument was used to measure carbon dioxide concentration in each expiration in stage C. The concentration of oxygen and carbon dioxide in bag 2 (FeO2, Fco2) was measured by an oxygen–carbon dioxide analyser (Penyves and Gut). Arterial PO2 and Pco2 were measured by oxygen and carbon dioxide electrodes (ABL 2, Radiometer). The results were calculated on the Hewlett-Packard 85 computer.

STATISTICAL ANALYSIS
The relations between the derived and measured blood gas pressures were explored by the method of Bland and Altman. The limits of agreement for the two measurements were calculated from the mean (x) of the differences (wPAO2 – PAO2) or (wPAO2 – PAO2) and from the standard deviation of the differences (SD) (limits of agreement = x ± 2 SD). The 95% confidence intervals (CI) for the bias was calculated as x ± 2 × SEm.

Results
ALVEOLAR PO2
PAO2 ranged from 4 to 9·3 kPa. The mean difference between wPAO2 and PAO2 was 0·01 kPa (95% CI = 0·19 to −0·17 kPa; table). The SD of the differences was 0·7 kPa. Alveolar carbon dioxide tension estimated

Analysis of the results according to the method of Bland and Altman showing the degree of agreement between the values for alveolar carbon dioxide tension obtained by the helium washout technique (wPAO2) and arterial carbon dioxide tension (PAO2) and between the helium washout alveolar oxygen tension (wPAO2) and arteriole oxygen tension estimated from the ideal air equation

<table>
<thead>
<tr>
<th>Measuring agreement</th>
<th>wPAO2 (eqn 1) related to PAO2</th>
<th>wPAO2 (eqn 2) related to PAO2 (ideal air eqn)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean of the differences (kPa)</td>
<td>0·01</td>
<td>0·02</td>
</tr>
<tr>
<td>Standard deviation of the differences (kPa)</td>
<td>0·70</td>
<td>0·93</td>
</tr>
<tr>
<td>Limits of agreement (kPa)</td>
<td>1·41</td>
<td>1·87</td>
</tr>
<tr>
<td>Upper</td>
<td>1·39</td>
<td>1·83</td>
</tr>
<tr>
<td>Lower</td>
<td>−1·39</td>
<td>−1·83</td>
</tr>
<tr>
<td>95% confidence interval for the bias (kPa)</td>
<td>0·19 to −0·17</td>
<td>0·26 to −0·22</td>
</tr>
</tbody>
</table>
Figure 2  Relation between the individual values of the helium washout alveolar carbon dioxide tension \( \text{wPACO}_2 \), estimated from equation 1, and those of the arterial carbon dioxide tension \( \text{PACO}_2 \). The line is the regression line.

Figure 3  Individual values of the helium washout alveolar oxygen tension \( \text{wPAO}_2 \), estimated from equation 2, in relation to those of alveolar oxygen tension estimated from the ideal air equation. The line is the regression line.
from equation 1 (wPAco2) was related to PAco2 according to equation a:

\[
wPAco2 = 0.1610 + \, 0.9763 \times PAco2 \, kPa \quad (a)
\]

(in traditional units wPAco2 = 1.2078 + 0.9763 \times PAco2 mm Hg) (fig. 2).

**ALVEOLAR P02**

PAo2, derived from the ideal air equation, ranged from 8 to 14.7 kPa. The mean difference between wPAO2 and PAO2 was 0.02 (95% CI 0.26 to 0.22) kPa (table). The SD of the differences was 0.93 kPa.

Alveolar oxygen tension calculated from equation (2) (wPAO2) was related to PAO2 according to equation (b):

\[
wPAO2 = 0.7358 + 0.9388 \times PAO2 \, kPa \quad (b)
\]

(in traditional units wPAO2 = 5.5186 + 0.9388 \times PAO2 mm Hg) (fig. 3).

The mean value of wPAO2 was 11.96 (SD 1.68) kPa. The mean value of PAO2, calculated from the ideal air equation on the basis of wPAO2 instead of PAO2, was 11.95 (SD 1.68) kPa.

The mean difference between duplicate measurements was 0.33 (range 0-0.87) kPa for wPAO2 and 0.23 (range 0-0.65) kPa for wPAco2.

**Discussion**

The alveolar air composition is still a matter of debate, because PAO2 and PAco2 cannot be measured accurately while a subject breathes quietly. A traditional approach to determining PAco2 is to use the Bohr equation,

\[
Vd/Vt = 1 - \text{FEco2/PAco2}
\]

given that the deadspace/tidal volume ratio for carbon dioxide (Vd/Vt) is known. In normal subjects and in patients with chronic bronchitis, asthma, and pulmonary fibrosis the Vd/Vt ratio for carbon dioxide is very similar to that obtained by the helium washout technique (wVd/Vt). The close relation between wVd/Vt and Vd/Vt can be explained on theoretical grounds. In an ideal lung (Vd = 0) the decay in helconcentration in the expired air during the washout procedure follows a power equation of the form \(F_e = F_o \times x^{-n}\) (where \(x = 1 + Vd/VT\)) the mean value of this change is FEi. As there is no deadspace the mean fractional concentration of helium in the alveolar air (Fia) is equal to FEi. In real lungs (Vd \(\neq 0\)) the mean fractional concentration of helium in mixed expired air (Fie) is smaller than FEi. The terms in the above power equation have the same value in real and ideal lungs, so the difference (FEi – FEi) is solely due to the decrease in helium concentration in the collecting bag resulting from the helcon free volume of deadspace air \([n \times (VT - Vd)]\). As the volume of helcon expired from real lungs during the multibreath washout procedure is equal to that from the ideal lungs, the ratio of the alveolar part of the tidal volume (VA) to tidal volume (VT) is equal to FEi/Fie. The ratio VA/VT is also incorporated in the Bohr equation for carbon dioxide (FEco2/PAco2). If the mechanisms of intrapulmonary gas mixing responsible for the reduction in gas concentration from mean alveolar to mixed expired gas during quiet breathing are equally effective for helcon and carbon dioxide, the ratio FEi/Fie must equal the ratio FEco2/PAco2. This has been shown for helcon and sulphur hexafluoride, the washout curves of which are very close. FEco2 and FEi represent the mean carbon dioxide and helcon fractional concentrations respectively in the collection bag, obtained from all alveolar compartments whether slow or fast emptying. In these compartments the alveolar carbon dioxide fractional concentrations, which depend on the local VA/Qc ratios, can be represented by a mean value, PAco2, the term used in the Bohr equation to calculate the overall physiological deadspace/tidal volume ratio. PACO2 is the perfusion weighted mean value of carbon dioxide partial pressures in blood from all perfused alveolar compartments, complete equilibration between alveolus and end capillary blood being assumed. The wVd/Vt ratio expresses only the gas distribution within the airspace of the lungs whereas Vd/Vt, calculated on the basis of PAco2 as an estimate of PACO2, is affected by abnormalities in the pulmonary circulation and by diffusion defects in the alveolar membrane. In most instances, however, membrane diffusion defects and pulmonary right to left shunt (except when large) do not affect the Vd/Vt ratio for carbon dioxide. wVd/Vt therefore provides a good estimate of PAco2. There are certain conditions in which differences would be expected between wVd/Vt and Vd/Vt and between wPAco2 and PAco2. In non-steady state hyperventilation and in pulmonary embolism, for example, wVd/Vt will be less than Vd/Vt and wPAco2 lower than PAco2. This requires further investigation; no patient with pulmonary embolism was included in our study.

As shown in figure 2, there was a reasonably close linear correlation between wPAco2 and PAco2. The difference between wPAco2 and PAco2 values in individual subjects was up to 1.4 kPa (mean difference with 2 SD) (table). This difference will to some extent represent the noise of the two methods but may also reflect a real difference between these two terms in the patients studied.

There was also a reasonably close linear relation between alveolar oxygen tension measured from the ideal air equation (PAo2) and wPAO2 (fig. 3). The difference between wPAO2 and PAO2 was abolished when wPAO2 was used instead of PAO2 in the ideal air equation, because both the Bohr equation for oxygen and the ideal air equation are derived from the equation of the respiratory exchange ratio.

The rebreathing method of Campbell and Howell for measuring alveolar carbon dioxide tension takes less time and equipment than the method described here, but there is no accurate way of predicting arterial PCO2 from the oxygenated mixed venous value. The procedure we describe requires no special cooperation from the patient, who has only to breathe tidally at his own rate, whether in the laboratory or in the ward. Static lung volumes, the
physiological deadspace: tidal volume ratio, alveolar oxygen and carbon dioxide tension, the respiratory exchange ratio, carbon dioxide production and oxygen uptake, tidal volume, and minute ventilation can all be measured easily with acceptable accuracy and reproducibility. Patients with respiratory failure can be monitored non-invasively after an initial arterial sample has been taken for blood gas analysis. Measurement of alveolar carbon dioxide tension (w\(P_{aco2}\)), arterial oxygen saturation by ear or pulse oximetry, or tissue oxygen tension by the transcutaneous electrode (\(P_{to2}\)) may reduce the need for an arterial puncture. Arterial blood sampling is needed only when alveolar gas tensions have to be related to arterial blood gas tensions, mainly to determine the alveolar-arterial oxygen gradient.

We would like to express our thanks to Dr Neil Pride for his constructive criticism.


Appendix
The alveolar carbon dioxide and oxygen fractional concentrations were calculated according to equations 1 and 2 respectively.*

\[wF_{aco2} = \frac{F_{e} - V_{D} \times \left(\frac{1}{V_{t}} - \frac{1}{V_{t}}\right)}{F_{e} + V_{D} \times \left(\frac{1}{V_{t}} - \frac{1}{V_{t}}\right)}\]  
and \[wF_{ao2} = \frac{F_{e} - F_{i} \times V_{D} \times \left(\frac{1}{V_{t}} - \frac{1}{V_{t}}\right)}{F_{e} + V_{D} \times \left(\frac{1}{V_{t}} - \frac{1}{V_{t}}\right)}\]

and \[wF_{ao2} = wF_{aco2} \times (P_{a} - 47)\],

where \(F_{e}\), derived from the washout curve, is the ideal mean concentration of helium in the expired air if there were no deadspace, \(V_{D}\) is the deadspace of the valve system (0·1 L), \(V_{t}\) is the tidal volume during the helium washout from the lungs, and \(V_{t}\) is the tidal volume during the collection of expired air after complete washout of helium.

*The full formulae are available on request.