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Research Article

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Correction for Mechanical Dead Space in the Calculation of Physiological Dead Space

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ABSTRACT When physiological dead space (V_{D_p}) is calculated for a patient who has alveolar dead space, e.g., after pulmonary vascular occlusion, less than the full volume of attached mechanical dead space (V_{D_m}) appears in the measured dead space (V_{D_n}). Under these conditions the traditional subtraction of V_{D_m} from V_{D_n} leads to underestimation of V_{D_p} and can give a falsely small ratio of V_{D_p} to tidal volume (V_T) when, in fact, an abnormally large V_{D_p}/V_T exists. To make the proper correction for V_{D_m}, two equations have been derived and validated with seven subjects having V_{D_p}/V_T from 0.29 to 0.87, using V_{D_m}'s from 120 to 322 ml. With only a small modification, these equations are suitable for routine clinical use and give V_{D_p}/V_T within 0.02 of that by the validated equations (32 of 33 comparisons). The fraction of V_{D_m} subtracted from V_{D_n} is the square of the ratio of effective alveolar to total alveolar ventilation and is never >1. This fraction is $(PA_{CO_2}/Pa_{CO_2})^2$, where PA_{CO_2} and Pa_{CO_2} are the mean partial pressures of expired alveolar and of arterial CO_2; in the other equation this fraction is $[PE_{CO_2}/Pa_{CO_2}(V_T - V_{D_{an}} - V_{D_m})]^2$ where PE_{CO_2} is mixed expired P_{CO_2} and $V_{D_{an}}$ is anatomical dead space. The second equation requires an estimated $V_{D_{an}}$ and is applicable when PA_{CO_2} is not measured or does not plateau (as in exercise).

INTRODUCTION

Physiological dead space (V_{D_p})[1] is becoming a more useful index of impaired perfusion of pulmonary vessels as normal values and conditions for V_{D_p} become more precisely defined (1). When a normal adult breathes spontaneously at a normal tidal volume (V_T), V_{D_p}/V_T is <0.45 and decreases with increased V_T (1, 2). V_{D_p}/V_T may increase with age (1) and with a variety of parenchymal lung diseases. However, a very large ratio (e.g., 0.8 at a normal V_T) or an increase of this ratio with the increased V_T of exercise (2) supports the diagnosis of pulmonary vascular occlusion.

In the traditional calculation of V_{D_p}, all of the mechanical dead space (V_{D_m}) is subtracted from the measured dead space (V_{D_n}).[2] As given in Enghoff's modified Bohr equation (3),

$$V_{D_p} = V_{D_n} - V_{D_m} = \frac{Pa_{CO_2} - PE_{CO_2}}{Pa_{CO_2}} \cdot V_T - V_{D_m}, \quad (1)$$

where Pa_{CO_2} and PE_{CO_2} are the partial pressures of CO_2 in arterial blood and mixed expired gas, respectively. Suwa and Bendixen have analyzed the change of Pa_{CO_2} with added V_{D_m} and have shown that total subtraction of V_{D_m} can lead to underestimation of V_{D_p} (4). This underestimation occurs whenever gas from V_{D_m} is inspired into nonperfused alveoli where it has no direct effect on gas exchange with alveolar capillary blood.

We have derived and validated two equivalent equations for making the proper calculation and present evidence that shorter modified forms give, with precision V_{D_p} at the V_T of the measurement (V_{T_n}).

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[1] *Abbreviations used in this paper:* f_p, fraction of ventilation to perfused alveoli; FA_{CO_2}, mean concentration of CO_2 in expired alveolar gas; FE_{CO_2}, concentration of CO_2 in mixed expired gas; PA_{CO_2} mean partial pressure of CO_2 (P_{CO_2}) in expired alveolar gas; Pa_{CO_2}, mean P_{CO_2} in arterial blood; PE_{CO_2}, P_{CO_2} in mixed expired gas; *r*, correlation coefficient; V_A, effective alveolar ventilation per breath; V_{CO_2}, volume of CO_2 expired per breath; $V_{D_{alv}}$, alveolar dead space; $V_{D_{an}}$, anatomical dead space; V_{D_m}, mechanical dead space; V_{D_n}, total measured dead space; V_{D_p}, physiological dead space; V_T, expired tidal volume.

[2] *Subscripts specific for this paper:* n, value measured with V_{D_m} attached; o, value without V_{D_m} attached.

METHODS

Derivation. The volume of $\mathrm{CO_2}$ expired in a breath ($\mathrm{V_{CO_2}}$) is given by

$$\mathrm{V_{CO_2} = FE_{CO_2}VT = FA_{CO_2}(VT - VD_{an} - VD_m)}, \quad (2)$$

where $\mathrm{FE_{CO_2}}$ and $\mathrm{FA_{CO_2}}$ are the mean concentrations of $\mathrm{CO_2}$ in the mixed expired gas and in the expired alveolar gas, respectively, and $\mathrm{VD_{an}}$ is anatomical dead space. Dividing by $\mathrm{Pa_{CO_2}VT}$ and converting concentrations to partial pressures:

$$\frac{\mathrm{VA_n}}{\mathrm{VT}} = \frac{\mathrm{PE_{CO_2}}}{\mathrm{Pa_{CO_2}}} = \frac{\mathrm{PA_{CO_2}(VT - VD_{an} - VD_m)}}{\mathrm{Pa_{CO_2} \cdot VT}}, \quad (3)$$

where $\mathrm{VA_n}$ is measured effective alveolar ventilation per breath.

To derive equations for $\mathrm{VD_p}$, we have assumed that addition of $\mathrm{VD_m}$ does not change the fraction of ventilation to perfused alveoli ($\mathrm{f_p}$). Using the equation for $\mathrm{f_p}$ derived by Julian, Travis, Robin, and Crump (5), and denoting, respectively, the conditions with and without $\mathrm{VD_m}$ by "n" and "o":

$$\mathrm{f_p} = \frac{\mathrm{PE_oCO_2}}{\mathrm{Pa_oCO_2 - PA_oCO_2 + PE_oCO_2}} = \frac{\mathrm{PE_nCO_2}}{\mathrm{Pa_nCO_2 - PA_nCO_2 + PE_nCO_2}} \quad (4)$$

Cross multiplying the middle and right sides of equation 4 and dividing by $\mathrm{Pa_oCO_2Pa_nCO_2}$:

$$\frac{\mathrm{PE_oCO_2}}{\mathrm{Pa_oCO_2}} - \frac{\mathrm{PE_oCO_2PA_nCO_2}}{\mathrm{Pa_oCO_2Pa_nCO_2}} = \frac{\mathrm{PE_nCO_2}}{\mathrm{Pa_nCO_2}} - \frac{\mathrm{PE_nCO_2PA_oCO_2}}{\mathrm{Pa_nCO_2Pa_oCO_2}}. \quad (5)$$

Substituting the left side of equation 3 (with appropriate subscripts) for the first term on each side of equation 5, and substituting the right side of equation 3 for $\mathrm{PE_{CO_2}/Pa_{CO_2}}$ in the second term on each side of equation 5:

$$\frac{\mathrm{VA_o}}{\mathrm{VT_o}} - \frac{\mathrm{PA_oCO_2PA_nCO_2(VT_o - VD_{an_o})}}{\mathrm{Pa_oCO_2Pa_nCO_2VT_o}} = \frac{\mathrm{VA_n}}{\mathrm{VT_n}} - \frac{\mathrm{Pa_oCO_2PA_nCO_2(VT_n - VD_{an_n} - VD_m)}}{\mathrm{Pa_oCO_2Pa_nCO_2VT_n}}. \quad (6)$$

Substituting ($\mathrm{VT_n - VD_n}$) for $\mathrm{VA_n}$ and ($\mathrm{VT_o - VD_{p_o}}$) for $\mathrm{VA_o}$:

$$\mathrm{VD_{p_o}} = \frac{\mathrm{VT_o}}{\mathrm{VT_n}}\left[\mathrm{VD_n} - \frac{\mathrm{PA_oCO_2PA_nCO_2}}{\mathrm{Pa_oCO_2Pa_nCO_2}} \cdot \left(\mathrm{VD_{an_n}} - \frac{\mathrm{VT_n}}{\mathrm{VT_o}} \cdot \mathrm{VD_{an_o}} + \mathrm{VD_m}\right)\right]. \quad (7)$$

Substitution for $\mathrm{PA_{CO_2}}$ from equation 3 gives an equivalent equation:

$$\mathrm{VD_{p_o}} = \frac{\mathrm{VT_o}}{\mathrm{VT_n}}\left[\mathrm{VD_n} - \frac{\mathrm{PE_oCO_2VT_o}}{\mathrm{Pa_oCO_2(VT_o - VD_{an_o})}} \cdot \frac{\mathrm{PE_nCO_2 \cdot VT_n}}{\mathrm{Pa_nCO_2(VT_n - VD_{an_n} - VD_m)}} \cdot \left(\mathrm{VD_{an_n}} - \frac{\mathrm{VT_n}}{\mathrm{VT_o}} \cdot \mathrm{VD_{an_o}} + \mathrm{VD_m}\right)\right]. \quad (8)$$

The validity of equations 7 and 8 can be tested by calculating $\mathrm{VD_{p_o}}$ for the same subjects with different $\mathrm{VD_m}$'s. If the assumption holds that $\mathrm{f_p}$ remains constant with added $\mathrm{VD_m}$, then $\mathrm{VD_{p_o}}$ (and $\mathrm{VD_{p_o}/VT_o}$) should remain constant.

In the routine measurement of dead space, $\mathrm{VD_{p_o}}$ is always calculated for $\mathrm{VT_o = VT_n}$. If $\mathrm{VD_{an_o} = VD_{an_n}}$, then equations 7 and 8 simplify to

$$\mathrm{VD_{p_o}} = \mathrm{VD_n} - \left[\frac{\mathrm{PA_oCO_2PA_nCO_2}}{\mathrm{Pa_oCO_2Pa_nCO_2}}\right] \cdot \mathrm{VD_m} \quad (9)$$

$$\mathrm{VD_{p_o}} = \mathrm{VD_n} - \left[\frac{\mathrm{PE_oCO_2VT}}{\mathrm{Pa_oCO_2(VT - VD_{an})}} \cdot \frac{\mathrm{PE_nCO_2VT}}{\mathrm{Pa_nCO_2(VT - VD_{an} - VD_m)}}\right] \cdot \mathrm{VD_m}. \quad (10)$$

Since equations 9 and 10 are equations 7 and 8 at the VT and $\mathrm{VD_{an}}$ of the measurement, experimental validation of equations 7 and 8 also validates 9 and 10.

If it can be shown that substitution of $\mathrm{PA_nCO_2/Pa_nCO_2}$ for $\mathrm{PA_oCO_2/Pa_oCO_2}$ (and the equivalent substitution in equation 10) result in very little error, then two good working equations are

$$\mathrm{VD_p} = \mathrm{VD_n} - \left[\frac{\mathrm{PA_nCO_2}}{\mathrm{Pa_nCO_2}}\right]^2 \cdot \mathrm{VD_m} \quad (11)$$

$$\mathrm{VD_p} = \mathrm{VD_n} - \left[\frac{\mathrm{PE_nCO_2 \cdot VT}}{\mathrm{Pa_nCO_2(VT - VD_{an} - VD_m)}}\right]^2 \cdot \mathrm{VD_m}. \quad (12)$$

These equations, like equations 9 and 10, give $\mathrm{VD_p}$ at $\mathrm{VT_n}$; but they require data from only a single collection.

Measurements. $\mathrm{VD_n}$ was measured in seven men chosen to represent a wide range of $\mathrm{VD_p/VT}$. The men sat upright and breathed spontaneously through a rubber mouth piece and Hans-Rudolph valve with a combined $\mathrm{VD_m}$ of 120 ml. Additional measurements were made with pipes of varying lengths and internal diameter of 2 cm between the mouth piece and valve. Expired gas was collected in a 350 liter gasometer. The subjects breathed through each $\mathrm{VD_m}$ for at least 8 min before each measurement was begun. Arterial blood was collected from an indwelling catheter during the middle minute of a 3 min gas collection. End-tidal $\mathrm{CO_2}$ at the mouth and mixed expired $\mathrm{CO_2}$ from the gasometer were measured with an infrared $\mathrm{CO_2}$ meter. Alveolar $\mathrm{CO_2}$ plateaued for each subject. Correction was made for the volume of gas lost through the $\mathrm{CO_2}$ meter, and the total volume of expired gas was corrected to BTPS (body temperature, pressure, saturated with water) $\mathrm{P_{CO_2}}$, $\mathrm{P_{O_2}}$, and pH were measured with an Instrumentation Laboratory blood gas analyzer (Instrumentation Laboratory Inc., Lexington, Mass.). Both the infrared $\mathrm{CO_2}$ meter and the $\mathrm{CO_2}$ electrode were calibrated with the same gases, previously analyzed with the Scholander 0.5 $\mathrm{cm^3}$ gas analyzer. Duplicate measurements using the same $\mathrm{VD_m}$ were made for six of the men. The reproducibility of $\mathrm{VD_n/VT}$ was within 0.02 for five men; the sixth (C. W.) had very disparate VT's with the same $\mathrm{VD_m}$. Of the 41 collections, one deviated inexplicably for C. O. from all the other results (duplicate measurement with 120 ml $\mathrm{VD_m}$) and was discarded; however, duplicate measurements with 218 ml $\mathrm{VD_m}$ were made with perfect agreement for $\mathrm{VD_n/VT}$.

Calculations. $\mathrm{VD_p}$ (and $\mathrm{VD_p/VT_n}$) were calculated for each collection using no correction ($\mathrm{VD_n}$), the traditional correction (equation 1), and equations 9–12. Equations 7 and 8 were tested by using the VT and P_{CO_2}'s of the initial condition (with 120 ml V_{D_m}) for the "o" condition (without V_{D_m}). Equations 8 and 10 include 120 ml V_{D_m} in the denominator of the ventilation ratio for the "o" condition. The last collection (instead of the first with the same 120 ml V_{D_m}) was used to calculate $V_{D_{po}}/V_{T_o}$ for C. W., because his initial VT far exceeded all subsequent VT's. The mean end-tidal P_{CO_2} was used for $P_{A_{CO_2}}$, and $V_{D_{an}}$ was estimated from ideal body weight (6, 7). Where $[P_{E_{CO_2}}V_T/Pa_{CO_2}(V_T - V_{D_{an}} - V_{D_m})]$ was >1 (C. O.), a value of 1 was used.

Regression lines (8) for V_{D_p}/V_T on V_{D_m}/V_T were calculated for each method and each subject. Comparisons of V_{D_p}/V_{T_n} by equations 11 with 9 and by 12 with 10 were made, and correlation coefficients (*r*) were calculated (8). The initial

TABLE I

V_{D_p}/V_T with Added V_{D_m} Calculated by (a) *No Correction for V_{D_m},* (b) *Traditional Correction,* (c) *Equation 7, and* (d) *Equation 8*

Subject, diagnosis, age, height, estimated $V_{D_{an}}$	V_{D_m}	V_T	Respiration rate per min	$P_{E_{CO_2}}$	$P_{A_{CO_2}}$	Pa_{CO_2}	$\frac{V_{D_n}}{V_{T_n}}$ (a)	$\frac{V_{D_p}}{V_{T_n}}$ (b)	$\frac{V_{D_{po}}}{V_{T_o}}$ (c)	$\frac{V_{D_{po}}}{V_{T_o}}$ (d)
	ml	*ml*		*mm Hg*	*mm Hg*	*mm Hg*				
C. O.	120	473	19.0	18.0	36.9	38	0.53	0.27	0.29	0.27
Asthma in remission,	170	515	20.7	16.4	36.1	37	0.55	0.22	0.26	0.25
40 yr, 69 inches,	218	538	21.3	14.9	37.8	41	0.64	0.23	0.31	0.27
141 ml	270	591	21.0	13.9	38.7	42	0.67	0.21	0.32	0.27
	322	652	21.3	13.6	39.2	42	0.68	0.18	0.30	0.26
	218	538	22.0	14.7	36.8	41	0.64	0.24	0.33	0.28
C. W.	120	891	10.7	22.4	37.8	40	0.44	0.31	0.42	0.42
Emphysema-bronchitis,	170	696	14.0	20.2	37.3	45	0.55	0.30	0.43	0.43
55 yr, 67 inches,	218	649	16.3	16.8	34.4	45	0.62	0.29	0.45	0.43
130 ml	270	732	14.3	16.8	36.9	45	0.63	0.26	0.44	0.42
	322	689	16.0	14.9	36.9	46	0.67	0.21	0.42	0.35
	120	518	16.7	19.0	34.4	44	0.57	0.33	0.42	0.40
J. R.	120	890	9.7	17.8	33.5	41	0.57	0.43	0.48	0.52
Bronchitis-emphysema,	170	800	13.0	17.3	30.9	42	0.59	0.38	0.45	0.50
70 yr, 66 inches,	218	890	11.7	16.3	32.8	42	0.61	0.37	0.46	0.52
120 ml	270	840	14.0	14.3	33.6	43	0.67	0.35	0.46	0.54
	322	900	14.0	13.0	32.0	43	0.70	0.34	0.48	0.57
	120	730	13.3	18.2	30.4	40	0.55	0.38	0.42	0.47
M. C.	120	692	22.0	19.1	32.0	45	0.58	0.40	0.49	0.50
Emphysema-bronchitis,	170	694	24.0	16.4	29.6	42	0.61	0.37	0.49	0.49
56 yr, 69.5 inches,	218	759	21.0	13.5	27.7	40	0.66	0.37	0.53	0.54
144 ml	270	734	21.0	14.5	31.6	42	0.66	0.29	0.47	0.47
	322	823	21.0	13.4	29.8	43	0.69	0.30	0.51	0.51
	120	727	21.7	15.5	25.9	37	0.58	0.42	0.51	0.51
H. V.	120	1013	21.7	16.3	27.1	40	0.59	0.47	0.53	0.55
Bronchitis-emphysema,	170	910	20.3	16.7	28.1	41	0.59	0.40	0.49	0.51
56 yr, 73 inches,	218	979	18.7	14.9	27.3	40	0.63	0.40	0.52	0.55
165 ml	270	1043	18.3	15.6	28.4	39	0.60	0.35	0.48	0.51
	322	1162	17.3	14.6	28.4	40	0.63	0.35	0.51	0.54
	120	1091	19.0	15.3	24.9	36	0.58	0.47	0.53	0.55
E. B.	120	580	19.0	16.3	32.4	59	0.72	0.52	0.66	0.67
Emphysema-bronchitis,	170	636	19.3	16.7	36.6	61	0.73	0.46	0.65	0.66
56 yr, 69 inches,	218	642	16.7	15.6	41.4	65	0.76	0.42	0.65	0.68
141 ml	270	712	16.0	15.1	38.2	64	0.77	0.39	0.66	0.67
	322	729	16.0	14.0	38.7	64	0.78	0.34	0.65	0.65
	120	556	20.7	16.0	32.3	57	0.72	0.50	0.65	0.66
L. H.	120	478	33.0	7.1	16.8	59	0.88	0.63	0.86	0.87
Embolism-emphysema,	170	470	34.3	6.5	19.6	63	0.90	0.54	0.87	0.88
62 yr, 63.5 inches,	218	501	36.0	5.9	22.0	62	0.90	0.47	0.86	0.88
113 ml	270	507	37.3	5.3	23.0	63	0.92	0.38	0.86	0.87

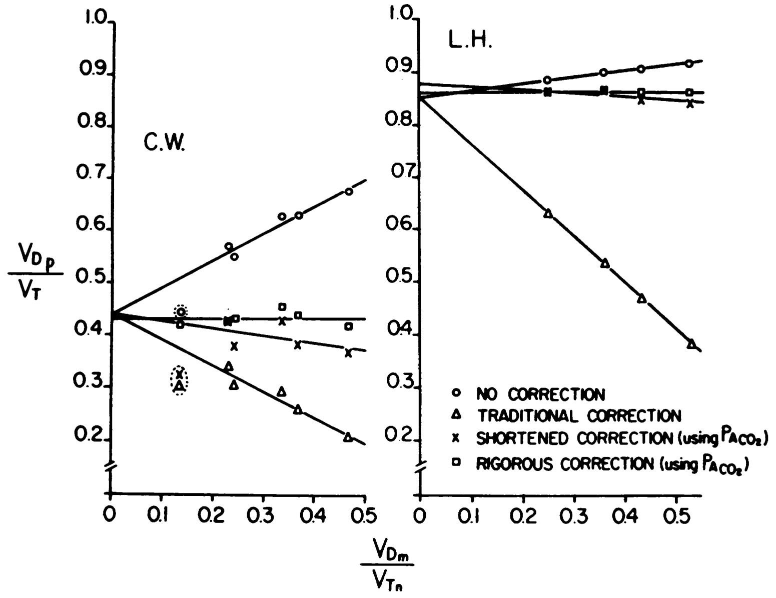

FIGURE 1 The change of V_{D_p}/V_T with added V_{D_m} for C. W. and L. H. Values plotted are by (*a*) no correction for V_{D_m}, (*b*) traditional correction (equation 1), (*c*) shortened equation 11, and (*d*) rigorous equation 7. Extrapolation of the regression lines to $V_{D_m} = 0$ indicates the approximate V_{D_p}/V_T of the subject when breathing without V_{D_m}. The decrease of V_{D_p}/V_T by equation 11 represents for C. W. a true decrease as a result of the increased V_T response to added V_{D_m} (see text). The three encircled points were calculated for an initial V_T 200 ml greater than any succeeding measurement. These data were not used in the calculation of regression lines because of the unusually large V_T.

measurements were not included in these correlations, because $P_{A_n}CO_2/P_{a_n}CO_2$ and $P_{A_o}CO_2/P_{a_o}CO_2$ (and their equivalents in equations 10 and 12) were identical.

RESULTS

Fig. 1 shows V_{D_p}/V_T calculated by four methods for C. W. and L. H. The intercepts of the regression lines at $V_{D_m} = 0$ indicate the approximate V_{D_p}/V_T ratios of the patients when breathing without V_{D_m}. As V_{D_m}/V_{T_n} increases, V_{D_n}/V_{T_n} and the traditional correction for C. W. appear to deviate equally from the intercept value of 0.44; neither gives the proper value. For L. H. (pulmonary embolism), the increase in V_{D_n}/V_{T_n} is only 0.06 with 0.53 added V_{D_m}/V_{T_n} (270 ml V_{D_m}); when the traditional correction is used, V_{D_p}/V_T is 0.38, a gross underestimation of the 0.85 intercept. Table I (column b) shows for the group that underestimation of V_{D_p}/V_T by the traditional correction increased as alveolar dead space increased.

Equations 7 and 8 give $V_{D_{po}}$ at a constant V_T (the assumed value for V_{T_o}). In Fig. 1 the results from equation 7 (rigorous correction using $P_{A_{CO_2}}$) produce horizontal regression lines for both patients. This constancy in $V_{D_{po}}/V_{T_o}$ is shown in Table I for each of the seven subjects and for both equations. For six of the seven men the intercepts of the regression lines for equations 7 and 8 at zero V_{D_m} are within 0.02 of those for V_{D_n}/V_{T_n}.

Equations 9 and 10 calculate V_{D_p}/V_T at the V_T of the measurement (rather than at a constant V_T as in equations 7 and 8). With added V_{D_m} the subjects tended to increase V_T slightly and V_{D_p}/V_T by equations 9 and 10 decreases accordingly. The decrease for C. W. in Fig. 1 by equation 11 is essentially the same as by equation 9. This slight decrease represents a true decrease in V_{D_p}/V_T with spontaneously increasing V_T (1, 2). The encircled measurement in Fig. 1 (V_T 373 ml greater than the repeat with the same V_{D_m}) is further evidence of this true decrease.

Values for V_{D_p}/V_T by equations 11 and 12 agree within 0.02 of the values by the more rigorous equations 9 and 10 in 32 of 33 comparisons for both pairs of equations. The correlations are extremely high ($r = 0.998$ for each comparison).

DISCUSSION

Dead space in the original Bohr equation (9) or measured by Fowler's method (10) is $V_{D_{an}} + V_{D_m}$, i.e. mechanical dead space is simply an extension of $V_{D_{an}}$. However, physiological dead space includes alveolar dead space ($V_{D_{alv}}$) which is a functional volume (11), defined as the difference between physiological and anatomical dead space (12). $V_{D_{alv}}$ is primarily caused by reduced perfusion of alveoli relative to their ventilation (13). If V_{D_m} were simply an extension of $V_{D_{an}}$ during measurement of V_{D_n}, $V_{D_{alv}}$ would also equal $V_{D_n} - V_{D_{an}} - V_{D_m}$. The fact that V_{D_p} is underestimated when all of V_{D_m} is subtracted from V_{D_n} indicates that this is not so. As $V_{D_{alv}}$ increases an increasingly smaller fraction of dead space gas from V_{D_m} is inhaled into the perfused areas of the lung where it decreases effective ventilation (increases dead space). In the nonperfused alveoli V_{D_m} gas has little effect on dead space, i.e. effective ventilation cannot be decreased below 0. The nonperfused alveoli do contribute indirectly to gas exchange by exhaling part of the CO_2 inhaled from $V_{D_{an}}$ and V_{D_m} in the previous breath (12). When V_{D_m} is added, a smaller volume of this gas escapes to the outside, but its CO_2 concentration is greater. Equations 7 and 8 take all these changes into account.

The nearly horizontal slopes of $V_{D_{po}}/V_{T_o}$ on V_{D_m}/V_T and the agreement of the intercepts at $V_{D_m} = 0$ with those for V_{D_n}/V_T indicate the validity of equations 7 and 8 and of the assumption used in their derivation (that f_p does not change significantly with added V_{D_m}).

Equations 11 and 12 are good working equations to use with data from a single collection. As with the traditional correction for V_{D_m}, they apply only to the conditions (V_{T_n}, posture, spontaneous or assisted ventilation, etc.) of the measurement. The substitutions of $P_{A_n}CO_2/P_{a_n}CO_2$ for $P_{A_o}CO_2/P_{a_o}CO_2$, and the equivalent substitution using $V_{D_{an}}$ introduce little error as shown by the comparisons of equation 11 with 9 and 12 with 10.

Since the ratio within the brackets of equations 11 and 12 is the ratio of effective to total alveolar ventilation, it can never be >1. When the calculated P_{ACO_2}/P_{aCO_2} in equation 11, or the equivalent ratio in equation 12 is >1, simply subtract V_{D_m} from V_{D_n}.

Both equations 11 and 12 can be applied at large tidal volumes. However, if alveolar CO_2 does not plateau, e.g., during the hyperventilation of exercise, then equation 12 using $V_{D_{an}}$ is preferable. Any of several equations from the literature can be used for estimating $V_{D_{an}}$ (14, 15). When comparing V_{D_p}/V_T during exercise with rest, 3 ml should be added to the estimated $V_{D_{an}}$ for every 100 ml over the subject's resting V_T (1, 16). When V_T is very small, e.g., <300 ml for normal adults, correction for V_{D_m} is not dependable because alveolar ventilation begins before washout of $V_{D_{an}}$ and V_{D_m} is complete (17).

Clinically, V_{D_p}/V_T at normal tidal volumes gives a better index of alveolar dead space than do arterial-alveolar CO_2 gradients when there is coexistent uneven ventilation. In addition, hyperventilation of exercise can be used to distinguish the normal decrease of V_{D_p}/V_T from the increased V_{D_p}/V_T accompanying pulmonary vascular occlusion (2). Since hyperventilation requires low resistance breathing valves having significant dead space, the proper correction for V_{D_m} is important.

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REFERENCES

1. Lifshay, A., C. W. Fast, and J. B. Glazier. 1971. Effects of changes in respiratory pattern on physiological dead space. *J. Appl. Physiol.* **31**: 478.
2. Nadel, J. A., W. M. Gold, and J. H. Burgess. 1968. Early diagnosis of chronic pulmonary vascular obstruction. Value of pulmonary function tests. *Am. J. Med.* **44**: 16.
3. Enghoff, H. 1938. Volumen inefficax. Bemerkungen zur Frage des Schädlichen Raumes. *Upsala Läkarefören. Förh.* **44**: 191.
4. Suwa, K., and H. H. Bendixen. 1968. Change in Pa_{CO_2} with mechanical dead space during artificial ventilation. *J. Appl. Physiol.* **24**: 556.
5. Julian, D. G., D. M. Travis, E. D. Robin, and C. H. Crump. 1960. Effect of pulmonary artery occlusion upon end-tidal CO_2 tension. *J. Appl. Physiol.* **15**: 87.
6. Radford, E. P., Jr. 1955. Ventilation standards for use in artificial respiration. *J. Appl. Physiol.* **7**: 451.
7. Spector, W. S., editor. 1956. Handbook of Biological Data. W. B. Saunders Company, Philadelphia. 181.
8. Snedecor, G. W., and W. G. Cochran. 1967. Statistical Methods. Iowa State University Press, Ames. 6th edition. 135, 172.
9. Bohr, C. 1891. Ueber die Lungenathmung. *Skand. Arch. Physiol.* **2**: 236.
10. Fowler, W. S. 1948. Lung function studies. II. The respiratory dead space. *Am. J. Physiol.* **154**: 405.
11. Folkow, B., and J. R. Pappenheimer. 1955. Components of the respiratory dead space and their variation with pressure breathing and with bronchoactive drugs. *J. Appl. Physiol.* **8**: 102.
12. Severinghaus, J. W., and M. Stupfel. 1957. Alveolar dead space as an index of distribution of blood flow in pulmonary capillaries. *J. Appl. Physiol.* **10**: 335.
13. Riley, R. L., and A. Cournand. 1949. "Ideal" alveolar air and the analysis of ventilation-perfusion relationships in the lungs. *J. Appl. Physiol.* **1**: 825.
14. Hart, M. C., M. M. Orzalesi, and C. D. Cook. 1963. Relation between anatomic respiratory dead space and body size and lung volume. *J. Appl. Physiol.* **18**: 519.
15. Wood, L. D. H., S. Prichard, T. R. Weng, K. Kruger, A. C. Bryan, and H. Levison. 1971. Relationship between anatomic dead space and body size in health, asthma, and cystic fibrosis. *Am. Rev. Respir. Dis.* **104**: 215.
16. Shepard, R. H., E. J. M. Campbell, H. B. Martin, and T. Enns. 1957. Factors affecting the pulmonary dead space as determined by single breath analysis. *J. Appl. Physiol.* **11**: 241.
17. Briscoe, W. A., R. E. Forster, and J. H. Comroe, Jr. 1954. Alveolar ventilation at very low tidal volumes. *J. Appl. Physiol.* **7**: 27.