LABORATORY REPORTS

Anesthesiology
62:54–59, 1985

Errors in Measurement of Oxygen Uptake due to Anesthetic Gases

Stanley J. Aukburg, M.D., Ralph T. Geer, M.D.,† Harry Wollman, M.D.,‡ Gordon R. Neufeld, M.D.†*

Errors in measurement of exhaled gas volume, mixed expired oxygen and carbon dioxide concentrations, and inspired oxygen concentration and the presence of exhaled anesthetic agents cause errors in on-line calculated oxygen uptake that increase geometrically with increasing inspired oxygen concentration. No one has quantified the decrease in the magnitude of the error that might be realized if directly measured nitrogen concentration were included in the calculation. We used a computer model to evaluate this improvement, assuming an oxygen uptake of 200 ml/min and normal ventilatory parameters. Using a Monte Carlo technique, we generated 100 sets of data points, with random errors averaging 0.5% around the expected gas concentrations, and compared the accuracy of oxygen uptake calculated with and without inclusion of directly measured inspired and expired nitrogen concentrations. When the inspired oxygen fractions were 0.2, 0.5, and 0.8, the calculated oxygen uptakes ±% standard deviation were 200 ± 4.3, 200 ± 12, and 196 ± 21 when directly measured nitrogen was included *versus* 200 ± 3.5, 196 ± 16, and 205 ± 71 when it was not. The procedure was repeated, assuming 50 ml/min of anesthetic excretion and the calculated oxygen uptakes were 200 ± 4.6, 202 ± 12, and 195 ± 17 *versus* 212 ± 3.8, 251 ± 17, and 398 ± 64. Including direct measurement of inhaled and exhaled concentrations of nitrogen or another insoluble inert tracer gas allows accurate measurement of oxygen uptake, even in the presence of exhaled anesthetic gases. It also decreases the error in oxygen uptake determination by a factor of nearly six when the inhaled oxygen fraction is 0.8. (Key words: Anesthetics, volatile. Measurement techniques: oxygen consumption; errors.)

WHILE STEADY STATE CO_2 excretion can be reliably and accurately determined in most patients, oxygen uptake determination is difficult because it is necessary to account for the difference between inhaled and exhaled volumes. Oxygen uptake can be computed without measurement of inhaled volume by using calculated concentrations on an insoluble inert tracer gas, usually nitrogen, in both inhaled and exhaled gas, to estimate the inhaled volume.[1] The technique is based on the assumption that under steady state conditions there is no net transfer of the tracer equation (1).[2]

$$\dot{V}_{O_2} = \left[\frac{F\bar{E}_{N_2}}{FI_{N_2}} \times FI_{O_2} - F\bar{E}_{O_2}\right] \times \dot{V}_E \qquad (1)$$

Nitrogen fractions can be inferred by subtracting measured fractions of carbon dioxide and oxygen, in dried inhaled and exhaled gases, from unity equation (2).

$$\dot{V}_{O_2} = \left[\frac{(1 - F\bar{E}_{O_2} - F\bar{E}_{CO_2})}{(1 - FI_{O_2})} \times FI_{O_2} - F\bar{E}_{O_2}\right] \times \dot{V}_E \qquad (2)$$

Most currently available commercial metabolic carts employ equation (2). Accuracy of this equation depends upon a low inspired oxygen concentration, the absence of gases other than the tracer and those stated in equation (2) in the exhaled mixture, and absence of uptake or excretion of the tracer.

At high inspired oxygen concentrations, as the FI_{O_2} approaches 1, inhaled and exhaled N_2 concentrations and hence both the numerator and denominator of the fraction in equation (2) approach zero.[2] Small errors in measurement of $F\bar{E}_{CO_2}$ and $F\bar{E}_{O_2}$ and FI_{O_2} then cause large errors in oxygen uptake measurement. Error also arises because dilution of exhaled gases by unmeasured quantities of anesthetic gases leads to computation of a falsely large inhaled volume.[3] Thus, measurement of oxygen uptake with a metabolic cart is most reliable in air breathing subjects who have not been anesthetized recently with inhalation agents. Since patients in the perioperative period often need increased inspired oxygen concentrations and may excrete significant quantities of anesthetic gases, oxygen uptake measurement in this group is less reliable.

A method with accuracy not dependent on the absence of anesthetics and with errors less amplified by a high FI_{O_2} would be of great benefit to anesthesiologists. Oxygen uptake determination based on direct measurement of an inert tracer gas in inhaled and exhaled volumes should meet these criteria if the tracer is sufficiently insoluble and if near steady state levels are maintained to avoid significant uptake or excretion of the tracer.[1]

To evaluate this premise, we calculated the effect of FI_{O_2} on errors in oxygen uptake, caused by errors of measurement of $F\bar{E}_{CO_2}$, $F\bar{E}_{O_2}$, FI_{O_2}, $F\bar{E}_{N_2}$, and FI_{N_2}. We also assessed the error in calculated $\dot{V}_{O_2}$,

* Assistant Professor.

† Associate Professor.

‡ Chairman, Department of Anesthesia, Robert Dunning Dripps Professor, Professor of Pharmacology.

Received from the Department of Anesthesia, Hospital of the University of Pennsylvania, Dulles Seven, 3400 Spruce Street, Philadelphia, Pennsylvania 19104. Accepted for publication July 3, 1984.

Address reprint requests to Dr. Aukburg.

caused by ignoring the anesthetic fraction in exhaled gas. We compared errors resulting from methods based on both direct measurement of inhaled and exhaled nitrogen, and on nitrogen inferred by subtraction. Formulas for correcting the error due to exhaled anesthetics are presented, and the potential improvement in the accuracy of metabolic measurements realized by directly measuring the inhaled and exhaled concentrations of an insoluble inert tracer is evaluated.

Methods

For the purposes of this error evaluation, it was assumed that the subject under test was exhaling five liters of gas, not including the exhaled volume of anesthetic gases, that the respiratory exchange ratio was either 0.8, 1, or 1.2, and that the subject's CO_2 excretion was 200 ml/min. It was assumed further that all measurements were either made at STPD or else appropriately corrected. Equations (3) through (9) in Appendix A were used to calculate what the observed concentrations of oxygen and CO_2 would be in inhaled and exhaled gases, and what the measured $\dot{V}_E$ would be, for selected combinations of $F_{I_{O_2}}$, and $\dot{V}_{Anes}$. We used equations 12 and 13 to calculate the correct $F\bar{E}_{N_2}$ and $F_{I_{N_2}}$. Equations describing the error in observed oxygen uptake were derived from equations (1) and (2), assuming errors in measurement of $F\bar{E}_{CO_2}$, $F_{I_{N_2}}$ and $F\bar{E}_{N_2}$, $F_{I_{O_2}}$, or $F\bar{E}_{O_2}$ as well as an error common to $F_{I_{O_2}}$ and $F\bar{E}_{O_2}$. The first derivative of the equation for calculating $\dot{V}_{O_2}$ (equation [1] or equation [2], as applicable) with respect to the gas parameter in question ($d\dot{V}_{O_2}/dG$) was taken. It was assumed that for small errors (<1%) the differentials in oxygen uptake and the gas in question could be replaced with increments and the resulting equation was solved for the increment in oxygen uptake. The increment in the gas in question was replaced by the correct concentration shown in Appendix B. Simplifying assumptions were made where appropriate (*i.e.*, $F_{I_{O_2}} \cong F\bar{E}_{O_2}$).

To test the potential accuracy of the inert tracer method, we used a Monte Carlo technique.[4] This technique allows the estimation of the error resulting from the interplay of multiple errors that would be difficult or impossible to derive directly. It uses the luck of the draw to select the error to be added to each independent variable from a table of randomly distributed errors. We calculated the error in oxygen uptake caused by adding a Gaussian random error of ±.5% to $F\bar{E}_{CO_2}$, $F_{I_{O_2}}$, $F\bar{E}_{O_2}$, $F_{I_{N_2}}$, and $F\bar{E}_{N_2}$ if measured nitrogen *versus* inferred nitrogen were used in the calculation. One hundred sets of gas concentrations with added random errors were created for each selected $F_{I_{O_2}}$.

TABLE 1. Empirically Derived Equations for Computing Oxygen Uptake Error Introduced by Errors in Measurement of Respiratory Gases

Gas Parameter in Error	Equation Used	Computing Equation	
$F\bar{E}_{CO_2}$	2	$\Delta\dot{V}_{O_2} = -EF \times \dot{V}_E \times \frac{F_{I_{O_2}} \times F\bar{E}_{CO_2}}{1 - F_{I_{O_2}}}$	(14)
$F_{I_{O_2}}$	2	$\Delta\dot{V}_{O_2} \cong EF \times \dot{V}_E \times \frac{F_{I_{O_2}}}{1 - F_{I_{O_2}}}$	(15)
$F\bar{E}_{O_2}$	2	$\Delta\dot{V}_{O_2} \cong -EF \times \dot{V}_E \times \frac{F_{I_{O_2}}}{1 - F_{I_{O_2}}}$	(16)
$F_{I_{O_2}}$ and $F\bar{E}_{O_2}$	2	$\Delta\dot{V}_{O_2} \cong EF \times \dot{V}_E \times \frac{F\bar{E}_{CO_2}}{1 - F_{I_{O_2}}}$	(17)
$F\bar{E}_{Anes}$	2	$\Delta\dot{V}_{O_2} = \dot{V}_E \times F\bar{E}_{Anes} \times \frac{F_{I_{O_2}}}{1 - F_{I_{O_2}}}$	(18)
$F_{I_{N_2}}$	1	$\Delta\dot{V}_{O_2} \cong -EF \times \dot{V}_E \times F_{I_{O_2}}$	(19)
$F\bar{E}_{N_2}$	1	$\Delta\dot{V}_O \cong EF \times \dot{V}_E \times F_{I_{O_2}}$	(20)
$F_{I_{N_2}}$ and $F\bar{E}_{N_2}$	1	$\Delta\dot{V}_{O_2} = 0$	(21)
$F\bar{E}_{Anes}$	1	See text	

Oxygen uptakes then were calculated from each set. The mean and standard deviation of the 100 oxygen uptakes calculated with each method then were computed and compared. The computations were repeated, assuming anesthetic excretions of 0, 50, and 100 ml/min. Such volumes are likely to be excreted during the first 2–3 h after termination of an inhalational anesthetic.[5]

Results

Mathematically derived equations for estimating the error in oxygen uptake introduced by an error fraction (EF) in each gas parameter and by exhaled anesthetics are listed in table 1.

Equations (14) through (18) refer to results determined from the inferred nitrogen method equation (2). In each case the error in oxygen uptake increases hyperbolically as the inspired oxygen fraction approaches 1. The calculated oxygen uptake error introduced by an error in measured $F\bar{E}_{CO_2}$ is opposite in direction to the error introduced in calculated carbon dioxide excretion. The oxygen uptake error never exceeds 5% if the $F\bar{E}_{CO_2}$ error does not exceed 1% (EF < 0.01) and the $F_{I_{O_2}}$ is 0.8 or less. The error in oxygen uptake introduced by $F_{I_{O_2}}$ or $F\bar{E}_{O_2}$ measure-

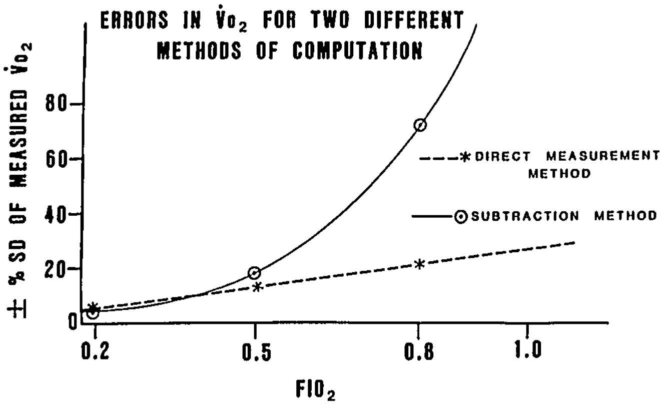

FIG. 1. Per cent standard deviation of calculated oxygen uptake *versus* F_{IO_2} for two different methods. Values for inhaled and exhaled respiratory gas fractions were calculated assuming $\dot{V}_E = 5{,}000$ ml/min, $\dot{V}_{O_2} = 2{,}000$ ml/min, and R = 1. Using a Monte Carlo technique, random errors of ±0.5% in a Gaussian distribution were added to all calculated respiratory gas fractions and oxygen uptake recalculated using both the direct nitrogen measurement method equation (1), solid line, and the nitrogen by subtraction method equation (2), dash line. One hundred oxygen uptakes were calculated for each F_{IO_2} of 0.2, 0.5, and 0.8. The per cent standard deviation of the oxygen uptakes for each method then was computed and plotted.

ment errors of 1% exceeds 100% when the F_{IO_2} is 0.8 or greater. Error common to F_{IO_2} and $F\bar{E}_{O_2}$ causes an oxygen uptake error that is very small compared with that produced by error isolated to F_{IO_2} or $F\bar{E}_{O_2}$.

The error in oxygen uptake introduced by ignoring exhaled anesthetic gas can be calculated from equation

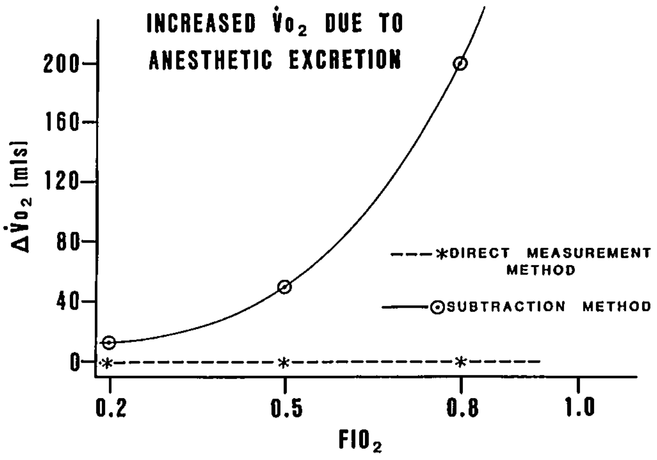

FIG. 2. Error in oxygen uptake (ml) from ignoring anesthetic excretion *versus* F_{IO_2} for two different methods. Values for inhaled and exhaled respiratory gas fractions were calculated as for figure 1 but assuming 50 ml/min of anesthetic gas excretion. One hundred oxygen uptakes were calculated for each F_{IO_2} of 0.2, 0.5, and 0.8. The difference between the mean oxygen uptake and the correct value were plotted against F_{IO_2} for each method.

(18) in table 1. If the exhaled anesthetic fraction is known, equation (18) can be used to correct an oxygen uptake value calculated from equation (2). Failure to correct for exhaled anesthetics renders the inferred nitrogen method almost useless in the immediate postoperative period if inhalational anesthetics have been used.

Equations (19) through (21) refer to results determined from equation (1). Errors in nitrogen determination cause errors in oxygen uptake that increase linearly as the inspired oxygen fraction increases. Errors in directly measured nitrogen concentrations cause smaller errors in computed oxygen uptake than occur when nitrogen is computed by subtraction and the oxygen concentration is in error. Matched errors in inhaled and exhaled nitrogen concentrations yield no error in computed oxygen uptake. When equation (1) is used, exhaled anesthetics introduce an error in calculated oxygen uptake reduced by the ratio of the solubility of N_2 to the solubility of the anesthesia gas. For N_2 and N_2O the error is 1/30 that introduced by equation (2).

The results of adding ±0.5% Gaussian random errors to all gas parameters in equations (1) and (2) are shown in table 2 and figures 1 and 2. Since the respiratory quotient (R) did not significantly affect the magnitude of the error, results are presented for R = 1 only. Each oxygen uptake value in the table represents the mean ± %SD of 100 observations. The subtraction technique equation (2) yields a smaller error than the measured inert gas technique equation (1) when the F_{IO_2} is 0.2 (±3.5% *vs.* ± 4.3%). When the F_{IO_2} is 0.5, the advantage reverses (±16% *vs.* ± 12%), and when the F_{IO_2} is 0.8, the advantage increases (±71% *vs.* ± 21%). Furthermore, the presence of exhaled anesthetic gas has no effect on calculated uptake when inert gas is measured directly but erroneously adds to the actual oxygen uptake if the inert gas fractions are computed by subtraction. Examination of figure 1 reveals the hyperbolic increase in oxygen uptake error resulting from equation (2) and the smaller linear increase resulting from equation (1).

Examination of figure 2 reveals the hyperbolic increase in oxygen uptake error with increasing inspired oxygen fraction secondary to failure to account for 1% anesthetic agent in exhaled gas when the inferred nitrogen method is used. Use of directly measured nitrogen eliminates the error.

Discussion

Our results indicate that errors that affect the apparent difference between inhaled and exhaled oxygen concentrations produce a far greater error in computed oxygen uptake than errors common to inhaled and exhaled concentrations. Therefore, matched O_2 analyzers for inhaled and exhaled gas or a multiplexed sampling technique with a single O_2 analyzer is preferred. Because matched error in inhaled and exhaled N_2 cancel, matched analyzers or a multiplexed sampling technique should be employed for the inert gas as well.

The postoperative patient may be excreting significant amounts of anesthetic gases,[5] which should be accounted for by expanding equation (2) into equation (22) if the inferred nitrogen method is used to compute oxygen uptake.

$$\dot{V}_{O_2} = \left[\frac{1 - F\bar{E}_{O_2} - F\bar{E}_{CO_2} - F\bar{E}_{Anes}}{1 - FI_{O_2}} \times FI_{O_2} - F\bar{E}_{O_2}\right] \times \dot{V}_E \quad (22)$$

Failure to account for excreted anesthetics leads to computation of a falsely high inhaled volume. The assumed increase in inhaled volume is that gas volume that would contain a volume of nitrogen equal to the exhaled volume of anesthetic. The error in oxygen uptake caused by ignoring exhaled anesthetics is the difference between that calculated by equation (2) and equation (22). Subtracting equation (2) from equation (22) yields equation (18). The extent of the $\dot{V}_{O_2}$ error depends on the inhaled oxygen fraction. Equation (18) should be used to correct for exhaled anesthetic gases when the inferred nitrogen method is employed.

It is not necessary to know the concentrations of exhaled anesthetic if the concentration of an insoluble tracer gas, such as N_2, is known in both inhaled and exhaled volumes and equation (1) is used. The resulting $\dot{V}_{O_2}$ will be nearly correct independent of the quantity of exhaled anesthetic gas as shown in figure 1. A small error in O_2 uptake will result from the uptake of N_2, which must occur when N_2 replaces anesthetic in inhaled gas, however, the magnitude of the error is smaller than that produced by anesthetic excretion because of the much lower solubility of N_2. Errors in estimation of the tracer gas introduce less error than errors in FI_{O_2} or $F\bar{E}_{O_2}$ if the FI_{O_2} is 0.5 or greater (fig. 2).

Our results are similar to those obtained by Ultman and Burzstein.[2] They compared errors in oxygen uptake that occur when inhaled and exhaled volume are measured directly to errors occurring when inhaled volume is inferred from nitrogen fractions calculated by subtraction. Extremely precise matching of the inhaled and exhaled volume transducers is required in order to achieve oxygen uptake measurements of reasonable accuracy. Currently available gas flow transducers are not capable of supplying the needed precision, especially if anesthetics are present in the exhaled gas stream.

TABLE 2. Error Introduced in Oxygen Uptake by Adding ±0.5% Gaussian Error to Respiratory Gas Fractions (n = 100)

FI_{O_2}	N_2O	$\dot{V}_{O_2}$ (ml/min actual)	$\dot{V}_{O_2}$ (ml/min ± %SD from eq. [1])	$\dot{V}_{O_2}$ (ml/min ± %SD from eq. [2])
0.2	0	200	200 ± 4.3	200 ± 3.5
0.5	0	200	200 ± 12	196 ± 16
0.8	0	200	196 ± 21	205 ± 71
0.2	50	200	200 ± 4.6	212 ± 3.8
0.5	50	200	202 ± 12	251 ± 17
0.8	50	200	195 ± 17	398 ± 64
0.2	100	200	201 ± 4.9	226 ± 3.9
0.5	100	200	200 ± 12	303 ± 16
0.8	100	200	200 ± 19	591 ± 75

We conclude that valid estimation of oxygen uptake by the inert gas method in postoperative patients requires that exhaled anesthetic vapors be accounted for. This can be accomplished by measuring the exhaled anesthetic concentration and applying the correction elaborated above or by measuring the concentrations of N_2 or another insoluble tracer (*e.g.*, He, Ar, or SF_6) in the inhaled and exhaled gases and then using equation (1). This latter technique is preferred, especially if the subjects FI_{O_2} is greater than 0.5.

The authors are indebted to Kenneth Beck, Ph.D., and Kai Rehder, M.D., for developing the derivations of the equations in Appendix B.

References

1. Heneghan CPH, Gilbe CE, Branthwaite MA: Measurement of metabolic gas exchange during anesthesia. Br J Anaesth 53:73–76, 1981
2. Ultman JS, Burzstein S: Analysis of error in determination of respiratory gas exchange in varying FI_{O_2}. J Appl Physiol 50:210–222, 1981
3. Abdul-Rasool IH, Chamberlain JH: Respiratory gas exchange before and after cardiac operations. J Thorac Cardiovasc Surg 85:856–863, 1983
4. Snedecor GW: Cochran WG: Statistical Methods, 7th ed. Ames, The Iowa State University Press, 1980
5. Frumin J, Salanitre E, Rackow H: Excretion of nitrous oxide in anesthetized man. J Appl Physiol 16:720–722, 1961

Appendix A

Equations Used to Calculate Equation (1) and Equation (2) Parameters

$$\dot{V}_E = 5000 + \dot{V}_{Anes} \quad (3)$$

$$F\bar{E}_{CO_2} = \frac{200}{\dot{V}_E} \quad (4)$$

$$\dot{V}_{O_2} = \frac{200}{RQ} \quad (5)$$

$$\dot{V}_I = 5000 + \dot{V}_{O_2} - \dot{V}_{CO_2} \quad (6)$$

$$\dot{V}I_{O_2} = \dot{V}_I \times FI_{O_2} \quad (7)$$

$$\dot{V}\bar{E}_{O_2} = \dot{V}I_{O_2} - \dot{V}_{O_2} \quad (8)$$

$$F\bar{E}_{O_2} = \frac{\dot{V}\bar{E}_{O_2}}{\dot{V}_E} \quad (9)$$

$$\dot{V}_{CO_2} = F\bar{E}_{CO_2} \times \dot{V}_E \quad (10)$$

$$R = \frac{\dot{V}_{CO_2}}{\dot{V}_{O_2}} \quad (11)$$

$$F\bar{E}_{N_2} = 1 - F\bar{E}_{CO_2} - F\bar{E}_{O_2} - \frac{\dot{V}_{Anes}}{\dot{V}_E}\left\{+\frac{\dot{V}_{N_2}}{\dot{V}_E}\text{ ignored, see text}\right\} \quad (12)$$

$$FI_{N_2} = 1 - FI_{O_2} \quad (13)$$

Appendix B

Derivation of Error Equations

Each of the error equations listed in table 1 was developed with the same four step process. The errors in oxygen uptake are expressed as functions of the inspired oxygen fraction.

1. The first derivative of the equation for calculating $\dot{V}_{O_2}$ (equation [1] or [2] as applicable) with respect to the gas parameter in question was taken: $d\dot{V}_{O_2}/dG$.
2. It was assumed that for small errors (<1%) $d\dot{V}_{O_2}/dG = \Delta\dot{V}_{O_2}/\Delta G$ and that $\Delta G = G \times EF_G$ so that $d\dot{V}_{O_2}/dG$ was replaced by $\frac{\Delta\dot{V}_{O_2}}{G \times EF_G}$
3. The equation was then solved for $\Delta\dot{V}_{O_2}$
4. Simplifying assumptions were made where appropriate (*i.e.*, $FI_{O_2} \cong F\bar{E}_{O_2}$)

I. Error expressions applicable to equation (2).

$$\dot{V}_{O_2} = \dot{V}_E \times \frac{FI_{O_2}(1 - F\bar{E}_{O_2} - F\bar{E}_{CO_2})}{(1 - FI_{O_2})} - F\bar{E}_{O_2} \quad (2)$$

A. $F\bar{E}_{CO_2}$ in error

1. $$\frac{d\dot{V}_{O_2}}{dF\bar{E}_{CO_2}} = \frac{FI_{O_2} \times \dot{V}_E}{1 - FI_{O_2}}$$

2. $$\frac{\Delta\dot{V}_{O_2}}{\Delta F\bar{E}_{CO_2}} = \frac{FI_{O_2} \times \dot{V}_E}{1 - FI_{O_2}}$$

$$\Delta F\bar{E}_{CO_2} = EF(F\bar{E}_{CO_2}) \times F\bar{E}_{CO_2}$$

3. $$\Delta\dot{V}_{O_2} = EF \times F\bar{E}_{CO_2} \times \frac{FI_{O_2} \times \dot{V}_E}{1 - FI_{O_2}} \quad (14)$$

B. FI_{O_2} in error

1. $$\frac{d\dot{V}_{O_2}}{dFI_{O_2}} = \frac{\dot{V}_E(1 - F\bar{E}_{O_2} - F\bar{E}_{CO_2}}{(1 - FI_{O_2})^2}$$

2 & 3. $$\Delta\dot{V}_{O_2} = EF \times FI_{O_2} \frac{\times \dot{V}_E(1 - F\bar{E}_{O_2} - F\bar{E}_{CO_2}}{(1 - FI_{O_2})^2}$$

4. Since $\frac{1 - F\bar{E}_{O_2} - F\bar{E}_{CO_2}}{1 - FI_{O_2}} \cong 1.0$

$$\Delta\dot{V}_{O_2} \cong EF \times \frac{FI_{O_2} \times \dot{V}_E}{1 - FI_{O_2}} \quad (15)$$

C. $F\bar{E}_{O_2}$ in error

1. $$\frac{d\dot{V}_{O_2}}{dF\bar{E}_{O_2}} = -\dot{V}_E \times \frac{1}{1 - FI_{O_2}}$$

2 & 3. $$\Delta\dot{V}_{O_2} = -EF\frac{F\bar{E}_{O_2} \times \dot{V}_E}{1 - FI_{O_2}}$$

4. $$\Delta\dot{V}_{O_2} \cong -EF \times \frac{FI_{O_2}}{1 - FI_{O_2}} \times \dot{V}_E \quad (16)$$

D. FI_{O_2} & $F\bar{E}_{O_2}$ in error

1, 2, and 3. Note: $\Delta\dot{V}_{O_2}$ = sum of $\dot{V}_{O_2}$ error for B & C above.

$$\Delta\dot{V}_{O_2} = \frac{EF\bar{E}_{O_2} \times \dot{V}_E \times FI_{O_2}}{1 - FI_{O_2}} - \frac{EFI_{O_2} \times \dot{V}_E \times FE_{O_2}}{1 - FI_{O_2}}$$

4. since $EF\bar{E}_{O_2} = EFI_{O_2}$

$$\Delta\dot{V}_{O_2} = \frac{EF \times \dot{V}_E \times (FI_{O_2} - F\bar{E}_{O_2}}{1 - FI_{O_2}}$$

and since $FI_{O_2} - F\bar{E}_{O_2} \cong F\bar{E}_{CO_2}$

$$\Delta\dot{V}_{O_2} \cong \frac{EF \times F\bar{E}_{CO_2}}{1 - FI_{O_2}} \times \dot{V}_E \quad (17)$$

E. $F\bar{E}_{A_n}$ not accounted for.

1. $$\frac{d\dot{V}_{O_2}}{dF\bar{E}_{A_n}} = \frac{\dot{V}_E \times FI_{O_2}}{1 - FI_{O_2}}$$

2 & 3. $$\Delta\dot{V}_{O_2} = -\frac{\dot{V}_E \times FI_{O_2} \times EF \times FE_{A_n}}{1 - FI_{O_2}}$$

4. Since FE_{A_n} is not measured the whole theory is considered an error and therefore EF is taken as one.

$$\Delta\dot{V}_{O_2} = -\frac{\dot{V}_E \times FI_{O_2} \times F\bar{E}_{A_n}}{1 - FI_{O_2}} \quad (18)$$

II. Equation 1

$$\dot{V}_{O_2} = \dot{V}_E FI_{O_2}\frac{F\bar{E}_{N_2}}{1 - FI_{O_2}} - F\bar{E}_{O_2}$$

A. FI_{N_2} in error

1. $$\frac{d\dot{V}_{O_2}}{dFI_{N_2}} = -\frac{\dot{V}_E \times FI_{O_2} \times F\bar{E}_{N_2}}{FI_{N_2}{}^2}$$

2 & 3. $\Delta\dot{V}_{O_2} = \dfrac{-EF \times \dot{V}_E \times FI_{O_2} \times F\bar{E}_{N_2}}{FI_{N_2}}$

4. Since $FI_{N_2} \cong F\bar{E}_{N_2}$

$$\Delta\dot{V}_O \cong -EF \times \dot{V}_E \times FI_{O_2} \qquad (19)$$

B. $F\bar{E}_{N_2}$ in error

1. $\dfrac{d\dot{V}_{O_2}}{dF\bar{E}_{N_2}} = \dfrac{-\dot{V}_E \times FI_{O_2}}{1 - F\bar{I}_{N_2}}$

2 & 3. $\Delta\dot{V}_{O_2} = \dfrac{-EF \times \dot{V}_E \times FI_{O_2} \times F\bar{E}_{N_2}}{FI_{N_2}}$

4. Since $FI_{N_2} \cong F\bar{E}_{N_2}$

$$\Delta\dot{V}_{O_2} \cong EF \times \dot{V}_E \times FI_{O_2} \qquad (20)$$

C. FI_{N_2} and $F\bar{E}_{N_2}$ in error

1, 2, and 3. Note: $\Delta\dot{V}_{O_2}$ = sum of $\dot{V}_{O_2}$ error for A & B above.

$$\Delta\dot{V}_{O_2} = \frac{-EF_I \times \dot{V}_E \times FI_{O_2} \times F\bar{E}_{N_2}}{FI_{N_2}} + \frac{EF_{\bar{E}} \times \dot{V}_E \times FI_{O_2} \times F\bar{E}_{N_2}}{FI_{N_2}}$$

4. Since EFI is taken as equal to EF$\bar{E}$ and nitrogen balance is assumed.

$$\Delta\dot{V}_{O_2} = 0 \qquad (21)$$