Tutorial

ACCURACY OF END-TIDAL CARBON DIOXIDE TENSION ANALYZERS

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ABSTRACT. Substantial mean differences between arterial carbon dioxide tension ($PaCO_2$) and end-tidal carbon dioxide tension ($PetCO_2$) in anesthesia and intensive care settings have been demonstrated by a number of investigators. We have explored the technical causes of error in the measurement of $PetCO_2$ that could contribute to the observed differences. In a clinical setting, the measurement of $PetCO_2$ is accomplished with one of three types of instruments, infrared analyzers, mass spectrometers, and Raman spectrometers, whose specified accuracies are typically ±2, ±1.5, and ±0.5 mm Hg, respectively. We examined potential errors in $PetCO_2$ measurement with respect to the analyzer, sampling system, environment, and instrument. Various analyzer error sources were measured, including stability, warm-up time, interference from nitrous oxide and oxygen, pressure, noise, and response time. Other error sources, including calibration, resistance in the sample catheter, pressure changes, water vapor, liquid water, and end-tidal detection algorithms, were considered and are discussed. On the basis of our measurements and analysis, we estimate the magnitude of the major potential errors for an uncompensated infrared analyzer as: inaccuracy, 2 mm Hg; resolution, 0.5 mm Hg; noise, 2 mm Hg; instability (12 hours), 3 mm Hg; miscalibration, 1 mm Hg; selectivity (70% nitrous oxide), 6.5 mm Hg; selectivity (100% oxygen), −2.5 mm Hg; atmospheric pressure change, <1 mm Hg; airway pressure at 30 cm H_2O, 2 mm Hg; positive end-expiratory pressure or continuous positive airway pressure at 20 cm H_2O, 1.5 mm Hg; sampling system resistance, <1 mm Hg; and water vapor, 2.5 mm Hg. In addition to these errors, other systematic mistakes such as an inaccurate end-tidal detection algorithm, poor calibration technique, or liquid water contamination can lead to gross inaccuracies. In a clinical setting, unless the user is confident that all of the technical error sources have been eliminated and the physiologic factors are known, depending on $PetCO_2$ to determine $PaCO_2$ is not advised.

KEY WORDS. Monitoring: carbon dioxide. Equipment: infrared analyzers; Raman spectrometer; mass spectrometer.

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The Standards for Basic Monitoring in Anesthesia, recently adopted by the American Society of Anesthesiologists, require continuous monitoring of ventilation and suggest the use of an end-tidal carbon dioxide (CO_2) monitor [1]. Several state societies have also established guidelines for monitoring that strongly urge the use of this instrument. Some medical malpractice insurance carriers have designated this device as a requirement for coverage while others have given discounts for their purchase and use [2]. The anesthesia community has responded with an unprecedented increase in the purchase of respiratory gas monitors, as reported by the major instrument manufacturers. Reducing the incidence of ventilatory mishaps is the primary motivation for advocating the use of these de-

vices. However, many anesthesiologists attempt to use the end-tidal CO_2 monitor to estimate arterial CO_2 tension ($PaCO_2$). Often, clinicians are surprised to find substantial differences between end-tidal CO_2 tension ($PETCO_2$) and $PaCO_2$.

Although most investigators have attributed the difference between $PaCO_2$ and $PETCO_2$ in anesthesia and intensive care settings to PHYSIOLOGIC DEAD SPACE [3–8], the contribution of *technical* factors to these differences cannot be ignored. The technical sources of error contributing to the apparent difference between $PETCO_2$ and $PaCO_2$ include inaccurate $PETCO_2$ measurement, inaccurate $PaCO_2$ measurement, and incorrect assumptions when comparing $PETCO_2$ and $PaCO_2$. This report will focus on errors in $PETCO_2$ measurement only.

The objectives of this tutorial are to enumerate the sources of error in $PETCO_2$ measurement and to illustrate the approximate magnitude of the error to be expected from each. In this way, users and developers of respiratory CO_2 monitors can evaluate the characteristics of their particular devices in an appropriate context. It is not the intent of this article to compare particular instruments or technologies to recommend them for purchase or use. Since the manufacturers of CO_2 instruments are continually changing and improving their devices, instrument-specific data will rapidly become obsolete.

BACKGROUND

Respiratory CO_2 monitoring during anesthesia is typically accomplished with one of 3 instruments: INFRARED (IR) ANALYZER, RAMAN SPECTROMETER, or MASS SPECTROMETER. Each of these technologies is reasonably accurate, reliable, and practical. However, the design of commercially available instrumentation is imperfect and substantial errors in measurement of $PETCO_2$ can result. We have used and evaluated many of these devices over the past decade in both laboratory and operating room settings and can enumerate their potential error sources.

Principles of Operation

IR ANALYZERS. Many respiratory and anesthetic gases and agents, including CO_2, absorb IR energy when atoms rotate or vibrate asymmetrically resulting in a change in dipole moment. CO_2, nitrous oxide (N_2O), water vapor, and fluorinated hydrocarbons exhibit strong absorption bands throughout the IR spectrum; the nonpolar molecules of argon, nitrogen, helium, xenon, and oxygen do not.

Measuring the energy absorbed from a narrow band of wavelengths of IR light passing through a gas is termed IR spectroscopy. IR analyzers measure the *partial pressure* of the gas of interest since the measurement is dependent on the number of gas molecules in the path of the IR light during measurement. There are many design alternatives for an IR instrument; all exhibit different performance characteristics (further description of design alternatives is available [9,10]).

Clinical IR monitoring instruments are classified as either MAINSTREAM or SIDE STREAM according to how they obtain the gas sample for measurement. In a mainstream instrument, the patient's respiratory gas stream passes through a wide-bore chamber (cuvette) in the airway. A miniature IR optical system is placed over the chamber and measures gas partial pressure through synthetic sapphire windows. To ensure that water vapor does not condense on the windows and obstruct the optical path, the cuvette is heated to slightly above body temperature.

Side-stream instruments continuously withdraw a sample of gas from the airway through small-bore tubing at a flow rate between 50 and 500 ml/min. The sample is sometimes channeled through a length of tubing made of Nafion, a semipermeable polymer that selectively allows water vapor to pass from its interior to the dry exterior [11]. Errors caused by water vapor are discussed later in this report. Liquid water in the sample cuvette can interfere with the transmission of the IR beam. A mechanical water trap is usually interposed between the patient sample tubing and the analyzer to protect effectively the optical system from liquid water and body fluids [12].

RAMAN SPECTROMETER. When visible or ultraviolet light strikes gas molecules, energy is absorbed and reemitted at the same wavelength and direction (Rayleigh scattering). A small fraction (approximately 10^{-6}) of the energy absorbed is reemitted at new wavelengths in a phenomenon called Raman scattering. At room temperature, Raman scattering usually results in reemission at a longer wavelength, producing a "red-shifted" spectrum. The wavelength shift and amount of scattering can be used to determine the constituents of a gas mixture. Raman scattering is not limited to gas species that are polar, as is IR spectroscopy. CO_2, oxygen, nitrogen, water vapor, N_2O, halothane, enflurane, isoflurane, sevoflurane, and desflurane all exhibit Raman activity.

The Raman spectrometer designed for use in clinical anesthesia was introduced relatively recently [13]. Like the IR instrument, the Raman spectrometer measures the *partial pressures* of the gases in its measurement cuvette. The instrument samples gas from the breathing circuit at 200 ml/min.

MASS SPECTROMETER. A magnetic sector mass spectrometer draws a small fraction of the gas sampled from the breathing circuit into an evacuated measurement chamber through a tiny "molecular leak," comprising either a fine needle valve, a sintered metal filter, or a vibrating crystal. Electrons bombard the gas mixture and ionize gas molecules into fragments of predictable mass and charge. The charged particles are accelerated by an electric field and pass through a magnetic field that deflects them on the basis of their mass and charge. The heaviest ions have the longest trajectories while the lightest travel the shortest. Appropriately located metal dishes collect ions of each species individually, producing minute electric currents. These currents are amplified and scaled to represent relative gas concentration.

The quadrupole mass spectrometer is similar to the magnetic sector device except that it uses a varying magnetic field to establish the trajectory of the ions and a single detector to receive and measure them.

All of the medical mass spectrometers measure CO_2 at mass 12. Other gases are measured and the reported concentrations are electronically normalized to 100%. In addition, organic molecules (e.g., anesthetic vapor agents) may produce ionic fragments of mass 12, and the CO_2 measurement is automatically adjusted accordingly.

Note that the mass spectrometer differs from the IR analyzer and Raman spectrometer in that it measures *fractional concentration in vol%* by assuming that all of the gases in the sampled mixture fall on a collector and are measured.

Mass spectrometers for clinical use are either "stand-alone," designed to continuously monitor a single patient, or "shared," designed to sequentially monitor several patients in different locations. In the stand-alone system, a vacuum pump is used to sample the respiratory gas and pass the sample stream past the molecular leak. The entire instrument is located in the individual operating room where the analysis and display of the results takes place.

There are two approaches to the shared systems. In the first, the gas is sampled simultaneously from all attached operating rooms by a large vacuum pump through long lengths of nylon tubing ($\sim$ 50 m) at a rate of about 250 ml/min. A rotary valve (multiplexer) is used to sequentially direct the gas samples to the mass spectrometer. When a particular location is being sampled, a second vacuum pump takes over, drawing the gas down the long tubing and through the rotary valve at the same sample rate.

In the second method, the gas is continuously sampled from all patient locations at 90 ml/min to a waste catheter [14]. All of the long sample tubes contain about 20 seconds of inspired and expired gas profile. Solenoid valves sequentially switch each of the sample catheters to the inlet manifold of the mass spectrometer, which is maintained at a substantially lower pressure. The gas from the sample tube is drawn into the evacuated inlet manifold at twice the original sampling rate. The data are then displayed at twice actual speed to recreate the proper gas waveform. Less time per patient location is required with this method compared with direct sampling. There appears to be little waveform degradation using this technique [15].

METHODS

Representative commercially available instruments were compared for accuracy in measuring $P_{ET}CO_2$. Since these data are presented to illustrate the range of errors to be expected from various sources, not to compare particular instruments, the instruments are not identified by manufacturer or model, but are merely denoted A through K. The devices included 7 sidestream IR analyzers, 2 mainstream IR analyzers, 1 Raman spectrometer, and 1 stand-alone quadrupole mass spectrometer. As we were unable to test clinical multiplexed mass spectrometers simultaneously with other devices in our laboratory, no data are shown for these devices. In this report, all measurements are expressed in terms of differences from specified standards in units of partial pressure (mm Hg) unless otherwise stated. When errors in measurement are estimated, a nominal $P_{ET}CO_2$ of 40 mm Hg is assumed.

The analyzers were compared for ACCURACY, WARM-UP TIME, STABILITY, NOISE, N_2O and oxygen interference, TIME RESPONSE, and pressure interference. Several instruments were tested simultaneously to ensure a valid comparison between devices. Each analyzer was carefully calibrated prior to each experiment at BASELINE and mid scale using certified gas compositions accurate to ±0.02% (5% CO_2 in air or 5.0% CO_2 in nitrogen as appropriate, Scott Medical Products, Plumsteadville, PA). The analog output from each analyzer was scaled appropriately and converted to digital values with a 12-bit Data Translation DT2801 analog-to-digital converter. The ASYSTANT+ Scientific Software package (MacMillan) was used to collect and analyze the data.

Analyzer accuracy was measured at room temperature (20 to 22°C) with gas compositions produced with a precision gas mixer [16]. In most cases, multiple measurements were made throughout the operating range of the devices and averaged.

Warm-up time was measured by running the analyzers overnight, calibrating the next morning, disconnecting the power and allowing them to cool for several

hours, and then restarting. The time required for the measurement to come within 1 mm Hg of the calibration value was used as a measure of warm-up time.

Analyzer baseline and SPAN stability were measured by alternating the measurement gas between a baseline gas (air) and the reference gas from a tank (5% CO_2 in air) using a solenoid valve switched every 20 seconds. A 1-Hz sample rate was used to collect the data and the measurements were averaged. The average baseline gas measurement was used to determine baseline stability. The difference between the average baseline gas measurement and the reference gas measurement during each 20-second epoch was used as a measure of span stability.

Analyzer noise was measured by collecting data at 100 samples per second while the device was sampling reference gas (5% CO_2 in air). The noise of the Raman spectrometer was determined by recording the number of photon counts on the CO_2 channel while sampling 38-mm Hg CO_2 (balance air). Noise was measured as one standard deviation of the photon counts.

N_2O and oxygen interference were measured at room temperature similarly to the accuracy experiment, with various concentrations of N_2O and oxygen produced by the precision gas mixer.

Response time of the analyzers was measured by rapidly removing the sampling catheter from a gas stream of reference gas flowing at 1 L/min. Measurements were taken in triplicate to ensure repeatability. Generally, the sample catheter and water trap provided with the instrument were used. Mainstream analyzer time response was measured by unclamping a bag filled with reference gas as described by Brunner and Westenskow [17].

Pressure interference was measured by sampling reference gas from a chamber where the pressure was increased by partially occluding the outlet. Pressure was measured with a water or mercury manometer (Dwyer).

RESULTS

Analyzer Accuracy

Figure 1 shows the measured accuracy of 9 IR analyzers, 1 quadrupole mass spectrometer, and 1 Raman spectrometer. The data are shown as a measured difference on the ordinate from the test gas CO_2 tension (PCO_2) on the abscissa. They demonstrate that most of the instruments were accurate in laboratory testing to within 1 to 2 mm Hg in the PCO_2 range typically encountered in clinical practice. Many of these instruments showed less accuracy at the high end of the scale.
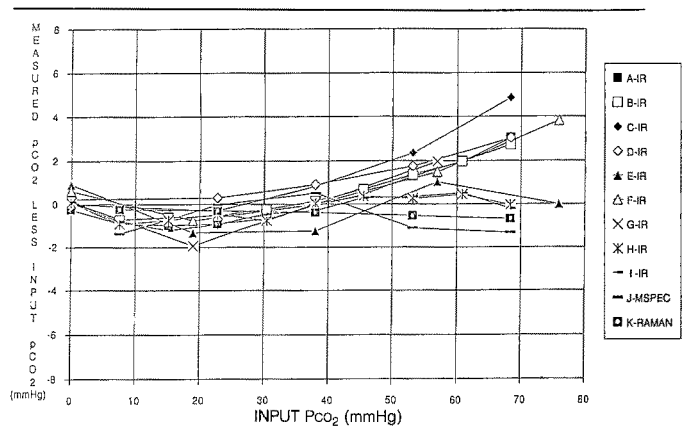

Fig 1. *Carbon dioxide tension (PCO_2) measurement accuracy of 9 infrared (IR) analyzers, a quadrupole mass spectrometer (MSPEC), and a Raman spectrometer (RAMAN). The difference between the measured PCO_2 and the input PCO_2 in 20% oxygen, balance nitrogen, is shown. All instruments were calibrated at a baseline (air) and span (5% carbon dioxide in air) prior to the experiment.*

Warm-up

Figure 2 shows the warm-up characteristic of 3 IR analyzers. IR instrument A came to within 1 mm Hg of its calibration value almost immediately. IR instrument I started within 1 mm Hg of its calibration, but fell below this range before stabilizing in about $1^1/_2$ minutes. IR instrument B demonstrated a gradual stabilization, taking just over 4 minutes to come to within 1 mm Hg of its calibration value.

Instability

Figure 3 demonstrates the baseline and span stabilities of 2 IR respiratory CO_2 analyzers over a 13-hour period. IR instrument D showed a small initial baseline drift followed by good stability over the remaining 10 hours. There was also a small upward drift of the span in this instrument. The total change in the IR instrument D reading over the 13-hour period including baseline and span drift was only about 1 mm Hg. IR instrument C showed excellent baseline stability. However, this device is a good example of the apparent instability from inaccurate compensating variables. Sudden shifts in the data are seen that affect the span stability. These were likely produced from an incorrect measurement of a compensating variable such as oxygen, N_2O, or pressure.

Noise

Five-second epochs from 5 IR analyzers and a quadrupole mass spectrometer measuring a PCO_2 of approxi-
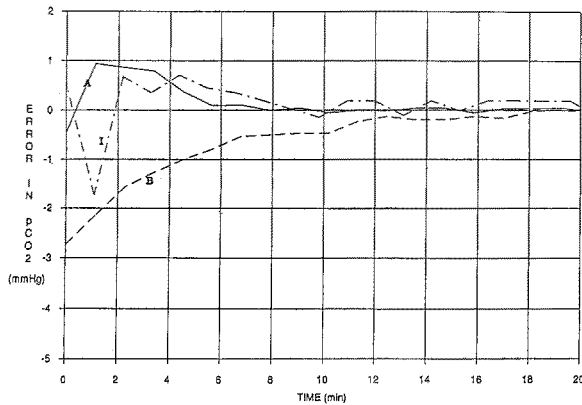
Fig 2. Warm-up characteristics of 3 infrared (IR) analyzers (units A, I, and B). The analyzers were allowed to warm up for several hours, calibrated, allowed to cool for several hours, and restarted. The time for the instruments to achieve their precooling calibration values is shown. PCO_2 = *carbon dioxide tension.*
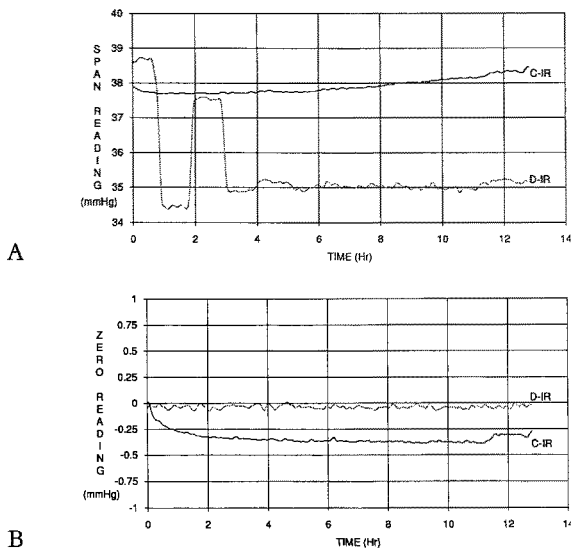

Fig 3. The stabilities of 2 infrared (IR) analyzers (C-IR, D-IR) over about 13 hours at zero carbon dioxide (CO_2) (100% nitrogen) and span CO_2 (5% CO_2, balance air), switching every 20 seconds were measured. (A) shows the span readings corrected for zero drift. (B) shows the zero stability.

mately 38 mm Hg showed substantial differences in the measured noise (Fig 4). One IR instrument (H) demonstrated noise of about ±2 mm Hg. The data show a low-frequency noise component, probably coming from a system that controls the temperature of one of the analyzer's optical components. The quadrupole mass spectrometer showed substantial noise at 20 and 0.5 Hz.

The Raman spectrometer exhibited about ±0.3 mm Hg of noise on the CO_2 channel.

Collision Broadening

As shown in Figure 5, representative IR analyzers exhibited inaccuracies owing to an N_2O of about 0.1 to 1.4 mm Hg CO_2 per 10% N_2O. Some analyzers automatically compensated for this effect by measuring or estimating concentrations of N_2O. IR instruments A, C, F, and G employed automatic compensation. Instrument E had no automatic compensation but showed relatively little COLLISION BROADENING effect.

Oxygen also had a substantial collision broadening effect on representative IR analyzers (Fig 6), though it was smaller than the effect of N_2O. Except for IR instruments C and F, the analyzers exhibited an effect of 0.15 to −0.5 mm Hg PCO_2 per 10% oxygen. IR instruments C and F incorporated an oxygen sensor and an algorithm that automatically compensated for the effect of oxygen. Instrument F appeared to overcompensate slightly and instrument C undercompensated. The residual effect was about ±0.10 mm Hg PCO_2 per 10% oxygen.

Time Response

Figure 7 shows the response of 4 respiratory PCO_2 analyzers to a change from a PCO_2 of 38 mm Hg to baseline. The 90 to 10% response times of the IR analyzers ranged from 168 ms for analyzer I to 326 ms for analyzer B. Instrument I was a mainstream analyzer. IR instruments A and B were side-stream analyzers without water traps. Instrument D had a water trap. Note that B had a distinctly slower multiexponential response characteristic.

Pressure Effects

The effect of positive end-expired pressure (PEEP) on 3 IR analyzers exposed to a fixed concentration of 5 vol% CO_2 is shown in Figure 8. The theoretical line was the direct effect of pressure increase in the cuvette. IR instruments D and I showed the combined results of direct pressure increase and pressure broadening. An increase in the reading of 2 mm Hg can be observed when 28 cm H_2O of PEEP was applied. Instrument C compensated for the applied PEEP with a built-in pressure transducer.

End-Tidal CO_2 Detection Algorithms

Figure 9 shows 4 examples of respiratory waveforms from an awake volunteer and the $P_{ET}CO_2$ reported by 4 instruments. Note that in each example, 1 or more of the analyzers erroneously read a late peak as the $P_{ET}CO_2$.
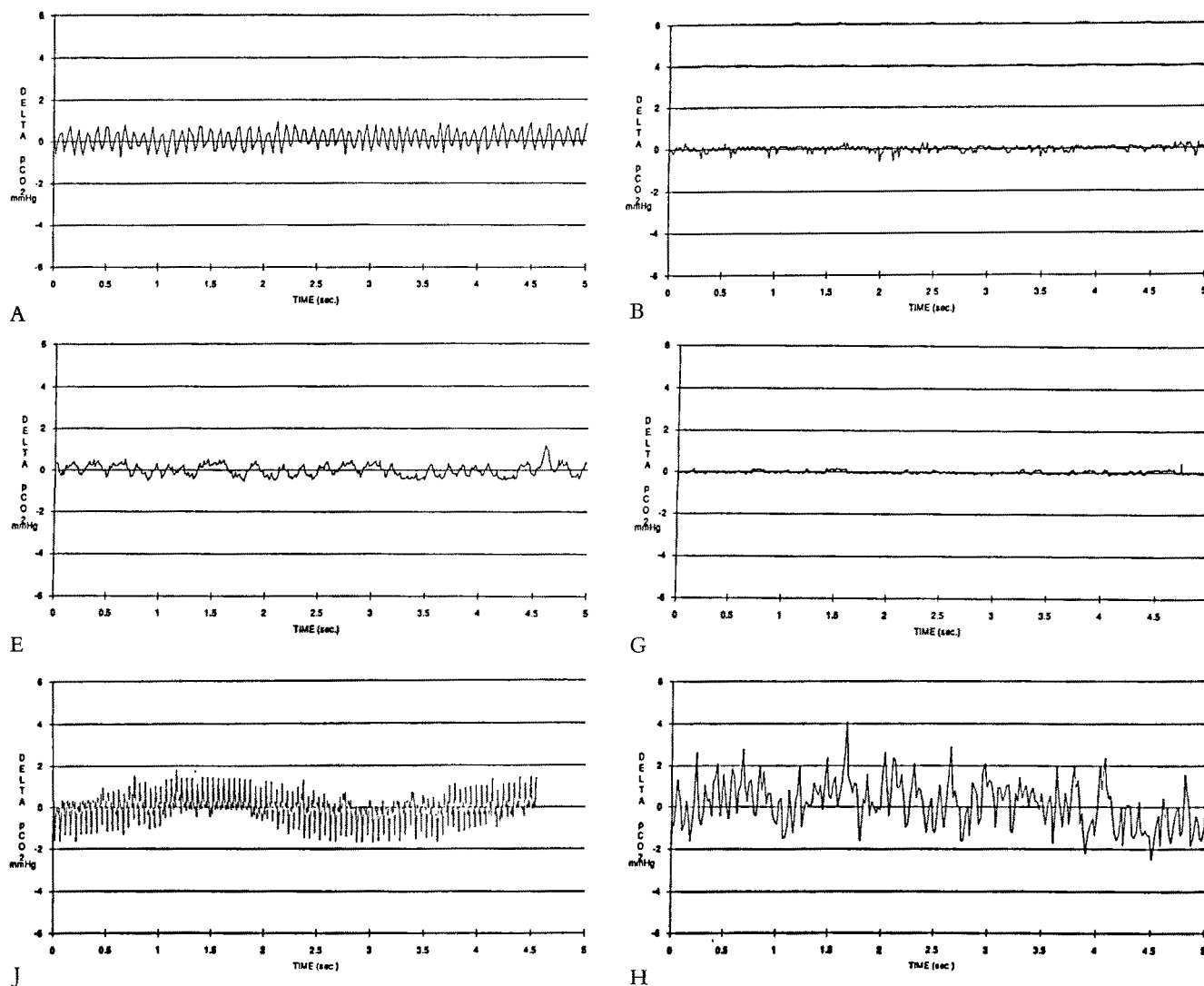
Fig 4. The measurement noise of 5 infrared analyzers (A, B, E, G, and H) and a quadrupole mass spectrometer (J) while measuring 5% carbon dioxide (38 mm Hg) test gas. Data were collected from the analog output of the instruments for 5 seconds at a 100 samples per second. P_{CO_2} = carbon dioxide tension.

DISCUSSION

Specified Analyzer Accuracy

The SPECIFIED ACCURACY of a respiratory CO_2 monitor is generally provided by the manufacturer as a percentage of the reading at mid or full scale. It is assumed that the measurement is made under nearly ideal conditions, including recent calibration and absence of interfering gases. Mass spectrometers are reported to have accuracies of about ±1.5 mm Hg [16]. The Raman spectrome-

ter has been shown to have a CO_2 measurement accuracy of about ± 0.5 mm Hg [18]. IR analyzers typically have specified accuracies within ± 2 mm Hg at mid scale (~40 mm Hg). Our data show that most analyzers can be expected to fall within these accuracy specifications under laboratory conditions. Some error results from nonlinearity, although the deviations of readings from the mid scale calibration point indicate that other factors such as instability, environmental variables, or experimental errors are primarily responsible.

Sources of End-Tidal CO_2 Analyzer Error

Although the *specified accuracy* of respiratory P_{CO_2} analyzers appears adequate for clinical interpretation, there are additional errors that may occur during actual use. We have categorized these error sources into four areas:
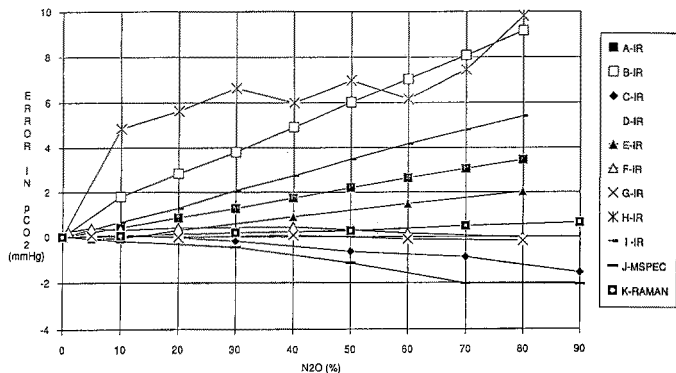
Fig 5. The effect of nitrous oxide (N_2O) on measured carbon dioxide tension (PCO_2) for 8 infrared (IR) analyzers, a quadrupole mass spectrometer (MSPEC), and a Raman spectrometer (RAMAN). Automated compensation for N_2O interference and collision broadening is found in A, C, F, and G. Instruments that require the user to input the N_2O concentration were not compensated in this experiment.
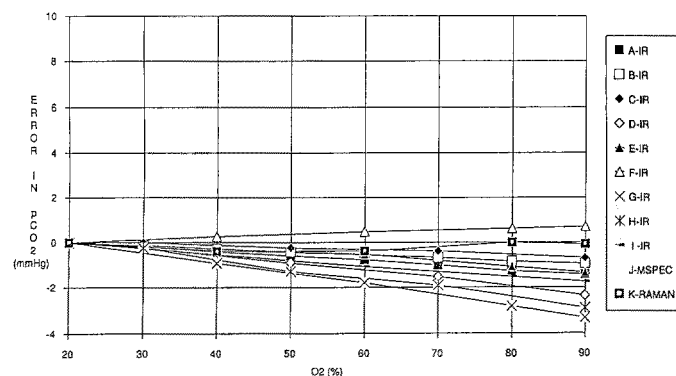

Fig 7. The response of 4 infrared analyzers (B, D, A, and I) to a sudden change in carbon dioxide (CO_2) tension from approximately 40 to 0 mm Hg. The 90 to 10% fall times were measured to be 213 ms (A), 326 ms (B), 256 ms (D), and 168 ms (I).

Fig 6. The effect of oxygen (O_2) concentration on measured carbon dioxide tension (PCO_2) for 9 infrared (IR) analyzers and a Raman spectrometer (RAMAN). Automatic compensation for oxygen collision broadening is found in C and F. Instruments that require the user to input the oxygen concentration were not compensated in this experiment.

Fig 8. Deviation from 5% carbon dioxide tension (PCO_2) (38 mm Hg) versus positive pressure applied to the sample tubing input to simulate positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) for 3 infrared analyzers. The Theoretical line shows the direct effect of pressure in the measurement cuvette. Instrument C does not deviate with sample tubing pressure, indicating it measures and compensates for pressure in the measurement cuvette. Instruments D and I exceed the effect predicted by the Theoretical line owing to pressure broadening.

(1) analyzer, (2) sampling system, (3) environment, and (4) instrument.

1. Analyzer

CALIBRATION. The accuracy of an analyzer is dependent on the calibration procedure, the reference gases, and the instrument's internal algorithm using the calibration data.

Calibration procedure. In normal clinical use, the accuracy of an analyzer depends on whether the analyzer was calibrated at one or two points, and the frequency of recalibration. Generally, side-stream IR analyzers re-
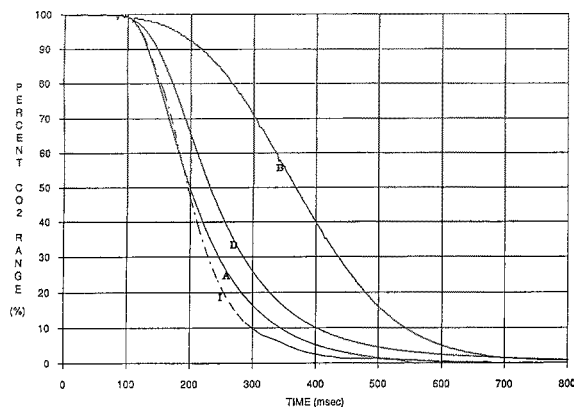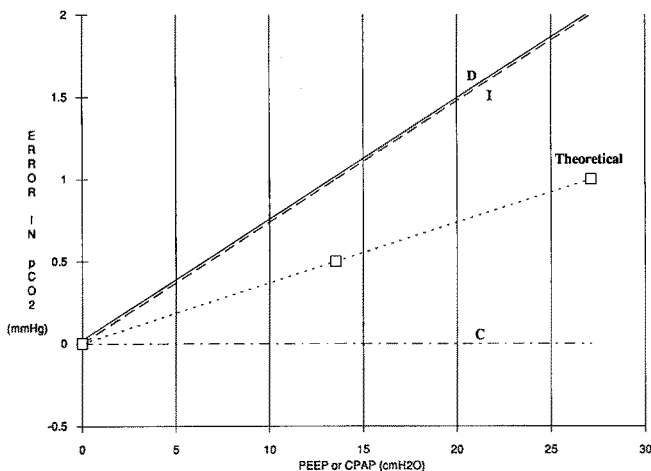
quire a regular (e.g., daily) gas calibration for baseline. Some require regular span calibration using a reference gas as well. Others specify occasional (e.g., 6 months) span calibration. A few analyzers automate the baseline and/or the span calibration using room air and an internal reference tank. Most mainstream IR analyzers use two sealed calibration cells containing a CO_2-free sample for baseline calibration and a reference PCO_2 for span calibration. One mainstream analyzer requires a CO_2-
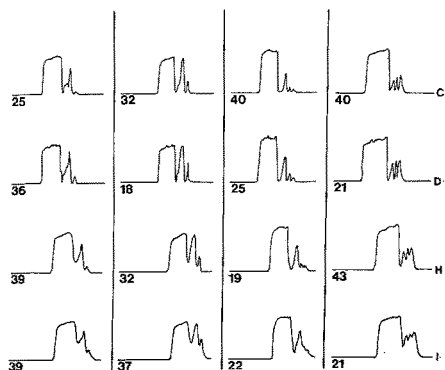
Fig 9. Four examples of the comparison of waveforms from 4 carbon dioxide tension (PCO_2) infrared analyzers (C, D, H, I) during spontaneous breathing by volunteers showing the end-tidal (PCO_2) values as displayed on each instrument's display screen. Note that each instrument can occasionally be fooled by an irregular breath pattern.

free flow of air or nitrogen in the airway adapter for baseline calibration. Another mainstream analyzer uses gas in the inspiratory cycle of ventilation to perform a periodic baseline calibration. This method can lead to serious errors if CO_2 is present in the inspiratory gas.

The Raman spectrometer baseline is established with argon from a small tank. Room air is used to set the span of oxygen and nitrogen channels. All other gases are measured with the assumption that the responses for their measurement channels are in constant proportion to the oxygen and nitrogen response. Medical mass spectrometers generally require periodic calibration by trained personnel.

We have noted that poor calibration technique can introduce substantial errors. The reference gas is introduced under pressure through a flow regulator, and sufficient pressure relief must be provided to calibrate at or near atmospheric pressure. In addition, the sample tubing or equivalent resistance must be used for introducing calibration gas, lest a pressure difference between calibration and measurement result. Alternatively, the cuvette pressure must be measured and compensated by the instrument.

Reference gases. All IR instruments require a periodic baseline calibration and the specified reference gas is usually air or, occasionally, nitrogen. Atmospheric air has a nominal PCO_2 of 0.03 mm Hg [19]. Room air can contain higher concentrations of CO_2 owing to human and combustion sources. We have measured CO_2 as high as 3 mm Hg in a poorly ventilated instrument case near the calibration inlet. A few instruments use a soda lime filter to absorb CO_2 from the baseline gas. Most rely on adequate instrument ventilation in the region of the baseline sample port to ensure a good sample.

The reference gases for span calibration are prepared gravimetrically by the major suppliers and may be specified to contain various components. Several grades are available with absolute accuracy from 0.01 to 1% tolerance. Recently, suppliers have offered gas mixtures specifically for respiratory gas analyzer calibration. The tolerance on these preparations is usually 0.03% absolute accuracy.

The tanks supplied by respiratory PCO_2 analyzer manufacturers are usually aerosol cans or 11-in (28-cm)-tall PD canisters prepared by a gas supplier to specification. These tanks typically are specified at a midrange CO_2 value (5%) of ±0.03% or 38.0 ± 0.23 mm Hg at 1 atm.

Severinghaus and Young [15] have advocated a gas mixer system for calibrating the mass spectrometer. They have found the accuracy of this calibrator to be comparable to that of gravimetrically prepared gas mixtures. In general, the accuracy of a respiratory PCO_2 analyzer is not compromised by the small errors tolerated in calibration gas standards.

Internal calibration. The interpretation of calibration data by the respiratory gas analyzer is the most important factor in the quality of the calibration. In an IR analyzer, the relationship between the absorption measured and PCO_2 is approximately exponential as idealized by the Lambert-Beer law [20]. The actual curvature of the relationship seen by an instrument is a function of the cuvette distance, the incident IR power, and scattering. The respiratory analyzer must linearize the output from the optical measurement system to report PCO_2. Typically, the optical measurement system produces an analog electrical voltage proportional to the measured absorption. This analog voltage is converted to a digital value in a microprocessor and the appropriate PCO_2 is determined from a table. Linearization tables are determined in the factory during the development of the instrument. The linearization table is usually determined for about 50 points and is tailored to minimize error caused by variation between IR filters. Thus, the basic accuracy of the instrument is highly dependent on calibrating the measurement of a gas of known PCO_2 to its correct point on the linearization table.

If an IR analyzer measures and compensates for errors caused by other gases such as N_2O and oxygen, then these gases may be included in the calibration mixture. Such analyzers incorporate a second IR channel to measure N_2O and an independent analyzer to measure oxygen. Each must be calibrated to ensure accurate measurement. Some IR analyzers do not measure or employ compensation for the effects of other gases. For these analyzers, a calibration gas mixture that approximates the respiratory samples expected during clinical use is

recommended. In this way, error caused by interference effects may be minimized, though not eliminated.

The industry standard multigas references for IR analyzers are 5% CO_2, 21% oxygen, balance nitrogen; 5% CO_2, 30% oxygen, balance N_2O; or 5% CO_2, 50% N_2O, balance air. All of these are specified to 0.03% tolerance.

DRIFT. *Warm-up.* Any instrument requires a period of warm-up to produce accurate results, as seen in the 1- to 4-minute times we measured. IR analyzers are thermally sensitive and employ temperature control or compensation or both. Most of the optical component housing materials are metal and require some time to come to temperature.

A mass spectrometer requires about 12 to 24 hours to establish an adequate vacuum after a cold start. If the vacuum is maintained, up to 15 minutes may still be needed to achieve readings within the accuracy specifications at start-up. The Raman analyzer requires about 2 minutes to reach stability after a cold start [21].

Instability. Long-term instability of a respiratory CO_2 analyzer can result in a substantial change from the accurate measurements obtained just after calibration.

Traditionally, two components of stability are measured: span and baseline. Because of the ratiometric techniques used in most IR analyzers, the sensitivity to P_{CO_2} over the entire measurement range (i.e., span) is expected to be relatively constant over time. The nature of these designs, however, makes them more prone to absolute shifts in the measurements (i.e., baseline). Our data show, however, most instruments will maintain reasonable baseline and span stability when they are left undisturbed.

As seen in one example (IR analyzer C), a paradoxical source of instability is the use of compensating variables. Known sources of inaccuracy such as temperature at various points in the system and sensitivity to pressure and other gases are often measured and introduced into the measurement of P_{CO_2} as corrections. If any of these measurements are inaccurate, the result will be an apparent instability in the measurement of P_{CO_2}.

Mass spectrometers sometimes exhibit erratic stability characteristics. Severinghaus and Young [15] stated: "Radical change may occur within a few minutes, particularly after startup in the morning or after a momentary standby period for calibration, or they may occur after a long period of sampling only oxygen or only air. These drifts are neither predictable nor repeatable." They report that drifts of 9 mm Hg/hr can occur as often as 20% of the time over several months.

The Raman spectrometer has a self-calibrating feature that compensates for the instrument's drift. This calibration consists of an 8-second injection of argon into the instrument to correct for baseline offset and a sample of air to adjust the span. This process is repeated automatically every 20 minutes. We have confirmed that the instrument remains within its accuracy specification between these calibration intervals, exhibiting about a ±0.1 mm Hg change over this period.

Noise. Noise is usually considered any component of the measurement that is unwanted and cannot be explained from known error sources. We have shown that the noise can be substantial in some $P_{ET}CO_2$ analyzers (e.g., IR analyzer H) and may contribute to inaccuracy. Noise can result from many sources including local thermal changes in the optical system, mechanical instability in the chopper wheel, electronics, analog-to-digital converter, round-off errors in digital processing, and electromagnetic interference.

SELECTIVITY. Selectivity of a respiratory P_{CO_2} analyzer is the ability to accurately measure P_{CO_2} in the presence of other gases in the respiratory mixture (e.g., nitrogen, argon, helium, xenon, oxygen, water vapor, N_2O, and anesthetic agents). For the IR analyzers, oxygen and N_2O are known to strongly influence P_{CO_2} measurements by either or both of two different mechanisms: DIRECT INTERFERENCE and collision broadening. The mass spectrometer measurement of CO_2 is affected by the anesthetic vapor agents and must be compensated.

Direct interference. There are wavelengths in the IR region of the spectrum where each of the respiratory and anesthetic gases exhibits unique absorption. As seen in Figure 10, some of these bands are quite near each other; CO_2 absorbs strongly between 4.2 and 4.4 μm while N_2O absorbs strongly between 4.4 and 4.6 μm. At the 4.4-μm edges of both absorption bands, CO_2 and N_2O overlap slightly. Consequently, some CO_2 analyzers exhibit inaccuracy in the presence of high concentrations of N_2O [22]. Most of the other gases, including anesthetic agents and water vapor, do not overlap with the CO_2 band and their DIRECT INTERFERENCE is negligible.

The mass spectrometer can experience direct interference in CO_2 measurement from carbon fragments of organic molecules (e.g., anesthetic agents), which are produced during the ionization process. Since CO_2 is usually measured at mass 12, a mass spectrometer can't distinguish carbon atoms from other organic sources.

Collision broadening. A separate phenomenon, collision broadening, may cause inaccuracy in an IR analyzer or Raman spectrometer. Molecules in the gas mixture being analyzed are constantly colliding with each other and exchanging energy with each collision. Depending on the size, dipole moments, and other characteristics
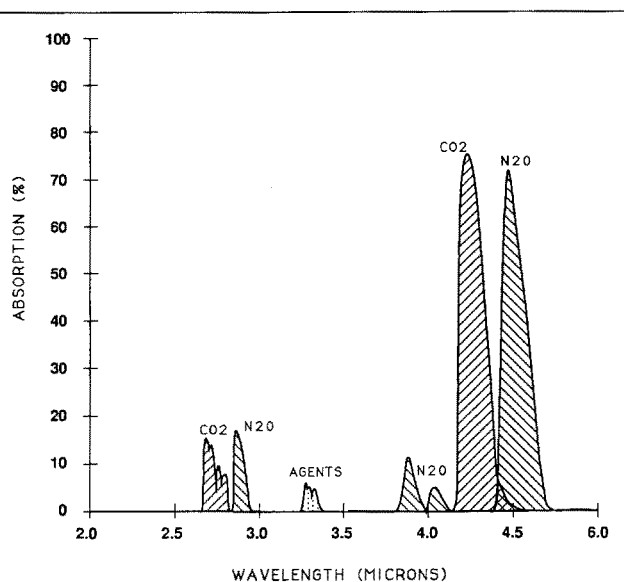
Fig 10. The infrared absorption spectrum for the gases carbon dioxide (CO_2) and nitrous oxide (N_2O) and the volatile anesthetic agents.

of the gas molecules, energy will transfer to or from the gas being measured. As a result, individual peaks within the IR absorption spectrum of the gas are broadened (or narrowed) and the apparent absorption at the measurement wavelength is altered [23]. Of most concern for respiratory gas monitoring, oxygen and N_2O cause collision broadening when CO_2 is measured. Left uncompensated, the collision broadening effect of N_2O can substantially alter CO_2 measurements (up to 6.5 mm Hg), as our data demonstrate. Collision broadening from oxygen is smaller in magnitude (up to -2.5 mm Hg), but is not negligible in most instruments.

The Raman spectrometer shows a slight effect due to N_2O of about 0.2 mm Hg per 10% N_2O, but little effect from oxygen. The quadrupole mass spectrometer is not affected by N_2O or oxygen to any appreciable extent (not shown in the figures).

Pressure broadening. The total pressure in the measurement cuvette causes a shift in the absorption spectrum for CO_2 and is often called the PRESSURE BROADENING effect. Severinghaus et al [22] developed a relationship for this effect of about 0.4 mm Hg Pco_2 per 100 mm Hg of total pressure.

It should be noted that the pressure broadening effect and the collision broadening effects are complex physical phenomena and, in many circumstances, difficult to separate. The two terms often are used interchangeably.

2. Sample System

SAMPLING SYSTEM ERRORS. As we have demonstrated, changes in measurement cuvette pressure can result in

erroneous measurements. An IR CO_2 analyzer or Raman spectrometer using a side-stream sampling system can be directly influenced by any changes in the sampling catheter or pneumatic system that change the measurement cuvette pressure. In most sampling systems, a pump draws gas through sample tubing and the measurement cuvette, resulting in a slightly negative pressure with respect to ambient. So long as this pressure does not change between the time of calibration and the time of measurement, no error results. However, if water or foreign substances collect in the sample tubing, the total pressure in the cuvette will become more negative. As a result, the Pco_2 reading will be erroneously low in proportion to the pressure change. Some analyzers measure pressure at the cuvette to correct for changes in pressure due to sample tubing resistance changes. These analyzers will be relatively insensitive to increased sample catheter resistance. Other analyzers have sampling systems that measure and automatically maintain sample *flow*. These systems will not, however, keep the *pressure* within the cuvette constant and may exhibit substantial sensitivity in the Pco_2 reading to increased sample catheter resistance. We have observed that a typical instrument will tolerate an increase in sample tubing resistance that results in a change in the Pco_2 reading of 1 or 2 mm Hg before an occlusion is detected.

INTERFERENCE FROM LIQUID WATER. Most sampling systems incorporate a water trap to prevent liquid water and other foreign substances from entering the measurement cuvette. There are almost as many water trap designs as there are respiratory Pco_2 analyzers. Some separate the liquid from the gas via a tortuous sample path, where gravity coaxes the liquid portion into a collection bottle. Others use a hydrophobic membrane to exclude the liquid portion of the sample. We have found that many water traps are easily overwhelmed and water enters the measurement system. The result is often total obscuration of the optical path and the inability to obtain a reading. When the optical path is not totally blocked, the readings are generally accurate owing to the ratiometric design of most IR instruments.

INADEQUATE TIME RESPONSE. The time response of a respiratory Pco_2 analyzer to a change in Pco_2 can substantially affect the accuracy of the measurement of $PetCO_2$ [17]. For "normal" Pco_2 waveforms, this is not a problem since the gradual plateau phase allows time for the analyzer to react. However, at high respiratory rates the change in Pco_2 to its maximum may challenge the response of an instrument. Also, small sharp peaks sometimes appear during the plateau phase that may

represent the maximum value of P_{CO_2}. These peaks may not be faithfully recorded by a sluggish analyzer.

The ability of an analyzer to follow an abrupt change in P_{CO_2} is determined by the response time of the optical system and the gas mixing properties of the sample catheter, pneumatic system, and cuvette at the given sample rate. Generally, the response of the optical system is rapid in comparison with the other factors. The mixing characteristics of the sample catheter, pneumatic system, and cuvette are complex and are a function of the sample rate [24]. The total response generally cannot be modeled as a first-order process. Therefore, a 10 to 90% rise time or 90 to 10% fall time is often used as a time-response figure of merit. A response time less than 250 ms is usually considered adequate to faithfully reproduce clinical P_{CO_2} waveforms at respiratory rates up to 60 breaths per minute [9]. All except 1 of the instruments we measured were acceptable according to this criterion. The instrument that failed to meet the criterion (IR analyzer B) had an unusually large effective pneumatic system volume.

Thirteen commercial IR analyzers were tested by the Emergency Care Research Institute for adequacy of response time [24]. They found that all analyzers were capable of reporting $P_{ET}CO_2$ to within 1 mm Hg of actual at simulated respiratory rates up to 60 breaths per minute.

3. Environment

ATMOSPHERIC PRESSURE. Atmospheric pressure directly influences the readings of respiratory IR or Raman P_{CO_2} analyzers since they measure partial pressure. Also, an indirect effect is seen when an IR or Raman spectrometer reports measurements in vol% or a mass spectrometer reports measurements in mm Hg.

The direct effect of atmospheric pressure changes on IR and Raman analyzers can be eliminated by knowing the atmospheric pressure during calibration. Calibration is usually accomplished from a tank whose contents are known in vol%. If the atmospheric pressure at calibration time is known accurately, the analyzer can compute the partial pressure of the calibration gas (or vol% of 1 atm). Thus, its readings will always reflect the partial pressure of the gas within its measurement cuvette regardless of changes in the atmospheric pressure.

The indirect effect of atmospheric pressure results when a side-stream IR or Raman analyzer is required to report results in vol%. The atmospheric pressure at measurement time must be known to compute the values correctly. Similarly, the mass spectrometer that measures fractional composition must consider the atmospheric pressure when converting to units of partial pressure.

Some mainstream IR instruments are calibrated from sealed gas cells whose partial pressure (and fraction) are known absolutely. These instruments will always report measurements in units of partial pressure correctly regardless of the atmospheric pressure. If this analyzer is required to report results in vol%, the atmospheric pressure at measurement time only must be known.

Some instruments incorporate a barometer to compensate for changes in atmospheric pressure. Others require the user to enter the correct atmospheric pressure manually and then compensate appropriately. It should be noted that the maximal changes in atmospheric pressure due to the weather are on the order of 20 mm Hg. This would result in a change in the P_{CO_2} of about 1 mm Hg. Changes in altitude, such as calibrating in Boston and measuring in Denver, can result in a decrease in P_{CO_2} readings of 6 mm Hg!

BREATHING CIRCUIT. The location in the breathing circuit from which the respiratory gas sample is taken can influence the value recorded for $P_{ET}CO_2$. In an anesthesia circle system, the sample should be taken as far from the interface of fresh gas and expired gas (Y piece) as possible, preferably near the distal end of the tracheal tube. This prevents premature mixing of the expired gas with fresh gas in the vicinity of the sample catheter.

Leaks in the breathing system or the sample system itself will lower measured P_{CO_2} from dilution by entrained air. Under special circumstances of positive-pressure ventilation and a large leak at the circuit sample port, the P_{CO_2} waveform may be very distorted with no reduction of $P_{ET}CO_2$ [25]. In a mass spectrometer or Raman spectrometer system, the appearance of nitrogen in both inspired and expired gas is often a sign of a leak in the sample system.

The location of the sample site may also have an effect on the shape of the P_{CO_2} waveform. Very small pressure fluctuations during expiration can result in small shifts in the interface between the end-expired gas volume and inspired gas. Such pressure fluctuations are thought to be caused by the heart beating against the lungs. If the sample catheter is located near the interface of expired and inspired gas, oscillations may occur in the P_{CO_2} waveform. These patterns are termed "cardiogenic oscillations" and are sometimes misclassified by breath-detection algorithms, as discussed in the following section.

For instruments that inherently measure partial pressure (not the mass spectrometer), airway pressure will be transmitted to the measurement cuvette and change the measurement. During spontaneous ventilation, pressures negative to atmosphere are developed. The magnitude of these pressures is usually quite small (<5 cm H_2O or <3.5 mm Hg) and will have little effect

on the measurements. Airway pressures at end-expiration are virtually atmospheric, and instruments that measure PETCO$_2$ at this time will be relatively unaffected.

When PEEP is applied to the patient circuit, this pressure is transmitted to the cuvette and will increase the measurement, as shown by our data. Typical values of 10 cm H$_2$O (7 mm Hg) will have a small influence on the measurement of PETCO$_2$. The PCO$_2$ analyzer should report values without compensation for the effect of PEEP. The alveolar PCO$_2$ will be elevated by the PEEP and the analyzer will correctly reflect this fact. The PaCO$_2$ will (theoretically) be increased by the PEEP as well.

WATER VAPOR CONSIDERATIONS. Water vapor produced by the patient as part of expired gas is a very important factor in the measurement and reporting of PETCO$_2$. Some instruments report body temperature and pressure, saturated (BTPS), values for PCO$_2$ assuming that the gas sampled from the patient was fully saturated with water vapor at 37°C. Other instruments report ambient temperature and pressure, dry (ATPD), values for PCO$_2$ by removing water vapor from the sample. Still others report values in between BTPS and ATPD and ignore the effects of water vapor all together. The error in reporting PCO$_2$ at ATPD when it should be reported at BTPS is about 2.5 mm Hg. Severinghaus [26] has recommended that respiratory PCO$_2$ analyzers report their results in the conventional BTPS units. We agree strongly with this convention.

Analyzers that use Nafion tubing in their sample catheters to remove water vapor will essentially measure dried patient gas. Some of these analyzers report the PCO$_2$ at BTPS, by decreasing the dry gas reading by the fraction, $(P_{ATM} - 47)/P_{ATM}$. P_{ATM} is the atmospheric pressure in mm Hg and 47 is the vapor pressure of water at 37°C. Others report the results in ATPD, expecting the user to apply the above conversion to get BTPS values. (Note.—Nafion actually equilibrates the water vapor pressure inside the tubing to that outside the tubing. The atmospheric water vapor pressure is the saturated water vapor pressure at atmospheric temperature times the relative humidity. At 20°C and 50% relative humidity, the water vapor pressure is about 10 mm Hg. At a PCO$_2$ of 40 mm Hg, the error resulting from considering the sample truly dry is about 0.5 mm Hg.)

If Nafion tubing is not used in the sample catheter, then the respiratory gas cools to nearly ambient temperature as it passes through the breathing circuit and into the pneumatic system. The water vapor pressure when the gas reaches the measurement chamber will be the saturated water vapor pressure at the point of lowest temperature along the gas path. Generally, this temper-

ature will be unknown and some analyzers just ignore the resulting error of about 1 mm Hg.

Mainstream IR analyzers measure the gas in the breathing circuit, which is generally nearly saturated at body temperature. They will naturally report readings near BTPS. The exact water vapor pressure in the breathing circuit will depend on many factors, including the use of heated humidification, fresh gas flow, length of time in use, CO$_2$ absorber used, and temperature. A reduction in temperature of 5°C in the breathing circuit from a body temperature of 37°C will result in a PCO$_2$ reading about 0.5 mm Hg less than the correct BTPS value.

Medical mass spectrometers do not have ion collectors for water vapor. Thus, they effectively "dry" the sample by ignoring water and summing the remaining gases to 100%. They report PCO$_2$ at BTPS by multiplying the measured CO$_2$ fraction by the atmospheric pressure less 47 mm Hg.

4. Instrument

END-TIDAL CO$_2$ DETECTION ALGORITHMS. In clinical practice, various perturbations occur in the upstroke, plateau, and downstroke of the PCO$_2$ waveform. Technical causes include the ventilator mechanics (e.g., stops, accordion bellows, and valve flutter). Physiologic causes include voluntary and involuntary contractions of the respiratory muscles, cardiogenic oscillations, abdominal movements, and airway reactivity. Waveform perturbations can also be caused by pressure against the patient's chest or abdomen or even against the bed. In addition, clinical maneuvers such as adjusting the airway apparatus, suctioning the airway, and repositioning the bed can perturb the waveform. Spontaneous ventilation by a patient often results in an irregular PCO$_2$ pattern without well-defined plateaus.

As seen in the example data, disturbances in the PCO$_2$ waveform make identification of the breath by an instrument's algorithm difficult. Misidentification of breaths can lead to incorrect reporting of PETCO$_2$. For example, if an algorithm incorrectly identifies a cardiogenic oscillation as a breath, PETCO$_2$ may be reported as the peak of this waveform. Usually the cardiogenic oscillation occurs during the downslope of the true breath and its peak value is substantially less than the true PETCO$_2$.

RESOLUTION ERROR. Limited RESOLUTION in the PETCO$_2$ displayed by the respiratory gas analyzer produces a small error in the estimate of the PaCO$_2$. Most respiratory CO$_2$ analyzers report values to the one unit's digit. Thus, a limit of resolution of ±0.5 mm Hg is implied.

A few instruments report P_{CO_2} to one decimal digit, implying a limit of resolution of ± 0.05 mm Hg.

CONCLUSIONS

Estimating $PaCO_2$ from measured $P_{ET}CO_2$ is fraught with difficulties, not the least of which are related to $P_{ET}CO_2$ measurement accuracy. Accurate measurement of $P_{ET}CO_2$ is dependent on the instrumentation used and a number of factors that can influence the measurement. Instrument inaccuracy, lack of display resolution, temperature dependence, miscalibration, drift, noise, poor selectivity, pressure effects from the sampling system or the patient environment, and the effects of water and water vapor can all contribute errors. These errors can be independent and additive, resulting in substantial inaccuracies. The Table lists the expected magnitude of these errors, when present, as discussed in the results section. These estimates assume that no automatic or manual compensation is built into the analyzer. Also, the conditions for each source of error are assumed to be at their extreme (e.g., an instrument calibrated at 0% N_2O and measured at 75% N_2O). Ambient pressure of 1 atm and a nominal $P_{ET}CO_2$ of 40 mm Hg are assumed.

In addition to the errors given in the Table, other systematic mistakes can lead to gross inaccuracies. The end-tidal detection algorithm may mistake cardiogenic oscillations or plateau disruptions for breaths. The user may miscalibrate the instrument by applying substantial pressure to the inlet port or by using a tubing connection with different resistance than the patient sample

Estimate of Typical Errors for
an Uncompensated Infrared Analyzer

Error Source	Typical Magnitude (mm Hg)
Inaccuracy	2.0
Resolution	0.5
Noise	2.0
Instability (12 hours)	3.0
Miscalibration	1.0
Selectivity	
70% Nitrous oxide	6.5
100% Oxygen	−2.5
Atmospheric pressure change	<1.0
Airway pressure, 30 cm H_2O	2.0
Positive end-expiratory pressure or continuous positive airway pressure, 20 cm H_2O	1.5
Sampling system resistance	<1.0
Water vapor	2.5

tubing. Liquid water may accumulate in the optical measurement system, rendering the instrument inoperable or grossly inaccurate.

In a clinical setting, unless the user is confident that all of the technical error sources have been eliminated and the physiologic factors are known, depending on $P_{ET}CO_2$ to determine $PaCO_2$ is not advised.

GLOSSARY

ACCURACY The ability of an instrument to measure the actual CO_2 composition of a gas under all possible conditions.

AMBIENT TEMPERATURE AND PRESSURE, DRY (ATPD) CO_2 measurements reported as if the sample were measured under conditions of ambient temperature and pressure, dry.

BASELINE The output of an analyzer measuring a gas containing no CO_2, or the calibration of an analyzer with a gas containing no CO_2.

BODY TEMPERATURE AND PRESSURE, SATURATED (BTPS) CO_2 measurements reported as if the sample were measured under conditions of body temperature and pressure, saturated with water vapor.

COLLISION BROADENING A phenomenon where the spectral absorption peaks of a gas (CO_2) are broadened owing to the collision or proximity of molecules of another gas (e.g., N_2O, oxygen). Collision broadening is sometimes called line broadening and is often used interchangeably with the term pressure broadening (see below).

DIRECT INTERFERENCE In an IR analyzer, one gas (e.g., N_2O) can absorb light of the wavelength used to measure another gas (e.g., CO_2). In a mass spectrometer, a gas (e.g., anesthetic vapor agents) can cause ions to fall on the measurement channel of the gas of interest (e.g., CO_2).

INFRARED (IR) ANALYZER A type of analyzer that uses the absorption or transmission of IR radiation (as opposed to scattering) as a basis for measuring the quantity of a gas within its measurement cuvette.

MAINSTREAM ANALYZER An instrument that analyzes gases by passing the entire respiratory gas flow through the instrument's measurement cuvette.

MASS SPECTROMETER An instrument that ionizes a gas sample and uses the ratio of the mass to the charge of the resulting ions to identify and measure the fractional concentrations of that gas sample.

NOISE Any component of the measurement that is unwanted and cannot be explained from known error sources.

PHYSIOLOGIC DEAD SPACE The volume of gas free of CO_2, equivalent to the portion of the expired gas not in equilibrium with $PaCO_2$.

PRESSURE BROADENING   A phenomenon where the spectral absorption peaks of a gas (e.g., CO_2) are broadened owing to the absolute pressure of the gas sample.

RAMAN SPECTROMETER   An instrument that uses the scattering of a monochromatic light source by gases in a sample at wavelengths specific to each gas to identify and measure the composition of that sample.

RESOLUTION   The ability of an instrument to distinguish between two measured values that are different.

SIDE-STREAM ANALYZER   An instrument that draws gas samples into the measurement cuvette from respiratory gas.

SPAN   The output of an analyzer measuring a gas containing CO_2 equivalent to the mid- or full-scale reading of the instrument; or, to calibrate the instrument at a mid- or full-scale reading using a reference gas.

SPECIFIED ACCURACY   The ability of an instrument to measure the actual CO_2 composition of a particular gas under a limited set of conditions.

STABILITY   The ability of an analyzer to accurately read a baseline and a span gas over time.

TIME RESPONSE   The time required for an analyzer to respond to a change in the composition of the measurement gas. Time response is often measured by making an instantaneous change between a baseline and a span gas and recording the time required for an analyzer to change its reading. The period between the instantaneous change in gas composition and its first appearance at the analyzer is known as the delay time. Delay time does not affect the accuracy of measurement. The rise from 10 to 90% of the baseline and span readings is often referred to as the response. Alternatively, a 90 to 10% response for a change from span to baseline gas is used along with the delay time to reflect the instrument time response.

WARM-UP TIME   From a cold start, the time required for an instrument's readings to stay within its specified accuracy limits.

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