METHODS OF MEASUREMENT OF BLOOD AND GAS CARBON DIOXIDE DURING ANESTHESIA

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THIS section will deal with the measurement of carbon dioxide content and tension in gases, blood and in tissue, and the special problems introduced by the presence of anesthetic agents and apparatus. In the gas phase, the partial pressure may always be calculated from content in volumes per cent, by multiplying by barometriic pressure minus the water vapor pressure at body temperature. We will not consider separately instruments for analysis of gas partial pressure, although some instruments are sensitive to pressure rather than content. Further reference to these instruments may be found in Glasser.[1]

CARBON DIOXIDE ANALYSIS OF GAS SAMPLES CONTAINING ANESTHETIC AGENTS

Haldane. The Haldane analyzer can be adapted to measure gas CO_2 concentration fairly accurately in the presence of nitrous oxide by using extremely concentrated alkali and eliminating rubber tubing connections.[2] The errors are due to solution of the anesthetic in the absorbent.

Scholander. The small volume of absorbent used in the micro Scholander makes it possible to correct for this error. In order to make this correction, one computes the volume of anesthetic agent which went into solution in the absorbent. The volume of added absorbent is measured at the end of the analysis by setting the mercury-absorber interface at the hair line in the capillary, recording it as "V" micrometer divisions (below zero). The solubility (S) of the anesthetic agent may be estimated by blank analysis of undiluted anesthetic, or a known fractional concentration (Co) of the anesthetic without CO_2. Using M_1 and M_2 as the micrometer readings before and after adding a volume (Vo) of CO_2 absorber,

$$S = \frac{M_1 - M_2}{CoVo}.$$

Then the CO_2 concentration of a sample containing an anesthetic gas is given by

$$\text{Per Cent } CO_2 = \frac{M_1 - M_2 - SCV}{M_1} \times 100.$$

where C is the fractional concentration of the anesthetic. *Example:* A gas sample containing 80 per cent N_2O was analyzed. M_1 read 12.312, M_2 read 11.741. The absorber volume (V) read −.135. In analyzing pure N_2O, a value for $M_1 - M_2$ of .057 with a Vo of −.225 was obtained. Then $S = .057/.225 = 0.253$. So the sample had [12.312 − 11.741 − (0.253) (0.80) (.135)]/12.312 × 100 = 4.41 per cent CO_2. If no correction were made for N_2O absorption, the answer would be 4.64 per cent CO_2. Other common sources of error in Scholander analyses are (1) use of Van Slyke reagents which have the wrong vapor tension, and (2) dilution of sample by air through the end of the transfer pipette if the mercury is not allowed to fall continuously during transfer from gas source to Scholander apparatus.

The Infrared Carbon Dioxide Analyzer. The most satisfactory instrument for continuous rapidly responding indication or recording of alveolar or airway CO_2 in anesthesia is the infrared analyzer. The instrument most used in the United States, the Beckman-Spinco, (formerly Liston Becker), is available with two types of sample cells, the large bore (43 ml.) "breathe-through" and the 0.2 ml. "microcatheter" cell. For use in anesthesia the breathe-through cell has several disadvantages. Its large dead space is undesirable for breathing bi-directionally. It may not wash out completely if put in the expiratory tubing with a valved Y piece. It is awkward to support it in a close fixed relationship to the patient's head, and it must be removed from the breath-

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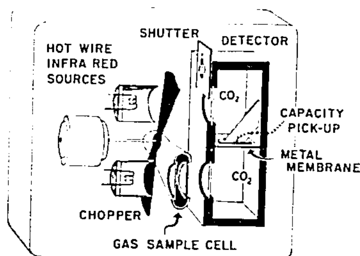

FIG. 1. Schematic diagram of the principal of the infrared CO_2 analyzer. Infrared light, interrupted 60 times per second, enters two sealed chambers containing some CO_2 (usually 50 mm. of mercury pressure in the Beckman instrument) where wave lengths of 2.6 and 4.3 micra are absorbed by this CO_2, causing it to expand. When the two chambers receive equal amounts of these wave lengths, the pressure rise is the same in both chambers. The chambers are separated by a very thin metal membrane pressure manometer which will be displaced when some of the infrared light is absorbed by a sample placed in one of the light paths in the sample cell. The signal is logarithmically proportional to the optical density (for just these two wave lengths) of the gas in the sample cell.

ing system for calibration. The problem of cross infection arises with the instrument mounted directly in the airway. For these reasons the microcatheter cell is preferable, and the remainder of this discussion will refer to its use.

Interference of Anesthetic Agents in Infrared Analyzers. The Luft principle which is used in all modern IR analyzers is a detector cell filled with the gas to be analyzed (fig. 1). This detector absorbs only specific wave lengths of infrared light, which for CO_2 are 2.6 and 4.3 micra. These absorption bands are quite sharp, so only when the same gas is placed in the light path (in the sample cell) are some of these same wave lengths absorbed, reducing the energy absorbed in the detector. Of the common anesthetics, only N_2O has a significant overlap of these wave lengths, and this is surprisingly minor considering that it has the same molecular weight as CO_2. 100 per cent N_2O reads about 0.5 per cent CO_2 when introduced in the IR CO_2 analyzer.[3] Fortunately, this effect may be eliminated by filling the entire analyzer head with N_2O, absorbing the overlapping wave lengths before they reach the detector. No overlap is detectable with cyclopropane, ether or halothane.

Another and more difficult problem is the increased light which CO_2 absorbs when mixed with some anesthetic gases, notably cyclopropane and nitrous oxide. This effect, known as pressure broadening, is a general phenomenon of infrared absorption of gases.[1] The increase in the apparent reading of 5 per cent CO_2 when various other gases are added is shown in table 1.[5,6] Fortunately, the ratio of the apparent reading to the actual CO_2 concentration in the presence of a fixed anesthetic concentration, remains approximately constant from 0 to 10 per cent CO_2.[7] Therefore, calibration curves for CO_2 in anesthetics can be prepared from the CO_2 in O_2 curve by multiplying the concentration at all points on the curve by this ratio determined at one particular meter deflection.

Since the response of the instrument is nonlinear, and this non-linearity varies with the pressure in the sample cell (fig. 2) it is best to

TABLE 1

Background Gas and Concentration (per cent)	Reading Given on CO_2 - O_2 Curve by 5% CO_2 (per cent)	Correction Ratio	Reference
Oxygen 95	5.00	1.00	—
Air 95	5.4	.925	3
	5.5	.91	31
	5.35	.935	10
Nitrous oxide 95	6.2	.81	3
	5.77	.87	9
Nitrous oxide 47.5 Oxygen 47.5	5.7	.88	3
Nitrous oxide 60-80	5.7	.88	5
Cyclopropane 95	6.7	.75	3
Cyclopropane 20	5.5	.91	6
Cyclopropane 40	5.8	.86	6
Ether, all conc. 0-20	5.0	1.00	6
Air 95	5.15	.97	*
N_2O 70	5.25	.95	*
Cyclopropane 25	5.15	.97	*
Cyclopropane 10	5.05	.99	*

* We obtained these values in a Beckman-Spinco LB-1 CO analyzer with microcatheter cell. The pressure in the sampl cell was regulated at 100 mm Hg below ambient. The head was filled with 100 per cent N_2O. The detector was filled wit pure CO_2 gas at 50 mm. of mercury. Carbon dioxide concentrations were determined to ±0.2 mm. of mercury with a C electrode. This correction factor was constant over the rang 0-10 per cent CO_2; *i.e.*, in a sample containing 70 per cent N_2 the actual CO_2 concentration is .95 times the CO_2 concentratio read from the CO_2 in O_2 calibration curve.

Our data show much less collision broadening than any othe published data. Dr. Max Liston of Beckman Company (per sonal communication) has found a ratio of .965 for N_2O 95 pe cent, CO_2 5 per cent, in close agreement with ours. Some of th other investigators did not eliminate crossover of absorptio bands by filling the analyzer head with N_2O. The earlier work ers also used higher partial pressures of CO_2 in the detecto which increases pressure broadening. However, several othe workers appear to have used the same detector pressure an have filled the analyzer head with N_2O. It may be that othe unrecognized differences in the apparatus affect collisio broadening.

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establish the shape of the curve frequently with 3 to 6 known CO_2 mixtures. Generally it is most convenient to adjust the gain to bring the highest gas deflection to full scale on either the meter or recorder. Frequent checks and resetting can be done using only this gas. It should be noted that even nitrogen has a small pressure broadening effect making the calibration curve for CO_2 in air read 2–4 per cent higher than CO_2 in O_2. Ramwell[8] has taken advantage of this proportionality over the 0 to 10 per cent CO_2 range to suggest a simple method of calibration using a single plotted curve. He establishes one curve accurately for CO_2 in O_2. He then introduces a sample of known CO_2 concentration mixed with the desired N_2O (or cyclopropane) concentration, and resets the gain to make the CO_2 read correctly. A further simplification is to then re-read the meter deflection produced by the original highest CO_2–O_2 mixture, and in the future, set this gas to this reading instead of to full scale. The alternative is to prepare a series of calibration curves for various anesthetics, always setting full scale with a CO_2–O_2 mixture. It has recently been suggested that the pressure broadening effect is reduced by lowering the detector cell P_{CO_2} from 50 to 10 mm. of mercury.[9] However, this adjustment cannot be done except by the manufacturer. Greater accuracy can be obtained by optically suppressing zero, to make the instrument read zero with a known CO_2 concentration up to about 5 per cent, and full scale with some higher known CO_2 mixture.

Water Vapor Effect on Infrared CO_2 Analyzers. The pressure broadening effect of water vapor very nearly counteracts its dilution effect in the sample cell. Experimentally, the greatest difference we have been able to detect between extreme drying and saturation at 40 C. is about 2 per cent, whereas the dilution effect should have been about 7 per cent. In practice, without this extreme drying, there is no difference in reading of wet and dry gas of the same CO_2 concentration (as determined by chemical analysis). Chemical analysis gives the dry gas concentration (even though the gases are wet in the Scholander, the answer is in dry gas per cent CO_2). Therefore, the IR CO_2 analyzer may be treated as a dry gas analyzer.[10] The end-tidal P_{CO_2} is computed

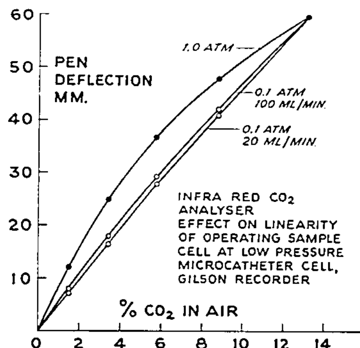

FIG. 2. The effect on linearity of response produced by maintaining low pressure in the sample cell of the infrared CO_2 analyzer.

from per cent CO_2 by multiplying by barometric pressure minus the water vapor pressure (at patient temperature).

Mass Spectrometer. Unfortunately, N_2O and CO_2 are both of molecular weight 44, and coincide in the output of a mass spectrometer. Carbon dioxide must be read using the carbon fragment at 12, and this means loss of sensitivity and usually problems in variation of the amount of breakdown of the gas. Considering its cost and complexity, this instrument is inappropriate for CO_2 measurements in anesthesia.

Nonspecific Analyzers Sensitive to CO_2. The catharometer is a hot wire forming part of a Wheatstone bridge, the cooling of which is affected by the gas around it. It can distinguish CO_2 from anesthetic gases only by comparing two samples of the same gas, from one of which the CO_2 has been absorbed. It has the advantage, when used for analysis of CO_2 in air, of a linear direct reading output with constant sensitivity. An analysis requires several minutes and several hundred milliliters of gas. Unfortunately, the calibration is altered by anesthetics. The Sonic Analyzer is very sensitive to CO_2 but has a different calibration curve for each different combination of background gases, and is totally impractical for CO_2 analysis of anesthetic gas mixtures. Mead's[11] critical orifice CO_2 analyzer is a simple, nonelectrical device using chemical CO_2 absorp-

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tion. It also has slow response (4 minutes) and requires large samples (500 ml.) and the effect of anesthetics has not been described.

The Carbon Dioxide Electrode. This instrument, which will be described under blood CO_2 analyzers, can also be used for gas analysis. It is totally specific for CO_2 and unaffected by anesthetics.

Carbon Dioxide Analysis of Blood Samples Containing Anesthetic Agents

The buffers in blood combine with CO_2 to form bicarbonate. The amount of bicarbonate is more an index of the acid-base buffer state than of the P_{CO_2} of the blood. Content must be known if P_{CO_2} is to be computed from the Henderson Hasselbalch equation. On the other hand, P_{CO_2} is only indirectly related to acid-base balance (via the respiratory center) but is quantitatively related to alveolar ventilation. The methodology of both P_{CO_2} and CO_2 content determination has changed considerably in the past few years, and this section will deal primarily with the newer methods and the effect, if any, of anesthetics on the methods.

Methods for Carbon Dioxide Content: Manometric analysis in the Van Slyke apparatus is still most widely used, but suffers from errors and complications when soluble gases are present. Two procedures for correction have been described, neither being precise. These were compared recently by Holaday and Verosky[12] who found the Goldstein method to be better.[13]

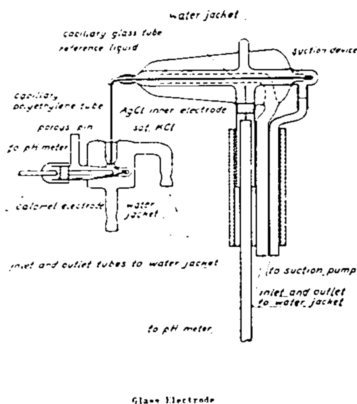

Fig. 3. The Astrup micro-capillary glass electrode and reference electrode.

The Astrup method[14, 15] is particularly applicable in anesthesia. It provides values for P_{CO_2}, pH, CO_2 content, buffer base and standard bicarbonate. It is not affected by anesthetic agents. The only measuring instrument is a pH meter. The apparatus includes a tonometer for equilibrating blood with several known gas CO_2 tensions at 37 C. The new Astrup apparatus (Welwyn International Inc.) uses a micro-capillary glass pH electrode (fig. 3) which requires only 0.025 ml. of blood to fill it, and the tonometers are therefore only required to equilibrate about 0.1 ml. of blood which they will do in 3 minutes. The pH of the sample is first measured, and then remeasured after equilibration with several known CO_2 tensions. These data can be plotted on a pH-log P_{CO_2} diagram and the other values derived. The diagram is dependent on fixed values for solubility, pK′ and temperature of the patient, so for CO_2 content and standard bicarbonate it is not accurate except at 37 C. Diagrams can be prepared for use at other temperatures. A small error is introduced by the complete oxygenation of the blood sample, due to loss of the hemoglobin buffer, especially if venous blood is being determined.

Carbon Dioxide Content of Blood Measured with a CO_2 Electrode. The CO_2 present as bicarbonate in blood may be converted to free dissolved CO_2 in solution by dilution of 1 ml. of blood with 20 ml. of 0.1N lactic acid in a syringe. The P_{CO_2} of the resulting solution, determined with a CO_2 electrode, is a linear function of the original CO_2 content. Calibration is accomplished by performing the same maneuver with 1 ml. of a standard solution of sodium carbonate (25.00 millimoles per liter) instead of blood. The accuracy is about that of the dilution, ±1 per cent. Anesthetic agents in the blood have no effect on the results.

Methods for Determination of P_{CO_2}: *Computed from pH and CO_2 Content.* Anesthetic agents have no effect on pH measurements, but as noted above affect

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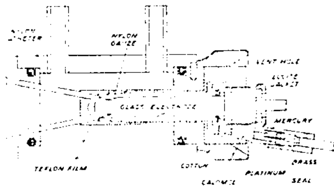

FIG. 4. Design of the P_{CO_2} electrode (National Welding Company). The material used to hold a very thin film of water between the sensitive glass electrode and the Teflon membrane may be cellophane, glass wool or nylon (stocking).

the Van Slyke determination of CO_2 content. There are a number of excellent new electrode systems and *p*H meters now available for blood *p*H determination. The Radiometer and Metrohm Company instruments use the Sanz type [16] capillary electrodes in which the blood volume is kept very small. The sensitive glass membrane is the capillary itself, and is surrounded by the HCl. When the capillary has been filled with blood, one end of it is dipped in a pool of saturated KCl which connects with the calomel electrode. This forms a better and more reproducible junction than the fiber or sleeve junctions which had been used. These capillary electrodes have water jackets for precise temperature control with a circulating thermostat (Haake, Godart). Beckman Company have improved their micro-blood *p*H electrode assembly by arranging for a continuous flow of KCl through the fiber liquid junction (Model 46850).

P_{CO_2} Electrode.[17] The CO_2 electrode measures the *p*H in a very thin film of a bicarbonate solution which is separated from the blood sample by a Teflon membrane permeable to CO_2 (as a gas in solution) but not to ions which could change the *p*H of the water film. The *p*H is a linear function of the log of the blood P_{CO_2} over the range from at least 7 to 700 mm. of mercury. The accuracy is limited only by the temperature regulation and the readability of the *p*H meter, and is within 1 per cent (*i.e.* ±0.07 mm. at 7 mm. of mercury). Response time is about one minute for full equilibrium. The stainless steel cuvette (Fig. 4) has a volume of 0.2 ml. There have been several modifications in the device (National Welding Co.) since the published description. The reference electrode was changed from silver-silver chloride to 0.1*N* calomel for stability. A special glass electrode was designed with a flatter sensitive membrane and a groove to retain the cellophane spacer which holds the bicarbonate solution film. We have recently found that if the cellophane spacer is replaced with very sheer nylon netting (7 denier, especially prepared through the courtesy of the Philadelphia Textile Institute) the electrode is faster in response, more sensitive and linear to lower P_{CO_2} (2 mm. of mercury).

The Effect of Body Temperature on Meas-

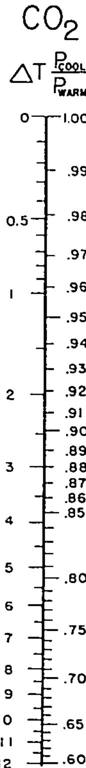

FIG. 5. Factors for correcting whole blood P_{CO_2} for a difference of temperature between the patient and the measuring instrument. For example, if a patient is 3 degrees C. cooler than the P_{CO_2} electrode, multiply the determined P_{CO_2} by 0.88 to obtain P_{CO_2} at the patient's temperature.

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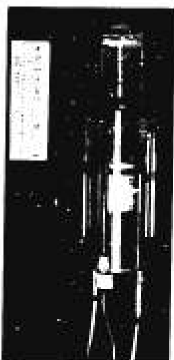

FIG. 6. Tissue P_{CO_2} electrode with self-contained water jacket.

urement of P_{CO_2} and pH. Large errors are introduced by small differences between temperature of the patient and the temperature of measurement. The factor is 0.015 pH units per degree and about 4 per cent change in P_{CO_2} per degree centigrade (fig. 5).[18] Correction cannot be accurately made over large ranges of temperature. When pH and P_{CO_2} measurements are to be made in connection with hypothermia using pump oxygenators and temperatures of less than 20 C. are anticipated, it is probably more accurate to operate the electrodes at an intermediate temperature of about 25 C. The most accurate way is, of course, to adjust the electrode temperature to that of the patient. This can be done if the electrodes are thermostated by an easily regulated bath. However, the CO_2 electrode response time becomes very long at low temperatures.

Tissue P_{CO_2} with the CO_2 Electrode. The lucite electrolyte jacket may be removed from the stainless steel CO_2 electrode cuvette and the active surface applied to the surface of tissues to measure tissue P_{CO_2} directly. A temperature jacket must be used around the electrode (fig. 6). This has been done in dogs and man. Average for the cerebral cortex was 55 mm. of mercury (with arterial P_{CO_2} held at 40 mm. of mercury). Active metabolizing tissues were higher than had been anticipated (the values for liver, gastric mucosa and jejunal mucosa were 55–75 mm. of mercury). Skin varied from arterial levels when warmed to over 130 mm. of mercury when blanched with slight pressure on the electrode.

COLLECTION OF SAMPLES

Blood Sampling. We no longer use oil to seal syringe barrels, using the anticoagulant to fill the dead space and make the seal. No more than the dead space should be filled with heparin, and the dilute heparin (10 mg./ml.) is preferred, the more concentrated being more acid and therefore tending to elevate P_{CO_2} and reduce pH. The blood and heparin can be mixed by closing the syringe either with mercury filled caps and swirling, or with blood filled caps, and rolling the syringe between the palms. Carbon dioxide content values should be corrected for dilution by anticoagulant (1.5 per cent in a 10 ml. sample, 10 ml. syringe). Filled syringes should be kept under water until analysis to prevent barrel sticking.

For respiratory studies, arterial blood is usually necessary. Blood taken from hand veins after the hand has been thoroughly soaked in hot water has been shown to be within 2 mm. of mercury of arterial P_{CO_2}. For accurate work however, arterial blood is usually preferred.

Percutaneous arterial catheterization has been greatly facilitated by the procedure introduced by Seldinger.[19] His contribution was the idea of threading a solid leader into the artery through the needle, withdrawing the needle and then sliding a catheter in over the leader. In its simplest form, this requires only three parts, as follows: (1) standard 18 gauge 1½-inch intravenous needle, (2) 24-inch piece of monofilament 3 pound test (0.7 mm. O.D.) nylon fishing leader, sterilized, and (3) 10-inches of PE-160 polyethylene catheter, one end of which has been tapered sharply by pulling to form a sharp leading edge which will just pass over the nylon leader. When the leader has been threaded through the 18 gauge needle into the artery, the needle is withdrawn, the leader wiped with a moist gauze, and the catheter passed over it, screwing it into the artery while withdrawing the leader. When the leader is out, the same needle may be used to adapt the catheter to a stopcock. These catheters may be left in for many days if they are kept filled with heparin saline solution.

Gas Sampling. Gas samples may be collected by hand from various parts of anesthetic

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breathing systems using a large glass syringe wet with dilute HCl or oil, a 1 or 3 way stopcock and an 18 to 22 gauge needle. For example, the effectiveness of absorbers may be checked by aspiration from the inspiratory tubing while momentarily stopping all fresh gas inflow. An approximate end-tidal sample can be collected from the expiratory tubing provided the directional valves are in the Y piece and not on the circle. Sampling must be done in small aliquots during the end of expiration. With care, reasonable end-tidal samples can be collected from an endotracheal tube during the latter phase of exhalation, but before outflow stops. It is best to either sample from the carina with a catheter or add a dead space (20 ml.) between the sampling needle and Y piece. Generally the gas under a mask is not suitable for collection of end-tidal samples because of the large dead space.

Several automatic end-tidal samplers have been described. By far the simplest method, applicable only with positive pressure controlled respiration, was pointed out by Capel and Hodgson.[20] If the directional valves are in the Y piece, a small needle inserted just beyond the expiratory valve will deliver a flow of end-expiratory gas during each positive pressure inflation of the lungs. The Rahn sampler [21] utilizes the negative airway pressure occurring during inspiration in a valved Y piece to draw air from beyond the expiratory valve into a thin walled balloon. The negative airway pressure is transmitted to a bottle surrounding this balloon. Lambertsen and Benjamin,[22] Nunn and Pincock [23] and Hesser [24] have described more complicated automatic samplers which can select a particular phase of the breath for sampling. All these devices were designed to permit collection of samples for analysis in devices with response times which were too slow to follow the instantaneous changes during the breathing cycle. The rapidly responding infrared CO_2 analyzer has largely eliminated the need for these methods. It can sample continuously from the airway permitting the CO_2 concentration to be recorded through the breath cycle with a time lag of about 0.2 second.

The leakage of CO_2 through plastic and rubber may be high.[2] Anesthesia bags made of latex rubber can lose 5 per cent of the CO_2 in a 500-ml. sample in 10 minutes. Polyethylene and vinyl tubing should not be used to transfer samples or calibrating gas to analyzers. They can lose measurable amounts of CO_2 while flow of gas exists through the tubing. Nylon tubing (Polymer Corporation of America) is almost impermeable to gases, and is much cheaper than polyethylene. A new plastic film, Mylar (solid Dacron), with polyethylene film bonded to one side, has low permeability and can be made into bags by heat welding the polyethylene.

End-tidal Sampling Methods with Infrared CO_2 Analyzers. Suction must be used to permit continuous sampling (except with the breathe-through cell). The resistance of the inlet tubing is such that at most reasonable flows the pressure in the light path is subatmospheric.[10] The absorption of light depends on the number of CO_2 molecules in the light path, so the instrument is in fact sensitive to P_{CO_2}, not percentage CO_2. This fact requires that the pressure be kept constant at all times both for calibration and for measurement. For example, if a catheter (nylon or polyethylene) is used to conduct samples from the airway to the inlet to the microcatheter cell, calibration must be done by allowing the same catheter or one of the same length and diam-

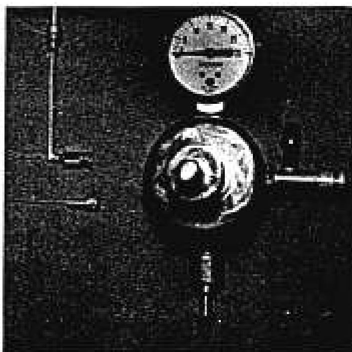

FIG. 7. Sampling needle and regulator for low pressure operation of infrared CO_2 analyzer. The needle stylette is flattened on one side so flow can be adjusted by rotating it. The infrared analyzer sampling tip was drilled to permit wedging in a small nylon catheter.

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eter to draw in calibrating gas flowing past the tip at atmospheric pressure. If a needle has been inserted into the airway to withdraw samples, the same or a duplicate needle should be used to sample the calibrating gas. If this is not done, any change in the inlet circuit may change the pressure in the cell and incorrectly calibrate the instrument. The volume of the inlet system should be as small as possible if rapid response time is desired.

Low Pressure Operation. We have found the most satisfactory method is to use a needle with adjustable orifice for controlling flow rate (fig. 7), and a negative pressure regulator (model 903-B, C. M. Sorensen Co.) set to 0.1–0.5 atmosphere. The disadvantages are: (a) pressure broadening may be increased and (b) the sensitivity setting must be increased, a disadvantage in terms of noise level on some instruments. Advantages are: (a) response time is faster because of the expansion of gas beyond the needle, (b) the instrument is much less sensitive to pressure variations in the airway or calibration gas, (c) water vapor condensation is eliminated, (d) the response curve is more linear (fig. 2), since 1 per cent CO_2 at 1 atmosphere gives the same deflection that 10 per cent CO_2 gives at .1 atmosphere, and (e) variations in the vacuum pump or wall suction have no effect on calibration because of the regulator. This system can be used to obtain rapid response with very low flows (20 ml./minute flow with the cell at 0.1 atmosphere pressure gives the same response time as 200 ml./minute at 1 atmosphere). This is useful in recording end-tidal CO_2 in very small animals (*e.g.* rats) where higher flows will exceed the total expiration of the animal and therefore be contaminated with air. Mead (personal communication) has used another method to permit sampling from guinea pigs at very low flow rates. The technique must solve the dual need for sampling at the nostril at a rate of about 20 ml./minute maximum but needing a flow through the analyzer of about 200 ml./minute to obtain the speed of response needed to record the individual end-tidal samples. He constructed a diluter which drew in, for example, 180 ml./minute of fresh air together with the 20 ml./minute of sample. The resulting signal is, of course, decreased by a factor of 10, as it was in the low pressure technique above, but gain is sufficient to recover most of this. The most serious problem is to keep the 1/10 dilution factor constant. This ratio is extremely sensitive to pressure variations at the sample tip. For this reason we found it more satisfactory to accomplish the same thing by working at reduced regulated pressures.

The Meaning of End-Tidal Sampling

End-tidal sampling is done in order to estimate the arterial P_{CO_2}. It is known that there is no difference between the P_{CO_2} in alveolar gas and capillary blood in any particular alveolus. However, mean alveolar and peripheral arterial blood may differ, and end-tidal CO_2 concentration may fail to represent even average alveolar CO_2. We need to examine these problems separately.

Causes of Differences Between Arterial and Alveolar (End-Tidal) CO_2. The principal source of this difference arises in the ventilation of certain alveoli which have no blood flow. The CO_2 concentration in such alveoli will approximate zero (except for CO_2 inspired from dead space), and during expiration will dilute the gas coming from normally perfused alveoli. This dilute mixture will be sampled as end-tidal gas, and will be lower than arterial blood in regard to its P_{CO_2}. The ventilation of such alveoli is called alveolar dead space, being wasted ventilation,[25] and has been used in attempts to measure the quantity of unperfused alveoli, or the size of pulmonary embolism.[26-28] The lung has a compensatory mechanism recently described[29] in which areas having no blood flow, and hence a low CO_2, develop bronchoconstriction and atelectasis, diminishing their ventilation about 25 per cent.

In general, patients with severe lung disease of any kind tend to have lower end-tidal than arterial P_{CO_2}. In emphysema we have found this difference to average 7–9 mm. of mercury (unreported) and Scherrer *et al.*[30] report 14 patients with emphysema and cor pulmonale having an average gradient of 23 mm. of mercury.

Patients having maldistribution of ventilation usually have a steeply sloping alveolar plateau when expired CO_2 is continuously recorded so that the actual end-tidal concentration is highly variable with the time and volume o

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expiration. Since the poorly ventilated alveoli empty last, one might expect to obtain end-tidal values above the arterial blood, but this is not found in practice.

Two observations can be made during recording of end-tidal CO_2 to check the adequacy of the recorded sample. One is to perform a forced expiration at the end of a normal breath. This may be done in anesthetized subjects by manual compression of the chest cage at the proper time. Normally, the value of CO_2 recorded in this manner will be a few mm. of mercury higher than the end-tidal CO_2. If a great increase is found, one may suspect that the end-tidal P_{CO_2} is not an adequate reflection of arterial blood P_{CO_2}. The other observations relate to the uniformity of successive end-tidal CO_2 concentrations. When ventilation becomes too shallow to wash out dead space, no plateau is recorded, and successive breaths reach differing concentrations. The same irregularity may result from too much lag in the analyzer or its sampling system, for example from partial plugging.

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