

ELECTRODE SYSTEMS FOR CONTINUOUS MONITORING IN CARDIOVASCULAR SURGERY

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Instruments capable of continuously indicating the chemical composition of blood have proved to be useful in controlling heart-lung machines, in regulating operative and postoperative management of patients, and in teaching and research. At first, such instruments were used with sensors mounted directly in the extracorporeal blood circuit that is used for perfusion of open-heart surgery patients.¹ Later, continuous monitoring of both machine and patients was conducted by means of continuous withdrawal of blood pumped into external cuvettes equipped with appropriate sensors.

Improvement in the design and construction of electrode systems and their associated electronic instrumentation, together with the commercial development and availability of stable amplifiers and recorders, has now provided entirely satisfactory systems for the rapid and accurate measurement of blood pH , pCO_2 , and pO_2 . Electrodes for measurement of blood pO_2 and pCO_2 can also be used for recording these tensions in gases. By mixing blood with certain reagents, these electrodes can be used to record blood gas *contents* as well as tensions.

Intravascular electrodes are being used to time hydrogen appearance, to detect changes in oxygen tension, and to record ascorbate indicator dilution curves. Such electrodes are proving valuable in cardiac catheterization and in evaluation of the effectiveness of corrective endocardiac surgical procedures. Speed of response, ease of use, autoclavability, smallness of size, and the practicability of using multiple electrodes simultaneously is often sufficient advantage to overcome the present lack of quantitative response of these relatively simple electrodes.

By withdrawing blood through microcatheters, continuous recording of blood composition for many hours, even days, is possible, using only about 10 cc. of blood per hr. Continued development of electrode systems may extend their usefulness to the measurement of blood ions, sugar, and urea and finally result in instruments with which analyses can be performed with a minimum of reagents and with but little delay. Electrode systems readily lend themselves to either intermittent, semiautomatic, or continuous analytical processes.

Blood oxygen tension. Electrodes available at present, mounted in thermostated cuvettes, have proved very satisfactory for the measurement of pO_2 in blood samples. Thousands of analyses have been performed with the several units available here. We have evaluated several means of utilizing electrodes to follow blood pO_2 under conditions encountered in cardiovascular operating rooms and have found that analysis of individual samples, withdrawn in plastic syringes, is the least troublesome and most

accurate. Electrodes placed directly in the blood stream of extracorporeal circuits are useful for assuring arterial oxygenation, especially in normothermia, but become somewhat clumsy to interpret when hypothermia is used, owing to the necessity for temperature corrections.

We are now routinely *continuously withdrawing* arterial blood for indication of pO_2 , pCO_2 , and pH and venous blood for recording oxygen content *during* cardiopulmonary by-pass, but continuously analyzing mixed venous blood for oxygen content and intermittently analyzing arterial blood for gas tensions and pH *postoperatively*. When the arterial oxygen tension is below 100 mm., use is made of the continuous arterial oxygen content recording method described in the following.

Blood carbon dioxide tension. The measurement of blood pCO_2 , using the commercially available electrodes, has also proved to be reliable and easy to perform by the individual sample technique. When many samples require analysis, the addition of carbonic anhydrase to the electrode electrolyte is undoubtedly worth-while in speeding the electrode response. To preserve the activity of the enzyme, it is desirable to fill the analytical chamber with a solution or gas having a measurable pCO_2 , since a low pCO_2 (or a high pH) hastens irreversible inactivation of the enzyme.²

The many publications dealing with design, theory, and use of pCO_2 and pO_2 electrodes may be consulted for further details.^{3, 4}

Electrodes mounted in individual jacketed cuvettes, rather than in a single bath, have been most useful because they are readily placed in convenient locations and can be replaced singly, without disturbing the remainder, in the event of difficulty. To avoid undesirable possible electrical interferences from heating baths and other electrical disturbances, we prefer to use silicone oil (10 cnsk. viscosity) as the circulating thermal control fluid.

Blood oxygen content. Recording of blood gas contents has been conducted using the general scheme shown in FIGURE 1. For blood oxygen content, the blood is first mixed with hemolyzing solution and the released

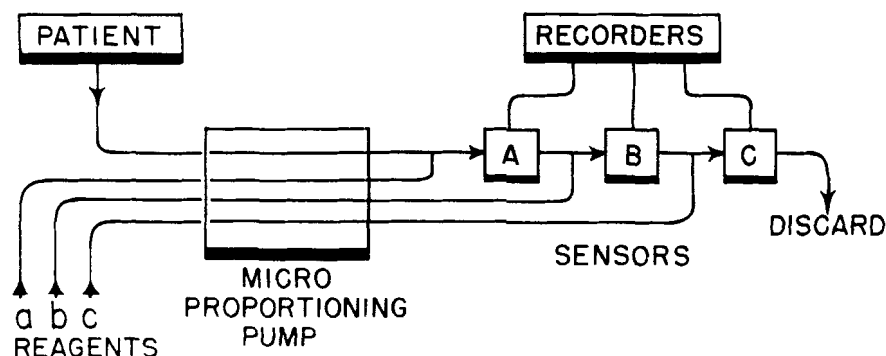


FIGURE 1. Principle of continuous analysis of blood.

oxygen measured with sensor A. This solution can then be acidified and the carbon dioxide recorded with sensor B.

In FIGURES 2 and 3 is shown the diagram of the unit used for a two-

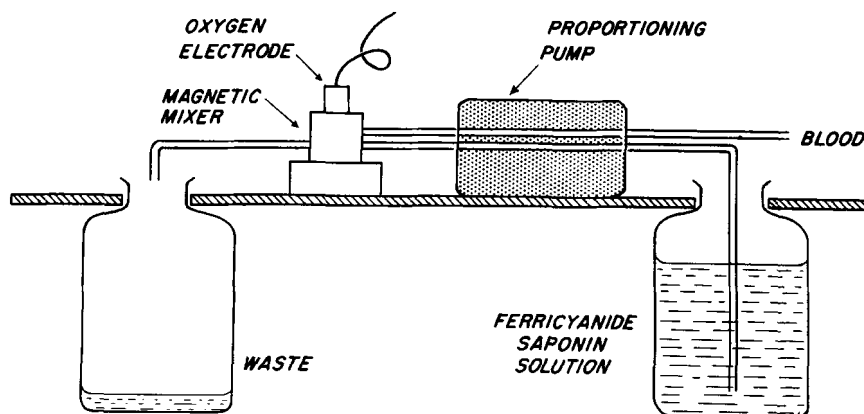


FIGURE 2.

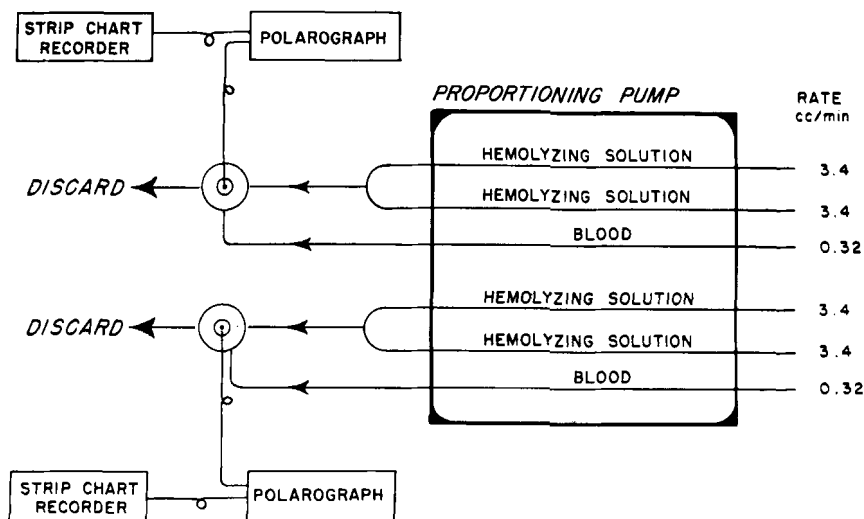


FIGURE 3.

channel system for blood oxygen content. De-aerated ferricyanide-saponin solution is continuously pumped into an anaerobic stirred cuvette having an oxygen electrode. Blood is withdrawn continuously from the patient through a microcatheter (P.E. 50 polyethylene) placed in the pulmonary artery, radial artery, jugular vein, or elsewhere and pumped directly into the cuvette. Heparinization of the blood is not necessary, providing the

microcatheter is less than 3 or 4 ft. in length. The magnetic mixer ensures rapid and uniform hemolysis and provides the stirring necessary when a macroplatinum cathode (*i.e.*, ca. 2-mm. diameter) is used. The base line is set to zero with the degassed hemolyzing solution and to 100 with oxygen-saturated blood. Usually, changes in the patient's hematocrit are such that recalibration with fully oxygenated blood is advisable every half hour, at which time the zero setting can be checked and reset if required. Ease of calibration and interpretation has led us to utilize per cent saturation as the most practical for use in the clinical setting. A two-channel system, one reading mixed venous blood from the pulmonary artery and thus providing an index of cardiac proficiency, the other reading arterial saturation and providing an indication of pulmonary function and ventilation, has proved to be most useful in hundreds of hours of recording.^{5, 6}

FIGURE 4 compares results obtained by continuous automatic analyses with samples analyzed by Van Slyke procedures. In addition, comparison

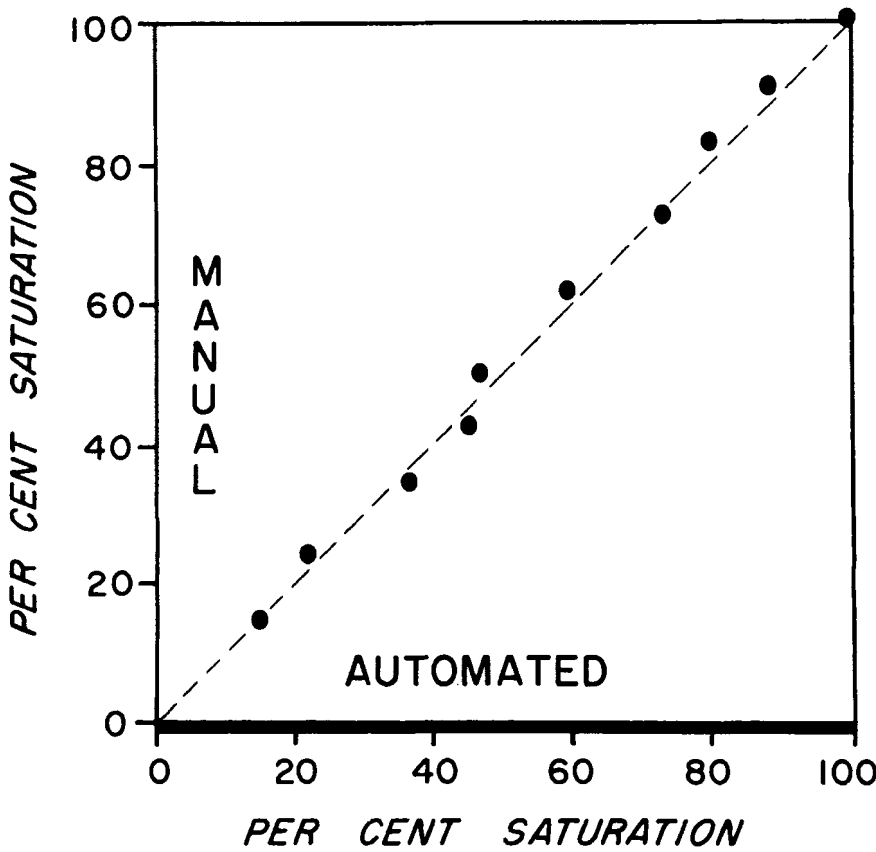


FIGURE 4.

of manual- and automatic-analyzed samples drawn at random during post-operative recording indicates an average deviation of about 1.4 per cent with the occasional large differences (up to 12 per cent) found during periods of rapid changes in blood oxygen content.

Instead of using a single cuvette for the anaerobic hemolysis and measurement, the blood can be hemolyzed in an anaerobic mixer and the resulting solution circulated through a thermostated pO_2 cuvette equipped with a microcathode, stir-insensitive, thermostated pO_2 electrode. Such a system facilitates calibration of the instrument in terms of volumes per cent oxygen, should this be desired. The same cuvette used for measuring



FIGURE 5.

blood pO_2 can, in other words, be used to measure and record oxygen content. The circuits⁷ used for the macro cathode are relatively simple and inexpensive; they depend, of course, upon the use of galvanometers or potentiometric recorders for sensing the currents (in the order of 2 or $3\mu A$).

Photographs of the two-channel unit (FIGURE 5), used here for several years, and our new unit (FIGURE 6) illustrate improvements in design that make such equipment more presentable in the operating room and more readily acceptable by those who must learn its operation. A major improvement in function and design has been the perfection of a 12-tube

panel or flush mountable proportioning pump (FIGURE 7) having a concealed mechanism and a transparent platen.

The thermostated cuvette shown in FIGURES 8 and 9 has been used primarily in recording blood oxygen content, but is so designed that it can be adapted for reading with other electrodes and so that various reagents can be continuously injected into it through a removable base plate.

That the recording of mixed venous oxygen content has been useful in understanding the cardiovascular status of postoperative patients is shown by the information given in FIGURE 10. The patients having residual shunts, as indicated by other means, were not included in this figure. Those hav-

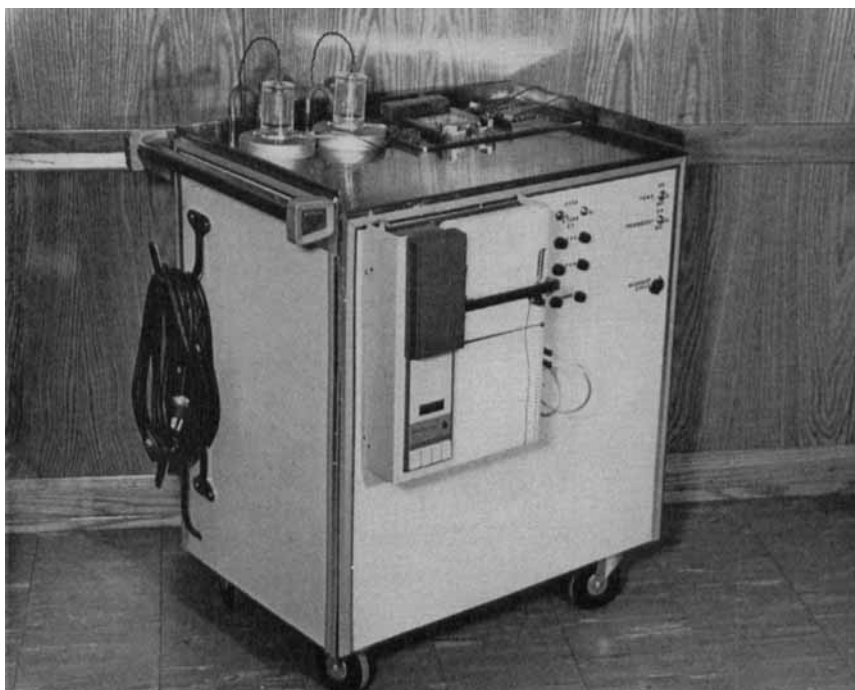


FIGURE 6.

ing oxygen saturations above 60 per cent, and hence a good cardiac output in the 4-hr. postoperative period upon which this data is based, all survived. Those in the 50 to 60 per cent range had roughly two chances in three of surviving, while those below 50 per cent had roughly one chance in seven of surviving. All of those above 60 per cent saturation could be given more-or-less routine postoperative management, those between 50 and 60 per cent required intensive care, and a certain amount of heroics was required to salvage those having such poor cardiac function as is represented by the below 50 per cent group. Having the information regarding mixed venous oxygen saturation continuously recorded by the

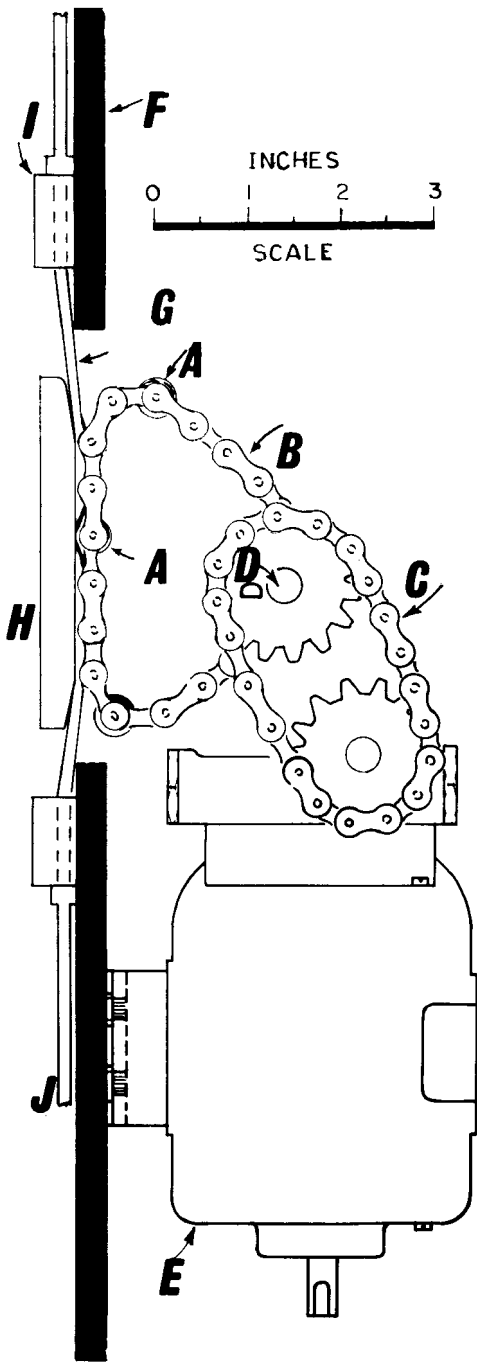


FIGURE 7. Flush mounted 12 tubing proportioning or ratio pump. Key: A, rollers; B, roller drive chain; C, main drive chain; D, axle for roller chain drive mounted on guide plates for chains; E, 1/50 hp. 110 v. 60 cycle motor; F, main plate, stainless steel, which is bolted to panel, and which supports the entire mechanism; G, plastic tubing; H, hinged, transparent platen; I, slotted movable L-shaped plate for adjusting tubing tension; J, inlet side of tubing.

Not shown is power switch, fuse, and details of hinge. The roller unit is designed so that it can be adjusted to compress the tubing accurately to its wall thickness and no further. The transparent platen makes it possible to see the tubing as it is being compressed and is hinged to facilitate loading. The entire driving mechanism is located safely behind the panel. The pump can be operated either vertically or horizontally. Detailed blue prints of the pump will be available at cost.

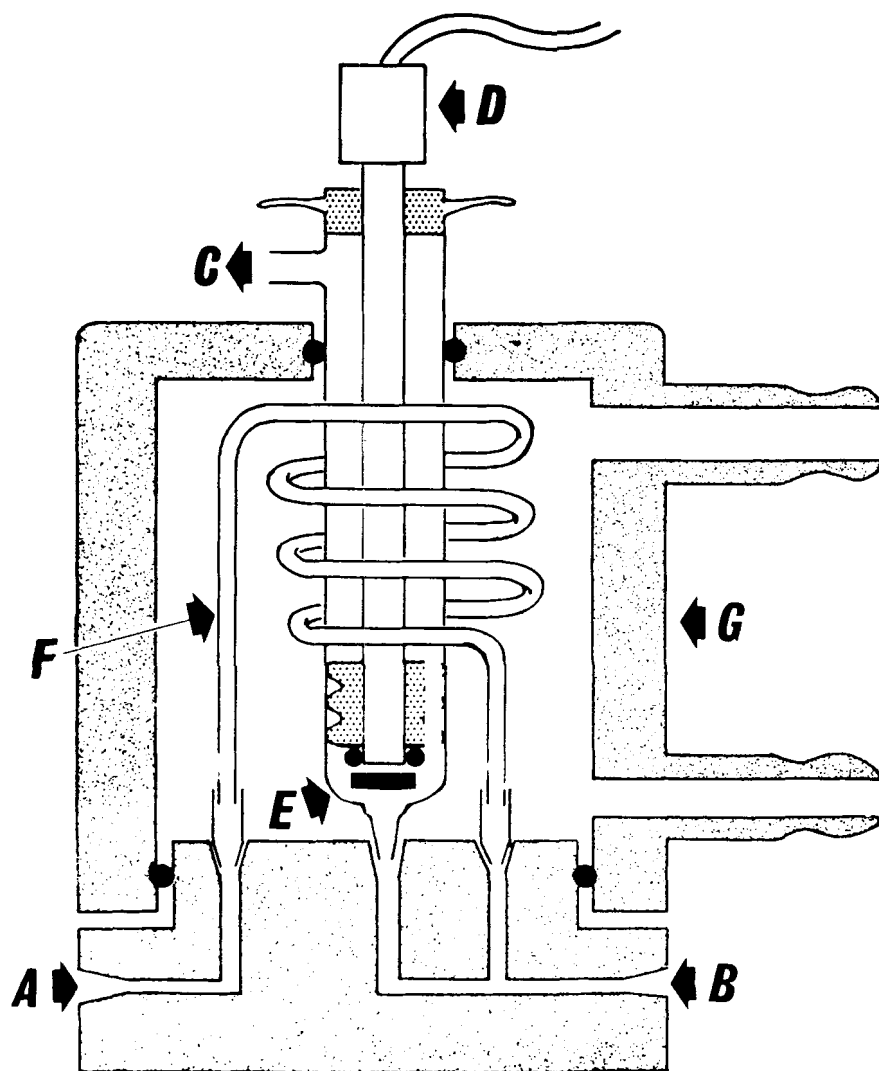


FIGURE 8. *Thermostated stirred anaerobic electrode cuvette.* The apparatus consists of a removable base plate and a cylinder (G), having inlet and outlet for circulating constant temperature fluid. For use for blood oxygen content, hemolyzing solution enters (A), circulates through the coil (F), and returns to the base plate to be mixed with blood entering at (B). The hemolyzed solution flows to a syringe equipped with a micromagnetic stirring bar (E), and pO_2 electrode (D). The solution flows upwards and out (C). Various size syringes may be used depending upon the speed of response required and the types of electrodes used. The volume of the reaction chamber can be changed by moving the electrode as a syringe plunger. Vertical flow of fluid facilitates clearing the unit of air in starting the analysis.

bedside not only helps plan the general type of care required but, of course, makes it possible in any given patient to determine the best course of action regarding blood replacement, optimum venous pressure, ventilation procedures, type and rate of administration of various drugs, and the many other details connected with the management of these patients.

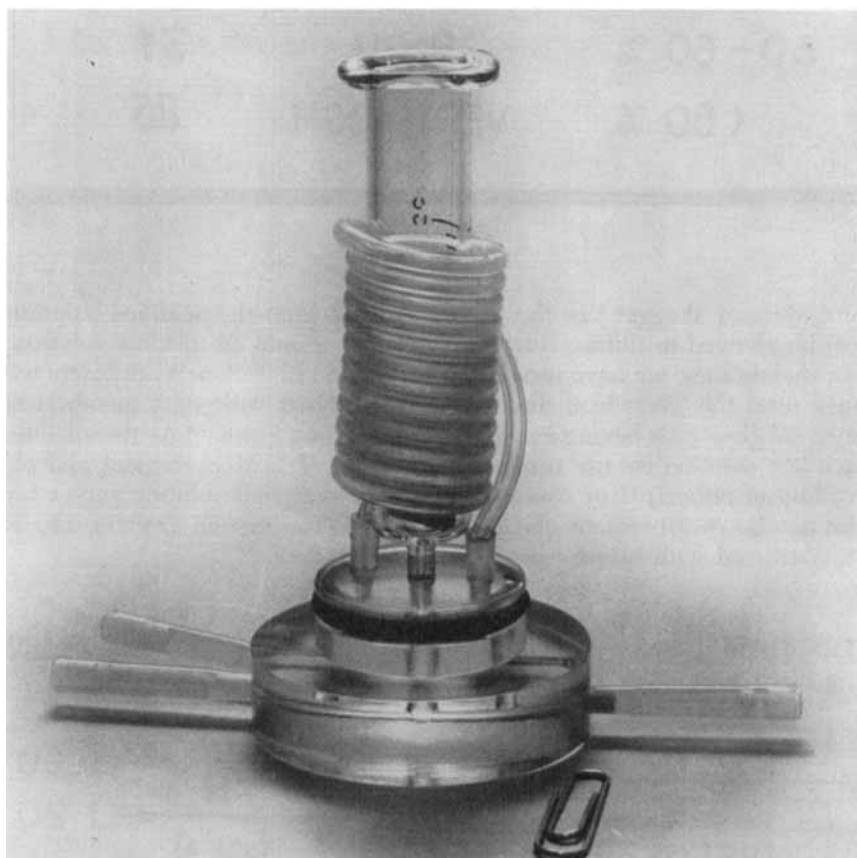


FIGURE 9. *Syringe electrode cuvette and coil.* The base plate can be drilled to program various mixing procedures and has tapered holes to accommodate standard Luer fittings for inlets, outlets, coils, and syringes. Cast Lucite or Plexiglass, annealed by overnight treatment at 80° C., has proved durable. The outer jacket (G, in FIGURE 8) and the electrode (D, in FIGURE 8) are not shown.

Carbon dioxide content. Continuous recording of blood carbon dioxide content is done by acidifying and diluting whole blood or by acidifying hemolyzed blood from the oxygen content cuvette. The carbon dioxide tension of such solutions can be read; the carbon dioxide can be separated in a gas phase and absorbed in an alkaline solution as in the colorimetric

PA SATURATION RANGE	MORBIDITY	PER CENT MORTALITY
60 + %	LOW	0
50 - 60 %	HIGH	31
< 50 %	VERY HIGH	85

FIGURE 10.

procedure of Skeggs^{8, 9} or the carbon dioxide from the acidified solution can be allowed to diffuse through a membrane into an alkaline solution. For membranes, we have used Silastic and 0.5 mil Teflon. As diffusers we have used the Technicon dialyzer unit equipped with such membranes or spiral glass coils having a coil of Silastic tubing inside.²¹ As the alkaline recipient solution we use tris buffer (ca. 0.01 M.). Measurement and recording of either pH or conductivity of the recipient solution serves for the precise measurement of carbon dioxide. The system (FIGURE 11) is standardized with bicarbonate solutions.

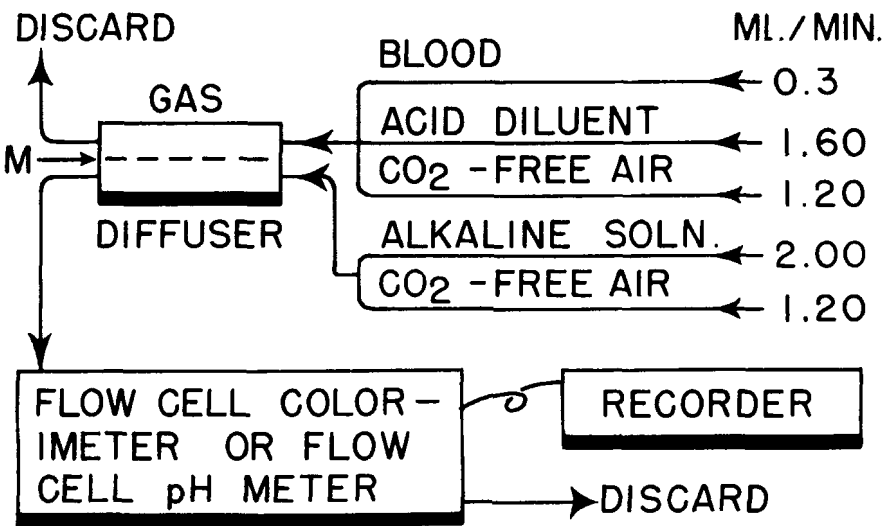


FIGURE 11. Continuous analysis of blood CO₂ content.

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Intravascular electrodes. The potential, with respect to a reference electrode, of a platinum electrode is a function of the pH , pO_2 , pH_2 , and the oxidation-reduction potential of the electrolyte in which it is immersed. Such an electrode can be used, in the form of a tiny pellet or ring on a catheter for example, to detect *changes* in any of these variables. The potential developed is not related to the size of the electrode. In the blood stream, changes in potential, of about 50 mv. or so, are observed as an electrode passes from venous to arterial blood. Larger changes of opposite polarity are observed if hydrogen is breathed while the same electrode is in blood. Changes in potential are readily recorded when the redox potential is altered, as following injection of sodium ascorbate, or when the pH is changed, as following the injection of sodium carbonate. The potentiometric platinum electrode is thus useful in timing the appearance of gaseous indicators (hydrogen)¹⁰ of injected indicator solutions (ascorbate)¹¹ and in detecting streams of blood having divergent oxygen tensions.¹² As an anode, it is depolarized by ascorbate, providing a sensitive rapidly responding electrode for following this indicator.¹³⁻¹⁵ Polarographic measurement of ascorbate appears to be preferable to potentiometric measurement because of the more reproducible and rapid response of the former. A versatile circuit for polarographic and potentiometric recording has recently been developed for use with the Electronics for Medicine oscillograph.

Indwelling pulmonary artery electrodes have been used to determine the presence or absence of residual shunts following open-heart surgery.¹⁶ This same electrode can be utilized as an intracardiac pacemaker by withdrawing it to the right ventricle, its location being assured by observation of the EKG. Small platinum anodes, threaded into the aorta through a radial artery, are proving to be useful in analyzing for the presence or absence of right-to-left or left-to-right shunts directly following surgery. Such ascorbate electroindicator dilution curves are performed while the extracorporeal perfusion apparatus is turned off but on stand-by and capable of being used again in the event that significant shunts are observed. Intravascular electrode systems are particularly useful for diagnostic evaluation in small children; but the wide use of hydrogen electrodes during catheterization of all types of patients indicates that such electrodes offer readily obtained confirmatory evidence and often can "clinch" a diagnosis.

Enzyme containing membranes. Although still in the exploratory stage, I want to mention the possibilities for use of enzyme layers trapped between membranes used with electrodes. The principle is illustrated by FIGURE 12, which shows how the specificity of response is regulated by the placement and nature of the enzyme, the nature of the detector electrode, and the nature of the membranes. The active electrode surface bears against a double layer of membrane between which is trapped a thin layer of concentrated enzyme.

The determination of glucose, using a Cuprophane-glucose oxidase-

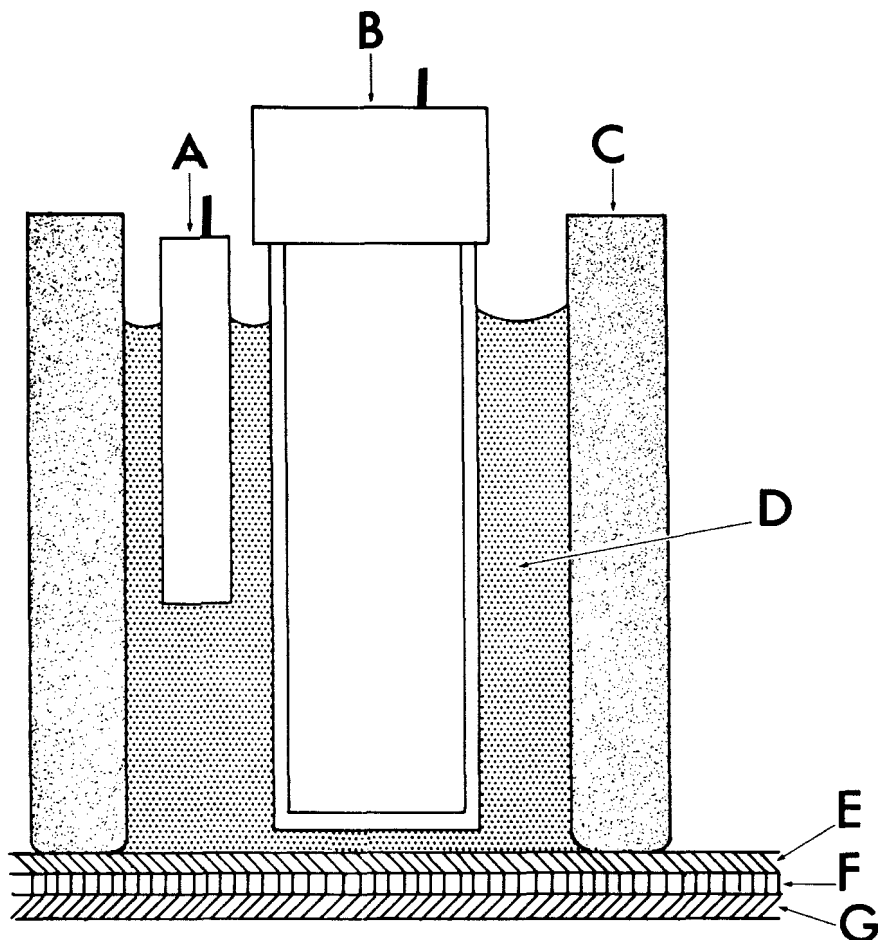


FIGURE 12. *Enzyme membrane electrode design.* The electrode cell, shown in principle, consists of a reference electrode (A), and a sensing electrode (B) held in a cylinder (C), the end of which is covered with a multiple membrane. The cell is filled with a suitable electrolyte, the composition of which is varied according to the particular application, and which may also contain enzyme. The membranes (E) and (G) have a layer of concentrated enzyme (F) between them. If the product involved in the reaction occurring at (F) is a gas, such as oxygen, carbon dioxide, or ammonia, the inner membrane (E) is perhaps best made of ion impermeable plastic so that the electrodes are electrically and ionically isolated from the system being analyzed. The sensing electrode may be a pH, pO_2 , conductivity electrode, or other type of sensor that can be pressed tightly against the membrane transducer. The cell should be thermostated. Layers between (B) and (E) and between (E) and (G) are very thin, since in practice the sensor projects somewhat and the membranes are stretched tightly.

Cuprophane membrane and a pH electrode, illustrates one use of this system. Glucose diffusing through such a membrane is converted to gluconic acid, which then diffuses both toward the pH sensitive glass and back into

the donor solution. This causes a drop in pH , the magnitude of which is largely determined by the concentration of the glucose, the rate of the flow and buffering capacity of the glucose containing solution, the temperature, and the pH . It is thus possible to regulate the sensitivity of the system over a wide range and to standardize it. It is easily possible, for instance, to obtain a pH response of 1 pH unit for a 10 mg. per cent solution of glucose flowing at a rate of 3 cc. per min. This enzyme electrode system is stable for hours of continuous recording and may possibly be usable for weeks because of the great excess of enzyme activity that can be trapped between the membranes. By using a hydrophobic (eg., polyethylene) membrane, a dialysis membrane, glucose oxidase, and a pO_2 electrode, a system can be arranged that is sensitive to glucose by virtue of the fact that oxygen is consumed from the flowing glucose solution in proportion to its glucose content.

Such enzyme membranes can be used with conventional continuous analysis systems as a part of the dialyzer unit. For example, by using Cuprophane-urease-Cuprophane, we have analyzed for low concentrations of urea with the alkaline phenate method for ammonia, obtaining full scale response from only 0.1 mg. per cent solutions. Such a membrane may find use with pH sensing or conductivity electrodes to measure urea.¹⁷

Enzymes may thus be useful in extending the specificity of electrode systems and in eliminating the use of reagents and the time lag inherent in most spectrophotometric methods. Further, expensive enzymes, such as lactic dehydrogenase, could be conserved, and systems depending for response upon thermodynamically available ions, such as calcium, may possibly be designed.

The application of the sodium electrode for continuous recording of blood sodium^{18, 19} and the recent advances in the chemistry of glass electrodes sensitive to divalent ions²⁰ suggest that it may not be too long before blood ions can be determined with the same ease as pO_2 , pCO_2 , and pH .

Safety. Devices that withdraw blood from patients should be well below the level of the patient so that if the pumping fails, blood (possibly contaminated by unsterile pump parts) will not siphon back to the patient. As an added precaution all reagent supplies must be as near the floor as possible so that they cannot be siphoned to the patient if the rollers fail to occlude the tubing. If blood is being sampled from a line that is under suction, such as the venous line to a heart-lung machine, provision should be made to pump with a separate line that is discontinuous with the analytical blood sampling tube. Thus, this suction can never be applied accidentally via a closed system and draw reagent in the venous line.

All components of these units should be completely grounded electrically. Only three wire systems should be used, and all points should be tested for secure and adequate grounding, using an appropriate meter.

Clinical research units. The successful continuous monitoring of blood gases in surgical patients has suggested that a versatile system may be

developed for recording a number of chemical variables in patients requiring intensive study and surveillance. Mobile chemical recording units have been used up to the present, but a plan to combine a number of systems in a special room has been developed in order to determine the feasibility of extending these analytical systems. Automatic and semi-automatic systems for blood analysis are being designed so that patients of research interest, such as patients in traumatic shock, may be studied and treated under conditions where blood chemistry is continuously recorded with a minimum delay. This room (FIGURE 13), to be centrally

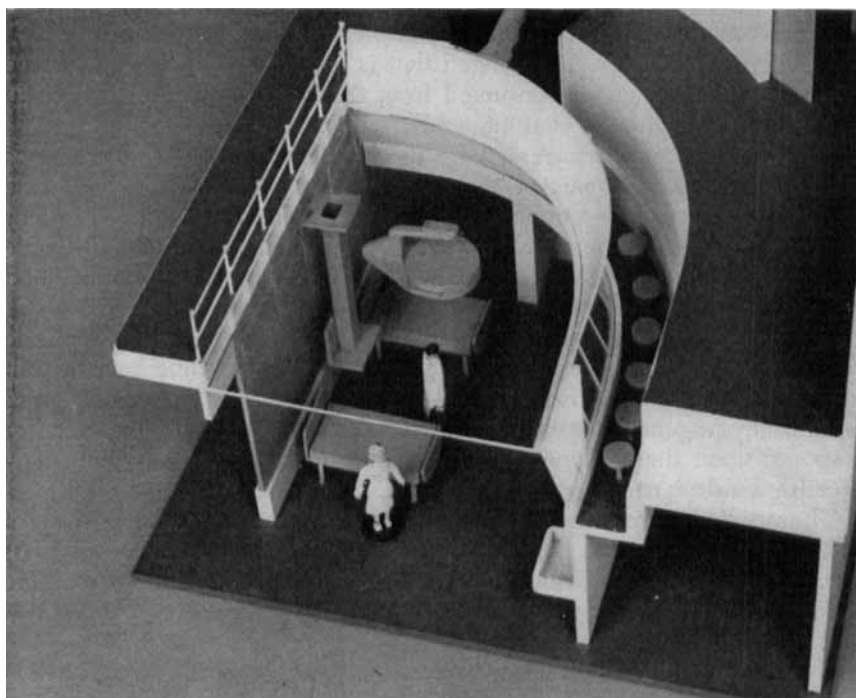


FIGURE 13. The room, shown as an engineer's model, is designed to provide facilities for intensive study of one or two patients. The wall at the left, at the head of the beds, will be constructed so as to allow panel mounting of a variety of chemical and physiological instrumentation. Instruments displaying information, and those necessary to visualize or manipulate to ensure proper operation, will be positioned on the face of the wall. Sources of reagents, constant temperature fluids, standards, power, drains, those processors that require only occasional attention, and working access will be provided behind the wall. Observation areas and additional working space are directly above the room.

located, and having a panel wall containing the processing, sensing, and recording equipment, is to be located within a short distance of the cardiovascular and main operating rooms. In addition to the chemical recording instrumentation, it will be provided with equipment for cannulation, partial perfusion, emergency surgery, cardiac resuscitation, and physiological

monitoring. The instrument wall has been constructed in prototype (FIGURE 14), and the final unit is scheduled for construction by the end of this year.

Summary

Continuous recording of blood chemistry in surgical patients has been conducted for many hundreds of hours. External electrode systems are being used to record, quantitatively, blood pH , oxygen, and carbon dioxide tensions and contents. Intravascular electrodes are being used for hydrogen

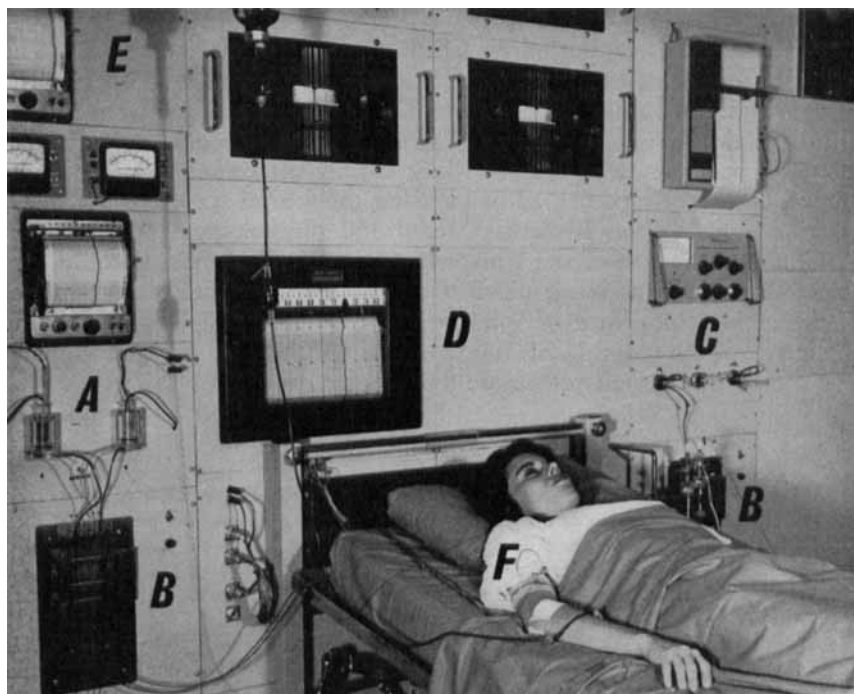


FIGURE 14. This is a working prototype of the analytical wall constructed to determine the practicality of mounting various types of proportioning pumps, sensors, recorders, and indicators in this way. Directly below (A) are two blood oxygen content cuvettes and directly above is a recorder that cycles between the two sensors. At (B), on the patient's right, is one of the panel-mounted proportioning pumps used primarily for the oxygen content analysis and that will also be used for CO_2 content. A similar pump, to the patient's left, is being used for continuous recording of arterial pO_2 , pH , and pCO_2 with the cuvettes shown directly below (C) and the amplifier shown above. Recording of pH is done by the recorder near (D) and pO_2 and/or pCO_2 by the recorder above (C). At the top left of the figure is equipment for recording temperature. At (F), possibly not visible in the final figure, is a microcatheter, sampling blood from the pulmonary artery. The vertical members of the panel are designed so as to accept 19- or 24-in. panels. Attempts are being made to design the unit so that most automatic procedures can be programmed as desired. Standard physiological monitoring, central suction, central oxygen, equipment for respiratory gas monitoring, and instruments for indicator dilution curves will be added to the final unit.

detection, for sensing oxygen tension changes, and for ascorbate indicator dilution curves. Electrochemical detection systems in general provide information rapidly with a minimum of reagents and chemical manipulation. Accurate, continuous recording of blood oxygen content is possible with as little as 6 cc. of blood per hr. Knowledge of mixed venous saturation is of practical value in judging cardiac output, while knowledge of arterial gas tensions is useful in evaluating pulmonary function. Knowledge of the variables measured can be used to provide optimum surgical management.

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