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 [21] Appl. No. **453,281**
 [22] Filed **May 5, 1965**
 [45] Patented **Sept. 29, 1970**
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2,756,203	7/1956	Gilbert	204/195.1
3,098,813	7/1963	Beebe et al.	204/195.1
3,224,433	12/1965	Von Dalebor	128/2
3,224,436	12/1965	Le Massena	128/2.1

FOREIGN PATENTS

358,937	1/1906	France	128/350
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OTHER REFERENCES

Adler: "Scientific Apparatus," in Science for Oct. 25, 1940, pages 385, 386.

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[54] **ELECTRODE FOR MAKING IN VIVO IONIC MEASUREMENTS OF VENOUS BLOOD**
5 Claims, 2 Drawing Figs.

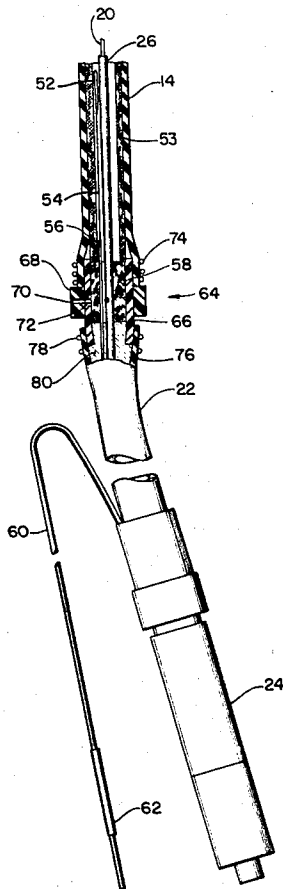
[52] U.S. Cl.....	128/2,
	204/195
[51] Int. Cl.....	A61b 5/00
[50] Field of Search.....	128/2.1.2;
	204/1.1, 195.1, 195; 128/1.05

References Cited

UNITED STATES PATENTS

2,168,867	8/1939	George	204/195X
3,244,607	4/1966	Leonard et al.	204/195
3,334,623	8/1967	Hillier et al.	128/2.05

ABSTRACT: A miniature electrode for making in vivo ionic measurements of venous blood in which the ion measuring electrode is positioned entirely in front of the reference electrode to minimize the cross sectional area of the assembly. The reference electrode includes a flexible catheter tube which holds the electrolyte of the reference electrode. The catheter tube may be filled with a sufficient quantity of electrolyte to expand the tube whereby the tube exerts a positive pressure on the electrolyte therein and thereby produces a constant flow of electrolyte through the liquid junction of the reference electrode regardless of the position of the assembly.



Patented Sept. 29, 1970

3,530,849

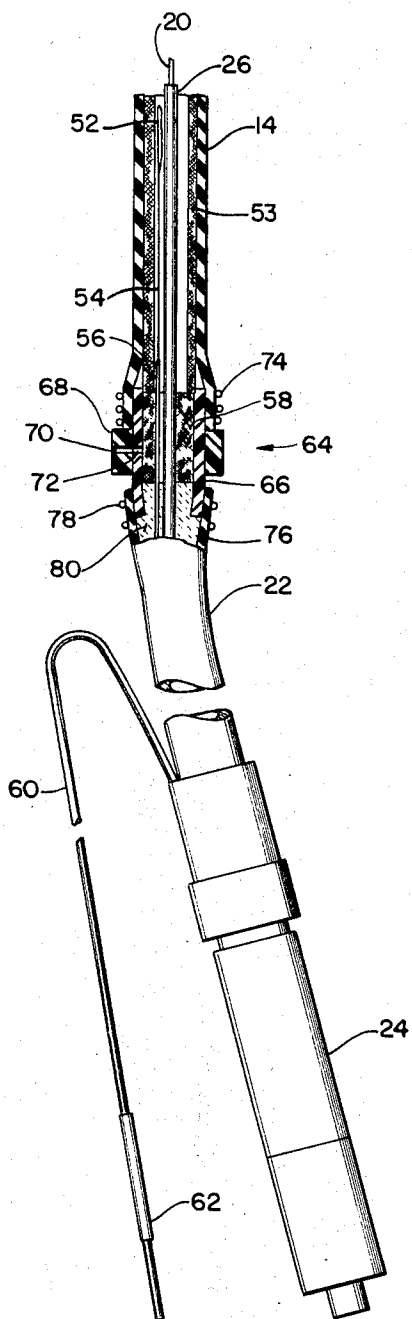


FIG. 2

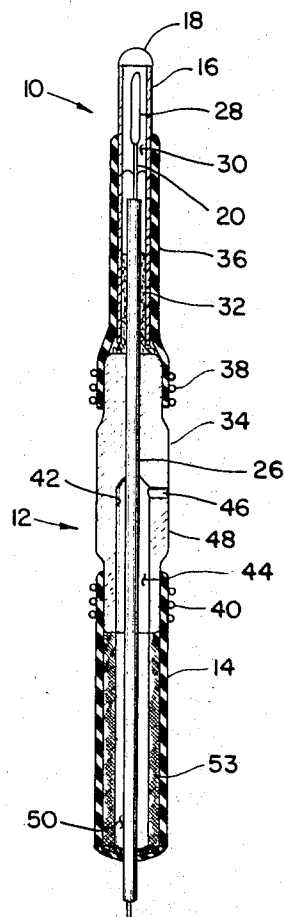


FIG. 1

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ELECTRODE FOR MAKING IN VIVO IONIC MEASUREMENTS OF VENOUS BLOOD

This invention relates to an electrochemical electrode assembly for measuring the ionic concentration of a sample medium and, in particular, to an electrochemical electrode assembly for making in vivo pH measurements of venous blood or tissues of human or animal subjects.

Current medical research indicates that low tissue and venous blood pH in human or animal subjects may be used as an indicator for primary hemorrhagic shock. Furthermore, it is believed that correction of the low pH of venous blood and vital organs by means of intravenous injection of adequate quantities of sterile bicarbonate buffer may improve the prognosis for a subject in shock. In other words, if the tissue acidosis resulting from ischemia can be neutralized, the subject will be better able to survive and re-establish adequate circulation.

At the present time there is no instrument available which is capable of making in vivo pH measurements in the venous lumina of major internal organs to permit the diagnosis and treatment described above. It is the conventional practice today to measure the pH of venous blood by withdrawing blood from a vein by a syringe and delivering the blood to a flow cell having pH electrodes mounted therein. This method has the disadvantage, however, that the pH of the blood may not be measured completely anaerobically, that is, without exposure to air, thus possibly resulting in some errors in the pH measurement. Also, it is necessary that the flow cell in which the blood sample is measured have close temperature control to simulate the temperature of the subject being diagnosed. Any difference in the temperature of the blood being measured in the flow cell and that inside the body might also produce a source of error. Furthermore, by the present method only the pH of blood withdrawn from peripheral veins may be measured which may be different than the pH of blood at points inside the body in the venous lumina of certain major internal organs.

Therefore, what is needed is an instrument for making in vivo pH measurements of venous blood in deep tissue or near major internal organs. The instrument should be capable of being positioned in the veins of a patient or experimental subject with a minimum of surgical trauma. Also, it must be capable of making the required measurement with accuracy and precision; preferably the accuracy should be better than .1 pH unit as a minimum. In addition, the instrument should establish a stable, well-coupled reference point and preclude interference from the electrical activity of the heart or other muscles and nervous tissue and from the electrical impedance differences from various points of the body. This requires that the reference electrode for the pH measuring instrument be positioned very close to the pH electrode, yet the assembly must be sufficiently small to permit it to be readily inserted through the veins of the subject being examined. Also, a stable pressurized reference junction should be provided for the reference electrode of the instrument.

It is an object of the present invention to provide an electrochemical electrode assembly for making in vivo ionic measurements of venous blood or tissues of human or animal subjects having the above desired characteristics.

According to a principal aspect of the present invention, there is provided a miniaturized combination ion measuring-reference electrode assembly in which the ion measuring electrode portion of the assembly is sealed to one end of the reference electrode portion of the assembly thus permitting the assembly to have a substantially smaller cross section than that of conventional combination measuring-reference electrodes. Hence, the assembly may be made sufficiently small to be mounted in an elongated flexible tube of very small diameter, generally referred to as a catheter, which can be positioned in a vein or other small organ of a human or animal subject for making in vivo ionic measurements. Also, the catheter forms a part of the reference electrode in that it provides a salt bridge space whereby a sufficient supply of salt bridge solution is available to maintain ionic communication between the in-

ternal half cell of the reference electrode and the sample medium for a substantial period of time.

According to another aspect of the invention, the salt bridge space provided by the catheter in the above-described assembly is filled with a sufficient quantity of salt bridge solution so as to expand the elastic wall of the catheter. The expanded catheter exerts a positive pressure on the salt bridge solution thereby providing a pressurized reference junction for the assembly. Consequently, by this feature the assembly may be disposed at any position and salt solution will still flow through the liquid junction so long as the solution remains pressurized by the expanded catheter. According to still another aspect of the invention, a fibrous material is positioned in the salt bridge space provided by the catheter so as to ensure continuous electrolytic communication between the leak structure and the internal half cell of the reference electrode for a substantial time even though bubbles might eventually form in the salt bridge space.

Other objects, aspects and advantages will become apparent from the following description taken in connection with the accompanying drawing wherein:

FIG. 1 is a greatly enlarged cross sectional view of the forward portion of the electrochemical electrode assembly of the invention; and

FIG. 2 is an enlarged partial cross sectional view of the rear portion of the assembly including the connectors for connection to an external electrical circuit, not shown.

Referring now to the drawing in detail, there is illustrated the electrochemical electrode assembly of the present invention which comprises generally an ion measuring electrode 10 and a reference electrode 12 having as a portion thereof an elongated flexible tube or catheter 14 formed of an elastic nonconductive material such as silicone rubber. The ion measuring electrode 10 and the reference electrode 12 together with the catheter 14 are sufficiently small in cross section to permit the insertion of the entire assembly into the veins of animal or human subjects, which requires that the outside diameter of the assembly be no more than about 3 millimeters. The assembly also must be of sufficient length to permit the insertion of the assembly in the vein of an animal or a human subject so that the sensing portion of the ion measuring electrode 10 will reach the heart or other internal organs where the in vivo ionic measurement of blood or tissues is required.

The ion measuring electrode 10 comprises a tubular member of nonconductive material 16, preferably a conventional stem glass for glass electrodes, and an ion sensitive barrier 18 closes the forward end of the tubular member 16. The ion sensitive barrier may be formed of any material which is sensitive to the ions that are desired to be measured and may take the form of a bulb, as illustrated, or a flat barrier if desired. In the preferred embodiment of the present invention, the barrier 18 is formed of pH sensitive glass formed in the configuration of a bulb which is sealed by fusion to the end of the tubular member 16.

A conductor 20 is positioned in the tubular member 16 and extends through the rear open end of the tubular member and through the entire reference electrode assembly 12 including the catheter 14 for connection to a cable 22 having a connector 24 at the end thereof for connection to a suitable external circuit, such as a conventional pH meter (not shown). The conductor 20 is coated with a nonconductive material such as rubber to form an insulating sleeve 26 along its entire length except for the portion in the glass tubular member 16 which is connected to a half cell 28 immersed in a suitable electrolyte solution 30. Preferably, the conductor 20 is a silver wire and the half cell 28 comprises a coating of silver chloride formed on the end of the silver wire 20. The rear portion of the tubular member 16 is sealed off from the remainder of the electrode assembly by cementing the insulating sleeve 26 into the rear portion of the tubular member by silicone cement or other suitable insulating cement 32.

The reference electrode 12 of the assembly includes a glass tubular member or sleeve 34, which may be formed also of

other nonconductive materials such as ceramic. The sleeve 34 surrounds the insulating conductor 20 and is cemented at its forward end to the insulating sleeve 26 of the conductor. Also, as seen in FIG. 1, the forward portion of the sleeve 34 is cemented to the rear end of the glass tube 16 by the cement 32. To ensure that the tube 16 and sleeve 34 are durably secured together, a rubber sleeve 36 surrounds a substantial part of the tube 16 and a forward reduced portion of the sleeve 34 and is cemented thereto. Also, a suitable clamp 38 shown as a wire wound about the rubber sleeve 36 over the forward portion of the sleeve 34 mechanically fixes the ion measuring electrode 10 to the reference electrode assembly 12. An alternative to the rubber sleeve 36 and clamp 38 would be a sleeve of heat shrinkable plastic which could be slipped over the tube 16 and sleeve 34 and, upon application of heat, would permanently conform to the irregular shapes of the tube and sleeve, thus firmly securing the two parts together. An additional clamp 40 similar to clamp 38 secures the forward portion of the catheter 14 to the rear of the sleeve 34. The catheter 14 may take the form of any flexible nonconductive material, but preferably is formed of silicone rubber.

A cavity 42 is provided in the rear portion of the sleeve 34 to provide a salt bridge space 44 and a liquid junction or leak structure 46 is provided in the wall 48 of the sleeve 34 to provide electrolytic communication between the space 44 and the outside of the electrode assembly. Preferably the leak structure 46 comprises a palladium wire sealed in an opening in the wall 48 as described in U.S. Pat. No. 2,705,220. However, it is understood that other leak structures may be provided as, for example, porous ceramic plugs or asbestos fibers sealed into the wall 48. It is merely important that the leak structure provide a sufficiently slow passage of salt bridge solution from the reference electrode outside the assembly so that the blood or internal organs of the subject being examined are not exposed to appreciable quantities of reference electrolyte.

The wall of the catheter 14 is spaced from the insulated conductor 20 to provide additional salt bridge space 50 in communication with the space 44. The spaces 44 and 50, when filled with a suitable salt bridge solution such as saturated KCl, provide electrolytic connection between a half cell 52 at the rear of the catheter 14 and the sample medium through the leak structure 46. Since the space 50 is of substantial length, a sufficient supply of salt bridge solution for the reference electrode 12 is available to ensure continuous electrolytic communication through the leak structure 46 when the electrode assembly of the invention is implanted in a subject for monitoring the pH of venous blood over a substantial period of time.

According to one of the important features of the invention a sheath 53 of fibrous material such as braided cloth is disposed in the catheter 14 to facilitate the filling of the space 50 with salt bridge solution and, most importantly, since the sheath is impregnated with the salt solution, the half cell 52 remains in electrolytic communication with the sample through the leak structure 46 even though bubbles form in the space 50.

It is understood that the half cell 52 may be positioned any place within the salt bridge space 50 or even the space 44 in the sleeve 34, but it is preferred to mount the half cell at the rear of the catheter 14 as shown in FIG. 2, particularly if it results in increasing the diameter of the assembly. However, the increased diameter of the end of the assembly would be of no consequence since it would be external of the subject being examined. The half cell 52 may comprise a silver wire 54 coated with silver chloride. The wire 54 is covered with an insulation 56 and passes through a body 58 of fibrous material into the cable 22 and terminates in a lead 60 having a connector 62 for connection into the reference electrode terminal of a pH meter, not shown. The cable 22 is fixed to the rear of the catheter 14 by a salt bridge filling assembly 64.

The filling assembly 64 comprises a tube 66 of nonconductive material surrounding the braided cloth body 58 and a ring 68 rotatably mounted on the tube. The ring has an opening 70

therein which is adapted to be positioned in alignment with an opening 72 in the tube 66 to permit delivery of salt bridge solution into the space 50 as will be described in detail later. The rear of the catheter 14 is secured to the forward end of tube 66 by a suitable clamp 74, similar to clamp 38, while the sheath 76 of the cable 22 is secured to the rear of tube 66 by another clamp 78. An epoxy material 80 fills the rear portion of tube 66 and ensures that the catheter is firmly connected to the cable 22.

It is seen from the above description and the drawing that the reference electrode 12 including the catheter 14 is mounted entirely behind the rear portion of the ion measuring electrode 10, thereby producing a combination measuring-reference electrode assembly having a sufficiently small cross section to permit its insertion into veins or other small organs. Also, by the construction of the assembly of the present invention, good insulation is provided between all electrical parts of the assembly, which is essential in ion measuring equipment, yet the assembly is still compact.

The space 50 of the catheter may be filled with salt solution by inserting the needle of a syringe containing the solution through the openings 70 and 72, when aligned as shown in FIG. 2, and by forcing the solution into the space. However, it is extremely difficult to fill the space 50 in this manner without a considerable amount of bubbles forming in the space, which, of course, is undesirable. Therefore, it is preferred to fill the space 50 with salt solution by immersing the filling assembly end of the catheter 14 in a vessel of salt bridge solution with the openings 70 and 72 aligned. Then an inverted bell jar is placed over the electrode assembly and the vessel and a vacuum is drawn in the jar. This will cause the evacuation of the air in the catheter 14 through the openings 70 and 72. Thereafter, the bell jar is removed to break the vacuum so that atmospheric pressure forces the salt bridge solution in the vessel to completely fill the space 50 in the catheter without the formation of any air bubbles in the space.

In order for the assembly to operate it is necessary that there be adequate flow of salt bridge solution through the leak structure 46 to the sample media. This requires that a positive pressure be applied to the salt bridge solution in the catheter. If, when the electrode assembly is used it is disposed so that a portion of the catheter 14 is above the leak structure 46 then, due to the head of pressure of the salt solution, a flow of the solution through the leak structure will result. However, in many cases the electrode assembly will be so disposed in the body being examined that there will be no positive pressure on the salt solution in the vicinity of the leak structure 46. Therefore, according to another feature of the invention, a slight positive pressure is applied to the salt bridge solution regardless of the disposition of the electrode assembly. This is achieved by taking advantage of the elastic nature of the catheter 14. After the salt bridge space 50 in the catheter has been filled with solution in the manner described above, an additional amount of solution is supplied under pressure to the space 50 via openings 70 and 72 by a syringe. This will cause the catheter to expand to accommodate the additional amount of solution. Thereafter the ring 68 is rotated to a position to close the opening 72. Since the expanded elastic catheter will tend to contract, a constant slight positive pressure is applied to the solution in space 50 thereby causing a continuous flow of solution through the leak structure 46 so long as sufficient solution remains in the catheter to keep it expanded. Generally, this pressurization of the solution by the catheter will continue for a sufficiently long period, due to the slow flow of the solution through the leak structure 46, to meet most applications for the electrode assembly of the invention.

An electrochemical assembly has been constructed in accordance with the invention having a length of about three feet and a diameter of approximately 3 millimeters. The diameter of the ion sensitive barrier 18 was about 1.75 millimeters whereas the leak structure 46 of the reference electrode was positioned approximately 5 milliliters behind the ion sensitive barrier 18, which is sufficiently close to the barrier to

preclude interference from electrical activity from various points elsewhere in the body. Also, tests of the electrode assembly of the invention show that the impedance of the assembly, its accuracy and reproducibility were well within the required limits for satisfactory measurements of the pH of venous blood.

Although the present invention has been described as being ideally suitable for measuring in vivo the pH of venous blood, the invention has applications for the same general use in any system where access may be limited, particularly through a tubular passage or where remote ionic measurements are desired.

Although only one embodiment of the invention has been disclosed herein for purposes of illustration, it will be understood that various changes can be made in the form, details, arrangement and proportions of the various parts in such embodiment without departing from the spirit and scope of the invention as defined by the appended claims.

We claim:

1. In an electrochemical electrode assembly for making in vivo ionic measurements of venous blood or the like, the combination of:
 - a reference electrode including an elongated elastic tube having a salt bridge space therein;
 - a liquid junction in said electrode adjacent to one end of said tube to permit ionic communication between said salt bridge space and the exterior of the electrode;
 - closure means closing the other end of said tube;
 - an internal half cell positioned in said salt bridge space;
 - a conductor connected to said half cell and extending through said closure means for connection to an external electrical circuit;
 - a wall of said closure means having an unoccluded passage extending therethrough to provide communication between said salt bridge space and the exterior of said electrode;
 - said reference electrode being closed except for said liquid junction and said passage; and
 - a valve element movably mounted on the outside of said wall between two positions, in one position said valve element closing said passage and in the other position said valve element exposing said passage whereby in said other position of said valve element salt bridge solution may be introduced into said space under pressure to expand said elastic tube and said solution may be maintained under pressure by shifting said valve element to said one position to close said passage and, further, whereby said expanded elastic tube will exert a positive pressure on said solution in said salt bridge space.
2. An electrochemical electrode assembly for making in vivo ionic measurements of venous blood or the like comprising:
 - reference electrode means including an elongated flexible tube of relatively small diameter adapted to be inserted into the veins or other organs of humans or animal subjects;
 - ion measuring electrode means at one end of said reference electrode means and comprising a tubular member of nonconductive material having an ion sensitive barrier closing one end of said member, a first half cell in said tubular member for contacting an electrolyte solution therein, a first conductor connected to said half cell and extending beyond the other end of said tubular member and through said flexible tube for connection to an external circuit, and an insulating sleeve surrounding said first conductor and sealed to said other end of said tubular member;

said reference electrode means also including a second tubular member of nonconductive material surrounding said insulating sleeve and having one end sealed to said other end of said first tubular member, the wall of said second tubular member at its other end being spaced from said sleeve to define a first salt bridge space, a leak structure in said wall at said other end of said second tubular member providing ionic communication between said salt bridge space and the exterior of said assembly;

said flexible tube having one end sealed to said other end of said second tubular member and the wall of said flexible tube being spaced from said insulating sleeve to define a second salt bridge space communicating with said first salt bridge space; and

a second half cell in one of said salt bridge spaces and a second conductor connected to said second half cell and extending through said other end of said flexible tube for connection to an external circuit.

3. An electrochemical electrode assembly as set forth in claim 2 wherein said first conductor is a silver wire and said first half cell comprises a coating of silver chloride on said silver wire.

4. An electrochemical electrode assembly as set forth in claim 2 including a sheath of fibrous material extending substantially the length of said second salt bridge space in said elongated flexible tube for facilitating the filling of said first and second salt bridge spaces with salt bridge solution.

5. An electrochemical electrode assembly for making in vivo ionic measurements of venous blood or the like comprising:

reference electrode means including an elongated flexible tube having a sufficiently small cross section to permit its insertion into the veins or other organs of human or animal subjects;

ion measuring electrode means entirely at one end of said reference electrode means and comprising a tube of nonconductive glass having an ion sensitive glass barrier closing one end thereof, electrolyte solution in said glass tube, a first half cell in said glass tube contacting said electrolyte solution, a first conductor connected to said half cell and extending beyond the other end of said glass tube and through said flexible tube for connection to an external circuit, and an insulating sleeve surrounding said first conductor and sealed in said other end of said glass tube;

said reference electrode means also including a sleeve of nonconductive glass surrounding said insulating sleeve and having one end sealed to said sleeve and to said other end of said glass tube, the wall of said glass sleeve at its other end being spaced from said insulating sleeve to define a first salt bridge space, a leak structure in said wall at said other end of said glass sleeve providing ionic communication between said salt bridge space and the exterior of said assembly;

said flexible tube having one end sealed to said other end of said glass sleeve and the wall of said flexible tube being spaced from said insulating sleeve to define a second salt bridge space communicating with said first salt bridge space;

a second half cell in one of said salt bridge spaces and a second conductor connected to said second half cell and extending through said other end of said flexible tube for connection to an external circuit; and

a sheath of fibrous material extending substantially the length of said second salt bridge space in said elongated flexible tube for facilitating the filling of said first and second salt bridge spaces with salt bridge solution.