Jan. 21, 1964 B. W. TAYLOR 3,118,736

METHOD FOR BLOOD GAS ANALYSIS

Filed June 30, 1959 2 Sheets-Sheet 1

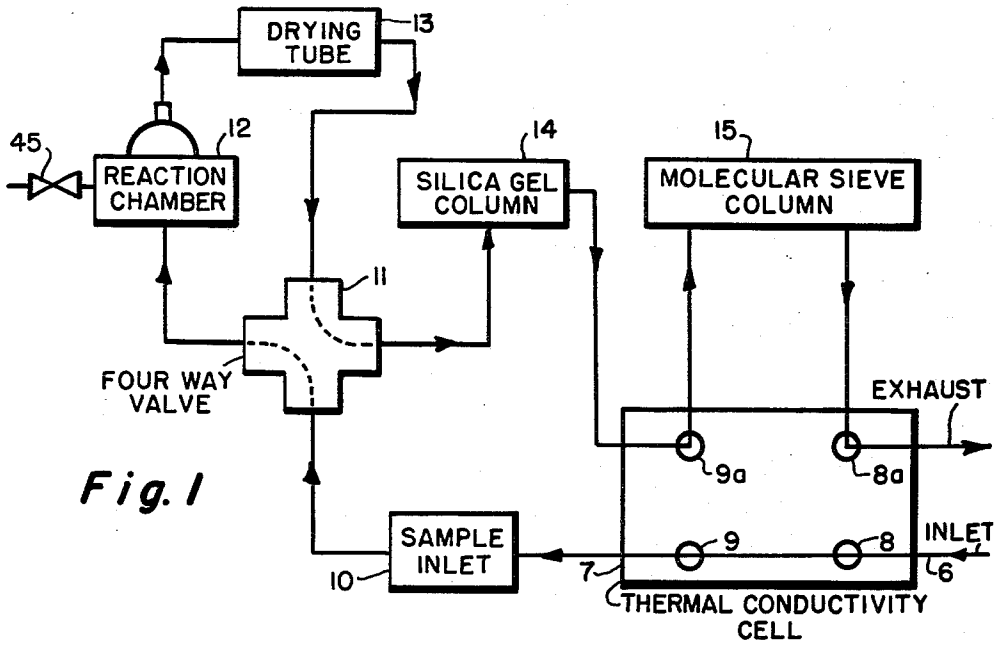


Fig. 1

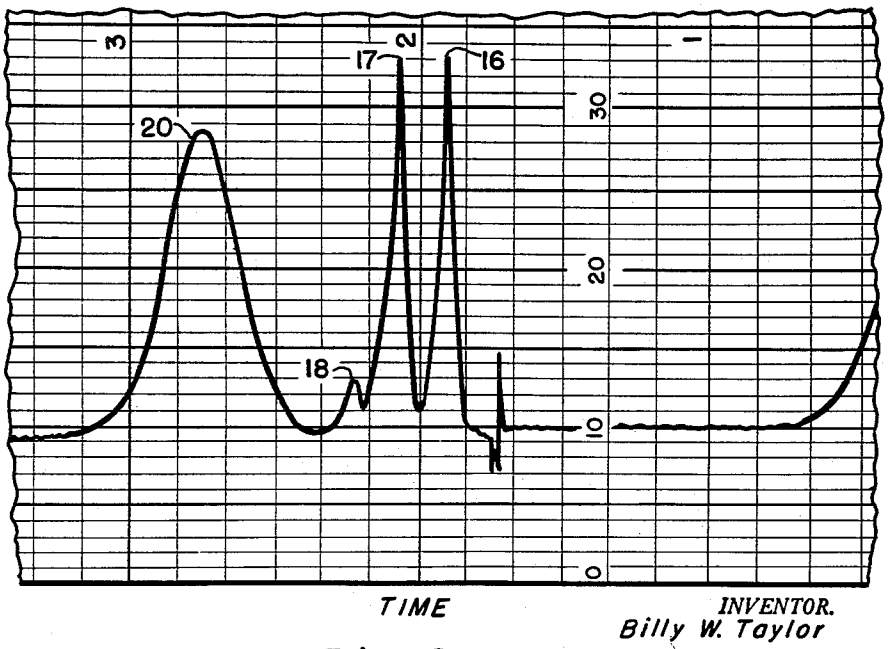


Fig. 2

INVENTOR.
Billy W. Taylor

BY
Webb, Mackey & Burden
HIS ATTORNEYS

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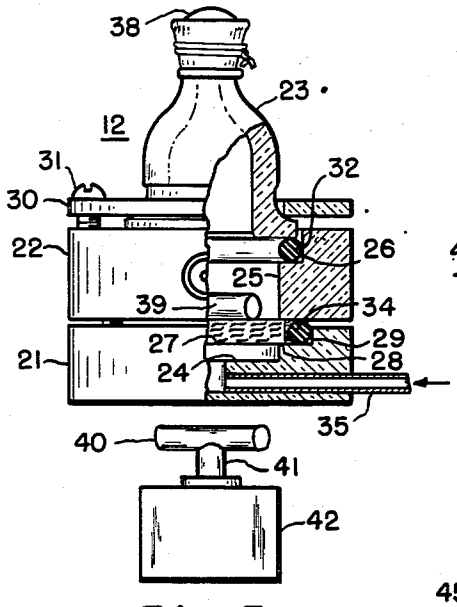


Fig. 3

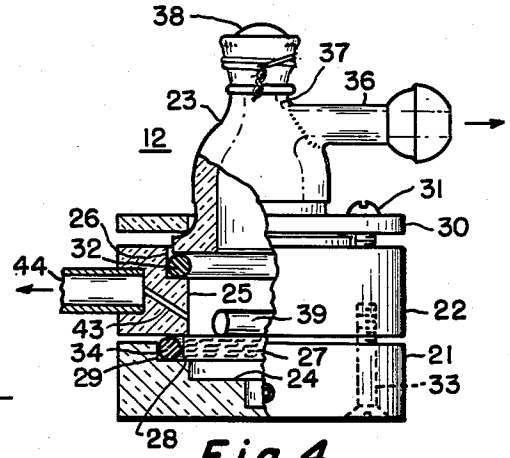


Fig. 4

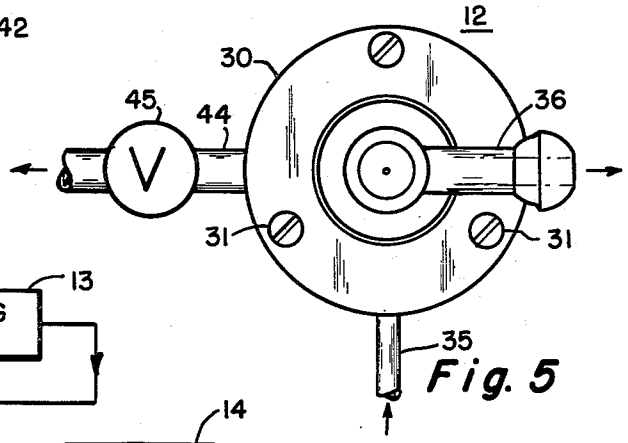


Fig. 5

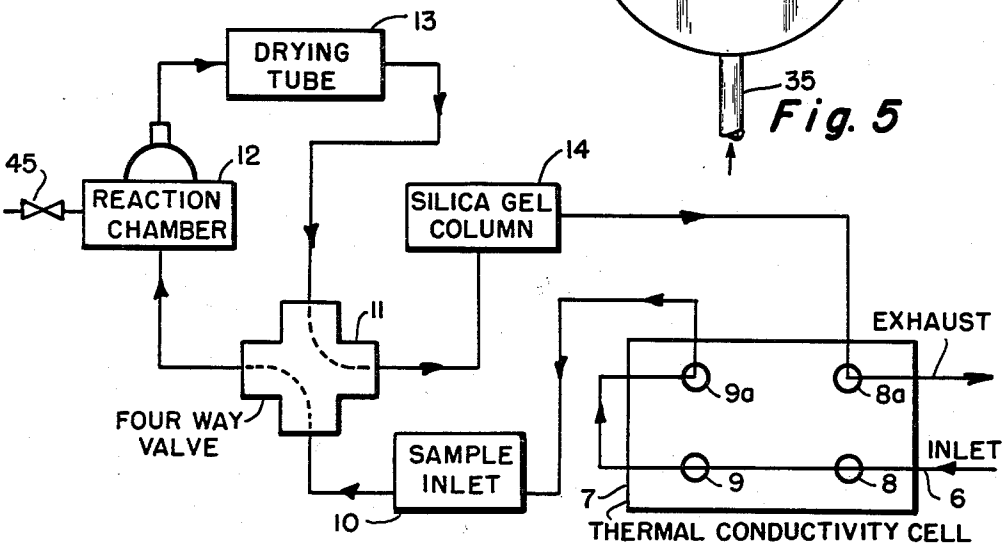


Fig. 6

INVENTOR.
Billy W. Taylor

BY
Wilson Mackey & Burden
HIS ATTORNEYS

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3,118,736

METHOD FOR BLOOD GAS ANALYSIS

Billy W. Taylor, Pittsburgh, Pa., assignor to Fisher Scientific Company, Pittsburgh, Pa., a corporation of Pennsylvania

Filed June 30, 1959, Ser. No. 824,038
1 Claim. (Cl. 23—230)

This application relates to method and apparatus for measuring gases found in blood, specifically nitrogen, oxygen, and carbon dioxide, although other gases occasionally present in the blood may also be measured by my inventions.

The quantity of gases present in human and animal blood is used by physicians and research personnel as an indication of the state of the health of the body from which blood is taken and analyzed. The physician is particularly interested in the presence and quantity in the blood of oxygen and carbon dioxide.

Animal and human blood consists of plasma in which are suspended red corpuscles, white corpuscles, and blood platelets. The red corpuscles contain oxygen, carbon dioxide in the form of potassium bicarbonate, and protein membrane, and the white corpuscles contain carbon dioxide in the form of sodium bicarbonate and protein membrane. Heretofore, blood has been analyzed by carrying out the well-known Van Slyke procedure. This procedure, although standard for at least 30 years, is time consuming, requires a highly skilled operator, and also requires a relatively large blood sample. Thus, the Van Slyke technique requires 15 to 20 minutes to run a complete analysis for both oxygen and carbon dioxide in whole blood, from 1 to 3 weeks is required to train an operator to carry out the process, and an analysis requires approximately 1 ml. of blood.

By my method and apparatus, a complete oxygen and carbon dioxide determination of whole blood can be carried out in five minutes and an operator can be trained to use my apparatus in approximately one-half day. An analysis requires approximately 0.1 ml. of blood.

In my method and apparatus, I use a standard Van Slyke solution to liberate gases contained in the blood. Using the special apparatus which I have invented, I pick up the liberated gases in a stream of inert gas and conduct the inert gas stream with the liberated blood gases contained therein through one or more chromatographic columns. The gases are separated in the columns and passed to a thermal conductivity cell which records their presence and quantity by sending an appropriate signal to conventional recording or reading apparatus. My method and apparatus can be used both for the analysis of whole blood and also for the determination of carbon dioxide in serum and plasma.

In the accompanying drawings, I have illustrated certain presently preferred forms of apparatus for carrying out my process, in which:

FIGURE 1 is a schematic block diagram of my apparatus for analyzing whole blood;

FIGURE 2 is a reproduction of a chart made by an electric recorder in carrying out my method of blood gas analysis;

FIGURE 3 is a side elevation, partially in section, of a reaction chamber used for liberating gas from a blood sample;

FIGURE 4 is a front elevation, partially in section, of the reaction chamber of FIGURE 3;

FIGURE 5 is a plan view of the reaction chamber of FIGURES 3 and 4; and

FIGURE 6 is a schematic block diagram of apparatus for analyzing blood serum for carbon dioxide.

FIGURE 1 is a diagram showing the arrangement of my apparatus for use in analyzing whole blood for carbon dioxide and oxygen. Referring to that figure, I supply a stream of inert gas, such as helium, to an inlet 6 of a thermal conductivity cell 7. This cell, which has two reference thermistors 8 and 9 and two detecting or sample thermistors 8*a* and 9*a*, is described and claimed in the copending application of Billy W. Taylor and Albert Anthony Poli, Jr., Serial No. 762,472, which application is owned by the same assignee as the assignee of this application.

The helium carrier gas flows past the two reference thermistors 8 and 9 and then to a sample inlet 10 and from the sample inlet to a four-way valve 11. The purpose of the inlet 10 and valve 11 will be later described.

Carrier gas then flows into a reaction chamber 12. As will be later described, a sample of the blood being tested is treated in the reaction chamber with reagents which will liberate the gases in the blood. These liberated gases are entrained in the carrier gas as a group; that is, the liberated gases are removed from the reaction chamber all at substantially the same time. From the reaction chamber, the carrier gas and the entrained blood gases flow through a drying tube 13 and back to the four-way valve 11.

After the blood gases entrained in the carrier gas leave the valve 11, they are separated and measured in accordance with a chromatographic technique described and claimed in said Taylor and Poli application, Serial No. 762,472. Thus the carrier gas and the blood gases flow into a chromatographic column 14, which, in this instance, is a silica gel column.

The column 14 is constructed in accordance with known chromatographic techniques so that oxygen and nitrogen pass together through the column at a higher rate than the carbon dioxide, with the result that, while the carbon dioxide is still passing through the silica gel column 14, oxygen and nitrogen elute from the column and pass over a detecting thermistor 9*a* in the thermal conductivity cell 7 which transmits a signal to a recording or reading device, as is also described in the said copending Taylor and Poli application, Serial No. 762,472. Preferably, the signal is sent to an electrical recorder which records on a chart oxygen and nitrogen together.

The oxygen and nitrogen then pass through a second chromatographic column 15, which, in this instance, is a molecular sieve column such as is described in said Taylor and Poli application, Serial No. 762,472. The oxygen and nitrogen flow at different rates through the molecular sieve column 15. They therefore elute at different times from the column 15 and pass at different times over the sample thermistor 8*a* in the thermal conductivity cell 7. The cell sends to a recorder a signal as oxygen and nitrogen each pass over the thermistor and the recorder records the presence and quantity of each gas on a chart in accordance with the signal received from the thermistor 8*a*. From the thermistor 8*a*, the gases flow to exhaust.

In accordance with known chromatographic techniques, the silica gel column 14 is so designed that carbon dioxide does not elute from the column 14 until after the oxygen and nitrogen have been recorded. The carbon dioxide then flows in the carrier gas past the thermistor 9*a* in the cell 7 which sends a signal to the recorder proportional to the quantity of carbon dioxide present.

FIGURE 2 is a reproduction of a typical chart recorded by a conventional electrical recorder in response to signals received from a thermal conductivity cell. Referring to that figure, it will be seen that the chart records against time the occasion and extent of each signal as the blood gases pass over the thermistors 9*a* and 8*a*. In the chart illustrated in FIGURE 2, time is the abscissa and runs from right to left. The first large signal 16 recorded both oxygen and nitrogen; the second signal 17

recorded oxygen; the next signal 18, nitrogen; and the last signal 20, carbon dioxide.

The area under each signal peak indicates the quantity of each gas present and, in order to obtain the actual amount present, it is necessary to calibrate the chromatographic portion of the apparatus shown in FIGURE 1. This is done by turning the four-way valve 11 so that carrier gas flows directly from the sample inlet 10 to the silica gel column 14. Samples of known quantities of air are then injected into the sample inlet and readings taken on the recorder for oxygen and nitrogen. From these recordings, a calibration curve may be obtained from which signals recorded on a chart may be read directly to give volume. To calibrate the instrument for carbon dioxide, the four-way valve is turned to the position shown in FIGURE 1. Carrier gas then flows through the reaction chamber and drying tube before reaching the column 14. Acid is charged into the reaction chamber and purged by flowing carrier gas therethrough. Different known quantities of sodium bicarbonate are then charged into the reaction chamber to generate carbon dioxide. Readings are then taken of the carbon dioxide present in the sample and a calibration curve for carbon dioxide is made from these readings.

FIGURES 3 to 5 show the reaction chamber 12 in which blood gases are liberated and entrained in the stream of carrier gas. The chamber comprises a cylindrical base 21, a hollow cylindrical body 22, and a glass cap 23. The base 21 has formed in its top surface a recess 24, and the body 22 is placed on the base so that its interior 25 is in line with the recess 24. The body has on its upper surface an annular recess 26 in which the cap 23 is placed.

Between the recess 24 in the base and the interior of the body 22, there is a porous partition 27 which extends completely across the recess 24 and rests on shoulders 28 formed by a second annular recess 29 which is larger in diameter than the recess 24. The partition 27 divides the interior of the reaction chamber 12 into two compartments and is porous so that carrier gas supplied in the compartment on one side of the partition 27 may flow through the partition 27 and be diffused into any reaction mixture which is present in the compartment on the other side of the partition. I have found that a disc of porous polytetrafluoroethylene makes an excellent partition for this purpose.

The cap 23 is secured to the body 22 by a ring 30 held to the base by three screws 31. The reaction chamber must be leakproof and, therefore, the cap 23 rests against an O-ring 32 within the recess 26.

The body 22 is secured to the base 21 by three screws 33, one of which is shown in FIGURE 4. The joint between the base 21 and the body 22 is sealed by an O-ring 34 which rests in the recess 29.

A passageway 35 in the base 21 leads from the exterior of the base to the recess so that carrier gas may be supplied to the recess 24. The carrier gas flows through the partition 27 into the body 22 and then into the cap 23. The cap 23 has an outlet passage 36 to which tubing leading to the drying tube 13 can be connected.

The cap 23 also has means whereby blood samples and reagents may be inserted into the chamber. These means comprise a hollow stem 37 extending upwardly from the top of the cap 23 and a serum cap, i.e., a rubber diaphragm 38 which is tied over the end of the stem 37. Blood samples and reagents are inserted into the reaction chamber through the cap 38 by filling them into hypodermic syringes, stabbing the syringe needle through the serum cap and forcing the sample or reagent out through the needle into the chamber.

It is important that the blood sample and the reagent chemicals be thoroughly stirred while in the reaction chamber. For that purpose, I provide a magnetic stirrer which comprises a bar magnet 39 which is covered with glass or polytetrafluoroethylene and which rests on the partition 27. Beneath the base 21, I install a second bar magnet 40 which is mounted on the shaft 41 of an electric motor 42. The motor when supplied with current will rotate the bar magnet 40 and the bar magnet 39, being magnetically attracted to the bar magnet 40, will turn with it.

In carrying out a blood analysis, I add reagent to the reaction chamber through the serum cap 38, as described. For a whole blood analysis, this reagent is a standard Van Slyke solution containing lactic acid, saponin, N. octyl alcohol, and potassium ferrocyanide. After the reagent is added, the supply of carrier gas is turned on and carrier gas is allowed to flow through the entire system to remove any gases which may be present in the reagents. Prior to this time, the four-way valve is thrown so as to flow the carrier gas through the chromatographic portion of the equipment and to stabilize the thermal conductivity cell and the recorder. After purging of the reagent and stabilization of the chromatographic apparatus, carrier gas is flowed through the reaction chamber and blood samples are inserted one at a time into the reaction chamber and analyzed as described above.

The same reagent solution may be used several times before replacing. When it is necessary to replace the solution, I clean out the reaction chamber by injecting water into the chamber through the serum cap and by blowing the water and the residue of the reagents out through a small passageway 43 which extends through the side of the body 22 to a tube 44 which is closed by a valve 45. The tube 44 leads to drain. It will be noted that the passageway 43 is relatively small because, as will be explained, I have found it advisable to restrict the size of the reaction chamber.

The size of the reaction chamber is quite important to the success of the operation. When a blood sample is added to the reagent solution, there is considerable effervescence and frothing and if the reaction chamber is too small some of the froth will carry over into the drying tube. On the other hand, in order to obtain good separation and measurable results on the liberated gases in the chromatographic portion of the apparatus, it is necessary that the gases liberated from the blood sample become entrained in the carrier gas as a group and at substantially the same time. If the volume of the reaction chamber is too large, the different components of the blood gases will not become entrained in the carrier gas and enter the chromatographic system at substantially the same time. I have found that best results are obtained with reaction chambers varying in volume from 5 ml. to 10 ml.

In order to obtain reproducible results, and particularly in order to calibrate the chromatographic system, it is necessary that certain variables in the apparatus be kept constant. These are the current to the thermistors in the thermal conductivity cell, the room temperature, the flow rate of the carrier gas, and the sample volume. It is not important that these variables be kept at any particular value, but it is important that they be kept constant.

In many instances, the only medical subject of interest is the quantity of carbon dioxide present in blood serum. As stated previously, my inventions can be used to analyze blood serum for carbon dioxide. To accomplish this analysis, certain changes are required in the chromatographic portion of the apparatus, and these changes are illustrated in FIGURE 6. Since only carbon dioxide is to be analyzed, only one chromatographic column, a silica gel column, is required, and the arrangement of the thermal conductivity cell, sample inlets, silica gel column, etc. are shown in FIGURE 6. The actual analysis is conducted in the same way as has been described for the analysis of whole blood. However, only a dilute acid is required for the reagent. This acid is inserted in the reaction chamber and thereafter samples of blood serum are inserted to react with the acid. Carbon dioxide and other gases released from the blood serum are entrained in the carrier gas and they pass with the carrier

gas through the drying tube and four-way valve into the silica gel column. The carbon dioxide moves more slowly through that column than the balance of the gases so that it is separated from them in the column and passes last over the thermistor 8*a*, which reads the gas as it passes. In order to determine from the graph made by the recorder the actual volume of the carbon dioxide, the apparatus is calibrated by adding in the reaction chamber known quantities of sodium bicarbonate and acid and reading the quantities of carbon dioxide released by the different sodium bicarbonate samples. From these readings, a calibration curve can be made.

While my apparatus and method as described are designed primarily for the analysis of oxygen and carbon dioxide in either whole blood or blood serum, it is possible to analyze other gases which may be found in the blood, for example ether and carbon monoxide. To separate and read these additional gases, a chromatographic system such as is shown in FIGURE 7 or FIGURE 8 of the said copending Taylor and Poli application, Serial No. 762,472, may be used.

While I have described certain presently preferred embodiments of my inventions, it is to be understood that they may be otherwise embodied within the scope of the appended claim.

I claim:

The method of analysis of gases contained in samples of whole blood, blood serum, and blood plasma which comprises, introducing into a closed reaction chamber a stream of inert gas from one side of said chamber, said reaction chamber containing a reagent capable of breaking down samples to be analyzed, flowing the inert gas through said reagent, introducing directly into said chamber from a side of the chamber removed from said side from which the stream of inert gas is introduced a sample of the material to be analyzed, breaking down said sample in the chamber to release all gases from the sample substantially instantaneously, entraining the gases from the sample as a group in the stream of inert gas, withdrawing said stream of inert gas from said reaction chamber with the gases released from the sample entrained in said stream as a group, and passing said inert gas and group of released gases through at least one chromatographic column to separate at least one of the components of the released gases from the balance of said gases and determining the quantity of said separated component.

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