

[54] **APPARATUS FOR
FILTRATION-LEUKOPHERESIS FOR
SEPARATION AND CONCENTRATION OF
HUMAN GRANULOCYTES**

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[*] Notice: The portion of the term of this
patent subsequent to Apr. 9, 1991,
has been disclaimed.

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[58] Field of Search 128/213, 214 R, 214 F,
128/214 B, 214 C, 214.2, 276, 278;
23/258.5; 210/23

[56] **References Cited**

UNITED STATES PATENTS

2,876,769 3/1959 Cordova 23/258.5

3,014,481 12/1961 Rumble et al. 128/214 F
3,075,524 1/1963 Clark 23/258.5
3,448,041 6/1969 Swank 210/23
3,462,361 8/1969 Greenwalt et al. 210/23
3,648,694 3/1972 Mogos et al. 128/214 F

FOREIGN PATENTS OR APPLICATIONS

856,792 11/1952 Germany 128/DIG. 12

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[57]

ABSTRACT

Apparatus of simple character is provided for continuous withdrawal of blood from a human donor, forced extracorporeal circulation of blood of the donor with separation of granulocytes, and return by gravity of the leukocyte-poor whole blood to the donor.

8 Claims, 2 Drawing Figures

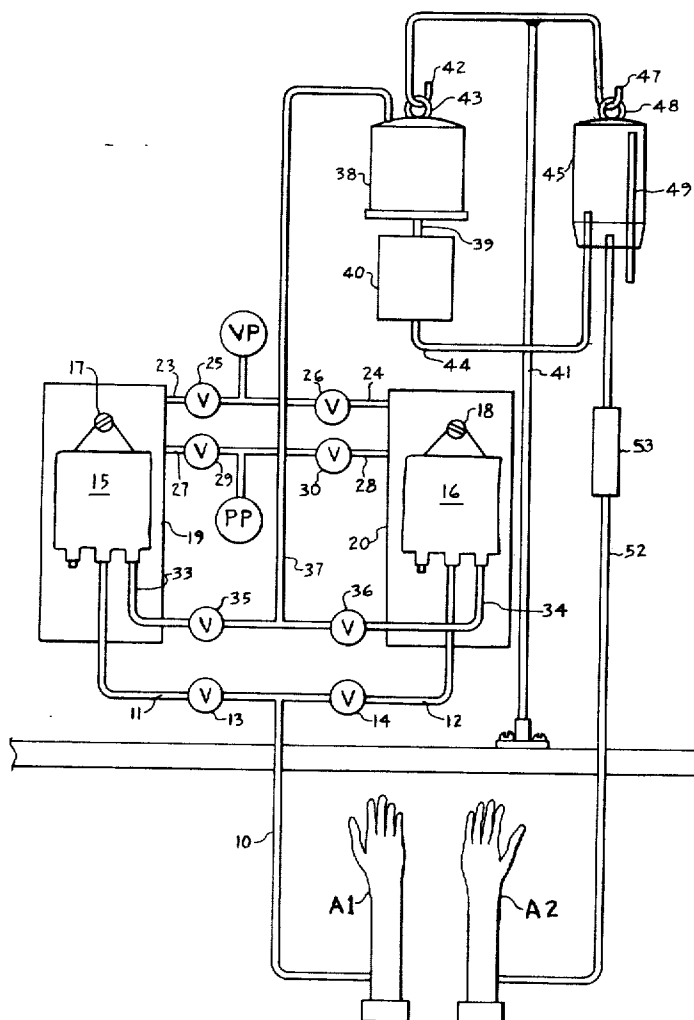


Fig. 1.

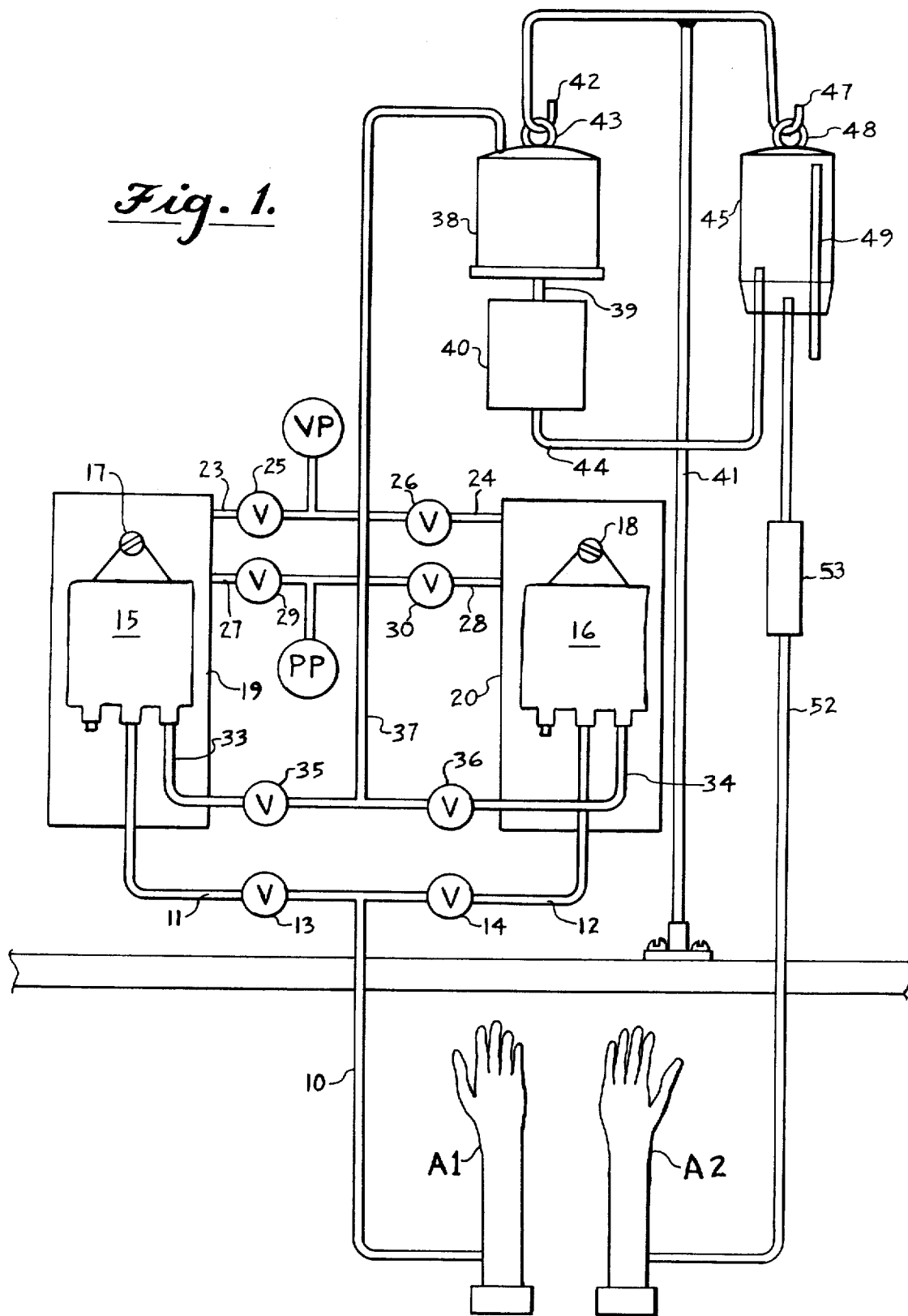
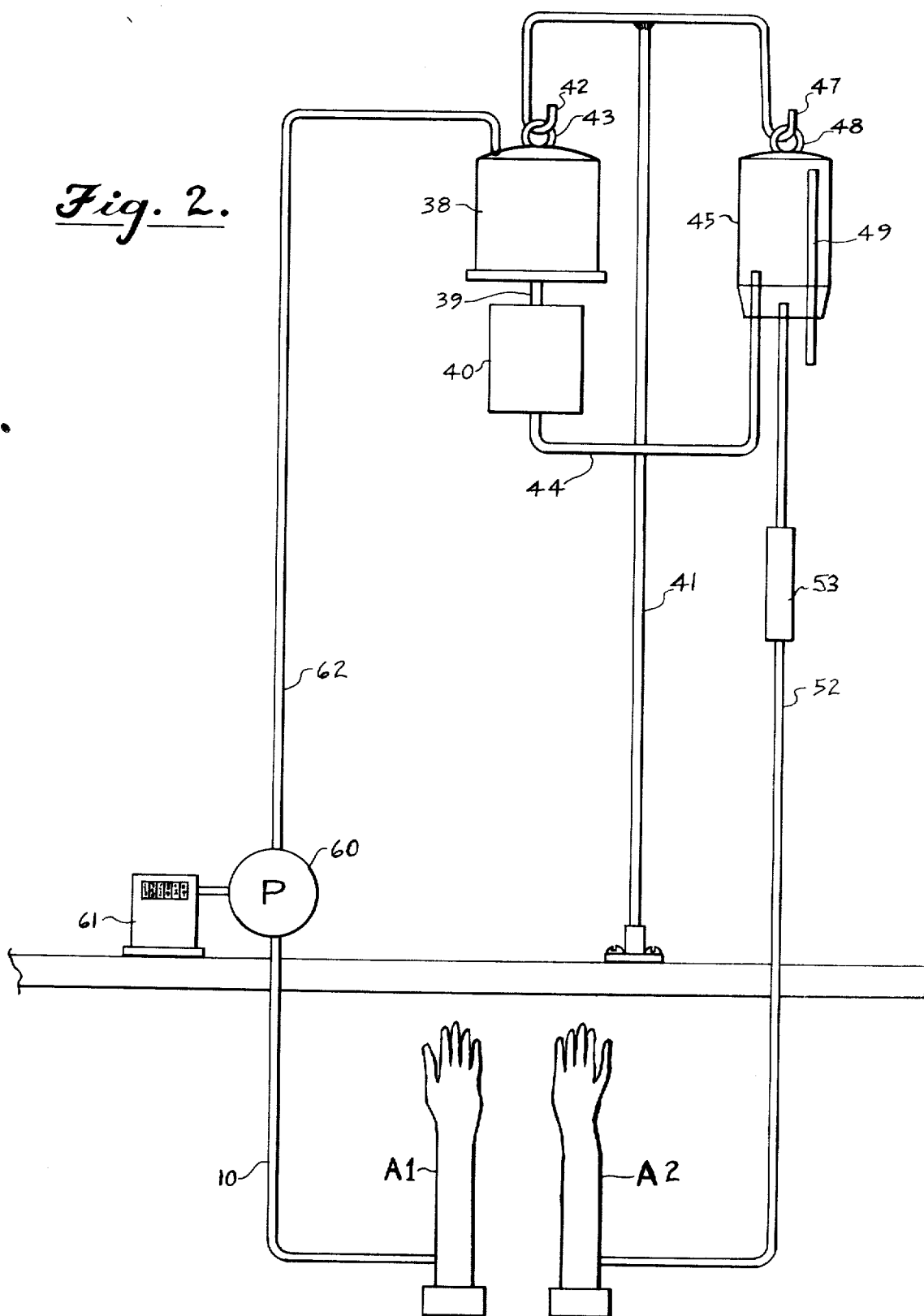


Fig. 2.



APPARATUS FOR FILTRATION-LEUKOPHERESIS FOR SEPARATION AND CONCENTRATION OF HUMAN GRANULOCYTES

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to apparatus for filtration-leukopheresis for separation and concentration of large amounts of normal human granulocytes.

2. Description of the Prior Art

It has heretofore been proposed to extract blood from a human donor for use as whole blood, for separation of plasma, for separation of granulocytes or other blood components primarily for the purpose of transfusion to individuals in need of such components.

Blood removal and collection apparatus has taken various forms and reference may be had to the U.S. Pat. Nos. to Strumia, 2,845,929, Gewecke et al., 2,757,669, Welch, Jr., 2,982,286, Rieutord et al., 2,757,375, Poitras, 2,784,932 Erikson, 2,597,715, and Judson et al., 3,489,145.

The delivery of blood plasma and the like to a patient for transfusion can be effected by gravity or by applied pressure as shown in the U.S. Pat. No. to Rundhaug, 2,842,123.

The harvesting of normal granulocytes with special continuous flow centrifugation (Freirach, E. J., et al., Separation and collection of leukocytes. Cancer Res. 25: 1516-1520 (1965)) is inefficient and impractical for widespread use.

The batch treating of whole blood to remove leukocytes with a filter is shown in the U.S. Pat. No. to Greenwalt, 3,462,361.

It has heretofore been undertaken to withdraw blood from a donor, in a plastic bag with saline solution and a mixture of heparin, saline and sodium citrate selectively delivered to the plastic bag and then transferring the fluid through two leukocyte filters and then advance the blood by manual manipulation to another plastic bag for return through a tube to the donor, a second source of saline solution being connected to the return tube. The respective tubes were controlled by hemostats for manual regulation and the entire procedure was manual.

Very close supervision and control by trained personnel has been required and the time for the filtration-leukopheresis has required about some 4 hours or more with each individual donor.

In my prior application for U.S. Letters Pat. filed May 18, 1972, Ser. No. 254,609, now U.S. Pat. No. 3,802,432 issued Apr. 9, 1974, there is described apparatus for separation and retention of human granulocytes with which the weight of the blood in intermediate receptacles in its circuit from and to the body of the donor is utilized to control the flow.

In my prior application for U.S. Letters Pat. filed Dec. 20, 1972, Ser. No. 317,057, improved apparatus is shown.

The present invention comprises simplified apparatus utilizing in one embodiment constant volume of blood from the donor and to and through the granulocyte separating filter and in another embodiment constant pressure of the blood from the donor to and through the filter in both instances for effecting the flow through the apparatus to a receptacle for gravity return of leukocyte-poor whole blood to the donor.

SUMMARY OF THE INVENTION

In accordance with the present invention apparatus is provided for harvesting granulocytes from a single donor and within a relatively short period of time and which includes a filter connected to a vented blood return receptacle, the blood being delivered to and through the filter to the return receptacle either by constant volume or by constant pressure delivery to the filter.

It is the principal object of the invention to provide apparatus for harvesting granulocytes from human blood of a donor with return of the leukocyte-poor blood to the donor which is of simplified construction, which requires a minimum of attention and which will permit of rapid cycling and attendant short period of retention of the donor.

It is a further object of the invention to provide apparatus of the character aforesaid in which the filter and the blood return receptacle and associated tubing may be supplied as a disposable unit for connection to a permanently installed withdrawal and delivery apparatus.

It is a further object of the invention to provide apparatus of the character aforesaid in which the withdrawal and delivery apparatus may selectively be such as to effect a constant volume or a constant pressure transfer of the blood from the donor.

Other objects and advantageous features of the invention will be apparent from the description and claims.

BRIEF DESCRIPTION OF THE DRAWINGS

The nature and characteristic features of the invention will be more readily understood from the following description taken in connection with the accompanying drawings forming part hereof, in which:

FIG. 1 is a diagrammatic view of a preferred form of apparatus in accordance with the invention utilizing constant pressure for blood delivery; and

FIG. 2 is a diagrammatic view of another preferred form of apparatus in accordance with the invention, utilizing constant volume for blood delivery.

It should, of course, be understood that the description and drawings herein are illustrative merely and that various modifications and changes can be made in the structure disclosed without departing from the spirit of the invention.

Like numerals refer to like parts throughout the several views.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring now more particularly to FIG. 1 of the drawings, a fluid connection 10 of flexible tubing, has a needle (not shown) of well known type, and preferably of 15 gauge, on its free end for insertion into a vein in one arm A1 of the donor for withdrawing blood.

The fluid connection 19 preferably extends to branch connections 11 and 12 of flexible tubing and past inlet control valves 13 and 14, which may be non-return valves or positively positioned valves. The valves 13 and 14 preferably act externally of and are adapted to pinch or release the tubes 11 and 12. The pipes 11 and 12 extend to flexible blood receiving receptacles 15 and 16, preferably of inert transparent or translucent synthetic plastic, suspended from fixed brackets 17 and 18 in rigid enclosing cylinders 19 and 20. The cylinders

19 and 20 are preferably transparent for observation of the receptacles 15 and 16 and each has its interior alternately placed under vacuum and under pressure and phased so that when cylinder 19 is under vacuum cylinder 20 is under pressure.

Vacuum pipes 23 and 24, connected to a suitable source of vacuum VP and connected to the cylinders 19 and 20 through control valves 25 and 26 and pressure supply pipes 27 and 28, connected to a suitable source of pressure PP through control valves 29 and 30, permit alternate pressure and vacuum application in cylinders 19 and 20.

The receptacles 15 and 16 are connected by fluid delivery connections 33 and 34, of flexible tubing, past control valves 35 and 36, which may be non-return valves or positively positioned valves. The valves 35 and 36 preferably act externally of and are adapted to pinch or release the tubes 33 and 34. The pipes 33 and 34 extend to a pipe 37 which is connected to a filter 38 which delivers blood either directly to pipe 44 or through pipe 39 to and through a transparent chamber 40 in which the flow of blood can be observed directly. The filter 38 can be of any suitable type which separates and retains granulocytes and permits the passage of leukocyte-poor whole blood for return to the donor. Filters identified as Leuko-Pak Leukocyte Filter available from Fenwal Laboratories, Division of Travenol Laboratories, Inc., Morton Grove, Illinois, and which utilize nylon fibers for adherence thereto of the granulocytes, have been found satisfactory.

The unit comprising the pendant filter 38 and chamber 40, if used, are preferably supported by a stand 41 having a hook 42 for detachable engagement by a ring 43 on the bag 37.

The filter assembly 38 and 40 is connected by a pipe 44 to the lower part of a vented blood return receptacle 45.

The receptacle 45 is preferably supported on the stand 41 by a hook 47 for detachable engagement by a ring 48 on the receptacle 45.

The receptacle 45 has an air vent tube 49 extending upwardly to close to the top of the receptacle 45 to prevent pressure build-up within the receptacle 45.

The receptacle 45 is connected through a transparent sight tube 53 by a flexible tube 52 which has a needle (not shown) of well known type and preferably of 15 gauge on its free end for insertion into a vein in the other arm A2 of the donor for return, by gravity of granulocyte-poor whole blood to the donor.

The structure, irreversibly connected, comprising the fluid connection 10, tubes 11 and 12, receptacles 15 and 16, pipes 33 and 34, pipe 37, filter 38 with or without chamber 40, pipe 44, vented receptacle 45 and pipe 52 with its sight tube 53 can be made as a single use unit one for each donor pre-sterilized and in a sealed protective package. The necessity for breaking sterile points of connection at the time of usage will thus be avoided. Quick removal and replacement can be effected.

Referring now to FIG. 2 of the drawings, a fluid connection 10 of flexible tubing is provided, as before, to a needle for withdrawing blood from a vein in one arm A1 of the donor.

The fluid connection 10 is connected to the inlet side of a variable speed positive displacement liquid pump 60. The pump 60, as a positive displacement pump, will have a constant volume delivery per revolution irre-

spective of the speed of rotation and can have a revolution counter 61 connected thereto and calibrated, if desired, in accordance with the liquid volume delivery of the pump 60.

The delivery side of the pump 60 is connected by a flexible pipe 62 to a filter 38, of the type previously described, for delivery to a vented blood return receptacle 45.

The receptacle 45 is connected by a flexible tube 52 for return by gravity, of granulocyte-poor whole blood to a needle in a vein in the arm A2 of the donor.

When suction of the blood through filter 38 by the pump is preferred, the pump is located to apply its action on pipe 44. In this case pipe 44 may be of special material with increased resiliency such as siliconized rubber or plastic.

The structure, irreversibly connected, comprising the pipe 62, filter 38, with or without chamber 40, pipe 44, vented receptacle 45, and pipe 52 with or without a transparent chamber, can be made as a single use unit similar to that previously described.

In the form of the invention shown in FIG. 1, the blood is withdrawn from a vein in the arm A1 of the donor by the suction alternately created in the cylinders 19 and 20 and therein on the flexible receptacles 15 and 16 and therefrom in the fluid connection 10. The blood in the receptacles 15 and 16 is then alternately delivered under pressure through the pipe 37, through the filter 38 under pressure and through the pipe 39 and chamber 40 under pressure which pressure by reason of the alternating delivery from the receptacles 15 and 16 is substantially constant.

In the filter 38 the granulocytes are separated from the whole blood, and collected in the filter 38 for subsequent recovery, the leukocyte-poor whole blood still under pressure being delivered to the vented receptacle 45.

The leukocyte-poor blood is then returned by gravity to a vein in the arm A2 of the donor through the return pipe 52, the height of the receptacle 45 being such as to insure adequate rate of return of the blood and the receptacle 45 providing the desired storage capacity for continuous return of blood.

In the form of the invention shown in FIG. 2, the blood is withdrawn from a vein in the arm A1 of the donor by the suction of the pump 60 and continuously delivered with constant volume through the pipe 62 to the filter 38.

The blood is delivered to and through the filter 38 under pressure or by suction through the filter 38 by the continuity of flow and to the vented receptacle 45, as before.

The granulocyte-poor whole blood in the receptacle 45 is returned by gravity to a vein of the donor as previously explained.

The quantity of blood delivered by the pump 60, can be measured by the counter 61 which functions as a volume meter.

I claim:

1. Apparatus for filtration-leukopheresis comprising a venous blood supply connection adapted to be connected to a donor,
- a venous blood return connection adapted to be connected to the donor,
- a leukocyte separating and retaining filter interposed in series with said connections and in fluid commu-

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- nication therewith for extracting leukocytes from blood passing therethrough.
a permanently vented receptacle in continuous communication with the atmosphere interposed in series between said filter and said return connection 5 and in fluid communication therewith.
fixedly mounted detachable supporting members for said filter and said vented receptacle, and
power driven pump means upstream of said receptacle for continuously delivering blood from said supply connection to and through said filter and to said vented receptacle. 10
2. The combination defined in claim 1 in which said last mentioned means includes members for impelling said blood under constant positive air pressure. 15
3. The combination defined in claim 1 in which said last mentioned means includes a plurality of flexible receptacles for alternate receipt and delivery 20

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- of blood from the donor, and
pressure and vacuum applying means for activating said flexible receptacles.
4. The combination defined in claim 1 in which said last mentioned means includes a constant volume continuous impelling member.
5. The combination defined in claim 4 in which said impelling member is a constant volume pump.
6. The combination defined in claim 5 in which said pump has a counter actuated thereby.
7. The combination defined in claim 1 in which said filter and said receptacle are interconnected and have supply and delivery connections to provide a replaceable unit for individual use by a donor.
8. A replaceable unit as defined in claim 7 in which said supply pipe has a plurality of flexible blood receiving receptacles interposed therein.

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