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


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References Cited

UNITED STATES PATENTS
2,876,769 3/1959 Cordova ...................... 128/DIG. 3

ABSTRACT

Apparatus is provided for continuous withdrawal of blood from a human donor, separation preferably of granulocytes therefrom by extracorporeal circulation and filtration of the blood and return of leucocyte-poor whole blood to the donor, controls being provided for the flow of the blood within the apparatus so that the volume of the blood processed can be known and controlled at any particular time.

9 Claims, 3 Drawing Figures
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, primarily for the purpose of transfusion to individuals in need of such treatments.

2. Background 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 and for separation of granulocytes or other blood components.

Blood removal and collection apparatus has taken various forms and reference may be had to the U.S. patents to Strumia, No. 2,845,929; Gewecke et al., No. 2,757,669; Welch, Jr., No. 2,982,286; Riectord et al., No. 2,757,375; Portras, No. 2,784,932; Erikson, No. 2,597,715; Judson et al., No. 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. patent to Rundhag, No. 2,842,123.

The methods in current use for separation and concentration of platelets and leukocytes for transfusion rely on differential centrifugation. Note Judson et al., U.S. Pat. No. 3,489,145.


It has heretofore been ascertained that granulocytes adhere to foreign substances such as siliconized glass wool and many of the newer synthetic plastics. A filter of the latter type and employing nylon fibers is available under the name Leuko Pak — Leukocyte Filter from Fenwal Laboratories, Division of Travenol Laboratories, Inc., Morton Grove, Illinois. These filters have heretofore been used for administration of leukocyte-poor whole blood to multitransfused patients with antileuko-cyte antibodies.

The adhering takes place when the medium carrying the granulocytes is heparinized blood and when the filter is perfused with more acid medium (example ACD or Citrate-Dextrose Plasma) the granulocytes are eluted and can be recovered in the outflowing carrier fluid and then separated therefrom.

It has heretofore been undertaken to withdraw blood from a donor, in a plastic bag with a mixture of heparin saline and sodium citrate selectively delivered to the plastic bag and then transferring the fluid through leukocyte filters and then advance the blood by manual manipulation to another plastic bag for return through a tube to the donor, a source of saline solution being connected to the return tube to keep it open when not in use. 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.

Leukocyte transfusions using granulocytes obtained from patients with chronic myelogenous leukemia have been used to support patients with infections who lack adequate numbers of granulocytes (Schwarzenberg, L. et al.: Study of factors determining the usefulness and complications of leukocyte transfusions. Amer. J. Med. 43:206, 1967; and Morse, E.E. et al.: Effectiveness of granulocyte transfusion from donors with chronic myelocytic leukemia to patients with leukopenia. Cl. Res. 9:32, 1961). The use of such transfusions is limited by the availability of donors with chronic myelogenous leukemia and the frequency of preexisting or developing antileukocyte antibodies in the recipient leading to severe and often life-threatening transfusion reactions.

Normal leukocyte "buffy coats" have also been used for support of infected leukopenic patients with inconclusive results. The transfusion of "buffy coats" from normal donors is handicapped by the need for each transfusion of large numbers of leukocyte concentrates (all ABO type specific) and especially by their low content of granulocytes. The latter sediment on centrifugation of the whole blood with the top layer of the red cells and are not included in the buffy coat which consists mainly of lymphocytes and platelets.

Even if adequate yields of granulocytes are harvested from each unit of whole blood, large numbers of donors are needed for each single transfusion thus greatly increasing the risk of sensitizing the patient to subsequent transfusions of granulocytes thus increasing the risk of severe reactions as well as of hepatitis and other infections.

Large amounts of granulocytes, all obtained from one donor as much as possible compatible with the recipient, could however be given repeatedly to leukopenic patients in order to prevent or overcome already existing infections. Obtaining normal granulocytes for transfusion using continuous flow centrifuges is limited by the low efficiency of separation by centrifugation (Freireich, E.J., et al.: Separation and collection of leukocytes. Cancer Res. 25:1516, 1965). Simple methods and suitable apparatus for repeated harvesting of large amounts of granulocytes from single donors, applicable to standard blood banks and donor centers, are needed to use transfusions of granulocytes routinely.

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 time period and which includes structure for withdrawal of blood from the donor and transferred under pressure, the pressure application being effective to transfer the blood to filters for retention of the granulocytes by selective absorption-elution. The filters are connected to leukocyte-poor whole blood collecting receptacles from which a connection is provided to pumping apparatus for return through an air vented bottle to the donor.

Provision is made for weighing the leukocyte-poor blood in the collecting receptacles and for limiting the amount by weight in the system so as to limit the total amount of blood out of the donor at any time and to provide knowledge of the volume of blood already processed.

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 will be effective in its action, will protect the donor against excessive withdrawal of blood at any time, will insure effective filtration of the blood and its safe return to the donor, which will reduce the burden upon the attendant and which will permit of relatively rapid cycling, thus allowing the processing of larger volumes of blood within the time available to the donor.

It is a further object of the invention to provide apparatus of the character aforesaid which will be reliable in its action, fool proof in regard to potential harm to the blood donor and which can be readily made available for use.

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 drawing forming part hereof, in which:

FIG. 1 is a diagrammatic view of a preferred form of apparatus in accordance with the invention;

FIG. 2 is a schematic diagram of the electrical circuitry employed; and

FIG. 3 is a view of a modified form of circuitry.

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.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring now more particularly to FIG. 1 of the drawings, a fluid connection 10 in the form of plastic tubing is shown 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 one arm A1 of the donor for withdrawing blood.

The fluid connection 10 preferably extends to the fluid inlet of an electric motor driven pump 12. The outlet or delivery connection of the pump 12 is connected by a fluid connection 14 to an elevated vessel 15 suspended above the location at which the donor is situated. The pump 12 can be of any desired type, rotary or tandem diaphragm or piston, but is preferably of a variable speed type to provide the desired rate of withdrawal from the donor and delivery to the vessel 15.

The vessel 15 is connected by a fluid connection 20 and branch pipes 21 to a plurality of leukocyte filters 22, four being preferred. The filters 22 are connected by fluid connections 23 through infusion chambers 24 which allow observation of the blood dripping or flowing out of the leukocyte filters after retention of the granulocytes. The filters 22 can be of any suitable type which separate and retain granulocytes and permit the passage of leukocyte-poor whole blood for return to the donor, Leuko-pak Leukocyte Filters available from Fenwal Laboratories, Division of Travonel Laboratories, Inc., Morton Grove, Ill. having been found satisfactory.

The infusion chambers 24 are connected by interconnected branch tubes 25 which is connected by a flexible tube 26 and flexible tubes 27 and 28 to collection bags 29 and 30 which are resting on scales of the spring or lever type. The tubes 27 and 28 have solenoid controlled valves 32 and 33 therein.

The collection bags 29 and 30 are carried on weighing scales 34 and 35 having normally open switches 55 and 56 closed when a predetermined weight is effective in either bag 29 or 30.

The collection bags 29 and 30 are connected by flexible pipes 35 and 36 which have solenoid controlled valves 38 and 39 therein to a fluid connection 40 which extends to the fluid inlet of an electric motor driven pump 42.

The pump 42 is preferably similar to the pump 12.

The delivery side of the pump 42 is connected by a fluid connection 43 to a vented receptacle 44 with a vent pipe 45 communicating with the atmosphere. The receptacle 44 has a fluid connection 46 extending therefrom 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 the return of granulocyte-poor whole blood to the donor.

Referring now to FIG. 2, one form of electrical circuitry is shown suitable for control of the system shown in FIG. 1.

A suitable source of electric energy such as 115 volt 60 Hz alternating current is connected by a conductor 50 through a main power control switch SW1 and conductor 51 and blood pump control switch SW2 conductor 53, and contact arms 54 and 55 of a manually positioned blood pump selector switch SW3 engaged with contacts 56 and 57 connected to conductors 58 and 59 to one terminal of each of the motor driven pumps 12 and 42. The other terminals of the pumps 12 and 42 are connected to return conductor 60.

The contact arms 54 and 55 of SW3 can also be selectively connected to contact 62 connected to conductor 58 and to contact 63 when operation of pump 12 only is desired.

The contact arms 54 and 55 of the switch SW3 can also be selectively connected to contact 64 and to contact 65 which is connected to conductor 59 when operation of pump 42 only is desired.

A spare blood pump 70 can also be provided if desired and which can be substituted by shifting of fluid inlet and delivery connections thereto. The pump 70 can be energized by normally open switch 71 connecting the conductor 53 through the pump 70 to the return line 60.

The conductors 51 and 60 are also preferably connected to the primary of a step-down transformer T.

The secondary of the transformer T has one terminal thereof connected to a conductor 73 the other terminal being connected by a conductor 74 through a normally open contact 75 of switch SW5 to one terminal of solenoid winding K1 thereof which has the other terminal connected to conductor 73. The secondary of the transformer T is also connected by a conductor 76 connected to the conductor 74 and through a normally open contact 77 of switch SW6 to one terminal of winding of solenoid K2, the other terminal of which is connected to conductor 73.

The winding of solenoid K1 controls a contact arm 78 which in its down position engages a contact 79 which is connected by a conductor 80 to one terminal of each of the solenoid valves 32 and 39.
The contact arm 78 in its up position engages a contact 82 which is connected by a conductor 84 to one terminal of the winding of solenoid K2, the other terminal of which is connected to conductor 73.

The winding of solenoid K2 controls a contact arm 85 which is connected to conductor 74 and which in its up position engages a contact 86 which is connected by a conductor 87 to conductor 74 and thence to one terminal of the winding of the solenoid K1, the other terminal of which is connected to conductor 73.

The winding of solenoid K2 controls the contact arm 85 to a down position in engagement with a contact 88 which is connected by conductor 89 to energize the windings of the solenoid valves 33 and 38.

The transformer T also has a conductor 90 which is connected by conductors 91, 92, 93, and 94 to the solenoid valves 32, 33, 38, and 39.

A manually operable override switch SW7 with simultaneously operable contact arms 95 and 96 controls the independent energization of the solenoid valves 32 and 33 for closing these valves.

A manually operable override switch SW8 with simultaneously operable contact arms 97 and 98 controls the independent energization of the solenoid valves 38 and 39 for closing these valves.

In normal operation with switches SW1 and SW2 closed, and with the switch SW3 in normal operating position as shown in FIG. 2 the pumps 12 and 42 will be operated. With the switch SW5 in closed position and the switch SW6 in open position the solenoid K1 will be energized so that solenoid valves 32 and 39 will be closed for delivery of blood to the receptacle 30, the valves 33 and 38 being open. As blood is delivered to the receptacle 30 the switch SW6 will be closed to energize the solenoid K2. The flow of blood from the receptacle 29 and the closing of the contact 77 by the weight of the blood in the receptacle 30 will effect a reversal of the control of the valves 33 and 38 so that delivery to the receptacle 44 through valve 39 will be effected with the valves 33 and 38 closed. The alternating operation will be repeated as desired.

The blood from the receptacle 15 will pass by gravity through the filters 24 and will have the granulocytes extracted therefrom for subsequent separation and utilization.

The blood delivered by the pump 42 to the receptacle 44 is then preferably returned by gravity to the donor, any air in the blood being separated out in the receptacle 44.

A modified form of circuitry is shown in FIG. 3 in which the scale switches includes a switch SW5a with normally open contact arm 75a and switch SW6a with normally closed contact arm 77a to both of which conductor 74 is connected. A single solenoid K is employed with conductor 90 from switch SW5a connected to one terminal thereof, the other terminal being connected to conductor 73. A conductor 91 extends from switch SW6a to the normally closed contact arm 92 which when engaged with contact 93 connected to conductor 90 for energizing the winding of the solenoid K.

A normally down contact arm 94 when in engagement with a contact 95 is connected by a conductor 96 to both the solenoid valve 32 and the solenoid valve 39 for energizing the same, and when in an up position in engagement with a contact 97 is connected by a conductor 98 to both the solenoid valve 33 and the solenoid valve 38.

The alternating opening and closing of the valves controlling the delivery to and discharge from the receptacles 29 and 30 is similar to that previously described, initiated and continued by alternate closing of the scale switches SW5a and SW6a, these switches opening when the weight thereon is removed.

The processing of blood for separation and collection of granulocytes is greatly facilitated.

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 communication therewith for extracting leucocytes from blood passing therethrough,
a permanently vented receptacle in continuous communication with the atmosphere interposed in series between said filter and said return connection and in fluid communication therewith, and
power driven pump means upstream of the vented receptacle continuously delivering blood from said supply connection to and through said filter and to said vented receptacle.

2. Apparatus for filtration-leukopheresis comprising
a blood supply connection adapted to be connected to a donor,
motor driven pump means for delivering blood from the supply connection to a receptacle;
leukocyte separation filters to which blood from said receptacle is delivered for circulation through said filters,
means for receiving blood from said filters including receptacles with valves inlet and delivery connections,
weight responsive members associated with each of said second mentioned receptacles,
members controlled by said weight responsive members for controlling the flow to and from said second mentioned receptacles, and
means for returning the blood from said delivery connections to the donor by increased gravity flow and venting of admixed air including a blood return connection adapted to be connected to the donor.

3. Apparatus for filtration-leukopheresis as defined in claim 2 in which
said last mentioned means includes a motor driven pump interposed between said blood return connection and said delivery connection for the purpose to raise the blood to the level of the blood return connection and increase the flow by gravity back into the donor.

4. Apparatus for filtration-leukopheresis as defined in claim 2 in which
said blood return connection has air collecting and venting means interposed therein.

5. Apparatus for filtration-leukopheresis as defined in claim 2 in which
said flow controlling members include solenoid controlled valves.
6. Apparatus for filtration-leukopheresis as defined in claim 2 in which independent control means is provided for said first mentioned motor driven pump means.

7. Apparatus for filtration-leukopheresis as defined in claim 3 in which independent control means is provided for said second mentioned motor driven pump.

8. Apparatus or filtration-leukopheresis as defined in claim 5 in which independent control means is provided for the sole-noid controlled valves for at least one of said filter connected receptacles.

9. Apparatus for filtration-leukopheresis as defined in claim 2 in which said leukocyte separation filters are positioned for flow of blood also by gravity through said filters.