

"METHOD FOR SELECTIVELY REMOVING A SPECIFIC CELL
FROM BLOOD AND APPARATUS THEREFOR"

Background of the Invention

5 This invention relates to a method for selectively removing a specific cell such as leucocyte from blood or blood components, and also to an apparatus for carrying out the method.

10 In most of the transfusion of blood, with a view to effectively utilize the blood and to alleviate the burden on the blood donor, currently adopted is a component transfusion, i.e., a method of blood transfusion wherein blood from a blood donor is first separated through a centrifugation into plural parts according to blood components, and only a blood
15 component required for a patient is transfused into the patient.

Examples of blood preparation to be employed in this component transfusion include a plasma preparation, an erythrocyte preparation, a platelet
20 preparation, and a mixed solution comprising any one of these preparations and a cell preservation liquid.

One of the most important subject matters in preparing these blood preparations is to minimize as far as possible the inclusion of leucocyte in these
25 blood preparations. Because, if the inclusion ratio of leucocyte (in particular, lymphocyte) in these blood preparations is high, the probability of a patient

being infected with hepatitis, AIDS, GVHD etc. will be increased.

However, since a difference in specific gravity between leucocyte and platelet is very small, it is very difficult to distinctly separate leucocyte from platelet by means of centrifugation. In other words, there has been a limitation in enhancing the elimination ratio of leucocyte in a blood preparation by using the centrifugation.

Under the circumstances, a method has been so innovated that a leucocyte-eliminating filter is employed in the manufacture of a blood preparation for selectively adsorbing and removing leucocyte in blood or in a blood component. According to this method, the following procedures are performed.

First of all, the outlet port of a bag which is filled with a blood preparation containing a substantial amount of leucocyte to be removed is pieced with a needle which is attached to the distal end portion of a tube connected to the inflow side of a leucocyte-eliminating filter. Then, the blood preparation is allowed to be discharged from the bag so as to pass through the leucocyte-eliminating filter, thereby eliminating leucocyte in the blood preparation to obtain a blood preparation free from leucocyte.

However, these procedures including the operation of piercing of needle are not performed in an aseptical

way, so that the blood preparation to be obtained may possibly be contaminated with bacteria. In order to avoid the contamination of a blood preparation with bacteria, the sequence of these procedures is required to be carried out in a sterilized chamber. However, the procedures in a sterilized chamber are accompanied not only with various troublesome administrations, for example, in regard of a person entering into or leaving the sterilized chamber, or in regard of keeping the cleanness of the sterilized chamber, but also with troubles in carefully manipulating the procedures. In addition, there is certain imitation for this conventional method to assure the complete sterilization of blood preparation. As a result, it is almost impossible to completely prevent the blood preparation from being contaminated with bacteria.

Summary of the Invention

Accordingly, an object of the present invention is to provide a method for selectively removing a specific cell from blood or blood components in a simple manner while maintaining asepsis of a product, and also to provide an apparatus for carrying out the method.

Another object of the present invention is to provide a method for selectively removing a specific cell from blood or blood components, which is capable of realizing the automation and rationalization in the manufacture of blood preparations, thereby improving



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the manufacturing efficiency, as well as the uniformity and safety of blood preparations. Another object of the present invention is to provide an apparatus for carrying out the aforementioned method.

5 These objects have been accomplished by this invention as illustrated by the following items.

(1). A method for selectively removing a specific cell from blood or blood components, which comprises the steps of;

10 aseptically connecting a first tube attached to a first container filled with blood or blood components with a second tube attached to an inlet port of a cell-eliminating filter, by using a tube-connecting device;

 discharging the blood or blood components from
15 the first container thereby allowing the blood or blood components to pass through the cell-eliminating filter, whereby eliminating the specific cell from the blood or blood components; and

 recovering the blood or blood components
20 eliminated of the specific cell into a second container communicating with an outlet port of the cell-eliminating filter.

(2). A method for selectively removing a specific cell from blood or blood components, which comprises
25 the steps of;

 aseptically connecting a first tube attached to a first container filled with blood or blood components



with a second tube attached to an inlet port of a cell-eliminating filter by using a tube-connecting device;

5 aseptically connecting a third tube attached to an outlet port of the cell-eliminating filter with a fourth tube attached to a second container by using a tube-connecting device;

10 discharging the blood or blood components from the first container thereby allowing the blood or blood components to pass through the cell-eliminating filter to eliminate the specific cell from the blood or blood components; and

recovering the blood or blood components eliminated of the specific cell into the second container.

15 (3). The method according to the item (1) or (2), wherein the cell-eliminating filter is a leucocyte-eliminating filter for adsorbing and eliminating leucocyte.

20 (4). An apparatus for selectively removing a specific cell from blood or blood components, which comprises;

a first container-supplying means for supplying a first container filled with blood or blood components;

25 a filter-supplying means for supplying a cell-eliminating filter for selectively removing a specific cell from the blood or blood components;



a second container-supplying means for supplying a second container which is capable of being filled with a blood component passed through the cell-eliminating filter; and

5 a tube-connecting device for enabling a pair of tubes to be aseptically connected with each other;

wherein a first tube which is attached to the first container supplied from the first container-supplying means is aseptically connected, by using the tube-connecting device, with a second tube attached to
10 an inlet port of the cell-eliminating filter supplied from the filter-supplying means; the blood or blood components are discharged from the first container, thereby allowing the blood or blood components to pass
15 through the cell-eliminating filter; and then, the blood or blood components eliminated of the specific cell are recovered in the second container.

(5). An apparatus for selectively removing a specific cell from blood or blood components, which
20 comprises;

a first container-supplying means for supplying a first container filled with blood or blood components;

a filter-supplying means for supplying a cell-eliminating filter for selectively removing a specific
25 cell from the blood or blood components;

a second container-supplying means for supplying



a second container which is capable of being filled with a blood component which has passed through the cell-eliminating filter; and

5 at least one tube-connecting device for enabling a pair of tubes to be aseptically connected with each other;

10 wherein a first tube which is attached to the first container supplied from the first container-supplying means is aseptically connected, by using the tube-connecting device, with a second tube attached to an inlet port of the cell-eliminating filter supplied from the filter-supplying means; a third tube which is attached to an outlet port of the cell-eliminating filter is aseptically connected with a fourth tube
15 attached to the second container; the blood or blood components are discharged from the first container, thereby allowing the blood or blood components to pass through the cell-eliminating filter; and then, the blood or blood components eliminated of the specific
20 cell are recovered in the second container.

(6). The apparatus for selectively removing a specific cell from blood or blood components according to the item (5), which further comprises a tube-sealing means for sealing the third tube or
25 the fourth tube.

(7). The apparatus for selectively removing a specific cell from blood or blood components



according to any one of the items (4) to (6), which further comprises a tube-transferring means capable of transferring a tube to the tube-connecting device.

5 (8). The apparatus for selectively removing a specific cell from blood or blood components according to any one of the items (4) to (7), which further comprises a liquid-transferring means which is capable of transferring blood or blood components.

10 (9). The apparatus for selectively removing a specific cell from blood or blood components according to any one of the items (4) to (8), wherein the tube-connecting device is adapted for connecting a pair of tubes with each other by thermally fusing the tubes.

15 (10). The apparatus for selectively removing a specific cell from blood or blood components according to any one of the items (4) to (8), wherein the tube-connecting device comprises a pair of holding members which are adapted to hold a pair of tubes side
20 by side for connecting these tubes; and a heating plate which is exchangeably disposed between the pair of holding members for thermally cut off the pair of tubes held by the holding members; the holding
25 members are adapted to be moved in relative to each other so as to contact and connect the cut portions of the pair of tubes with each other.

(11). The apparatus for selectively removing



a specific cell from blood or blood components according to any one of the items (9) or (10), which further comprises a tube-reshaping means for restoring any deformation produced at an interconnected portion of the pair of tubes.

(12). The apparatus for selectively removing a specific cell from blood or blood components according to any one of the items (4) to (11), wherein the cell-eliminating filter is flat in shape, and the filter-supplying means comprises a magazine for holding a plurality of cell-eliminating filters superimposed one upon another, and a supplying mechanism for supplying the cell-eliminating filters one by one from the magazine.

(13). The apparatus for selectively removing a specific cell from blood or blood components according to any one of the items (4) to (12), wherein the second container is formed of a pliable bag, and the second container-supplying means comprises a magazine for holding a plurality of second containers superimposed one upon another, and a supplying mechanism for supplying the second containers one by one from the magazine.

(14). The apparatus for selectively removing a specific cell from blood or blood components according to the item (13), wherein the second container-supplying means is constructed such that



a second container disposed at the top of layers of the second containers housed in the magazine is kept in a predetermined posture.

5 (15). The apparatus for selectively removing a specific cell from blood or blood components according to any one of the items (4) to (14), wherein the cell-eliminating filter is a leucocyte-eliminating filter for adsorbing and eliminating leucocyte.

Brief Description of the Drawings

10 FIG. 1 is a perspective view showing one embodiment of a cell-eliminating apparatus according to this invention;

FIG. 2 is a front view showing one embodiment of a tube-transferring means;

15 FIG. 3 is a perspective view showing one embodiment of a head in the tube-transferring means;

FIG. 4 is a partially sectioned side view showing one embodiment of a head in the tube-transferring means;

20 FIG. 5 is a partially sectioned side view showing another embodiment of a head in the tube-transferring means;

25 FIG. 6 is a perspective view showing a main portion of a tube-connecting device according to one embodiment of this invention;

FIG. 7 is a side view showing one embodiment of a tube-reshaping means;

FIG. 8 is a side view showing another embodiment of a tube-reshaping means;

FIG. 9 is a side view showing one embodiment of a second container-supplying means;

5 FIG. 10 is a front view showing one embodiment of a filter-supplying means;

FIG. 11 is a sectioned side view showing one embodiment of a leucocyte-eliminating filter; and

10 FIG. 12 is a plan view showing one embodiment of a clamp.

Detailed Description of the Preferred Embodiment

The cell-eliminating apparatus and a method of eliminating a specific cell according to this invention will be explained in detail with reference to a preferred
15 embodiment shown in the drawings.

FIG. 1 shows a perspective view of an embodiment where the cell-eliminating apparatus according to this invention is applied to a leucocyte-eliminating apparatus. The structural constituents not shown in
20 FIG. 1 are supplementally shown in FIGS. 2 to 12.

Referring to FIG. 1, a leucocyte-eliminating apparatus (cell-eliminating apparatus) 1 according to this invention comprises a base table 2, a first
25 container-supplying means 100, a roller pump 200, a tube-transferring means 300, a pair of tube-connecting devices 400, a pair of tube-reshaping means 450, a second container-supplying means 600,

a filter-supplying means 700, a tube-sealing means 800, a control means 50 and an operation portion 60.

Specific constructions of these components will be explained as follows.

5 The first container-supplying means 100

 The first container-supplying means 100 is disposed at one end portion of the leucocyte-eliminating apparatus 1. The first container-supplying means 100 comprises a transferring belt 110 for transferring
10 a first container 10 to a blood component-transferring section 140, and a driving means (not shown) for driving the transferring belt 110.

 The transferring belt 110 is provided on its one side with a plurality of supporting members 120 each
15 being spaced apart from one another by a predetermined distance for supporting the first container 10. A tube-holding member 130 for holding a pliable first tube 15 is disposed in the vicinity of each supporting member 120 of the transferring 110, the first tube 15
20 being connected to the first container 10.

 The first container 10 is constituted by a bag which can be manufactured by superimposing a pair of soft resin sheets made for instance of flexible polyvinyl chloride and then the peripheries of the soft
25 resin sheets are fusion-bonded whereby forming the bag. The first container 10 may be filled with any one of various blood components (hereinafter generally

referred to simply as a liquid to be treated) such as blood (whole blood), blood added with an anti-coagulant, a concentrated erythrocyte, a concentrated erythrocyte added with an erythrocyte preservation liquid, a concentrated platelet, a concentrated platelet added with a platelet preservation liquid, a mixed solution comprising a concentrated erythrocyte and a concentrated platelet, a buffy coat, a mixed solution comprising a buffy coat and erythrocyte, a plasma contaminated with leucocyte, and a solution of any of these blood components diluted with physiological salt solution.

Roller pump 200

The roller pump 200 is mounted near the blood component-transferring section 140 as a transferring means for transferring the treating liquid. The roller pump 200 is provided with a head 210 which can be opened and closed, so that the first tube 15 attached to the first container can be loaded therein by opening the head 210. When the roller pump 200 is actuated after the first tube 15 is loaded as mentioned above and the head 210 is closed, the first tube 15 is caused to be squeezed by the rollers of the roller pump 200, thereby allowing the treating liquid to be discharged from the first container 10 at a flow rate of 10 to 50 ml/min. for instance.

The loading of the first tube 15 in the roller

pump 200 can be effected manually or by making use of a tube-transferring means 300 to be explained hereinafter. The controls for actuating the roller pump 200 and for opening or closing of the head 210 can be effected by way of a control means 50.

Tube-transferring means 300

The tube-transferring means 300 functions to transfer the first tube 15, a second tube 25, a third tube 35 and a fourth tube 45 (these tubes are generally referred hereinafter to simply as a tube) to a tube-connecting device 400 and load these tubes in the tube-connecting device 400. As shown in FIGS. 2 to 5, the tube-transferring means 300 is provided with a head 351 comprising a block-like base table 352, a couple of chucks 353 and 354 for holding the tube, and a driving means 370 for moving one of the chucks, i.e. the chuck 354.

The chucks 353 and 354 are mounted on the front side of the base table 352 with a predetermined space being kept therebetween. Specifically, the chuck 353 is fixed to the base table 352, whereas the chuck 354 is movably (in the direction of X) mounted on the base table 352. With this movement of the chuck 354, the distance between the chucks 353 and 354 can be changed.

As shown in FIGS. 4 and 5, the chuck 354 is composed of a casing 360 having an opening 360, a pair of plate-like nipping members 362 and 363, and

a driving mechanism for moving the nipping member 363. The nipping members 362 and 363 are partially protruded out of the casing 360 through the opening 361.

5 The nipping member 362 is fixed to the casing 360, whereas the nipping member 363 is movably (in the direction of Z) mounted on the casing 360. The upper portion of the nipping member 363 is L-shaped and connected to the distal end of the plunger 365 of a solenoid 364 housed fixedly in the casing 360.

10 As shown in FIG. 4, when the solenoid 364 is not actuated, the plunger 365 takes an extended state, so that the nipping members 362 and 363 are sufficiently spaced apart to allow a tube to be inserted therebetween.

15 As shown in FIG. 5, when the solenoid 364 is actuated, the plunger 365 is contracted, whereby causing the nipping member 363 to move toward the nipping member 362 to hold a tube therebetween.

20 The driving means 370 for moving the chuck 354 is composed of a rack gear 371 mounted fixedly on the underside of the casing 360, a motor 373, and a pinion gear 372 fixed to the distal end of the rotation axis 374 of the motor 373 and engaging with the rack gear 371. When the motor 373 is actuated, the pinion gear 372 is caused to rotate in a predetermined
25 direction, concurrently causing the rack gear 371 to move in the longitudinal direction thereof, or in the

direction of X. As a result, the chuck 354 is moved in the same direction as that of rack gear 371.

Since the motor 373 is capable of being rotated both normally and reversely, the chuck 354 can be reciprocatingly moved in the direction of X.

The construction of chuck 353 is the same as that of the chuck 354 except that the chuck 353 is not provided with a driving means 370. The constructions of both chucks 353 and 354 are not restricted to those explained above, but may be optionally modified. For example, the actuation of the nipping member 363 may also be effected by making use of any driving source other than the aforementioned solenoid, such as an air cylinder or oil hydraulic cylinder. The driving source and mechanism for the driving means 370 for moving the chuck 354 may also be suitably modified likewise.

In the aforementioned embodiment, only the chuck 354 is made movable. However, both of the chucks 353 and 354 may be made movable so as to change the distance between these chucks 353 and 354.

The head 351 composed of the aforementioned base table 352, a pair of chucks 353, 354, and driving means 370 is mounted so as to be moved two-dimensionally, i.e. in the X-direction and the Y-direction which is in perpendicular to the X-direction as shown in FIG. 1 by means of a moving mechanism 380 as shown in FIG. 2.

This moving mechanism is composed of a transferring rail 381, a moving body 390 and an elevator 395.

5 The transferring rail 381 is arranged in parallel with the longitudinal direction of the tube in the blood component transferring line, i.e. in the direction of X.

10 The moving body 390 is placed on the transferring rail 381 so as to be reciprocatingly moved along the transferring rail 381. The moving body 390 is provided with two pairs of rollers 391 and 392 for holding the transferring rail 381, and with a motor (not shown) for rotating these rollers 391 and 392. This motor is capable of being rotated both normally and reversely, so that the moving body 390 can be moved within
15 a predetermined range along the transferring rail 381 as the rollers 391 and 392 are rotated by the operation of the motor.

20 The moving body 390 is provided with an elevator 395 comprising a cylinder 396 (such as an air cylinder or an oil hydraulic cylinder) which is adapted to move up and down, and a piston rod 397 which is adapted to telescopically expand or shrink according to the operation of the cylinder 396. The head 351 is fixed to the lower end of the piston rod 397.

25 With this moving mechanism 380, the head 351 can be moved in the direction of X as shown in FIG. 1 following the movement of the moving body 390, as well

as in the direction of Y (upward or downward) as shown in FIG. 1 following the expansion or contraction of the piston rod 397.

5 The driving sources for the solenoid 364, driving means 370 and cylinder 396 are respectively electrically connected to the control means 50 so as to be controlled by the control means 50.

10 According to the aforementioned embodiment, a couple of tubes to be connected with each other are adapted be loaded in the grooves of the holders 410 and 420, respectively by moving the tube-connecting device 400 in the direction of Z, so that the moving mechanism 380 is made movable only in two-dimensional direction, i.e. in the directions of X and Y. However, this
15 invention is not restricted to as such, but the moving mechanism 380 may be made movable in three-dimensional direction, i.e. in the directions of X, Y and Z.

20 In this case, another moving means for enabling the moving mechanism 380 in the direction of Z should be mounted on the distal end portion of the piston rod 397 and the head 351 may be mounted on the underside of such a moving means.

25 According to the tube-transferring means 300 constructed in this manner, it is possible to transfer the tube to a desired location by holding the tube with the chucks 353 and 354 of the head 351 and then moving the head 351 by the movement of the moving mechanism 380.

When tubes are to be loaded in the grooves 411, 412, 421 and 422 of the tube-connecting device 400, the distance between the chucks 353 and 354 holding a tube therebetween is expanded so as to reduce the outer diameter of the tube, and then the tube is introduced into the grooves 411, 412, 421 and 422. Thereafter, the tube is set free from the chucks 353 and 354.

Only single tube-transferring means 300 may be used for a couple of tube-connecting devices 400, or a couple of such a tube-transferring means 300 may be mounted so as to be exclusively used for each of the tube-connecting devices 400.

Tube-connecting device 400

A mobile table 500 is disposed in the vicinity of the roller pump 200 in such a manner that it can be moved manually or through a driving mechanism (not shown) in the direction of Z. On this mobile table 500 are mounted the tube-connecting device 400 and a tube-reshaping means 450.

FIG. 6 is a perspective view illustrating one embodiment of the main part of the tube-connecting device 400. As shown in FIG. 6, the tube-connecting device 400 is a device for aseptically connecting a first tube 15 and a second tube 25, and comprises a pair of holders 410 and 420 arranged side by side along the longitudinal direction of the tube, a wafer (a plate-like heating element) 430 interposed between

the pair of holders 410 and 420, a transferring means (not shown) for the holder 410, a transferring means (not shown) for the wafer 430, and a power supply means (not shown) for the wafer 430.

5 The holder 420 is fixedly mounted on the tube-connecting device 400, whereas the holder 410 is mounted in such a manner that it can be moved by means of a driving mechanism (not shown) in the direction of Z. A pair of grooves 411 and 412 each having
10 a U-shaped cross-section are formed in parallel with each other on the upper surface of the holder 410, and a pair of grooves 421 and 422 each having a U-shaped cross-section are also formed in parallel with each other on the upper surface of the holder 420 as shown
15 in FIG. 6.

 The width W_1 of the groove 411 as well as the width W_3 of the groove 421 should preferably be smaller than the outer diameter under the normal condition of a tube to be loaded therein and larger than the outer
20 diameter under a stretched condition of the tube when the tube is stretched by the aforementioned chucks 353 and 354. Likewise, the width W_2 of the groove 412 as well as the width W_4 of the groove 422 should preferably be smaller than the outer diameter under the
25 normal condition of a tube to be loaded therein and larger than the outer diameter under a stretched condition of the tube.

Caps 413 and 423 are pivotally hinged on the upper edge portions of the holders 410 and 420, respectively. On the inner surfaces of these caps 413 and 423 are formed grooves 414, 415, 424 and 425 in conformity with the aforementioned grooves 411, 412, 421 and 422, respectively. The cross-sectional shape of these grooves 411, 412, 421, 422, 414, 415, 424 and 425 is not restricted to the aforementioned U-shape, but may be a rectangular shape or a V-shape. The caps 413 and 423 may be constructed so as to be actuated automatically by an opening/closing mechanism provided with any desired driving source.

Between the holders 410 and 420 is exchangeably interposed a wafer 430 in such a manner that it can be moved at least in the direction of Y (in the direction of up and down) by the operation of a wafer-transferring means (not shown). This wafer 430 is composed of a double-folded metal plate made for example of a copper plate, and a patterned exothermic resistor (not shown) interposed via an insulating layer in the middle of the double-folded metal plate. The terminals 431 and 432 provided at both sides of the resistor are exposed through openings formed in the metal plate.

When electric current is passed to these terminals 431 and 432 by way of a power supplying means, the wafer 430 is heated to 260 to 320°C for instance.

This wafer 430 should preferably be of a disposable type (or a single use), i.e. which can be discarded after every operation of connecting the tubes. In this case, the wafer 430 may be automatically exchanged by
5 an exchanging means provided with a predetermined driving source.

It is also possible to provide the holders 410 and 420 at the end portions thereof facing the wafer 430 with a tube-nipping member which is capable of
10 compressing the tube thereby collapsing and closing the inner passage thereof after the caps 413 and 423 are closed.

The actuating means for the holder 410, the actuating means for the wafer 430, the current-transmitting means for the wafer 430, the driving
15 source for the wafer-exchanging means and cap-opening/closing mechanism, and the transferring means for the transferring table 440 are electrically connected to the control means 50 respectively, thereby
20 making it possible to control all of them.

This tube-connecting device 400 can be operated as follows. Namely, first of all, one end portion of one of the tubes to be connected is loaded in the grooves 411 and 421 of the holders 410 and 420, and one end
25 portion of the other tube is loaded in the grooves 412 and 422 of the holders 410 and 420. After closing the caps 413 and 423, electric current is passed between

the terminals 431 and 432 so as to heat the wafer 430 to a prescribed temperature, thereby fusing and cutting both tubes. Then, the holder 410 is moved in the direction of Z by a distance corresponding to
5 an interval between the center of the groove 411 and the center of the groove 412, thereby making the cut portions of both tubes coincide with each other. Thereafter, the wafer 430 is allowed to be descended and removed, thereby fusion-bonding both tubes with
10 each other. As a result, both tubes can be hermetically connected.

According to this tube-connecting device 400, the end portions of both tubes are sealed due to the fusion thereof before these end portions are connected, and
15 the lumens of both tubes are prevented from being contacted with the outer atmosphere during the connecting step of the tubes, so that both tubes can be aseptically connected.

Although a short tube (not shown) will be left in
20 the groove 412 of the holder 410 as well as in the groove 421 of the holder 420 after the tubes 15 and 25 are connected, these short tubes are of no use, so that these short tubes are held and transferred by the tube-transferring means 300 to be finally recovered in
25 a waste material-recovering box (not shown).

Tube-reshaping apparatus 450

The tube-reshaping apparatus 450 is mounted beside

the tube-connecting device 400 on the mobile table 500. Since the connected portion of the tubes connected by means of the tube-connecting device 400 may be deformed into a flat shape or collapsed causing the inner facing
5 surfaces of the tube to adhere with each other at the occasion of fusion-boding step, the inner passage of this connected portion may be closed or reduced in cross-section, thereby making it difficult to obtain a sufficient flow rate due to this deformed connected
10 portion. The purpose of this tube-reshaping apparatus 450 is to reshape the aforementioned deformed connected portion of the tube so as to ensure the normal inner passage of the tube.

FIGS. 7 and 8 illustrate the front view of one
15 embodiment of such a tube-reshaping apparatus. This tube-reshaping apparatus 450 is composed of a pair of press rollers 460 and 470 mounted for pressing a tube, a pair of swinging arms 464 and 474, and a pair of reciprocating mechanisms 466 and 476 functioning as
20 a driving means for swinging, via the swinging arms 464 and 474, the press rollers 460 and 470.

The press rollers 460 and 470 cylindrical in shape are disposed side by side and rotatably supported by a pair of rotating axes 463 and 473 disposed in
25 parallel with each other. These press rollers 460 and 470 are spaced apart from each other, leaving a predetermined interval therebetween.

Groove-like cut portions 462 and 472 are formed respectively on the outer peripheries of the press rollers 460 and 470, these cut portions 462 and 472 being extended in the axial direction of these press rollers 460 and 470. When the press rollers 460 and 470 are rotated in the same direction with each other so as to locate the cut portions 462 and 472 to face to each other, a tube passage 480 for allowing a tube to pass therethrough is formed between these cut portions 462 and 472. Namely, this tube passage 480 is large enough to allow the tube having the normal circular cross-section to easily pass therethrough.

Furthermore, a corrugated surface is formed next to each of the cut portions 462 and 472, thereby forming corrugated pressing surfaces 461 and 471 on the outer peripheries of the press rollers 460 and 470, respectively. These corrugated pressing surfaces 461 and 471 constitute respectively a curved surface conforming to the curvature of the outer periphery of each of the press rollers 460 and 470. When these press rollers 460 and 470 are further rotated from the state where the cut portions 462 and 472 face to each other forming a tube passage 480, the corrugated pressing surfaces 461 and 471 are then caused to face to each other. Under this condition, the distance "T" between the corrugated pressing surfaces 461 and 471 is slightly smaller than the difference between the outer

diameter and the inner diameter of the tube.

The swinging arms 464 and 474 which are adapted to be pivoted around the axes 463 and 473 are fixed to the press rollers 460 and 470, respectively. Namely, the swinging arms 464 and 474 are radially extended from the axes of the press rollers 460 and 470, respectively, and elongated holes 465 and 475 respectively extending in the longitudinal direction of the swinging arms 464 and 474 are formed at the distal end portion of each of the swinging arms 464 and 474.

The distal end portions of the swinging arms 464 and 474 are connected with the reciprocating mechanisms 466 and 476, respectively. The driving source for these reciprocating mechanisms 466 and 476 according to this embodiment may be an air pressure actuator for instance. The distal end portion of each of the driving rods 467 and 477 of this air pressure actuator is provided with a pin 468 or 478 projecting therefrom. These pins 468 and 478 are engaged respectively with the elongated holes 465 and 475 of the swinging arms 464 and 474.

The reciprocating mechanisms 466 and 476 may be actuated by any suitable means such as an oil hydraulic cylinder, a cam mechanism or an electric driving means in place of the aforementioned air cylinder, thereby effecting the displacement of the reciprocating mechanisms 466 and 476.

The driving sources for these reciprocating mechanisms 466 and 476 are electrically connected with the control means 50, thus controlling the actuation of these reciprocating mechanisms. The rotations of press
5 rollers 460 and 470 may be actuated by any other means, such as a motor for rotating the axes 463 and 473.

This tube-reshaping apparatus 450 can be operated as explained below. First of all, the press rollers 460 and 470 are rotated so as to locate the cut
10 portions 462 and 472 to face to each other, and then a tube carried by the tube-transferring means 300 is introduced into the tube passage 480 in such a manner that the deformed portion formed as a result of the connection of tubes is located inside the tube passage
15 480 as shown in FIG. 7.

Then, the press rollers 460 and 470 are caused to swing back and forth at least once by actuating the reciprocating mechanisms 466 and 476. Namely, due to the extending or contracting action of the driving rods
20 467 and 477 resulting from the operation of the air actuator, the swinging arms 464 and 474 are caused to swing around the axes 463 and 473 via the engagement of pins 468 and 478 with the elongated holes 465 and 475, thereby causing the press rollers 460 and 470 to swing.

25 As the press rollers 460 and 470 are caused to swing, the tube disposed therebetween is pressed from both sides thereof and collapsed by the pressing

surfaces 461 and 471. As a result, the tube is twisted causing the facing portions of inner surface of the collapsed portion of the tube to be scrubbed one another as shown in FIG. 8. It may be possible to
5 remove any blockades adhered onto the inner surface of the tube by simply collapsing the tube. However, when the tube is rotated while keeping the collapsed state of the tube so as to cause the facing portions of inner surface of the tube to be scrubbed one another, the
10 blockades adhered onto the inner surface of the tube can be completely peeled away, thus restoring the original or normal cross-sectional shape and ensuring the normal flow passage inside the tube.

The tube-reshaping means 450 may be constructed
15 such that the press rollers 460 and 470 can be moved by a suitable driving mechanism (not shown) to take two kinds of arrangements, i.e. a departed state (corresponding to a state shown in FIG. 7) and an approached state (corresponding to a state shown in
20 FIG. 8) and a departed state. In this case, when the press rollers 460 and 470 take the aforementioned departed state, the tube passage 480 is enlarged thereby allowing a tube to be inserted therein. Thereafter, the press rollers 460 and 470 are caused
25 to take the aforementioned approached state and the reciprocating mechanisms 466 and 476 are actuated to remove blockades as mentioned above to ensure the flow

passage of the tube.

Another mobile table 510 which is of the same kind as the aforementioned mobile table 500 is interposed between the filter-supplying means 700 and the second
5 container-supplying means 600. On this mobile table 510 is mounted another tube-connecting device 400 and tube-reshaping means 450 of the same types as mentioned above in the same arrangement as explained above. The tube-connecting device 400 on the mobile table 510
10 is employed for aseptically connecting a third tube 35 with a fourth tube 45 as explained below, while the tube-reshaping means 450 is used for remedying the deformed connected portion between the third tube 35 and the fourth tube 45, thereby ensuring the normal
15 flow passage inside the tube.

Since the leucocyte filter 30 and the second container 20 are separated in advance from each other in this embodiment, the mobile table 510, the tube-connecting device 400 and the tube-reshaping means 450
20 each mounted on the mobile table 510 are required to be employed for connecting a third tube 35 with a fourth tube 45 as explained above. However, if the leucocyte filter 30 and the second container 20 which are connected in advance with each other via a tube are to
25 be employed, all of the mobile table 510, tube-connecting device 400 and tube-reshaping means 450 may be omitted.

The second container-supplying means 600

5 The second container-supplying means 600 for supplying an unused second container is mounted on the other end portion of the leucocyte-eliminating apparatus 1. FIG. 9 is a partially sectioned side view showing one embodiment of a second container-supplying means. As shown in FIG. 9, the second container-supplying means 600 comprises a magazine 602 functioning as a housing for accommodating the second
10 container 20, a table 603 disposed at the bottom of the magazine 602 for receiving thereon the second container 20, and a lift 610 for moving the table 603 up and down within the magazine 602.

15 The magazine 602 is constituted by a box having an open top, an open bottom and an inner space for accommodating a plurality of the second containers 20 superimposed one upon another with their sides attached with the fourth tube being orientated in the same direction.

20 A tube-holding member 607 having a linear slit 608 for introducing and holding the fourth tube 45 of the second container 20 is provided at the middle of the front side wall (the right side in FIG. 9) of the magazine 602. Therefore, the second container 20 is
25 housed in the magazine 602 in such a manner that the fourth tube 45 thereof is inserted into the slit 608 so as to be held therein.

The second container 20 is constituted by a bag which is manufactured by superimposing a pair of soft resin sheets made for instance of flexible polyvinyl chloride and then the peripheries of the soft resin sheets are fusion-bonded whereby forming the bag.

One end portion of the fourth tube 45 is connected to one edge portion (an upper edge portion of the bag) 21 of the second container 20 so as to be communicated with the interior of the bag (the second container 20). The connection of the fourth tube 45 to the second container 20 can be effected by inserting the end portion of the fourth tube 45 into an interface between the sheets constituting the periphery of the bag and then fusion-bonding the end portion of the fourth tube 45 to the periphery of the bag.

The second container 20 may be preliminarily filled with a preservation liquid which is suitably selected according to the kind of blood component to be filled therein. For example, when liquid to be treated is a concentrated erythrocyte, an erythrocyte preservation liquid may be preliminarily filled in the second container 20. On the other hand, when the liquid to be treated is a concentrated platelet or buffy coat, a platelet preservation liquid may be preliminarily filled in the second container 20.

Since the second container 20 is constructed as mentioned above, the upper edge portion 21 thereof is

made thicker than the opposite edge portion (the bottom edge of the bag) 22 thereof by a thickness corresponding to the outer diameter of the fourth tube 45.

Therefore, when a plurality of the second containers 20 are stacked in the magazine 602 as shown in FIG. 9, the difference in thickness between the upper edge portion 21 and the bottom edge portion 22 is accumulated or increased according to the number of the second containers 20..

Although there is no limitation regarding the number of the second containers 20 that can be housed in the magazine 602, the number of the second containers 20 may be 2 to 50 in general, more preferably 10 to 25.

The table 603 for mounting the second container 20 is disposed in the vicinity of the bottom of the magazine 602. This table 603 is formed of a plate-like (or a frame-like) member, and the proximal end portion 604 of the table 603 is pivotally secured via a pin 606 to a mobile member 617. Each of the second containers 20 is mounted on the table 603 in such a manner that the bottom edge 22 of the second container 20 coincides with the proximal end portion 604 of the table 603 and the upper edge 21 of the second container 20 coincides with the distal end portion 605 of the table 603.

Since the upper edge 21 of the second containers 20 is thicker than the bottom edge 22 thereof as

mentioned above, the table 603 is required to be inclined by positioning the distal portion 605 lower than the proximal end portion 604 in order to keep a horizontal state of the uppermost one of the second
5 containers 20 stacked on the table 603 as shown in FIG. 9.

The table 603 can be moved by means of the lift (an elevator) 610 in the direction of Y, and at the same time, the table 603 is allowed to swing around the
10 pin 606. The lift 610 is provided with two driving mechanisms which enable the proximal end portion 604 and the distal portion 605 of the table 603 to move upward at a different moving rate from each other. Specifically, the driving mechanism 611 for ascending
15 the proximal end portion 604 of the table 603 is composed of a motor 612 functioning as a driving source, a shaft 613 extending vertically and connected to the rotation axis of the motor 612, a pair of supporting members 615 and 616 rotatably supporting the
20 upper portion and lower portion of the shaft 613, and a mobile member 617 which is adapted to be moved along the longitudinal direction of the shaft 613.

The outer periphery of the shaft 613 is provided with a screw 614, and a nut 618 engaging with the screw
25 614 is attached to the mobile member 617. When the shaft 613 is rotated in a predetermined direction by means of the motor 612, the nut 618 is caused to move

upward, thus causing the mobile member 617 to move upward concurrently. When the shaft 613 is rotated in reverse to the aforementioned direction, the mobile member 617 is caused to move downward. As for the nut 618, a ball screw provided with a ball (a steel ball) disposed between the nut and the screw 614 can be employed.

On the other hand, the driving mechanism 621 for ascending the distal end portion 605 of the table 603 is composed of a motor 622 functioning as a driving source, a shaft 623 extending vertically and connected to the rotation axis of the motor 622, a pair of supporting members 625 and 626 rotatably supporting the upper portion and lower portion of the shaft 623, a mobile member 627 which is adapted to be moved along the longitudinal direction of the shaft 623, an arm 630 mounted on the extended end portion 629 of the mobile member 627, and a roller 631 rotatably supported on the top portion of the arm 630.

The outer periphery of the shaft 623 is provided with a screw 624, and a nut 628 (such as a ball screw) engaging with the screw 624 is attached to the mobile member 627. When the shaft 623 is rotated in a predetermined direction by means of the motor 622, the nut 628 is caused to move upward, thus causing the mobile member 627 to move upward concurrently. On the contrary, when the shaft 623 is rotated in reverse to

the aforementioned direction, the mobile member 627 is caused to move downward.

5 The roller 631 is disposed such that the bottom surface of the distal end portion 605 of the table 603 is supported by the outer periphery of the roller 631. When the arm 630 is moved upward, the roller 631 pushes up the distal end portion 605 of the table 603 while rotating along the bottom surface of the table 603.

10 The table 603 is supported not only by a pin 606 connecting the table 603 with the mobile member 617 but also by the roller 631 attached to the distal end portion of the arm 630. Accordingly, the table 603 can be moved upward as the mobile members 617 and 627 are moved upward. When a second container 20 disposed at
15 the top out of a plurality of second containers 20 stacked on the table 603 in the magazine 602 is taken out, the table 603 is moved up so as to place the next one of the second containers 20 in the same position (level) as the previous one.

20 In this case, the driving mechanisms 611 and 621 of the lift 610 are controlled such that the mobile members 617 and 627 are moved upward at a different rising rate from each other so as to move the proximal end portion 604 and distal end portion 605 of the table
25 603 upward at a different rising rate from each other. This difference in rising rate is controlled such that the second container 20 disposed at the uppermost

position takes a horizontal posture irrespective of the number of the second containers 20 to be housed in the magazine 602.

5 The control of rising rate of these mobile members 617 and 627 as mentioned above can be effected by individually controlling the rotational speed or driving time of the motors 612 and 622, or by suitably setting the pitches of the screws 614 and 624. The control of rising rate of these mobile members 617 and 10 627 may also be effected by suitably combining these control means. By the way, the controls of the motors 612 and 622 can be effected by the control means 50.

15 The second container-supplying means 600 is exchangeably loaded at the recessed portion (a loading section for a second container-supplying means) 3 formed in the base table 2 as shown in FIG. 1.

20 Alternatively, a mechanism corresponding to the lift 610 may be fixedly mounted underneath the recessed portion 3, and at the same time members corresponding to the magazine 602 and the table 603 may be exchangeably loaded at the recessed portion 3.

The filter-supplying means 700

25 The filter-supplying means 700 for supplying a leucocyte-eliminating filter is interposed between the mobile table 500 and the mobile table 510. FIG. 10 shows a partial sectional view of one embodiment of the filter-supplying means 700. As shown in FIG. 10, the

filter-supplying means 700 is composed of a magazine 702 functioning as a housing for the leucocyte-eliminating filters 30, a table 703 disposed at the bottom of the magazine 702 for sustaining the leucocyte-eliminating filters 30 thereon, and a lift 710 for moving the table 703 up and down within the magazine 702.

The magazine 702 is constituted by a box having an open top, an open bottom and an inner space for accommodating a plurality of the leucocyte-eliminating filters 30 superimposed one upon another with their inflow sides and outflow sides being respectively orientated in the same direction.

A tube-holding member 705 for holding the second tube 25 and a tube-holding member 706 for holding the third tube 35 are disposed respectively at the middle of the front side wall (the right side in FIG. 10) and at the middle of the back side wall (the left side in FIG. 10) of the magazine 702. Linear slits 707 and 708 for inserting and holding a tube therein are formed in these tube-holding members 705 and 706, respectively. Accordingly, the leucocyte-eliminating filters 30 are housed in the magazine 702 in such a manner that the second tube 25 and the third tube 35 attached to each of the leucocyte-eliminating filters 30 are inserted respectively into the slits 707 and 708 to be held therein.

As shown in FIG. 11, the leucocyte-eliminating filter 30 is generally flat in shape and is provided with a housing 31 made of a resin. One end of the housing 31 is connected with the second tube 25 in a liquid-tight manner, and the other end thereof is connected with the third tube 35 in a liquid-tight manner by means of fusion or adhesion. To one end portion of the second tube 25 extending into the housing 31 is attached a film-like filter 32 which is capable of adhering and removing leucocyte. With this film-like filter 32, the interior of the housing 31 is partitioned into an inflow side space 33 and an outflow side space 34.

As for the material of the film-like filter 32, a porous synthetic material, a woven fabric or a nonwoven fabric made of fine fibers may be employed. Specific examples of such a porous synthetic material are polyurethane, polyvinyl formal, polypropylene, polystyrene, nitrocellulose and polyvinyl chloride. Specific examples of material constituting aforementioned fine fibers are polyester, polyethylene, polypropylene, polyamide, cellulose, polyacrylonitrile, polymethyl methacrylate, polystyrene and polyfluorochloroethylene.

The film-like filter 32 is not limited to that composed of a single layer as shown in the drawing, but may be a laminate composed of plural layers which

differ one another in features, such as raw material, film thickness or porosity.

The operation of this leucocyte-eliminating filter 30 is performed as follows. Namely, a liquid to be treated (blood or blood components) is introduced via the second tube 25 into the inflow side space 33 to pass through the filtering material where any leucocyte contained in the liquid is adhered onto the filtering material 32 thereby eliminating the leucocyte, and the resultant liquid entering in the outflow side space 34 is discharged via the third tube 35 out of the housing 31.

There is any particular limitation regarding the number of the leucocyte-eliminating filter 30 to be housed in the magazine 702. However, the number of the leucocyte-eliminating filter 30 may be 2 to 50 in general, more preferably 10 to 25.

The table 703 for mounting the leucocyte-eliminating filter 30 is disposed in the vicinity of the bottom of the magazine 702. This table 703 is formed of a plate-like (or a frame-like) member, and the top portion of the arm 704 mounted on the extended end 719 of the mobile member 717 to be explained hereinafter is secured to the underside of the table 703.

The table 703 can be moved by means of the lift (an elevator) 710 in the direction of Y. This lift 710

is composed of a motor 712 functioning as a driving source, a shaft 713 extending vertically and connected to the rotation axis of the motor 712, a pair of supporting members 715 and 716 rotatably supporting the upper portion and lower portion of the shaft 713, and a mobile member 717 which is adapted to be moved along the longitudinal direction of the shaft 713.

The outer periphery of the shaft 713 is provided with a screw 714, while a nut 718 engaging with the screw 714 is attached to the mobile member 717. The nut 718 may be a ball screw as mentioned above.

When the shaft 713 is rotated in a predetermined direction by means of the motor 712, the nut 718 is caused to move upward, thus causing the mobile member 717 to move upward concurrently. Since the table 703 is fixed via the arm 704 to the mobile member 717, the table 703 can be moved upward as the mobile member 717 is moved upward. When the shaft 713 is rotated in reverse to the aforementioned direction, the mobile member 717 is caused to move downward together with the table 703.

When a leucocyte-eliminating filter 30 disposed at the top out of a plurality of leucocyte-eliminating filters 30 stacked on the table 703 in the magazine 702 is taken out, the motor 712 is energized to moved up the table 703 so as to place the next one of the leucocyte-eliminating filters 30 in the same position

(level) as the previous one. In this case, the operation of the motor 712 is controlled by the control means 50.

5 The filter-supplying means 700 is exchangeably loaded at the recessed portion (a loading section for a filter-supplying means) 4 formed in the base table 2 as shown in FIG. 1.

10 Alternatively, a mechanism corresponding to the lift 710 may be fixedly mounted underneath the recessed portion 4, and at the same time members corresponding to the magazine 702 and the table 703 may be exchangeably loaded at the recessed portion.

The tube-sealing means 800

15 The tube-sealing means 800 is disposed beside the filter-supplying means 700 for sealing the inner passage of the third tube 35 (or the fourth tube 45) after the third tube 35 is connected with the fourth tube 45.

20 This tube-sealing means 800 comprises a plurality of clamps 810 for blocking the inner passage of the third tube 35 by nipping and press-closing it, and a clamp magazine 820 for housing and holding these clamps 810.

25 As shown in FIG. 12, the clamp 810 is made of a plate-like member whose one side is provided with a V-shaped cut functioning as a guiding groove 811 and also with a slit 812 formed contiguous with the guiding

groove 811. The width "H" of the guiding groove 811 is designed such that it is slightly smaller than the value of difference between the outer diameter and the inner diameter of a tube to be sealed, i.e. the third tube 35 (namely, twice the tube wall thickness).

Therefore, when the third tube 35 is inserted into the guiding groove 811 and slid along the guiding groove 811 into the slit 812 to be set therein, the third tube 35 is pressed from both sides by the inner walls of the slit 812 and collapsed, the inner surface of the third tube 35 being contacted with one another, thus sealing the inner passage thereof.

The clamp magazine 820 is constructed such that a plurality of clamps 810 can be stacked and held therein, and the clamps 810 thus housed therein can be taken out manually or automatically one by one.

The tube-sealing means 800 may be constructed such that the clamps 810 can be taken out and at the same time the clamp 810 thus taken out can be attached to the third tube 35 or the fourth tube 45 for sealing these tubes.

According to this invention, the tube-sealing means 800 is not limited to the aforementioned clamp 810, but may be constructed such that an intermediate portion of the tube is fusion-bonded (by means of heat bonding or ultrasonic bonding) and the fusion-bonded portion is cut and separated from each other (namely,

a tube fusion-bonding apparatus).

The control means 50

The control means 50 is constituted by a central processing unit (CPU) of a personal computer or
5 a microcomputer. Optionally, the control means 50 may be provided with a memory, an external input means such as key-board, a recording medium such as a floppy disk and a hard disk, and a transmitting means for communicating with other computers.

10 This control means 50 is electrically connected with the first container-supplying means 100, the roller pump 200, a tube-transferring means 300, the driving mechanism for the tables 500 and 510, each of tube-connecting devices 400, each of tube-reshaping
15 means 450, the second container-supplying means 600, the filter-supplying means 700, the tube-sealing means 800, so as to control the operation of these devices.

The operation of each of these devices can be manually performed by making use of the operation
20 section 60, or automatically performed according to the sequence programmed in advance in the control means 50 (a sequence control).

The operation section 60

Various devices such as keys, levers, bottoms,
25 switches or dials may be provided and suitably arranged as required in this operation section 60. These devices can be manually operated so as to perform the

setting of a condition, the ordering of run/stop, the actuation of driving sections, and the selection of operation modes.

As for the sheet materials constituting the first container 10 and the second container 20, the employment of flexible polyvinyl chloride is preferable. As for the plasticizer useful in this non-rigid polyvinyl chloride, it may be selected from phthalate, adipate and trimellitate. Among them, di(ethylhexyl) phthalate (DEHP) and di-(n-decyl) phthalate (DnDP) are preferable. The content of these plasticizer should preferably be 30 to 70 parts by weight per 100 parts by weight of polyvinyl chloride.

As other kinds of sheet materials constituting the first container 10 and the second container 20, polyolefins, i.e., a polymer or copolymer of olefin or diolefin such as ethylene, propylene, butadiene and isoprene may be employed. For example, polyethylene, polypropylene, ethylene-vinyl acetate copolymer (EVA), a polymer blend comprising EVA and any kind of thermoplastic elastomer, or a combination of these polymers may be employed. Furthermore, polyesters such as polyethylene terephthalate (PET), polybutylene terephthalate (PBT) and poly-1,4-cyclohexane dimethyl terephthalate (PCHT); and polyvinylidene chloride may be employed.

As for the material for constituting the tubes 15,

25, 35 and 45, polyolefins such as polyvinyl chloride, polyethylene, polypropylene and EVA; polyesters such as PET and PBT; thermoplastic elastomers such as polyurethane, polyamide, silicone, polyester elastomer, polyamide elastomer and styrene-butadiene-styrene copolymer; or a combination of any of these polymers may be employed. Among them, polyvinyl chloride is most preferable in view of its suitability for an automated mass production.

10 The tubes to be connected with each other in the tube-connecting device 400 should preferably be formed of the same or similar material to each other in view of the easiness and reliability of connection. Additionally, the tubes to be connected with each other
15 should preferably be of the substantially same size in inner diameter and also in outer diameter.

 Now, one embodiment of leucocyte-eliminating method (cell-eliminating method) by making use of the aforementioned leucocyte-eliminating apparatus 1
20 according to this invention will be explained. This method comprises the following steps.

 (1) The first container-supplying means 100 is actuated to transfer the first container 10 containing in advance a liquid to be treated to the blood
25 component-transferring portion 140.

 (2) The tube-transferring means 300 is actuated to hold an intermediate portion of the first tube 15 of

the first container 10 which has been transferred to the blood component-transferring portion 140, and the first tube 15 held in this manner is transferred to the roller pump 200 where the head 210 is in an open state. After the first tube 15 is loaded in the head 210, the head 210 is closed, thus making it ready for transferring the liquid to be treated.

(3) The tube-transferring means 300 is actuated so that the tube-connecting device 400 mounted on the table 500 is loaded with the end portion of the first tube 15 as well as the end portion of the second tube 25 connected to the leucocyte-eliminating filter 30 which is positioned at the top of the stacked leucocyte-eliminating filters 30 in the magazine 702.

(4) The tube-connecting device 400 is actuated as mentioned above to connect the first tube 15 with the second tube 25.

(5) The mobile table 500 is moved in the direction of "Z", and at the same time the tube-transferring means 300 is actuated to transfer the first tube 15 and the second tube 25 to the tube-reshaping apparatus 450, thereby positioning these tubes in the tube-reshaping apparatus 450.

(6) The tube-reshaping apparatus 450 is actuated as mentioned above to reshape the deformed connected portion formed between the first tube 15 and the second tube 25, thereby ensuring the normal flow passage of

the tube.

(7) The tube-transferring means 300 is actuated so that the tube-connecting device 400 mounted on the table 510 is loaded with the end portion of the third tube 35 connected to the leucocyte-eliminating filter 30 which is positioned at the top of the stacked leucocyte-eliminating filters 30 housed in the magazine 702 as well as the end portion of the fourth tube 45 connected to the second container 20 which is positioned at the top of the stacked second containers 20 housed in the magazine 602.

(8) The tube-connecting device 400 is actuated as mentioned above to connect the third tube 35 with the fourth tube 45.

(9) The mobile table 510 is moved in the direction of "Z", and at the same time the tube-transferring means 300 is actuated to transfer the third tube 35 and the fourth tube 45 to the tube-reshaping apparatus 450, thereby positioning these tubes in the tube-reshaping apparatus 450.

(10) The tube-reshaping apparatus 450 is actuated as mentioned above to reshape the deformed connected portion between the third tube 35 and the fourth tube 45, thereby ensuring the normal flow passage of the tube.

The aforementioned steps (3) to (6) and the aforementioned steps (7) to (10) may be performed

concurrently, or the steps (7) to (10) may be performed prior to the steps (3) to (6). Otherwise, the steps (3) to (6) and the steps (7) to (10) may be performed alternately (in parallel).

5 (11) The roller pumps 200 are actuated to discharge and transfer the liquid to be treated from the first container 10. The liquid discharged from the first container 10 is introduced via the first tube 15 and the second tube 25 into the leucocyte-eliminating
10 filter 30 disposed at the uppermost position of the stacked leucocyte-eliminating filters 30, thereby allowing the liquid to pass through the leucocyte-eliminating filters 30, thus eliminating the leucocyte contained in the liquid. The resultant treated liquid
15 (blood components) passed through the leucocyte-eliminating filters 30 and removed of leucocyte is then introduced via the third tube 35 and the fourth tube 45 into the second container 20 disposed at the uppermost position of the stacked second container 20, and stored
20 therein.

(12) When a predetermined amount (almost the entire volume in this embodiment) of the liquid to be treated is discharged from the first container 10, the operation of the roller pump 200 is suspended.

25 The timing of suspension of the roller pump 200 may be effected by preliminarily setting the operation time of the roller pump 200 in a timer which is built

in the control means 50. In this case, the operation time of the roller pump 200 may be suitably determined, taking into consideration various conditions such as the rotation number (the amount of discharge) of the roller pump 200 and the volume of the liquid in the first container 10.

Alternatively, the operation and suspension of the roller pump 200 can be controlled on the basis of information from a detection means which is mounted for detecting a predetermined volume of the treating liquid that has been discharged from the first container 10. The detection means useful in this case may be an optical sensor which is capable of optically detecting the liquid level in the first container 10 disposed at the blood component-transferring section 140, an optical sensor which is positioned at an intermediate portion of the tube 15, 25, 35 or 45 to optically detect a passing of an interface of vapor/liquid within the tube or an interface of liquid/liquid (each differs in transmittance from the other), a weight sensor for detecting the weight of the first container 10, a weight sensor for detecting the weight of the second container 10, or a pressure sensor for detecting the pressure within the tube portion disposed on the upstream side of the roller pump 200.

(13) An intermediate portion of the third tube 35 is sealed by the clamp 810 by making use of the

tube-sealing means 800.

5 (14) A linked body comprising the first container 10, the leucocyte-eliminating filter 30 and the second container 20 is placed on a take-out section 5 of the table 2 (see FIG. 1). If required, a tube fusion-bonding apparatus (not shown) may be employed to fusion-bond an intermediate portion of the fourth tube 45 (by means of heat bonding or ultrasonic bonding) and the fusion-bonded portion is then cut to separate the 10 second container 20 from the linked body.

As a result, a blood preparation (the second container 20) which is free from leucocyte can be automatically prepared.

15 (15) The lift 610 of the second container-supplying means 600 is actuated to move the next second container up to the uppermost position (the container supplying position). Likewise, the lift 710 of the filter-supplying means 700 is actuated to move the next leucocyte-eliminating filter up to the uppermost 20 position (the filter supplying position).

(16) By repeating the aforementioned steps (1) to (15), a blood preparation removed of leucocyte can be automatically and continuously prepared.

Examples

25 This invention will be further explained with reference to the following specific examples.

A leucocyte-eliminating apparatus having

a construction as illustrated in FIGS. 1 to 12 was manufactured.

5 Ten pieces of blood collection bag (the first container) made of flexible polyvinyl chloride each containing whole blood from human body (added with an anti-coagulant), ten pieces of leucocyte filter provided with a porous polyurethane film as a filtering material, and ten pieces of blood components bag (the second container) made of flexible polyvinyl chloride were prepared. Each of the blood collection bags was set on the first container-supplying means. Each blood collection bag was housed in a magazine and positioned at the recessed portion 3. Likewise, each leucocyte filter was housed in a magazine and positioned at the recessed portion 4.

15 Under this condition, the leucocyte-eliminating apparatus was actuated to carry out the aforementioned steps (1) to (16), to obtain a plurality of blood component bags each containing blood components removed of leucocyte ($n=10$).

20 The blood (before a leucocyte-eliminating treatment) in the blood collection bag and blood components (after a leucocyte-eliminating treatment) in the blood components bag were sampled, and the samples thus obtained were subjected to a measurement for counting the number of cells by making use of an automatic blood cell counter (Toua Iryo Densi Co.;

Sysmex NE-6000). The results are shown in Table 1.

Table 1

	Before a leucocyte- eliminating treatment	After a leucocyte- eliminating treatment
Amount of liquid (ml)	458.6 ± 9.9	415.6 ± 11.5
Total number of erythrocyte	$20.5 \pm 1.5 \times 10^{11}$	$18.7 \pm 2.0 \times 10^{11}$
Total number of leucocyte	$25.8 \pm 7.0 \times 10^{11}$	$3.8 \pm 2.7 \times 10^5$
Total number of platelet	$10.9 \pm 2.0 \times 10^{11}$	$7.2 \pm 1.1 \times 10^{10}$

As shown in Table 1, the leucocyte-elimination ratio of the blood components (a mixture of concentrated erythrocyte and concentrated platelet) in the blood component bag was of a high level.

Then, a bag for preserving platelets (a platelet preservation bag) was provided, and the tube from the platelet preservation bag was aseptically connected with the tube from the blood component bag obtained in the aforementioned step by making use of a tube-connecting device of the same type as shown in the drawings, whereby obtaining a double-linkage bag.

Then, this double-linkage bag was subjected to a centrifugation (centrifugation conditions: $180 \times G$; 6.5 minutes) by making use of a centrifugal separator, thereby separating the blood components contained

in the blood component bag into two phases, i.e.
an erythrocyte layer and a platelet layer.

Then, the blood component bag was pressed to
discharge the platelet constituting the upper layer
5 contained therein and transferred into the platelet
preservation bag via the tube connecting the two bags.

Then, an intermediate portion of the tube was
fusion-bonded by using a tube fusion-bonding apparatus,
and the fusion-bonded portion of the tube was cut off,
10 whereby obtaining a concentrated erythrocyte
(erythrocyte preparation: $255 \pm 12\text{ml}$) filled in the
blood component bag and a concentrated platelet plasma
(platelet preparation: $158 \pm 18\text{ml}$) filled in the
platelet preservation bag ($n = 10$).

15 When the number of cells in these erythrocyte
preparation and platelet preparation was measured in
the same manner as explained above, the total number of
leucocyte in the erythrocyte preparation was found to
be $2.9 \pm 1.8 \times 10^5$, and the total number of
20 leucocyte in the platelet preparation was found to be
 $8.2 \pm 4.1 \times 10^4$, each indicating a low level of the
number.

Although this invention has been described with
reference to the specific embodiments of cell-
25 eliminating apparatus and the cell-eliminating method
shown in the drawings, this invention should not be
considered to be limited by these specific embodiments.

For example, the first container-supplying means may be constructed such that the transfer of the first containers is performed by suspending them by making use of a hook (or hanger), or by placing them on a turn
5 table or on a mobile table.

Furthermore, the liquid transfer means is not restricted to a roller pump, but may be formed of a mechanism where the liquid to be treated in the first container is transferred by making the most of a fall
10 (gravitation); an apparatus for pressing (pushing pressure) the first container; an apparatus for reducing the inner pressure of the second container (for example, a pressure-reducing chamber housing the second container); or any combination of these
15 apparatuses.

Further, the cell-eliminating filter is not limited to the aforementioned leucocyte-eliminating filter, but may be a filter which is capable of selectively eliminating platelet, erythrocyte, specific
20 lymphocyte (such as T cell, B cell and NK cell) in leucocytes, microglobulin, albumin, globulin or immune complex. The cell-eliminating filter may be those which are capable of eliminating two or more kinds of these cells.

25 In the above embodiment, both first and second containers are constituted by a pliable bag. However, at least one of the first and second containers may be

constituted by a different kind of container such as a bottle.

5 All of the aforementioned sequence of steps according to this invention should preferably be performed automatically. However, part of the steps may be performed manually.

10 As is explained above, according to the cell-eliminating apparatus and the cell-eliminating method of this invention, since a tube attached to a bag can be aseptically connected with a tube attached to another bag in transferring blood or blood components from the former bag to the latter bag and vice versa, a cell-eliminating treatment such as leucocyte-eliminating treatment can be performed while
15 maintaining a closed system (or aseptically), thus avoiding blood or blood components from being contaminated by bacteria.

20 It is possible according to this invention to automate or rationalize the cell-eliminating treatment such as leucocyte-eliminating treatment, in particular the operation of manufacturing a blood preparation, whereby avoiding troublesome procedures that have been involved in the manufacture of a blood preparation and improving the productivity.



Claims:

1. A method for selectively removing a specific cell from blood or blood components, which comprises the steps of;

5 aseptically connecting a first tube attached to a first container filled with blood or blood components with a second tube attached to an inlet port of a cell-eliminating filter;

 discharging the blood or blood components from
10 said first container thereby allowing the blood or blood components to pass through said cell-eliminating filter, whereby eliminating said specific cell from the blood or blood components; and

 recovering the blood or blood components
15 eliminated of said specific cell into a second container communicating with an outlet port of said cell-eliminating filter.

2. A method for selectively removing a specific cell from blood or blood components, which comprises
20 the steps of;

 aseptically connecting a first tube attached to a first container filled with blood or blood components with a second tube attached to an inlet port of a cell-eliminating filter;

25 aseptically connecting a third tube attached to an outlet port of said cell-eliminating filter with a fourth tube attached to a second container;





discharging the blood or blood components from
said first container thereby allowing the blood or
blood components to pass through said cell-eliminating
filter to eliminate said specific cell from the blood
5 or blood components; and

recovering the blood or blood components
eliminated of said specific cell into said second
container.

3. The method according to claim 1 or 2, wherein
10 said cell-eliminating filter is a leucocyte-eliminating
filter for adsorbing and eliminating leucocyte.

4. An apparatus for selectively removing
a specific cell from blood or blood components, which
comprises;

15 a first container-supplying means for supplying
a first container filled with blood or blood
components;

a filter-supplying means for supplying a cell-
eliminating filter for selectively removing a specific
20 cell from the blood or blood components;

a second container-supplying means for supplying
a second container which is capable of being filled
with a blood component passed through said cell-
eliminating filter; and

25 a tube-connecting device for enabling a pair of
tubes to be aseptically connected with each other;
wherein a first tube which is attached to said





first container supplied from said first container-supplying means is aseptically connected by means of said tube-connecting device with a second tube attached to an inlet port of said cell-eliminating filter supplied from said filter-supplying means; the blood or blood components are discharged from said first container, thereby allowing the blood or blood components to pass through said cell-eliminating filter; and then the blood or blood components eliminated of said specific cell are recovered in said second container.

5. An apparatus for selectively removing a specific cell from blood or blood components, which comprises;

15 a first container-supplying means for supplying a first container filled with blood or blood components;

20 a filter-supplying means for supplying a cell-eliminating filter for selectively removing a specific cell from the blood or blood components;

a second container-supplying means for supplying a second container which is capable of being filled with a blood component passed through said cell-eliminating filter; and

25 at least one tube-connecting device for enabling a pair of tubes to be aseptically connected with each other;





wherein a first tube which is attached to said first container supplied from said first container-supplying means is aseptically connected by means of said tube-connecting device with a second tube attached to an inlet port of said cell-eliminating filter supplied from said filter-supplying means; a third tube which is attached to an outlet port of said cell-eliminating filter is aseptically connected with a fourth tube attached to said second container; the blood or blood components are discharged from said first container, thereby allowing the blood or blood components to pass through said cell-eliminating filter; and then the blood or blood components eliminated of said specific cell are recovered in said second container.

6. The apparatus for selectively removing a specific cell from blood or blood components according to claim 5, which further comprises a tube-sealing means for sealing said third tube or said fourth tube.

7. The apparatus for selectively removing a specific cell from blood or blood components according to any one of claims 4 to 6, which further comprises a tube-transferring means which is capable of transferring a tube to at least said tube-connecting device.

8. The apparatus for selectively removing





a specific cell from blood or blood components according to any one of claims 4 to 7, which further comprises a liquid-transferring means which is capable of transferring blood or blood components.

5 9. The apparatus for selectively removing a specific cell from blood or blood components according to any one of claims 4 to 8, wherein said tube-connecting device is adapted for connecting a pair of tubes with each other by thermally fusing the tubes.

10 10. The apparatus for selectively removing a specific cell from blood or blood components according to any one of claims 4 to 8, wherein said tube-connecting device comprises a pair of holding members which are adapted to hold a pair of tubes to be
15 connected side by side for connecting these tubes; and a heating plate which is exchangeably disposed between said pair of tubes for thermally cut off said pair of tubes held by said holding members; said holding members being adapted to be shifted in relative to each
20 other so as to contact and connect the cut portions of said pair of tubes with each other.

 11. The apparatus for selectively removing a specific cell from blood or blood components according to any one of claims 9 or 10, which further
25 comprises a tube-reshaping means for restoring any deformed shape formed at an interconnected portion of said pair of tubes.





12. The apparatus for selectively removing
a specific cell from blood or blood components
according to any one of claims 4 to 11, wherein said
cell-eliminating filter is flat in shape, and said
5 filter-supplying means comprises a magazine for holding
a plurality of cell-eliminating filters superimposed
one upon another, and a supplying mechanism for
supplying said cell-eliminating filters one by one from
said magazine..

10 13. The apparatus for selectively removing
a specific cell from blood or blood components
according to any one of claims 4 to 12, wherein said
second container is formed of a pliable bag, and said
second container-supplying means comprises a magazine
15 for holding a plurality of second containers
superimposed one upon another, and a supplying
mechanism for supplying said second containers one
by one from said magazine.

14. The apparatus for selectively removing
20 a specific cell from blood or blood components
according to claim 13, wherein said second container-
supplying means is constructed such that a second
container disposed at the top of layers of said second
containers housed in said magazine is kept in
25 a predetermined posture.

15. The apparatus for selectively removing
a specific cell from blood or blood components



according to any one of claims 4 to 14, wherein said cell-eliminating filter is a leucocyte-eliminating filter for adsorbing and eliminating leucocyte.

5 16. A method for selectively removing a specific cell from blood and apparatus therefor, substantially as hereinbefore described with reference to the accompanying drawings.

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