**Chapter:**

**Technological and innovative automation in Immuno-Haematology**

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**Abstract**

*In order to perform major surgeries including open heart surgery, organ transplants, cancer, and anaemia therapies, as well as other forms of treatments, blood is required. People remain dying in numerous nations due to an insufficient availability of blood products. General paediatricians, surgeons, intensivists, and haematologists/oncologists treat many infants and young children who require blood component transfusions as an essential component of their care. Because blood was utilised so frequently and extensively, it quickly led to new issues like vascular overload. These issues have been treated by component treatment. Many advanced techniques for collection and compatibility testing with recipients have been developed in the field of blood banking practise.*

**Key words**

History, Introduction, Blood component preparation, Recent advances in the techniques of blood bank.

**History**

Blood has always been a source of fascination for people. Aristocracy drank it, artists and playwrights used it as a literary allegory, ancient Egyptians used it as a bathing fluid, and modern humans transfuse it. Even though it has been a difficult process, tremendous advancement has been made in creating a straightforward, secure, and efficient transfusion system. Blood was taken from three young men and given to Pope Innocent VII in 1492 in an attempt to treat him, but all four of them died. Despite the gloomy outcome, this was the first documented case of a blood transfusion in history.

Clotting was the biggest challenge to get beyond. When Braxton Hicks suggested sodium phosphate as a nontoxic anticoagulant in 1869, efforts to find one officially got under way. This was possibly the earliest instance of blood preservation study. In 1901, Karl Landsteiner identified the ABO blood types and provided an explanation for the severe reactions that follow from receiving blood from an incompatible donor in people. Early in the 20th century, his contribution was recognised with a Nobel Prize. The appropriate transfusion-related equipment then arrived. The first to be successful was Edward E. Lindemann. He transfused blood from vein to vein using numerous syringes and a specialised cannula for piercing the vein through the skin. However, many knowledgeable assistants were needed for this lengthy, difficult procedure. When Hustin reported using sodium citrate as a transfusion anticoagulant solution in 1914, it was a historical breakthrough in blood transfusion. Lewisohn later established the minimal concentration of citrate required for anticoagulation in 1915 and proved that it is harmless in tiny doses. The patient's safety and the practicality of transfusions improved. Following this, preservative treatments to speed up RBC metabolism were developed. In 1916, Rous and Turner published a citrate-dextrose solution for the preservation of blood, which marked the beginning of the use of glucose. However, the importance of glucose in RBC metabolism was not completely understood until the 1930s. Because of this, the traditional timing for adding glucose to the preservation solution was delayed.

Due to the rise in demand for blood and plasma during World War II, research into blood preservation was sparked. A global network of blood banks was established as a result of Charles Drew's innovative work in creating blood transfusion and blood preservation techniques during World War III February 1941, Dr. Drew was selected to direct the first American Red Cross Blood Bank at Presbyterian Hospital. The American Red Cross's nationwide programme for voluntary blood donors was modelled after the trial programme Dr. Drew developed. Scientists Loutit and Mollison from England developed the preservative acid-citrate dextrose (ACD) in 1943. As a result of efforts made in several countries, the significant July 1947 issue of the Journal of Clinical Investigation, which had more than a dozen studies on blood preservation, was published. Blood banks were established in numerous significant American cities in 1947 as a result of the swift action taken by hospitals, which prompted the widespread use of transfusions. Many other blood group systems were discovered as a result of the frequent transfusions. As advanced methods were created, antibody identification shot to the top. Citrate-phosphate-dextrose (CPD), a less acidic alternative to ACD that Gibson proposed in 1957, eventually took the role of ACD as the preferred preservative for blood preservation.

**Problems due to frequent transfusion**

Blood was used so extensively and frequently that it soon gave rise to new issues including vascular overload. Component therapy has been used to address these problems. Previously, just one patient could get a single unit of whole blood. However, component therapy allows for the use of a single unit for several transfusions. Today, without incurring the risk of the inherent dangers of whole blood transfusions, clinicians may select the precise component for the specific needs of their patients. Only the necessary percentage in the concentrated form may be transfused by doctors without overtaxing the circulatory system. A fuller utilisation of blood products is now possible thanks to appropriate blood component therapy. Component separation aided in advancing knowledge of erythrocyte metabolism during this period of heavy blood consumption and increased awareness of the problems associated with RBC storage. The American Association of Blood Banks (AABB) estimates that 8 million volunteers donate blood each year. Research from the National Blood Data Resource Centre (NBDRC) estimates that 15 million units of whole blood and RBCs were donated in the United States in 2001. According to the NBDRC, blood components were transfused in about 29 million units in 2001. Future population ageing and advancements in medical procedures requiring transfusions are expected to increase the demand for blood and blood components. The majority of these units are given away each year by less than 5% of healthy Americans who are eligible to donate blood, usually through blood drives hosted at their place of employment. A person can also give blood in a community blood centre or a hospital-based donor centre, which together supply 88 and 12% of the nation's blood supplies, respectively. In the United States, volunteers donate most of the blood that is transfused.

Modified plastic collection devices are used for collecting 500 mL of blood, and the volume of the anticoagulant-preservative solution is increased from 63 to 70 mL. The maximum volume of whole blood that can be acquired, including the quantity needed for sampling, is now specified by an AABB standard, which states that it must be "10.5 mL/kg of donor weight." This suggests that a 110-lb donor can yield a maximum volume of 525 mL. Red blood cells are replaced in the donor's body one to two months following the donation. Whole blood can be donated by a volunteer once every eight weeks. A unit of whole blood/prepared RBCs may be kept for 21 to 42 days, depending on the anticoagulant-preservative solution used to collect the whole blood unit and if a preserving solution was added to the separated RBCs. There is still a fee for each unit to cover the costs of gathering, storing, testing, and transfusing blood, despite the fact that the majority of nonprofit blood-collecting groups mislead the public into believing that donated blood is free (1).

**Introduction**

Blood is a material suspension in an electrolyte-containing aqueous colloid solution. Blood serves as an exchange channel between the body's fixed cells and the outside world. According to popular consensus, Landsteiner's discovery of the immunologic phenomena defining the physiological basis of the blood group system currently known as ABO served as the foundation for the science behind blood transfusion practise. Before that, a select few committed medical professionals, primarily obstetricians (most notably James Blundell), handled blood transfusions for patients suffering from postpartum haemorrhage who were in critical condition. The insight made by Landsteiner paved the way for the creation of straightforward techniques for compatibility analysis (2-4)

United States

The Cleveland surgeon GW Crile was the first to regularly employ transfusion in the United States. He had come to believe that blood was the best fluid to treat haemorrhagic shock as early as 1898. Using surgical anastomosis, French surgeon Alexis Carrel, who is currently practising in the United States and has a speciality in vascular surgery and transplantation, has developed a method for direct (donor) artery to (recipient) vein transfusion. Incorporating a cannula to connect the vessels, Crile modified Carrel's technique to create the direct artery to vein transfusion.

Both procedures posed practical challenges because to the need for sophisticated surgical abilities and the difficulty to accurately calculate the amount of blood transfused. As a result, efforts were made to create transfusion systems that would enable calibrated blood transfusions between donors and recipients quickly enough to accomplish appropriate transfusions before clotting could happen. Many such techniques or tools were developed. The surgeons who practised transfusion in the early years of the war usually named three since they were widely employed. At Bellevue Hospital in New York, Lindeman employed numerous syringes. Unger, who was also based in New York, created a 4-way stopcock that was attached to a sizable syringe and enabled for repeated blood transfusions from donor to recipient with saline flushes in between. Kimpton and Brown in Boston accelerated the transfusion by applying positive pressure to a cylinder coated with paraffin to prevent clotting. All these devices had drawbacks, including the need for numerous operators and the presence of the donor(s). Blood transfusions were discouraged due to the practical challenges of transfusion, the professional scorn that "specialists" like obstetricians received, the development in stature of and academic interest in experimental physiology, and other factors***,*** The consensus was that isotonic saline should be the preferred resuscitative fluid (although physiologists continued to recommend the use of nonblood colloid substances like 6% or 7% gum acacia in 0.9% saline as late as 1916). As a result, the British brought saline into the conflict as a remedy for "hemorrhagic shock." Ironically, Crile spent a month in 1895 at the University College of London's physiology lab (which was active in this field of research) and, after returning to the United States, carried out animal experiments that led him to believe that only blood would remain in the circulation and that saline had no long-term value as a blood substitute (5).

**Blood banking**

A blood bank is a facility where donated blood is gathered and stored for use in future blood transfusions. Typically, the term "blood bank" refers to a department of a hospital, frequently found inside a clinical pathology laboratory, where blood products are maintained and pre-transfusion and blood compatibility testing are performed. But it can also refer to a place where things are collected; some hospitals even do this. Procedures for collecting, processing, testing, separating, and storing blood are included in blood banking.

Blood banking and transfusion procedures have seen tremendous development throughout time. Two significant changes are the increased automation of compatibility testing and the use of electronic systems to track the transfusion process from the order to the adverse impact reports. Blood banks have challenges when utilising monoclonal antibodies to treat cancer patients since these medications obstruct pre-transfusion compatibility tests, causing a delay in the supply of blood.

Transfusion, one of the most widely used treatments, occasionally produces inappropriate episodes. The hazards and benefits of requesting a blood transfusion must be carefully considered. In the last 10 years, hemovigilance systems have observed a drop in the use of red blood cells, which, among other things, can be attributed to the adoption of restriction strategies based on new scientific results. In fact, patient blood management plans are being gradually included into clinical practises to reduce unnecessary blood exposure and improve patient outcomes.

**Blood component preparation**

Blood component therapy is the practise of dividing freshly donated blood into its constituent parts so that each part can be used to treat a particular clinical disease. RBCs, platelet concentrate, cryoprecipitate, and platelet and cryoprecipitate poor plasma are all products of one unit of whole blood.

Blood obtained through WB or apheresis donations is used to manufacture blood components. WB transfusions are uncommon in contemporary medicine. Blood priming for extracorporeal circuits, such as therapeutic apheresis in small patients, cardiovascular bypass, extracorporeal membrane oxygenation, and continuous hemoperfusion, neonatal exchange transfusions, and patients with active bleeding and significant volume loss are uses for WB or reconstituted WB units. Most blood centres rarely collect WB for allogeneic use due to the poor platelet function that occurs after 24 hours of storage and the declining levels of coagulation factors (particularly V and VIII) throughout storage. Components can be administered in the form of "reconstituted" WB (a plasma unit and an RBC unit in one bag) when RBC and coagulation factor supplementation is required.

**Component preparation from whole blood**

450 mL of blood from a healthy adult donor are used to make one unit of WB, which is then placed in a sterile plastic bag with 63 mL of an anticoagulant/preservative (AP) solution. RBCs, platelets, and plasma can be distinguished from one another by centrifugation because they have various specific gravities. The most common method in North America for doing this first involves doing a gentle spin, which separates the platelet-rich plasma from the heavier RBCs. The RBCs are subsequently collected and placed in an anticoagulant solution-filled sterile satellite bag. A vigorous spin is then used to separate platelets from plasma. The outcome is one unit of platelet concentrate (PC), containing at least 5.5 1010 platelets in around 50 mL of residual plasma. The generated PC can be pooled with other donor PCs or stored in multiples of single units. A unit of plasma obtained from WB typically has a volume of 250 ml. Within eight hours of collection, the plasma must be isolated from the other blood components and kept at 18 C in order to be designated as fresh frozen plasma (FFP).

**Anticoagulant/preservative solutions**

The product must be sterile, the cellular components must stay viable throughout storage, there in vivo survival after storage must be greater than 75% 24 hours after transfusion, and haemolysis should be less than 1% when RBCs are stored for transfusion. RBCs must be kept in solutions that can meet their metabolic requirements in order to maintain their viability and functional activity. Citrate, phosphate, and dextrose (CPD) are ingredients found in all anticoagulant solutions. These components each serve as an anticoagulant, a buffer, and a source of energy for the metabolism of the RBCs. Recent improvements in the creation of AP solutions are mostly attributable to the addition of nutrients that sustain ATP and 2,3-diphosphoglycenate levels in erythrocytes and stabilise the RBC membrane. Some AP solutions contain mannitol because it stabilises RBC membranes and allows adenine to enter RBCs and be incorporated into the nucleotide pools, increasing the amount of ATP in the RBC products. RBCs now have a shelf life of 42 days for the more recent AP solutions (Adsol, Optisol, and Nutricell), compared to 21 days for CPD and 35 days for citrate-phosphate-dextrose-adenine (CPDA)-1. However, extremely ill premature neonates needing massive transfusions (e.g., exchange transfusion, extracorporeal membrane oxygenation, or cardiopulmonary bypass), or those who have significant renal or hepatic insufficiency, may be at risk for metabolic abnormalities. The concentrations of additives in products with U.S. licences are safe for most children and neonates receiving simple transfusions. Small volume transfusions of newborns utilising anticoagulant/preservative solution 1 (AS-1) contain less than a tenth of the hazardous dose of adenine and mannitol (15 mL/kg RBCs). However, there are no clinical studies on metabolic problems in neonatal large transfusion. Therefore, until such data are available, some professionals advise against using RBCs that have been preserved on extended-storage media (such as Adsol, Optisol, or Nutricell). Inverted storage, centrifugation, or even washing the RBC product are a few methods for lowering the AP (6).

**Recent advancement in the techniques of blood bank**

**Multicomponent apheresis**

In the past, complete blood was used in transfusions; today, just blood components are used. Patients with burns and other injuries as well as those with clotting issues are treated with plasma. For every patient needing a transfusion, red blood cells are the most often used component (more than 60% of units used are red blood cells, according to South Texas Blood & Tissue Centre 2014). They are mostly used to treat anaemia, perform surgery, treat blood diseases, and care for premature infants. Finally, platelets aid in the regulation of bleeding and are employed in cancer treatments, organ transplants, and other surgical procedures to prevent significant blood loss. In addition to whole blood donation, current technical developments enable the donation of multiple blood products and/or multiple transfusable units of each product without endangering the safety of the donor based on the donor's qualifications and characteristics. Multicomponent apheresis (MCA), sometimes known as multicomponent collection (MCC), is the process that non-profit organisations and businesses employ to collect donations (7). As a result, using MCA, the donation procedure can be customised according to the eligibility of the donor and the component(s) to be gathered. One can give plasma every 28 days, double red blood cells every 112 days, entire blood or red blood cells every 56 days, and red blood cells every time. The following are the key benefits of MCA donation:

It can include the collection of many parts and/or multiple units. Savings are produced as a result of the higher yield per donation, shorter donor sessions, lower costs for extra bags, and less tests that must be completed before a transfusion, which considerably lowers testing expenses and time. Additionally, the finished product is ready immediately following the donation; there is no need for an additional processing stage to divide the donated blood into its constituent parts. Because whole blood must be transported from the donor site to a processing centre, this lowers the processing expenses as well as the logistics costs. Before being delivered to the storage facility, the product(s) that MCA has collected can be safely stored at the donation location.

1. Increased donor utilisation is possible. As an illustration, obtaining two units of red blood cells and one unit of platelets from a qualified donor yields more transfusable units than donating whole blood, which aids in effectively managing the limited pool of donors. A donor may also be qualified for a particular form of donation even if they are not able to donate whole blood thanks to various customised eligibility criteria for each type of donation that are made possible by technologically more advanced machines (8).
2. The patient only receives blood from a small number of donors, lowering the risk of infection.
3. By adapting the donations to the demand, it helps to stabilise the type-distribution inventory and/or match the supply and demand in a more cost-effective manner. MCA donations offer a chance to enhance the donation process's efficiency at a lower cost while making better use of the donor pool. A steadier inventory level can be maintained throughout the year by adjusting the donations utilising MCA devices, which also eliminates seasonal shortages during the summer and winter months. To overcome the shortage of donors and the fluctuation of donation/usage patterns and to reduce soaring health care costs by improving donor utilization, the usage of MCA donations is expanding in many countries. An enhanced blood supply network depends heavily on economic analysis of MCA donations and research into the possible advantages of creating customised schedules (9).

Although blood can save lives, excessive donations are not preferred due to high donation costs, inventory keeping costs, and excess donation disposal costs. By personalising donations depending on donors' eligibility, organisations are now able to increase donor utilisation and maintain desirable blood-type and product-specific inventory levels of this product that is in limited supply. One must consider several criteria when deciding the kind of donation for each donor, including the anticipated demand for specific blood types and products, the amount of inventory at the time, the cost of the donation and the cost of the inventory, the donors' history of contributions, and the interval between donations. Donation organisations can seek to encourage donors to make an eligible donation type that produces more platelets if there is a strong demand for platelets in a specific location at a certain time. Although MCA contributions help blood donation organisations use donors more effectively and maintain a better type inventory, there has not been much research into how to use MCA donations to create donation tailoring guidelines (10).

A pheresis donor may be characterized into one or all the following:

1. Plateletpheresis
2. Plasmapheresis
3. Leukopheresis
4. Double RBC pheresis

Each of these treatments has certain requirements for the donor, as per rules established by the AABB and FDA as well as suggestions provided by the American Society for Apheresis (ASFA). We begin by outlining the fundamentals of apheresis. Most apheresis centres use an automated cell separator, whose centrifugal force separates blood into components based on changes in density. Blood that has been anticoagulated from the donor is extracted and pushed into a rotating bowl or chamber. Blood components are divided based on cellular density. The proper fraction is extracted (for instance, platelets), and the donor is given the remaining parts.

**Plateletpheresis**

With a few exceptions, the donor requirements for plateletpheresis donors are comparable to those for whole blood. Donors using platelet pheresis may give more frequently. The delay between donations must be at least two days, and they cannot be made more frequently than twice per week or 24 times per year.49 Donors who have used aspirin or products containing aspirin will not be accepted. A platelet count is not required for the initial donation, but it is required if more than 4 weeks have passed after the last donation; in this case, the platelet count must be greater than 150,000/L. Any abnormal outcomes require approval from the blood bank's medical director or, in unusual circumstances, a physician.

**Plasmapheresis**

It is possible to categorise plasmapheresis donors as "occasional" or "serial." In the former, pheresis is performed on the donor no more frequently than once every four weeks, and donor selection is similar to that of whole blood collection; in the latter, donations are made more frequently than once every four weeks, and extra conditions are in place. A minimum of 48 hours should pass between donations, and no more than two can be made in a 7-day period. Serum or plasma must also undergo tests for total protein, serum protein electrophoresis, or quantitative immunoglobulins. Results must fall within acceptable bounds.

**Leukopheresis**

Granulocyte collection from the leukopheresis donor requires the use of special agents. These could consist of growth agents such granulocyte-colony stimulating factor, corticosteroids, or hydroxyethyl starch. Any approval for the use of any of these agents during the procedure must be included in the informed consent. According to AABB Standards, no leukopheresis-facilitating medicines or substances should be administered to donors whose medical histories indicate that doing so could worsen existing conditions (11).

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An alternative to WB collection and separation of blood components is the collection of a specific component by apheresis. During this process, blood is drawn into an external circuit, the blood's components are separated using centrifugation or filtration, the required component is collected, and the donor is given the blood's other components back. Even while historically, this has been used for platelet, plasma, and granulocyte collection, more recent approaches support the collection of RBCs. These strategies offer more of the desired component than WB collecting methods. In this instance, a single platelet unit obtained through apheresis contains nearly the same number of platelets as a collection of six to eight randomly chosen donor platelet units received through WB (5.5 1010 versus 3 1011 platelets/U for platelets from a single donor obtained from WB). In "double" batches, platelets and RBCs can also be collected. Since platelet and red cell apheresis products expose users to fewer donors, there is also the theoretical benefit of lessening the risk for alloimmunization and transfusion-transmitted infections in patients who get blood transfusions often. Donors can give more frequently than with WB collection since there is no RBC loss during platelet apheresis. (12).

**Modified and Automated Antiglobulin Test Techniques**

LISS, PEG, and albumin have been mentioned as changes to the antiglobulin test method; however, other modifications might be employed in unique situations. The automated low ionic polybrene (LIP) technique was modified for use as a human procedure, as described in A. The technique depends on low ionic conditions to rapidly sensitise cells to antibodies. The sensitised cells can move towards one another and allow the associated antibody to cross-link them when Polybrene, a potent rouleaux-forming agent, is added. The rouleaux is then reversed by adding a solution with a high ionic strength, but agglutination will still be present. If necessary, the test might be continued using an AHG approach. If a polyspecific anti-IgG reagent were used, the low ionic conditions would cause considerable amounts of C4 and C3 to coat the cells, leading to false-positive results. A monospecific anti-IgG reagent must be used in this case. Microplates have also been used to conduct the antiglobulin test. Crawley and associates. Microplate technology is increasingly used in blood group serology, and several processes are being changed to accommodate it. The LIP method has been modified for use in microplates by Redman and colleagues. Even though they did not mention it in their report, this extra step might easily be added. A test for enzyme-linked antibodies An RBC suspension is introduced to a microtiter well and then rinsed with saline for the enzyme-linked antiglobulin test (ELAT). It is combined with AHG that has been enzyme-labelled. To IgG-sensitized RBCs, the enzyme-labelled AHG will attach. After the extra antibody is removed, the enzyme substrate is added. According to spectrophotometric analysis, the amount of colour produced is inversely related to the antibody concentration. Typically, 405 nm is used to evaluate optical density. This method can also be used to estimate the IgG molecule density per RBC. Phase Solid Antiglobulin tests may be conducted using solid-phase technology. Test tubes or microplates have both been used in several different approaches that have been published. This improvement makes it possible to introduce semi automation because microplate readers are readily available. Both direct and indirect testing can be done using solid-phase technology. In the first, an antibody and RBCs are added to a microplate well. If the antibody is specific for the antigen on RBCs, the bottom of the well will be covered with suspension; otherwise, RBCs will sink to the bottom of the well. In the latter, a glutaraldehyde- or poly-L-lysine-treated well is used to fix detected RBCs. As previously noted, when test serum is added to RBC-coated wells and an antibody in the serum is specific for the antigen on fixed RBCs, a positive reaction occurs. Immucor Incorporated creates solid-phase technologies for the detection and classification of alloantibodies. The sides of the polystyrene microtitration strip wells have RBC membranes attached for the Group O reagent. IgG antibodies from patient or donor sera are bound to the membrane antigens. After incubation, unbound immunoglobulins are taken out of the wells, and the wells are then filled with a suspension of anti-IgG-coated indicator RBCs. During centrifugation, antibodies linked to the reagent RBC membranes come into contact with the indicator RBCs. If the test is negative, a pellet of indicator RBCs develops at the bottom of the wells. When a test is positive, the indicator RBCs stick together, creating anti-IgG-IgG complexes and an additional layer of immobilised RBCs. The RBC antigen-antibody responses are detected using the gel test, which employs a chamber filled with polyacrylamide gel. Due to the gel's trapping properties, free, unagglutinated RBCs condense into pellets at the bottom of the tube, whereas agglutinated RBCs stay in the tube for hours. Negative responses appear as pellets at the bottom of the microtube, but positive reactions are fixed in the gel. There are three types of gel tests: antiglobulin, specific, and neutral. A neutral gel does not contain any specific reagents; it simply acts by its capacity to catch agglutinates. Reverse ABO typing, identifying enzyme-treated or untreated RBCs, and screening for antibodies are the three main applications of neutral gel testing. Since they employ a particular reagent built into the gel, specialised gel tests are useful for detecting antigens. The low ionic antiglobulin test for the gel test is a helpful tool that can be used for both the IAT and the DAT. The AHG reagent is present in the gel. As an illustration, in an IAT gel, serum is added, 50 L of an RBC solution at 0.8 percent is pipetted onto an AHG gel, and the tube is centrifuged after an incubation period. At the beginning of centrifugation, the suspension medium is often left on top while the RBCs tend to flow through the gel. Because there is not a washing phase, the medium and RBCs separate. RBCs interact with AHG at the upper part of the gel, where favourable and unfavourable responses are identified. The tip of each microtube of the LISS/Coombs ID cards has been put 50 L of a 0.8 percent RBC suspension in LISS solution (ID-Diluent 2). At a speed of 910 rpm, the cards are centrifuged for 10 minutes. If the gel test yields a positive result, monospecific reagents (anti-IgG, anti-C3d) can be used (13).

**Solid Phase Technology**

The ABS200067 is recognised as the first completely automated walk-away system created to automate repetitive, labor-intensive operations while freeing up engineers to work on other projects. Hemagglutination is used for ABO/Rh, and solid phase technology is used for antibody screens/crossmatches. An automated pipette is used by the ABS2000 to transfer specimens, create RBC suspensions, log reagents and samples, incubate, wash, centrifuge, read and interpret results. The blood bank's or blood center's data management system can be interfaced with the online microprocessor. The ROSYS Plato68 and ABSHV 69 can do medium- to high-volume testing, while the ABS2000 can handle workloads with a low to medium volume. With a capacity of 1800 tests each shift, these instruments additionally employ a barcode scanner to positively identify samples, pipet reagent and samples, incubate, wash, and evaluate results. The Dias Plus System70 employs a robotic system and a closed washing system to do high-volume testing (more than 300 tests per hour), hence reducing biohazard exposure. High throughput and 24-hour operation are included into this instrument. The Galileo is the newest automated instrument in the Immucor line. The FDA has given the Galileo approval to be marketed in the United States and it is available in Europe. It can perform medium- to high-volume ABO, Rh, antibody screen donor, and compatibility testing with a fully automated, bidirectional interface. The FDA granted The Gel Technology approval in 1994 for use in American blood banking processes. This technology was artfully packed by Ortho Clinical Diagnostics and Micro Typing Systems Inc (Pompano Beach, FL) into a "gel card" with six microtubes or gel chambers. If antibody and RBCs have agglutinated, each chamber contains dextran acrylamide gel particles that make it easier to trap the agglutinates. ABO/Rh, direct antiglobulin testing, antibody screens and identification, and crossmatches are among the tests carried out using this method. To positively identify donor samples, the semi-automated Tecan Megaflex69 uses a barcode scanner. Pipets are used to transfer chemicals and create RBC suspensions. A photo-optical centrifuge is used to read agglutination. A CPU is used to process reports and interpret data. Gel technology eliminates the need for washing. The new ProVue system is known as the first completely automated blood banking system for use with the ID-Micro Typing System (ID-MTS) Gel Test. The Ortho ProVue can now be marketed by Micro Typing Systems thanks to FDA approval. It offers high-volume testing and STAT capability to the blood bank laboratory.

Successful automation of the solid phase test has been achieved. Such equipment is capable of carrying out pipetting operations and calculating the level of reactivity by taking multiple measurements of each well. A LISS reagent that changes colour when added to serum or plasma and a smaller sample size (compared to the tube test) are additional advantages that make it ideal for use in paediatric settings. This ensures that the test system has a big enough sample. Due to the small sample and reagent amounts, manual testing has the disadvantage of requiring precise pipetting. Insufficient indicator cells may result in a pattern that resembles a flimsy affirmative response. Staff personnel should be carefully trained to visually assess results if automation is not used. Staff members who had mostly used the tube test in the past can mistake the diffuse positive pattern for a negative reaction and the dense pellet of the negative reaction for a positive reaction. Centrifuges with well-holding capacities, washers, and incubators are the specific equipment needed for this technique. The last disadvantage of this approach is the cost increase caused by the obligation to do a positive and negative control with each batch of tests.

**Antiglobulin Crossmatch**

Like the instantaneous spin crossmatch, the antiglobulin crossmatch process starts with a 37 degrees Celsius incubation and concludes with an antiglobulin test. To improve antigen-antibody responses, a variety of enhancement media can be used. These could include albumin, low ionic strength solution (LISS), polybrene 270, polyethylene glycol, and low ionic strength solution. For optimal sensitivity, an antihuman globulin (AHG) reagent that contains both anti-IgG and anticomplement may be used in the final phase of this crossmatch technique. However, many laboratories frequently use mono-specific anti-IgG AHG reagents. An auto-control produced from the patient's own cells and serum may be used in addition to the crossmatch test. Some engineers still find the auto-control useful even though it is no longer needed by the most recent AABB Standards. Perkins33 considered the predictive value of a positive auto-control (3.6 percent) and decided to continue using the auto-control in pretransfusion testing after the antibody screen came up negative. The auto-control's results help clarify potential explanations for beneficial outcomes.

Computer Crossmatch

It has been established that an electronic (computer) crossmatch is equally safe as the serologic instantaneous spin test for detecting ABO incompatibilities. Many people believe that the computer crossmatch is more secure than the instantaneous spin because it can identify ABO incompatibility between the sample provided for pretransfusion testing and the donor unit. The computer crossmatch checks current ABO serologic data and interpretations maintained on file for both the donor and recipient being matched in order to confirm compatibility.

**Nucleic Acid Amplification Technology Blood Donor Testing**

The polymerase chain reaction (PCR), invented by Kary Mullis and winner of the Nobel Prize, is still the most efficient nucleic acid amplification technique (NAT) and has fundamentally changed diagnostics across a wide range of sectors (14). Alternative NATs, such as transcription-mediated amplification (TMA), for instance, are more challenging than PCR to build in-house in several laboratories throughout the world with little effort and at a reasonable cost. The inherent drawback of this technology was greatly reduced and made automatable with the advent of real-time PCR (15). It is best to minimise or even avoid amplification products' (amplicons') impact on lab and equipment contamination. Internal controls were easily incorporated and distinguished from the target sequences by labelling them with various fluorophores. Multiplexed PCRs can detect numerous viruses at once, and they can be separated from one another by employing different labels. This readily available technology allowed for the development of numerous applications that required the highest levels of sensitivity and specificity, as well as the highest feasible throughput and a reasonable price. These technical advancements have allowed blood safety to advance to previously unheard-of levels over the last 20 years.

Technical Principles of NAT

Utilising NAT, a variety of nucleic acid amplification techniques can be employed for genomic screening for infectious diseases. Numerous techniques, such as the polymerase chain reaction, ligase chain reaction, nucleic acid sequence-based amplification, and transcription-mediated amplification, are used to amplify nucleic acids in vitro. HCV and HIV are two examples of RNA targets that can be amplified using nucleic acid sequence-based amplification and transcription-mediated amplification, whereas polymerase chain reaction and ligase chain reaction require targets that are DNA or cDNA sequences, necessitating a reverse transcription step for amplifying RNA viruses. All of these techniques detect the presence of infectious bacteria in donor blood by amplifying the nucleic acid sequences particular to the bacterium. The employment of these strategies delivers a much higher level of sensitivity and specificity when compared to currently used standard testing procedures (such enzyme immunoassay [EIA]). Even with the diligent EIA screening of donor blood for the detection of antigens (HBsAg, HIV p24 antigen), and antibodies (anti-HIV-1/2, anti-HBc, anti-HCV), there is still a risk of posttransfusion infection from HIV or hepatitis viruses acquired from donors donating in the early window (or latent) of infection (16). The advantage of NAT is that it can directly recognise viral genomic nucleic acids rather than relying on the presence of antibodies to do so. The efficiency of such screening is based on the prevalence of infection in the community and the length of the window period, according to Lee and Allain7. In most Western nations, HCV has a higher frequency and a longer window period (80 days) compared to HBV (56 days) and HIV (16 days). This is why the primary focus of the implementation of this blood screening technique is NAT detection of HCV. The Gen-Probe, Inc. (San Diego, Calif.) approach calls for three steps in the NAT procedure for HIV-1 and HCV in donor blood: sample preparation, HIV-1 and HCV RNA target amplification, and detection of the amplified products (amplicons). During sample preparation, pooled plasma samples from donors are treated with a detergent to denature proteins, solubilize the viral envelope, and release viral genomic RNA. With oligonucleotides that are identical to highly conserved regions of the HCV genome and HIV polymerase, the RNA targets of HCV or HIV are hybridised. After being adsorbed onto magnetic microparticles, these hybridised targets are removed from the plasma using a magnetic field. Transcriptional-mediated amplification, which uses an RNA polymerase and a reverse transcriptase for the amplification process, amplifies the HIV-1 and HCV targets. The amplicon is subsequently hybridised with a complementary single-stranded nucleic acid probe to perform detection. A luminometer is used to detect the presence of chemiluminescent signals produced by the hybridised probes. This popular multiplex assay may detect the presence of HIV or HCV genomes but cannot differentiate between the two. Discriminating assays are performed on the samples that were identified as reactive in the multiplex assay to determine if they are positive for HIV, HCV, or both. These selective assays also employ the fundamental methodology of the multiplex assay. However, HIV-specific and HCV-specific probe reagents are used separately, not in concert as in the multiplex probe reagent. Roche Molecular Systems came up with a replacement plan. The COBAS AmpliScreen HCV Test is composed of five key steps:

1. Preparation of the specimen.
2. Target RNA reverse transcription to produce complementary DNA (cDNA)
3. Target cDNA polymerase chain reaction amplification using complementary primers unique to the HCV infection
4. Hybridization of the amplified products to oligonucleotide probes specific to the target(s), and
5. Colorimetric detection of the probe-bound amplified products.

The Multiprep procedure is used to test primary plasma pools of 24 samples and secondary plasma pools of 6 samples for follow-up testing, and the Standard procedure is used to test individual samples to identify the positive specimen(s) in the primary and secondary pools. The COBAS AmpliScreen HCV Test is used in conjunction with both of these specimen-processing methods. (17).

**Cord blood collection**

Umbilical cord blood (UCB) was first used in therapeutic settings after it was discovered that it contains cells capable of in vitro haematopoiesis reproduction and that these cells could be cryopreserved. The first attempt at UCB transplantation was reported in 1972, but Elianne Gluckman and her team in Paris performed the first successful UCB transplant in 1988 in a patient with Fanconi anaemia using cord blood from an HLA-identical sibling; the patient is still alive and well. Due to his achievement, Rubinstein founded the first cord blood bank (CBB) using voluntarily donated cord tissue in New York in 1999. The first two unrelated cord blood transplants were then carried out in 1993 with the help of units from this bank, and the first extensive series outlining the clinical results of unrelated cord blood transplants was published in 1996. These findings made it clear that a substantial quantity of well-characterized, high-quality CBUs, which might be easily accessible, would be needed globally to support cord blood transplantation. Procedures for gathering, preserving, and releasing CBUs for transplantation to prospective related and unrelated recipients were developed by several researchers. Currently, there are 54 public, unrelated CBBs with over 300,000 frozen units spread across the globe, making them instantly transplantable. In children and adults with both malignant and non-malignant diseases, such as acute and chronic leukaemia, bone marrow failure, immunodeficiencies, and hereditary metabolic disorders, these CBBs have made it possible to execute over 10,000 unrelated cord blood transplants (18). It is possible to collect UCB in utero or ex utero from full-term births. Before the placenta is delivered, a skilled member of the delivery team conducts in utero collections during the third stage of labour. Alternatively, after a full-term natural delivery or caesarean surgery, the UCB can be removed ex utero by qualified personnel from the recently delivered placenta. This is accomplished by hanging the placenta, cannulating the vein, and allowing the blood to flow naturally into a UCB collection bag that has been specially made.

In nations with modest family sizes and sparse or non-existent bone marrow donor registries, several public CBBs have recently developed. China, Singapore, and Japan, among others, are currently making investments in the creation of CBBs. Most of the current HSC transplant activity in Japan, or more than 4000 UCB transplants, is performed utilising CBUs from the Japanese Cord Blood Bank Network (JCBBN), which has more than 30 000 units on hand. Similar circumstances exist in China, where there are already at least six CBBs that are operational, with plans for another four. There have been reports of anything between 25,000 and 250 000 CBUs being banked in China, although exact numbers are unknown. Public cord blood banking has flourished and proven to be very cost-effective in other nations, such as Mexico**.** Despite the existence of a bone marrow donor registry there, the costs associated with importing a bone marrow donor harvest are too expensive when compared to the availability and provision of a CBU locally.

**Future challenges As cord blood transplantation**

As data availability grows, new clinical protocols are used, and other criteria relating to the effectiveness and quality of CBUs could become apparent. Despite the relative success of cord blood transplantation, there are still significant obstacles to be cleared, which might need modifying our current procedures. Investigating ways to increase the TNC content of the banked units in order to promote engraftment is one of these problems. Early attempts to expand cord blood stem cells ex vivo were not particularly effective because it seems that most of the methods that have been published so far have largely expanded mature progenitors. With or without CD34+ cells, several researchers have now tried injecting UCB into the bone, together with CD34+ cells, or with third-party bone marrow-derived mesenchymal stem cells, with minimal success in improving engraftment rates. A further difficulty is attempting to enhance immunological reconstitution in CBT patients to lessen infections and/or viral reactivation. Future applications of some immunotherapy techniques, including the development of viral-specific T cells or natural killer cells, which are currently used for bone marrow transplantation, may be possible for cord blood transplantation (19).

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