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

**(Author-** Ms. Yashika Bhardwaj, Mrs Shivani)

Assistant Professor, Department of Paramedical Sciences, Subharti Medical College, Swami Vivekanand Subharti University, Meerut, U.P

Demonstrator, Department of Paramedical Sciences, Subharti Medical College, Swami Vivekanand Subharti University, Meerut, U.P

**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. Blood was utilised so regularly and widely that it quickly caused new problems, such as vascular overload. Component therapy has been used to address these problems. 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. Ancient Egyptians used it as a bathing fluid, aristocracy drank it, writers and playwrights utilised it as a literary allegory, and modern humans transfuse it. Although it has been a challenging journey, significant progress has been made towards developing an effective, safe, and simple transfusion procedure. To heal Pope Innocent VII in 1492, blood was drawn from three young men and given to him; however, all four of them passed away. This was the first time a blood transfusion has ever been documented in history, notwithstanding the dismal conclusion.

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, it was not until the 1930s that the role of glucose in RBC metabolism was fully appreciated. As a result, the customary use of glucose in the preservation solution was postponed.

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 II. Dr. Drew was chosen to lead the first American Red Cross Blood Bank at Presbyterian Hospital in February 1941. The American Red Cross's nationwide programme for voluntary blood donors was modelled after the trial programme Dr. Drew developed.The preservative acid-citrate dextrose (ACD) was invented in 1943 by English scientists Loutit and Mollison. The important July 1947 issue of the Journal of Clinical Investigation, which had over a dozen publications on blood preservation, was published as a result of efforts in numerous nations. As a result of the quick action taken by hospitals, blood banks were formed in many major American cities in 1947, which led to 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. These issues have been handled via component therapy. A single unit of whole blood used to be limited to one patient. However, with component therapy, a single unit may be utilised for several transfusions. Today, doctors may choose the precise component for the unique needs of their patients without running the danger of the inherent risks of whole blood transfusions. 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.During this time, there was a lot of blood use, and component separation helped to expand understanding of erythrocyte metabolism and raise awareness of the issues with RBC storage. According to the American Association of Blood Banks (AABB), 8 million volunteers give blood annually. An estimated 15 million units of whole blood and RBCs were donated in the United States in 2001, according to research by the National Blood Data Resource Centre (NBDRC). Nearly 29 million units of blood components were transfused in 2001, according to the NBDRC. The need for blood and blood components is anticipated to grow in the future due to an ageing population and improvements in medical treatments that call for transfusions. Less than 5% of healthy Americans who are eligible to donate blood provide these units each year, mostly through blood drives held at their place of employment. A person can also donate blood at a hospital-based donor centre or a community blood centre, which together account for 88 and 12 percent of the country's blood supplies, respectively. Nearly majority of the blood used for transfusions in the United States is donated by unpaid volunteers.

When collecting 500 mL of blood, modified plastic collection systems are employed, and the amount of anticoagulant-preservative solution is raised from 63 to 70 mL. The greatest amount of blood that can be donated or collected at once is now determined by an AABB standard, which stipulates that the volume of whole blood obtained, including an amount for samples, shall be "10.5 mL/kg of donor weight." This indicates that a maximum volume of 525 mL can be taken from a 110-lb donor. Within one to two months after donation, the donor's red blood cells are replenished. Every eight weeks, a volunteer donor may provide whole blood. Depending on the anticoagulant-preservative solution used to collect the whole blood unit and if a preserving solution was added to the separated RBCs, a unit of whole blood/prepared RBCs may be preserved for 21 to 42 days. Although most nonprofit blood-collecting organisations lead the public to believe that given blood is free, there is still a fee for each unit to cover the costs of gathering, storing, testing, and transfusing blood (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 solution1 (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 considerseveral 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

According to regulations set forth by the AABB and FDA as well as recommendations made by the American Society for Apheresis (ASFA), each of these treatments has certain requirements for the donor. We start by providing a basic explanation of apheresis. Most apheresis facilities employ an automated cell separator, whose centrifugal force divides blood into components according to variations in density. Anticoagulated blood from the donor is drawn and pushed into a revolving chamber or bowl. Depending on their cellular density, blood components are separated. The appropriate fraction is collected (for example, platelets), and the other components are given back to the donor.

**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. Although a platelet count is not necessary for the first donation, it is necessary if there is fewer than 4 weeks between donations; in this situation, the platelet count must be greater than 150,000/L. The medical director of the blood bank or a doctor in special situations must approve any aberrant results.

**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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The collection of a particular component via apheresis is an alternative to WB collection and separation of blood components. This procedure involves drawing blood into an external circuit, separating the components using centrifugation or filtration, collecting the desired component, and giving the donor back the remaining blood components. Newer techniques support RBC collection even if historically this has been employed for platelet, plasma, and granulocyte collection. Compared to WB collection approaches, these techniques offer more of the desired component. In this case, a single apheresis platelet unit has roughly the same number of platelets as a pool of six to eight randomly selected donor platelet units collected from WB (5.5 1010 versus 3 1011 platelets/U for single donor WB obtained platelets). Platelets and RBCs can also be collected in "double" batches. There is also a theoretical advantage of lowering the danger for alloimmunization and transfusion-transmitted illnesses in persistently transfused patients since platelet and red cell apheresis products expose recipients to fewer donors. Given that there is no RBC loss during platelet apheresis, donors can donate more frequently than with WB collection (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. A described how the automated low ionic polybrene (LIP) approach was converted for usage as a human process. The method relies on low ionic conditions to quickly antibody-sensitize cells. The addition of Polybrene, a powerful rouleaux-forming reagent, enables the sensitised cells to move towards one another and allow the attached antibody to cross-link them. 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. The low ionic circumstances induce significant amounts of C4 and C3 to coat the cells, which would generate false-positive results if a polyspecific anti-IgG reagent were employed. Therefore, if this is done, a monospecific anti-IgG reagent must be utilised. The antiglobulin test has also been performed using microplates. Crawford and colleagues. Blood group serology uses microplate technology more frequently, and numerous procedures are being modified for 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. The enzyme substrate is introduced after the extra antibody has been removed. Spectrophotometric measurements show that the amount of colour produced is proportional to the amount of antibody present. 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 a number of different approaches that have been published. This improvement makes it possible to introduce semiautomation because microplate readers are readily available. Utilising solid-phase technology, testing can be conducted directly and indirectly. In the former, RBCs and an antibody are introduced to a microplate well. The bottom of the well will be covered with suspension if the antibody is specific for the antigen on RBCs; otherwise, RBCs will sink to the bottom of the well. In the latter, identified RBCs are fixed to a glutaraldehyde- or poly-L-lysine-treated well. A positive reaction happens as mentioned above when test serum is introduced to RBC-coated wells and an antibody in the serum is specific for the antigen on fixed RBCs. Solid-phase systems for the detection and identification of alloantibodies are produced by Immucor Incorporated. RBC membranes for the Group O reagent are affixed to the sides of polystyrene microtitration strip wells. The membrane antigens have IgG antibodies bonded to them from patient or donor sera. Unbound immunoglobulins are removed from the wells after incubation, and the wells are subsequently filled with a suspension of indicator RBCs that have been coated with anti-IgG. Antibodies attached to the reagent RBC membranes come into touch with the indicator RBCs during centrifugation. A pellet of indicator RBCs forms at the bottom of the wells if the test is negative. A positive test results in the indicator RBCs adhering, resulting in the formation of anti-IgG-IgG complexes and a second layer of immobilised RBCs. The gel test uses a chamber filled with polyacrylamide gel to identify RBC antigen-antibody responses. Free, unagglutinated RBCs form pellets in the bottom of the tube due to the trapping effect of the gel, whereas agglutinated RBCs remain in the tube for hours. Positive reactions are thus fixed in the gel whereas negative reactions manifest as pellets at the bottom of the microtube. Gel tests come in three varieties: neutral, specific, and antiglobulin. A neutral gel simply functions via its ability to capture agglutinates; it does not include any specialised reagents. The primary uses of neutral gel tests are reverse ABO typing, enzyme-treated or untreated RBC identification, and antibody screening. Specific gel tests are helpful for identifying antigens since they use a specific reagent included into the gel. The gel test's low ionic antiglobulin test is a useful application that can be utilised for either the IAT or the DAT. The gel contains the AHG reagent. For instance, in an IAT gel, 50 L of an RBC suspension at 0.8 percent is pipetted onto an AHG gel, serum is added, and the tube is centrifuged after an incubation period. The RBCs tend to pass through the gel at the start of centrifugation, while the suspension medium is left above. Without a washing phase, the RBCs and the medium separate as a result. In the upper portion of the gel, RBCs encounter AHG, and the favourable and unfavourable reactions are distinguished. The GLIAT test for unexpected antibody detection offers a safe, dependable, and simple-to-read alternative to traditional AHG procedures. Each microtube of the LISS/Coombs ID cards has 50 L of a 0.8 percent RBC suspension in LISS solution (ID-Diluent 2) added to the top for the DAT. The cards are centrifuged for 10 minutes at 910 rpm. Monospecific reagents (anti-IgG, anti-C3d) can be utilised in the gel test in the event of a positive reaction (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. For use with the ID-Micro Typing System (ID-MTS) Gel Test, the new ProVue system is recognised as the industry's first fully automated blood banking system. The FDA has gave Micro Typing Systems permission to start marketing the Ortho ProVue. It provides the blood bank laboratory with STAT capability and high-volume testing.

The solid phase test has been automated successfully. By obtaining several readings of each well, such equipment may execute pipetting processes and calculate the level of reactivity. Other benefits include a LISS reagent that changes colour when added to serum or plasma and a reduced sample size (as compared with the tube test), making it excellent in a paediatric context. This guarantees that the test system contains a sufficient sample. One drawback of manual testing is the requirement for precise pipetting due to the limited sample and reagent volumes.An insufficient number of indicator cells may produce a pattern resembling a weak positive reaction. If automation is not employed, staff members should be carefully taught to visually interpret outcomes. The diffuse positive pattern may be interpreted as a negative reaction and the dense pellet of the negative reaction as a positive reaction by staff members who had previously utilised the tube test predominantly. The specific tools required for this procedure include centrifuges that can hold the wells, washers, and incubators. The requirement to conduct a positive and negative control with each batch of tests raises the cost of this procedure, which is its last drawback.

**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 comprise polyethylene glycol, polybrene 270, low ionic strength solution (LISS), albumin, and LISS. For the final step of this crossmatch procedure, an antihuman globulin (AHG) reagent comprising both anti-IgG and anticomplement may be chosen for maximum sensitivity. However, mono-specific anti-IgG AHG reagents are often used in many laboratories. In addition to the crossmatch test, an auto-control made out of the patient's own cells and serum may also be used. Even though the auto-control is no longer required by the most recent AABB Standards, some engineers still find it beneficial. When the antibody screen came back negative, Perkins33 evaluated the predictive value of a positive auto-control (3.6 percent) and made the decision to keep utilising the auto-control in pretransfusion testing. Results of the auto-control assist in elucidating potential justifications for favourable outcomes.

Computer Crossmatch

An electronic (computer) crossmatch to identify ABO incompatibilities was shown to be as safe as the serologic instantaneous spin test. Because the computer software detects ABO incompatibility between the sample submitted for pretransfusion testing and the donor unit, many people think that the computer crossmatch is safer than the instantaneous spin. In order to verify compatibility, the computer crossmatch compares current ABO serologic data and interpretations stored on file for both the donor and recipient being matched.

**Nucleic Acid Amplification Technology Blood Donor Testing**

The Kary Mullis-developed polymerase chain reaction (PCR), which was awarded the Nobel Prize, is still the most effective nucleic acid amplification technology (NAT) and has completely transformed diagnostics in a variety of fields (14). Alternative NATs like transcription-mediated amplification (TMA), for example, are more difficult to construct in-house in many laboratories throughout the world with minimal effort and affordable costs than PCR. With the development of real-time PCR, this technology's intrinsic disadvantage was much diminished and it became automatable (15). Equipment and lab contamination from amplification products (amplicons) should be reduced or even avoided. Labelling internal controls with various fluorophores made it simple to incorporate them and distinguish them from the target sequences. Multiple viruses may be detected simultaneously with one test using multiplexed PCRs, and they could be distinguished from one another using distinct labels. Numerous applications needing the highest sensitivity and specificity along with the maximum throughput and affordable price were made possible by this easily accessible technology. Over the past 20 years, these technological developments have made it possible for blood safety to reach previously unheard-of heights.

Technical Principles of NAT

Several nucleic acid amplification methods can be used for genomic screening for infectious pathogens employing NAT. The in vitro amplification of nucleic acids is accomplished via a variety of strategies, including the polymerase chain reaction, ligase chain reaction, nucleic acid sequence-based amplification, and transcription-mediated amplification. HCV and HIV are 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 need DNA or cDNA sequences as targets, necessitating a reverse transcription step for amplifying RNA viruses. By amplifying the nucleic acid sequences unique to the bacterium, all of these methods immediately identify the presence of infectious bacteria in donor blood. When compared to existing standard testing methods (such as enzyme immunoassay [EIA]), the use of these approaches offers a significantly greater level of sensitivity and specificity. 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, 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) (16). The strength of NAT lies in its capacity to identify viral genomic nucleic acids directly rather than indirectly detecting the presence of antibodies. According to Lee and Allain7, the effectiveness of such screening depends on the population's infection prevalence and the window period's length. Compared to HBV (56 days) and HIV (16 days), HCV has a higher prevalence and a longer window period (80 days) in most Western countriesThis is why the deployment of this blood screening strategy places the primary emphasis on NAT detection of HCV. The NAT procedure for HIV-1 and HCV in donor blood will follow a three-step process under the method created by Gen-Probe, Inc. (San Diego, Calif.): sample preparation, HIV- 1 and HCV RNA target amplification, and detection of the amplified products (amplicons). In order to denature proteins, solubilize the viral envelope, and release viral genomic RNA, pooled plasma samples from donors are subjected to a detergent treatment during sample preparation. The RNA targets of HCV or HIV are hybridised with oligonucleotides that are identical to highly conserved sections of the HCV genome and HIV polymerase. A magnetic field is used to pull these hybridised targets away from the plasma once they have been adsorbed onto magnetic microparticles. The HIV-1 and HCV targets are amplified via transcription-mediated amplification, which employs a reverse transcriptase and an RNA polymerase for the amplification procedure. The amplicon is then hybridised with a single-stranded nucleic acid probe that is complementary to it in order to perform detection. The existence of chemiluminescent signals generated by the hybridised probes is determined using a luminometer.The presence of HIV or HCV genomes can be found using this common multiplex assay, however it is unable to distinguish between the two. In order to ascertain if the samples identified as reactive in the multiplex assay are positive for HIV, HCV, or both, discriminating assays are run on them. The multiplex assay's core methodology is also used by these selective assays. However, instead of working together as in the multiplex probe reagent, HIV-specific and HCV-specific probe reagents are utilised individually. Roche Molecular Systems created a substitute strategy. There are five main steps that make up the COBAS AmpliScreen HCV Test:

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 COBAS AmpliScreen HCV Test is used in conjunction with two specimen-processing techniques: the Multiprep procedure, which 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, which is used to test individual samples to find the positive specimen(s) in the primary and secondary pools (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 a number of 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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