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“Blood and Blood Products for Dummies”

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BLOOD DONATION TO STORAGE

A: Donation:

At the time of blood donation, two types of products are collected:

- Whole Blood and
- Products of apheresis
  (Definition of apheresis: the removal of one component of blood and the return of the remaining components to the donors. e.g. single donor platelet concentrate)

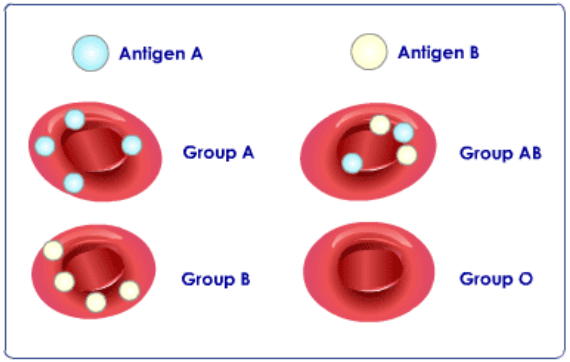
B: Mandatory Tests:

i. Red cell serology:

There are a total of 30 human blood groups that are recognized by the International Society of Blood Transfusion. Blood types are inherited. The two most important ones are:

- ABO System:

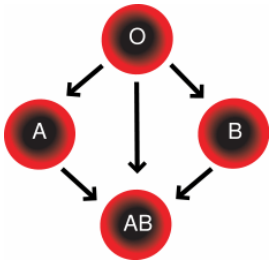
The ABO system is the most important blood group system in human blood transfusion. Red blood cells express a surface antigen (Ag) either A, B and A & B or no Ag at all. The body then develops antibodies (Ab) to the antigen that it lacks, within the first year of life.



Group A: lacks the B antigen and therefore develops anti-B.
Group B: lacks the A antigen and therefore develops anti-A.
Group AB: Doesn't develop any Ab.
Group O: lacks both A & B antigen and therefore develops anti-A and anti-B.

These antibodies are of the Immunoglobulin M (IgM) class. Determination of a patient's correct blood group is important because the most serious blood reactions occur with accidental transfusion of ABO-incompatible Blood.

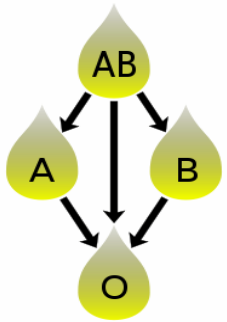
Red Cell Compatability



Group O donor red cell concentrate (RCC) can be given to O, A, B, and AB. It is therefore often referred to as a universal donor. In addition to donating to the same group, RCC from donors of group A and B type can be given to patients with AB blood type.

Plasma Compatibility

However it works conversely with the compatibility of the plasma of these patients with the different ABO blood groups.



Plasma from Group AB patient, because it doesn't include red blood cells expressing the specific blood group Ag and they don't have anti- A and anti-B antibodies , can be given to patients with blood group O, A, B and AB.

Plasma from group A and B, in addition to donating to the same group, can be given to group O.

- Rhesus Antigen System:
  This is the second most important blood group system in human blood transfusion.
  85% of individuals possess the D antigen and are classified as Rh+.
  The remaining 15% who lack the D antigen are classified as Rh-.
  Antibodies to the D antigen are not naturally occurring. Rh- individuals may become sensitized by exposure to the D antigen (e.g. Foetomaternal transfusion of blood during pregnancy), resulting in the development of Ig G anti-RhD. 60-70% of Rh- recipients are immunized (i.e. produce anti-D) if they are given a blood transfusion with Rh+ blood.

  Rh- blood from first time donors is not issued unless it is subjected to two independent D blood group tests and both have tested negative for D red cell antigen.

  Repeat donors who tested Rh+ do not need to be retested. Their unit of blood can be labeled as Rh+.

  Tabulated below is the red blood cell compatibility incorporating the ABO and Rh blood type and assuming the absence of atypical antibodies.

Recipient[1]	Donor[1]							
	O-	O+	A-	A+	B-	B+	AB-	AB+
O-	✓							
O+	✓	✓						
A-	✓		✓					
A+	✓	✓	✓	✓				
B-	✓				✓			
B+	✓	✓			✓	✓		
AB-	✓		✓		✓		✓	
AB+	✓	✓	✓	✓	✓	✓	✓	✓

Blood from donors of group O- blood can be given to all patients.
Patients with blood group AB+ can receive blood from all donors.

Incidence of the different ABO and Rh blood groups in South Arica.

Blood Group	Rh Positive	Rh Negative	Total
O	39%	6%	45%
A	32%	5%	37%
B	12%	2%	14%
AB	3%	1%	4%
Total	86%	14%	100%

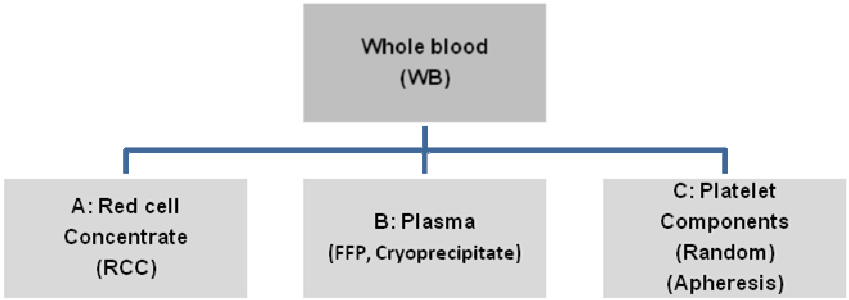
ii. Screening tests for transfusion transmissible diseases:

- Hepatitis B surface antigen (HBsAg).
- Antibodies to Hepatitis C Virus (Anti-HCV).
- Antibodies to HIV1 & 2 (Anti-HIV1 & 2).
- Serological test for Syphilis.
- In addition NAT (Nucleic Acid Amplification Testing) for the screening of: Hepatitis B & C and HIV1.
  NAT^2: This technology has been implemented by the South African National Blood Services since October 2005, and it was the first country in the world to implement it on such a large scale (i.e. each individual donor unit is tested with NAT). NAT decreases the window period for HIV, Hepatitis B & C viruses. Conventional serology technology, which is conducted in conjunction with NAT, detects the antigen or antibodies of the virus, but these can take time to develop and is only detected when it reaches a certain level. NAT looks for the RNA or DNA of the virus in the blood and can detect it even if there were a few virus particles in the blood sample. The window periods have been shortened for:
  - HIV from 16 to 5.6 days
  - HBV from 59 to 34 days
  - HCV from 82 to 23 days

C: Component Therapy

The two products of blood donation are whole blood and products of apheresis.

i. Whole Blood:



5% of the total blood that is donated is used as whole blood. The rest, 95%, is separated into various components. Clotting factor levels and platelet function decreases, within hours, after collection. Therefore, blood components need to be separated within 18 hours from collection.

Whole blood, which has a haematocrit of 40%, is centrifuged in a closed sterile system, resulting in its separation into:

- Red Cell Concentrate, which has a haematocrit of 70%,
- Platelets and
- Plasma which is fractionated into many products:
  - Fresh Dried Plasma/ Fresh Frozen Plasma
  - Cryoprecipitate
  - Cryosupernatant
  - Albumin
  - Immunoglobulins
  - Factor VIII and IX
  - Hyperimmune globulins (e.g. Rabies, Tetanus and Hepatitis B)

Red Cell Concentrate:

- **Red Cell Concentrate (Non-leucodepleted)**
  The red cell concentrates have a volume of 300-350ml excluding the 111mls of preservative solution. The haematocrit is between 0.55-0.70. One unit of red cell concentrate can be expected to increase the haemoglobin level of an average adult by 1-2g/dL.

- **Leucodepleted Red Cell Concentrate**
  Leucocytes in blood components are responsible for a number of adverse effects associated with blood transfusions. In many instances the pathogenesis has not been elucidated precisely, but it is likely that it is immunologically mediated.
  From the medical literature:
  - There is good evidence to support the avoidance of febrile non-haemolytic transfusion reactions (FNHTRs) by leucodepletion[4, 5]
  - Leucodepletion of platelet concentrates will reduce the incidence of platelet refractoriness to platelet transfusions[6]
  - Leucodepletion significantly reduces the risk of transfusion-transmitted CMV infection in susceptible individuals[7]
  - The evidence for reduction in postoperative infection is not consistent[8-11]
  - The evidence for reduction in cancer recurrence is not consistent[12]
  - Although meta-analyses do not provide convincing evidence of an overall reduction in postoperative mortality for leucodepleted products, subgroup analyses suggest a benefit for seriously ill and cardiac surgery patients[9, 11]
  - An association with reactivation of viral infections (HIV and CMV) and non-leucodepleted components has not been demonstrated[13]
  - Sensitization to transplant antigens can be ameliorated by leucodepletion where (human leucocyte antigen -HLA) allo-immunisation is important[14]
  - Leucodepletion may reduce prions in blood components but there is as yet no evidence that leucodepletion will avoid transmission of Creutzfeldt-Jakob disease (vCJD) by blood components[15]

A number of countries in the first world have adopted a policy of routinely leucocyte-depleting all red cell and platelet components by including pre-storage leucodepletion filtration in the component manufacturing process – so-called universal leucocyte reduction (ULR).

This however is a very costly process. It would require an increase of 24% of the SANBS budget. Given the competing health priorities in South Africa and weighing the cost benefit ratio of ULR, South Africa employs the selective leucocyte depletion of blood components.

The policy for selective leucocyte depletion of blood components makes the following recommendations:

1. All standard red cell concentrate in South Africa has its buffy coat removed. (A buffy coat is the ±0.5cm layer that sits on top of the red cells following centrifugation of a donated blood unit and it consists largely of young red cells (reticulocytes), platelets and leucocytes. This results in a decrease of leucocytes by 70-80% from the original whole blood.)
2. Random donor platelet concentrates will be prepared from buffy coats.
3. Single donor platelet concentrates collected by apheresis must incorporate a leucocyte-depletion process.
4. Patients on chronic transfusion regimens should receive leucodepleted products.
5. Patients at risk for CMV infection should receive leucocyte-depleted products.
6. Organ and stem cell transplant patients should receive leucocyte-depleted products.
7. Infants less than 1 year old should receive leucodepleted products.
8. Cardiac surgery and critically ill patients in ICU should receive leucocyte-depleted products.
9. Pre-storage (< 48 hours after donation) leucodepletion in blood-processing laboratories is recommended since there is better quality control of the finished product and there is some evidence to suggest that cytokines may accumulate with storage.[14] If this product is unobtainable it is recommended that the freshest units available be filtered in the blood bank for immediate use. Bedside leucodepletion filters should only be utilized when neither of the former two options is available.

- **Washed Red Cells**
  The red cell concentrate with the plasma and buffy coat removed is suspended in isotonic saline and centrifuged; the saline wash is removed and the red cells are then re-suspended in isotonic saline. They need to be used within 24 hours to decrease the risk of bacterial contamination and transmission, as these cells are manipulated in an open system.

Indications for washed red cells:

- Patients who have experienced severe, recurrent, allergic transfusion reactions not prevented by antihistamines.
- Patients with known IgA deficiency, who have developed IgA antibodies, may experience an anaphylactic reaction if transfused with blood products containing plasma.
- Neonates with necrotizing enterocolitis (NEC). The Thomsen-Friedenreich cryptantigen (TCA) is located on the surface of all red cells, but is concealed by a layer of neuraminic acid. When bacteria that produce neuraminidase disrupt this coating, the TCA can be exposed and activated. If blood products containing antibody to the TCA are subsequently administered, haemolysis can result. The bacteria causing NEC, causes the exposure of TCA.[16]
- The plasma potassium concentration in gamma irradiated blood increases significantly after 12 hours. Patients in whom this might be clinically significant may require washed red cells.
- Paroxysmal nocturnal hemoglobinuria (PNH) is an uncommon, acquired stem cell disorder primarily affecting red cells that have an abnormal sensitivity to complement lysis. For years (from the 1940's), these patients have been transfused with washed red cells to minimize haemolysis after transfusion. From the Mayo Clinic, Blood Bank and Blood Transfusion Services statistics, during the period 1950-1987 (23 patients), only one documented episode of post-transfusion hemolysis related to the underlying diagnosis of PNH was found and this was in a patient with AB + blood type transfused with O type whole blood that contained ABO incompatible plasma. The recommendation was therefore that the use of washed red cells in patients with PNH is not necessary, provided the donor red cells are of the same ABO group as the patient being transfused.[17] The SANBS has adopted this policy.

- **Irradiated Red Cells (also whole blood and platelets)**
  Blood and its components are irradiated in order to reduce the risk of Transfusion Associated Graft Versus Host Disease (TA-GVHD). TA-GVHD is a potential complication of blood transfusion. Usually, lymphocytes are identified as foreign and destroyed by the recipient's immune system.
  However, in situations where:
  - the donor and recipient share a Human Leucocyte Antigen (HLA) haplotype, as can occur in directed donations from first-degree relatives (The immune system uses the HLA to differentiate self cells and non-self/foreign cells. Any cell displaying that person's HLA type belongs to that person and is therefore a self cell. In directed donations from first degree relatives, where the donor is homozygous and the recipient is heterozygous, the recipient's lymphocytes doesn't recognize the donor lymphocytes as foreign and are therefore unable to destroy them)
  - or the recipient is immunocompromised

  the recipient's immune system is not able to destroy the donor lymphocytes. As a result, the donor T lymphocytes mount an immune response against the recipient's lymphoid tissue with the skin, gastro-intestinal tract, liver, spleen and bone marrow being particularly affected.
  Gamma irradiation is currently the only recommended method for the prevention of TA-GVHD. The cells are exposed to radiation of 25-50Gy which inactivates the T lymphocytes. Blood may be irradiated any time up to 14 days after collection and thereafter stored for a further 14 days after irradiation.

- **Frozen Red Cells**
  Selected rare donations are stored at -80ºC. They have a 10 year expiry date whilst frozen. Rare blood is blood that is negative for multiple blood group antigens or lacks a high frequency antigen. Occasionally patients may have an antibody directed against a high-frequency antigen that is present on the red cells of most donors. These patients benefit from transfusion from these rare donations.

Plasma (FFP/FDP & Cryoprecipitate)

- **Fresh Frozen Plasma (FFP):**
  FFP is separated from whole blood within 18 hours from donation by the centrifuge of whole blood in a closed sterile system and freezing the plasma to below -18ºC. It contains clotting factors at physiological levels.
  Donor Plasma Retest Quarantine Program was initiated by the SANBS 5 years ago whereby the FFP is stored and kept until the donor returns for a repeat donation. If the donor still tests negative for infectious diseases, the FFP is dispensed. If the donor doesn't return or tests positive, the FFP is discarded. This is feasible as FFP is stored for up to 2 years.
  It has a mean volume of 250ml

- **Freeze Dried Plasma (FDP):**
  It is produced by the National Bioproducts Institute (NBI). The NBI gets its pooled fresh human plasma from the SANBS having undergone all the tests mentioned above. However the FFP doesn't participate in the Donor Plasma Retest Quarantine Program. It is re-tested via serological testing for: HBsAg, anti-HCV, anti-HIV 1 & 2 and syphilis. The NAT for HBV, HCV, and HIV 1 is also repeated and includes a NAT for Hepatitis A and Parvovirus B19. It then undergoes a pathogen inactivation process using a solvent detergent, which inactivates the lipoprotein-coated viruses such as HIV, HBV, and HCV. Each 100ml contains 4-6g proteins and a minimum of 0.4IU/ml of each coagulation factor.
  It is available in 200ml or 50ml.

- **Cryoprecipitate:**
  It is produced by thawing FFP, which is stored at -18ºC, to 0-4ºC and spinning it through a centrifuge to remove the majority of the plasma. The insoluble fraction that remains is suspended in the remaining plasma or normal saline. It has a mean volume of 0-15ml.
  It contains:
  - Factor VIII and von Willebrand Factor ± 100 IU per unit
  - Fibrinogen 150-250mg per unit

- Fibronectin
- Factor XIII

It is also on the Donor Plasma Retest Quarantine Program (as described above)

- **Cryosupernatant**
  It is the plasma that is removed from the manufacture of cryoprecipitate. It contains plasma proteins and all the other clotting factors and can be used for all the same indications as FFP except, Haemophilia A and von Willebrands Disease. It is the component of choice in some haematology units for the exchange transfusion in patients with Thrombotic Thrombocytopaenic Purpura.

Platelets

Random Donor Pooled Platelets are prepared from the buffy coat of whole blood donations within 8 hours of collection. Five individual donations are pooled together to produce one platelet concentrate. Each unit contains a minimum of >2.4 x 10^{11} platelets with a volume of 200-300mls. One pooled platelet increases the platelet count by 20-40 x 10^{9}/L, the increment will vary depending on the patient's clinical condition e.g. DIC, septicaemia.

ii. Products of Apheresis:

Apheresis is the removal of one component of blood and the return of the remaining components to the donors. e.g. single donor platelet concentrate, FFP. It takes place at the bedside at the time of donation. And has the advantage that the complete dose of a product is derived from one donor.

For example the single donor platelet concentrate has a minimum yield of 2.4 x 10^{11} and a volume of 200-300mls which is the same as the pooled platelets from multiple donors.

It is recommended for patients who require long term platelet support e.g. Leukaemia, it decreases their exposure to multiple donors.

D: Storage

Blood donations prior to processing are stored at 1-6ºC within 8 hours.
After processing:

- Whole blood is stored at 1-6ºC
- Red Cell Concentrate:

Red Cell Concentrates are stored at 1-6ºC for up to 42 days.
Donated blood is collected into a solution containing sodium citrate. Citrate is a stable, minimally toxic anticoagulant with pH buffering prosperities. Citrate is metabolized in the Krebs cycle and after transfusion, is rapidly metabolized by most cells in the body, particularly the liver, muscle and renal cortex. However certain clinical scenarios may place the patient at risk for citrate toxicity manifesting as hypocalcaemia and its complications as citrate chelates plasma ionized calcium. Some of these conditions are liver disease, hypothermia and massive blood transfusions.

The red blood cells are then stored in a preservative solution that contains:

- Glucose which is a source of fuel for the red cells and allows them to continue glycolysis and maintain sufficient concentrations of ATP to ensure continued red cell metabolism and subsequent viability during storage.
- Adenine which allows the red cells to resynthesize adenine triphosphate (ATP) which is required to fuel metabolic reactions. Without adenine, red cells gradually lose ATP and their ability to survive after transfusion.
- Saline adjusts osmotic pressure
- Mannitol reduces haemolysis

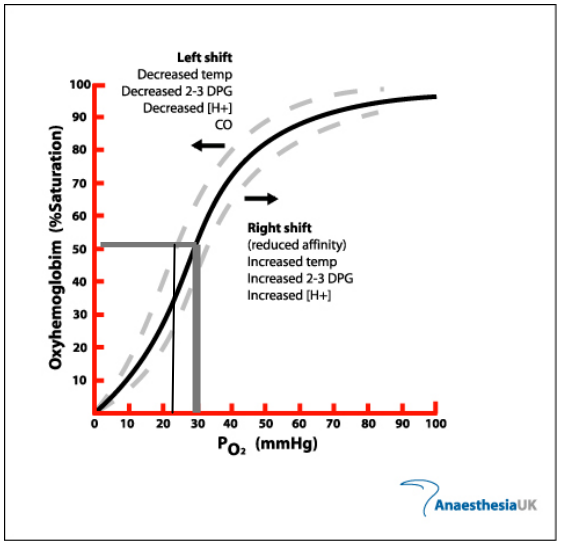
The storage at 1-6ºC assists the preservation of the red blood cells by slowing the rate of glycolysis by approximately 40 times the rate as that at normal physiological body temperature.

This time of 42 days is determined by the requirement that at least 70% of the transfused red blood cells remain in circulation for 24 hours after transfusion. Red blood cells that survive 24 hours after the transfusion disappear from the circulation at a normal rate. Those that don't survive are removed from the circulation by the recipient.

There is increasing evidence that stored red blood cells undergo time-dependent metabolic, biochemical and molecular changes. The Storage Lesion refers to the constellation of time dependant changes occurring in red blood cells. Some of these changes are irreversible and reduce post transfusion survival.

Some clinically significant storage lesions are:

- Electrolyte changes
  As discussed above, red cell concentrates need to be stored at 1-6ºC, however at these temperatures, the sodium-potassium pump is essentially non-functional and intracellular and extracellular levels of sodium and potassium equilibrate with time. Therefore the plasma K^+ levels increase and Na^+ levels decrease with increasing storage time. The K^+ load is rarely a clinical problem, however it may be in the setting of pre-existing hyperkalaemia.[18]



- Decrease in 2.3 Diphosphoglycerate (2.3 DPG)
  (Oxygen haemoglobin dissociation curve: Shifts in the curve are quantified by P_{50} which is the partial pressure of O_2 at which Hb is half saturated with O_2 at 37ºC and a pH of 7.4. With a left shift in the curve, the P_{50} is lower, which indicates that a lower than normal O_2 tension saturates Hb. As occurs with a decrease in 2.3 DPG where there is an increased affinity of O_2 for Hb.)

  Adequate levels of 2.3 DPG facilitate O_2 unloading from Hb particularly in the microcirculation where the partial pressure of O_2 is low and the majority of the O_2 is transferred to the tissue. With increasing length of storage, there is a decrease in 2.3 DPG, resulting in a shift of the O_2 haemoglobin dissociation curve to the left, as described above, where there is an increased affinity of O_2 for Hb hampering the delivery of O_2 to the tissues. However, clinical evidence to support this hypothesis is not consistent.

  This could be due to the fact that after transfusion, levels of 2.3 DPG are regenerated in vivo with approximately 50% being regenerated within 7 hours although full restoration of red blood cell 2.3 DPG can take up to 72 hours. It could also be due to the fact that patients who require blood transfusions are hypoxic, and have lactic acid production with a low pH and thus the O_2 dissociation curve is shifted to the right, increasing tissue O_2 delivery. They also increase their cardiac output, thereby increasing their O_2 delivery.

- Loss of deformability
  Red blood cells normally have a biconcave disc shape which is deformable allowing them to easily navigate the varied blood vessels in the body. However in time, with storage, the red blood cells gradually lose their deformability. There are so far only 2 randomized controlled trials in adults examining the effects of the storage time of transfused red blood cells. The one by Marik and Sibbald, found a decrease in gastric intramucosal pH (using gastric tonometry) in critically ill patients who had a transfusion of blood older than 20 days. It was postulated that the loss of deformability of stored red blood cells with time might contribute to microcirculatory occlusion in some organs thereby

promoting tissue ischaemia. However, in the other trial, Walsh et al. were not able to find a decrease in gastric mucosal pH with transfusion of blood more than 20 days old. The literature is thus conflicting and further studies are needed to shed more light on this area.[20, 21]

- Packaging of red cell concentrate
  The plasticizer (DEHP diethylhexly phthalate) has been shown to leach from the plastic container into stored blood and as storage time increases, the amount of DEPH detectable increasesd from 6.8 to 36.5µg/ml. The potential toxicity of transfused DEHP remains under investigation and to date, there are no studies indicating clinically significant effects.

- S-nitrosylated Haemoglobin (SNOHb) Hypothesis
  It has recently been discovered that Hb may have an autoregulatory role. Nitric oxide, an important regulator of vasomotor tone, binds to two sites on the Hb, one on the haem iron and the other on the cystein residue as SNOHb. At the level of the microcirculation, SNOHb donates it's NO causing vasodilatation. This occurs in proportion to the degree of tissue hypoxia. Thus suggesting that Hb may potentially autoregulate blood flow. With storage of red blood cells, even as early as 3 hours after collection, there is a decrease in SNOHb and thus Hb vasoactivity also declines. The addition of s-nitrosothiol (SNO) to stored blood is currently being investigated in the hope of increasing SNOHb. However clinical evidence for the significance of the decrease in SNOHb in stored blood is still lacking.[25, 26]

In recent years, numerous observational studies have highlighted the possibility that storage lesions may be responsible for transfusion associated complications.

TABLE 3. Association of RBC storage with clinical outcomes: observational studies

Study: first author, year	Population	Design	Number	Outcomes
Basran, 2006[115]	Cardiac surgery	Retrospective cohort	321	Increased mortality associated with mean age of RBC units and age of oldest RBC unit
Leal-Noval, 2003[104]	Cardiac surgery	Prospective cohort	897	Increased pneumonia associated with oldest unit
Keller, 2002[117]	Trauma	Retrospective cohort	86	Increased LOS with number of RBC units >14 days
Offner, 2002[105]	Trauma	Prospective cohort	61	Increased infections with number of units >14 and 21 days
Vamvakas, 2000[118]	Cardiac surgery	Retrospective cohort	268	No change in LOS or mechanical ventilation associated with age of RBC units
Vamvakas, 1999[103]	Cardiac surgery	Retrospective cohort	416	Increased risk of pneumonia with median age of transfused RBC units
Zallen, 1999[116]	Trauma	Prospective cohort	63	Increased multiorgan failure with number of units >14 and 21 days
Purdy, 1997[114]	Septic ICU	Retrospective cohort	31	Increased mortality associated with older median age of RBC units
Martin 1993[99]	ICU	Retrospective cohort	698	Increased LOS with number of units >14 days

Tinmouth et al Transfusion 2006[22]

LOS: length of stay

There is laboratory evidence suggesting that prolonged red blood cell storage may be deleterious and the above observational studies report a number of associations between prolonged storage and adverse clinical outcomes such as mortality and organ failure. Only two clinical trials, thus far, have been published assessing the clinical consequences of prolonged red blood cell storage (discussed above), but reach no consensus. Further clinical studies are needed to settle this heavily weighted question.

- FFP, Cryoprecipitate and Cryosupernatant: stored frozen at -18ºC for up to a year and -25ºC for up to 2 years

- Platelets:

Platelets are stored with continuous agitation at for up to 5 days They obtain most of their energy by oxidative phosphorylation in their mitochondria. Decreased oxygen tension suppresses oxidative phosphorylation and anaerobic glycolysis becomes more important for energy production. This results in the production of lactic acid as a byproduct. In the presence of sodium bicarbonate the lactic acid and the sodium bicarbonate will form: sodium lactate and carbonic acid. Carbonic acid dissociates into H_2O and CO_2, the latter of which is released from the gas permeable platelet bag. When the sodium bicarbonate is depleted, the

accumulation of lactic acid rapidly lowers the pH. A pH of 6.0-7.8 is critical in maintaining the viability of platelets and as a result, with this drop in pH, platelet viability decreases. Adequate gas exchange is essential to maintain an adequate pH and ensure platelet survival. Therefore during storage, platelets are agitated in a gas permeable bag to facilitate the influx of O_2 and the efflux of CO_2.[23]

Up to 24 hours without agitation, however, has not been shown to adversely affect platelet survival. Hunter S. et al. from the American Red Cross Blood Services found that disruption of agitation resulted in the accumulation of lactic acid in proportion to the number of platelets and duration of interruption. PO_2 increased suggesting a decrease in O_2 utilization. And there was no evidence of platelet damage until the pH < 6.5 which was not reached after only one day of interruption of agitation.[24]

Platelets are stored at 20-24ºC. Cold temperatures trigger platelet microtubule disassembly which results in platelet dysfunction.

The platelet storage lesion: numerous morphologic, biochemical and functional derangements occur during platelet storage. Platelets tend to become activated during storage. Over time, an increasing fraction of platelets in a concentrate will change from a discoid (resting) shape to spherical. Mediators of thrombosis such as ß-thromboglobulin and platelet factor 4 accumulate in the storage medium, reflecting granule release. Platelet surface levels of P-selectin (CD62P), another platelet activation marker, also increase during storage. Finally, functional derangements are observed in vitro. Platelet aggregation responses to a number of agonists drop significantly during storage. Still, beyond a few extreme cases (e.g., pH < 6.0) the significance of the in vitro abnormalities observed following platelet storage remains unclear. However there is good evidence suggesting that many of the platelet storage abnormalities seen in vitro are actually reversible upon transfusion.[25]

BLOOD SAMPLE FROM PATIENT TO BLOOD BANK

A: Ordering Priorities:

NO CROSSMATCH

- Blood can be issued from blood bank within 5-10 minutes
- This option is used in extreme emergencies.
- No blood group typing or crossmatch is carried out before the blood is dispensed and group O blood issued.
- There is a risk that the patient may have an irregular blood group Ab (may result in a haemolytic transfusion reaction)
- Standard compatibility tests are done afterwards.
- Emergency blood banks have been established in some hospitals, usually the more rural hospitals where they have a special emergency blood fridge that are only stocked with group O+ and group O- blood. Anti-D kits are available for rapid Rh typing of the patient requiring transfusion. Otherwise O- blood should be given to females before or during childbearing age.

CROSSMATCH – EMERGENCY

- The blood is available within 20-30 minutes
- Group specific blood is issued after the patient's ABO group and Rh type have been confirmed and the blood has been deemed compatible in the initial phase of crossmatch.
- The full crossmatch and Ab screen are completed after the blood has been dispatched.
- There is a risk that the patient may have an irregular blood group Ab (may result in a haemolytic transfusion reaction)

CROSSMATCH – STANDARD

- The blood is available after 2 hours
- Blood is fully crossmatched using standard compatibility testing methods.

TYPE AND SCREEN

- ABO grouping, Rh typing and antibody screening tests are performed on the specimen.
- Compatibility testing is only commenced on written or verbal request and is available on:
  - EMERGENCY in 20-30 minutes
  - STANDARD after 2 hours

CROSSMATCH AND HOLD

- The required number of units of blood are fully crossmatched and retained in blood bank for 24 hours, awaiting instructions for issue.
- The blood is available for issue immediately on request.

BLOOD ON RETURNABLE BASIS

- It needs to be specifically requested on the blood request form.
- The blood is dispensed in a special hamper where each unit of blood is compartmentalized, kept cooled and sealed with a cable tie.
- If any of the units are unused they can be returned to the blood bank for re-issue only if:
  - The cable tie of that compartment is still intact
  - The blood reaches the blood bank within 12 hours of issue
  - The blood temperature is <10ºC

B: Compatibility Testing

When the blood specimen drawn from the patient reaches the blood bank and blood is requested, the following tests are carried out:

- First the specimen is tested for ABO and Rh blood group and the antibody screen is initiated.
- The donor unit's ABO and Rh group is re-tested.
- Thereafter a crossmatch is carried out, which is a test of the compatibility between recipient serum and donor red blood cells. A crossmatch is essentially a trial transfusion in a test tube. The donor red blood cells are mixed with recipient serum to detect a potential for a serious transfusion reaction. It can be completed in

approximately 60 minutes and is carried out in 3 phases:

- First Phase

It takes approximately 1-5minutes.
It is conducted at room temperature.
It is a check against errors in ABO typing; detecting ABO incompatibilities and it also detects incompatibilities caused by naturally occurring Ab in the MN, P and Lewis system

- Second Phase: Incubation Phase

  It takes approximately 40-65 minutes.
  The phase one reactants are incubated at 37ºC in Albumin or a low ionic strength salt solution. The reason for this is that these solutions aid in the detection of incomplete Ab or Abs that are able to attach to a specific Ag but are unable to cause agglutination in a saline suspension of red blood cells.
  This phase primarily detects Ab in the Rh system.
  The incubation period is of sufficient duration to allow Ab uptake sensitization by cells so that incomplete Ab missed in this phase can be detected in the subsequent antiglobulin phase.

- Third Phase: Indirect Antiglobulin Test (Indirect Coombs Test)

  It detects the presence of Ab-Ag reactions. It involves the addition of Coombs reagent (anti-human Ab) to the incubated test tube where, if there were Abs in the recipient's serum to the Ag expressed on the donor red blood cells, they would have formed an Ab-Ag complex on the surface of the red blood cell.
  Antihuman Ab gets attached to this complex on the red blood cells, causing agglutination.
  This phase detects Ab in low titres, most incomplete Abs (i.e. those that don't agglutinate easily) in the blood group systems including Rh, Kell, Kidd and Duffy blood group systems.

- The Antibody Screen:
  This screen is used to detect unexpected Ab.
  The test also contains 3 phases and is similar in length to the crossmatch.

The screen is a trial transfusion between the recipient serum and commercially supplied red blood cells that are specifically selected to contain optimal numbers of red blood cells Ag that will react with Ab that commonly cause haemolytic transfusion reaction.

With regards to platelets and FFP, it is recommended that group specific concentrates be administered as there may be a few red blood cells in the platelet concentrate. And it is for this reason too that Rh- platelets be administered to females below and during the childbearing ages. If this is not possible, a different ABO group may be given provided the anti-A and anti-B titres are low and administration of anti-D immunoglobulin should be considered.

FDP is considered a universal donor and doesn't require blood group matching.

THE TRANSFUSION OF BLOOD

A: Checking the blood prior to transfusion:

1. Make a positive identification of the patient using the patient's name, surname and hospital number by directly asking the patient, if awake, or check the label on the name bands attached to the wrist, if in theatre. Then cross check this with the details on the certificate of compatibility on the unit of blood and the transfusion form.
2. Check the compatibility of the patient's blood group and the donor blood group (as discussed earlier).
3. Check the expiry date.
4. Inspection of the:
   Blood:
   - Leaks – especially in the port areas by inverting and applying light pressure to the unit.
   - Colour – the colour of a red cell concentrate unit should not be significantly darker than the attached segments. Plasma in the unit should not be murky, purple, brown or red.
   - Clots
   - Excessive air

Platelets: units will be cloudy yellow or straw coloured and should not contain grossly visible aggregates
Thawed FFP will be clear with the colour varying from yellow to straw coloured.
Cryoprecipitate will usually be a cloudy straw colour.

All the information is read out aloud by both attendants checking the blood. One of whom should be either a professional nurse or a doctor.

B: Filters and Administration Set:

All blood and blood products need to go through a filter to prevent the transfusion of clots and coagulation debris. The blood transfusion sets have a 170-240µm mesh filter that should be covered with blood to ensure that the full filtering area is used.

Using a platelet giving set is ideal for the transfusion of platelet concentrate. In emergencies, it is acceptable to use a standard blood transfusion set, however it may result in a greater loss of platelets due to a larger surface are for adhesion.

Blood that is leucodepleted by the blood bank does not need to be transfused through a bedside leucodepletion filter, if it is; it results in a further decrease in the red blood cells received by the patient.

Administration sets should be changed:

- When there is a transfusion reaction.
- Between red cell transfusions of different ABO groups, and between red cell transfusions and other blood product transfusions.
- Before transfusing other fluids.
- Every 12-24 hours or after 4 units of blood in patients requiring long term transfusions as material remaining in the filter may act as a culture medium for contaminating micro-organisms.

C: Transfusion

Blood:

- Should be transfused within 6 hours of opening the unit.
- Should be completed within 6 hours of warming the unit.
- Should not be heated to >37ºC
- No medication should be added to the blood, because of the risk of bacterial contamination, the therapeutic level of the drug may not be reached as the blood is administered slowly and for example dextrose may cause lysis/aggregation in the transfusion set.
- The only fluid that may be infused concurrently with blood is: normal saline, 4% Albumin, plasma protein fractions, ABO compatible plasma. There is a theoretical risk of clotting in the transfusion set when Ringers Lactate and blood are transfused concurrently because the citrate in blood reacts with the calcium in the Ringers Lactate. However it appears that this is not a major clinical concern.[28]

Platelets:

- Are stored at room temperature and usually don't need to be warmed.
- Should be transfused through a platelet giving set over 15-30 minutes.

FFP and Cryoprecipitate:

- Are thawed from their storage temperature of -18ºC or -25ºC to between 30-37ºC before being dispatched by blood bank.
- Maximum delay of transfusion, after thawing is 4 hours.
- Should be transfused as rapidly as possible (15-20 minutes)

FDP:

- Should be infused immediately after reconstitution, once all the powder has dissolved.
- The same concern with citrate in the FDP solutions and calcium containing solutions apply here. (see above)

HIV TRANSMISSION AND BLOOD TRANSFUSION

It is thought that blood transfusions are responsible for up to 10-15% of HIV transmission in Sub Saharan Africa.[29] Some of the reasons for this is that blood transfusion services in these parts were poorly developed until the mid 80's just around the time when HIV was recognized seroepidemiologically.

In 1994 Sitas et al. found the likely rate of HIV infected blood in South African blood transfusion supply ranges from 1.1-3.9 / 100 000 units. The data was found to be comparable to developed countries.[30]

Since then, great progress has been made with improvement of tests to detect transfusion transmitted pathogens. Most recently in October 2005 NAT (described above) was introduced by the South African Blood Services and there has, as yet, not been a reported case of HIV transmission as a consequence of a blood transfusion since its implementation.

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