TRANSFUSION MEDICINE

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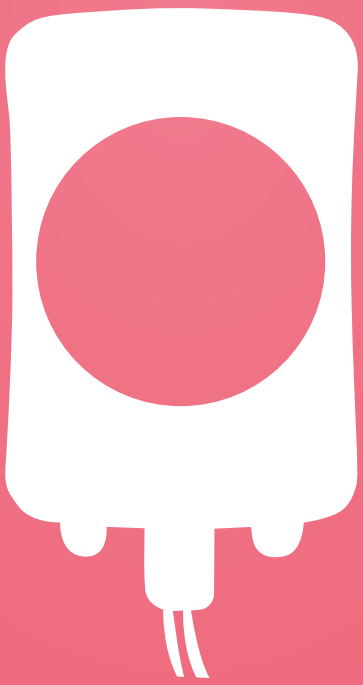
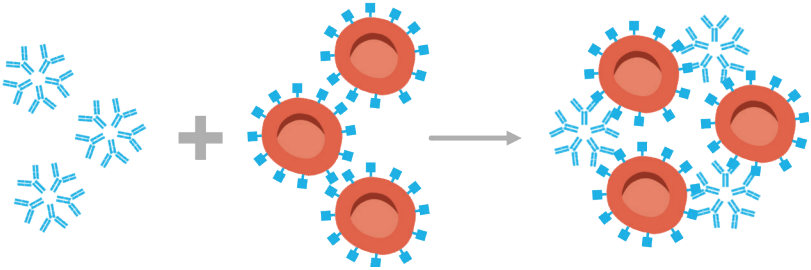
Chapter 1

WHAT IS BLOOD MANAGEMENT?

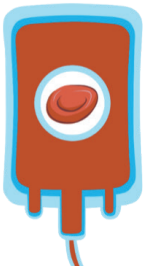


GETTING ACQUAINTED WITH BLOOD PRODUCTS

The breakthrough discovery of agglutinins by Karl Landsteiner, in the early 1900s, paved the way for modern transfusion medicine. Agglutinins, namely anti-A and anti-B, are naturally occurring anti-bodies that, if mixed with incompatible red blood cells, lead to agglutination and hemolysis.



Nowadays, we are able to safely transfuse specific blood components to patients in need. There are three groups of blood components:



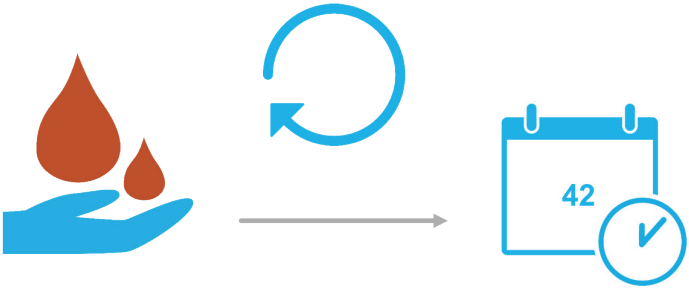
Red blood cells

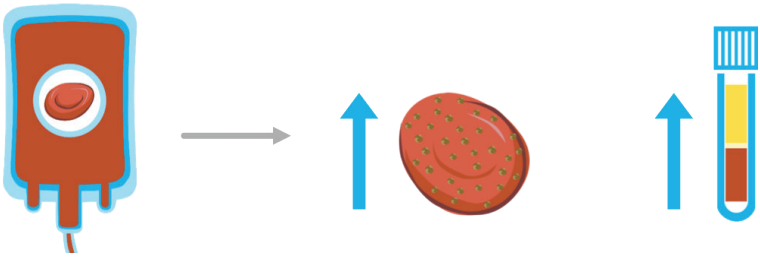
Platelets

Plasma

Red blood cells

One unit of red blood cells (RBCs) contains about 300–400 mL, including additive solutions. It must be stored at 2–6°C and expires approximately 42 days after donation. We call the period of time from donation to expiration the shelf life.





1 unit 1 g / dL 3%

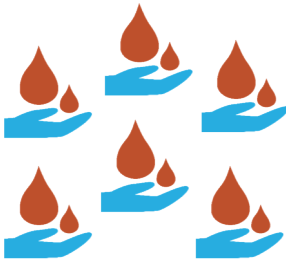
One unit of red blood cells increases the hemoglobin of an average-size, non-bleeding adult by about 1 g / dL, and the hematocrit by about 3%. One unit of RBCs also contains about 250 mg of iron. This is of interest for patients who receive RBC units regularly, like thalassemia patients. In these cases of iron overload, iron chelation therapy might be indicated.

Platelets

Platelets can be derived either from many donors, by whole blood donation, or from a single donor, by apheresis.

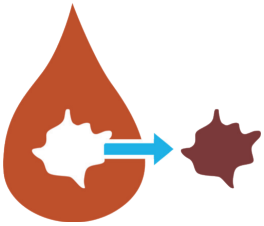
Random donor platelets

Random donor platelets are derived from many donors by whole blood donation. Each donor gives about 40–70 mL of plasma. For adults, 4–6 donations are usually pooled into one unit.

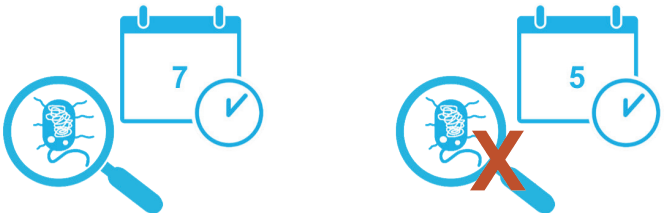


Single donor platelets

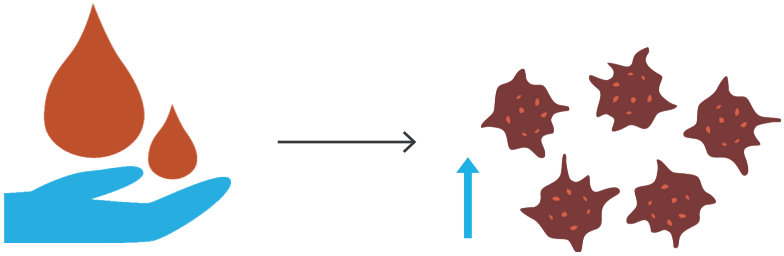
Platelets can also be derived from a single donor, by apheresis. These units contain about 100–500 mL of plasma. Nowadays, almost all platelet transfusions are apheresis, single donor platelets.



In general, platelets must be stored at room temperature (20–24°C) and must be gently agitated to maintain their function. If platelets are screened for bacteria, the shelf life is 7 days, if not, it's 5 days.



As a rule of thumb, one unit of single or random donor platelets increases the platelet count by about 30 000–50 000 / µL in adults.

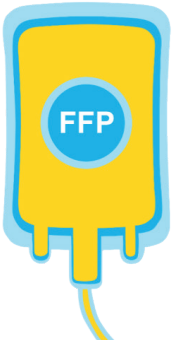


Fresh frozen plasma

Fresh frozen plasma (FFP) contains all coagulation factors.

One unit of FFPs contains about 200–300 mL of plasma. FFP units are stored at –18°C. They can be stored at this temperature for 3–4 years, depending on the product specifications. When thawed, the bag can be stored for another day at 1–6°C.

In general, a dose of 10–15 mL / kg is recommended in adults. For an adult weighing 70 kg that would be about 2–4 units, but more may be required depending on the clinical situation. The effectiveness is best evaluated by laboratory testing of coagulation function.

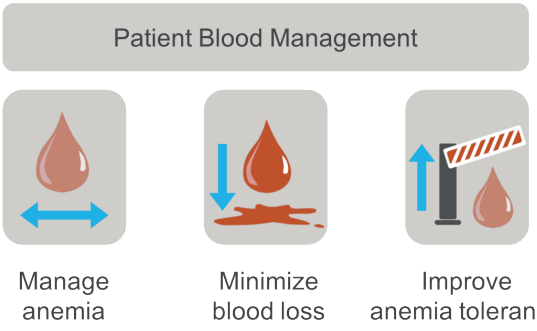


10–15 mL / kg

INTRODUCING
PATIENT BLOOD MANAGEMENT

Blood transfusion is the most common procedure performed during hospital stays in Western countries. Since transfusions are costly, put patients at risk for morbidity and even mortality, and supplies of blood products are finite, the rationale must be to perform transfusions only if necessary.

Patient Blood Management (PBM) is a concept in patient care, which promotes the safe and rational use of blood products. PBM focuses on managing or preserving the patient's own blood volume rather than simply resorting to, and relying on, donor blood. This can be achieved by preventing conditions that might otherwise result in the need for transfusion in the first place.



Restrictive versus liberal transfusion thresholds

A trial comparing a more liberal RBC transfusion strategy (with a typical transfusion threshold of hemoglobin of 9–10 g / dL) to a restrictive transfusion strategy (with a threshold of hemoglobin of 7 g / dL) showed that transfusing fewer RBC units not only led to reduced costs, but at the same time reduced patient mortality, the length of hospital stay, the number of hospital-acquired infections, and the incidence of heart attack and stroke. **(Reference: *Carson et al., 2013*)**

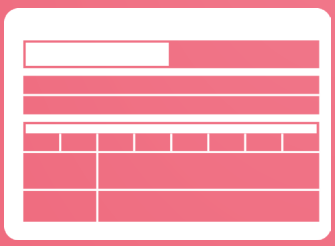
Thus, one important cornerstone of Patient Blood Management is to use restrictive, rather than liberal, transfusion thresholds.

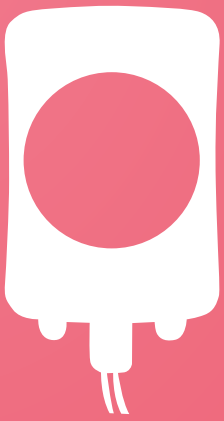
Examples of PBM strategies include

- Diagnosing and treating the cause of anemia before giving blood components (if clinically feasible)
- Using surgical techniques that are associated with decreased blood loss (e.g., laparoscopy)
- Assessing the patient's coagulation status and optimizing anticoagulant therapy

Chapter 2

ORDERING A TRANSFUSION





DETERMINING WHEN TO ORDER RED BLOOD CELLS

There is no single criterion to decide whether a unit of red blood cells (RBCs) is indicated for a given patient.

Various patient factors must be considered

- Symptoms and clinical status
- Bleeding status
- Comorbidities
- Hemoglobin levels
- Individual wishes

Hemoglobin levels help us to evaluate whether the given anemia is a risk for our patient, and whether the patient will benefit from a blood transfusion. In other words, we look for certain threshold hemoglobin levels below which we must consider blood transfusion. We distinguish a restrictive from a liberal transfusion threshold.

Restrictive versus liberal transfusion threshold

A **restrictive transfusion threshold** of 7–8 g / dL hemoglobin should be used for most hemodynamically stable medical and surgical patients.

A **liberal transfusion threshold** of 9–10 g / dL should be considered in patients

- Who are already symptomatic at those higher hemoglobin levels
- With acute coronary syndrome
- Who need massive transfusion
- At a very high risk of bleeding due to severe thrombocytopenia
- With chronic anemia who regularly receive blood transfusion

The main principle of blood transfusion is, *as many as necessary—as few as possible*.

In a stable patient who is not actively bleeding, order **one unit at a time.** Check the patient's blood count again before ordering multiple units that you may not actually need!

This strategy helps prevent the wasting of blood, and also prevents you from giving more blood than is medically necessary.

DECIDING WHEN TO ORDER PLATELETS

There is no single criterion to decide whether a unit of platelets is indicated. The decision should be made on an individual basis, based on your patient's history, clinical status, and present therapeutic goals.

In platelet therapy, we distinguish between **therapeutic** platelet transfusion, which would be used in actively bleeding patients or in preparation for an invasive procedure, and **prophylactic** platelet transfusion, which would be used to prevent spontaneous bleeding.

Therapeutic platelet transfusion

In actively bleeding patients with thrombocytopenia, platelets should be given if endogenous platelet levels fall below **50 000 / µL**.

For invasive procedures, it is recommended that platelets be maintained at a certain level to decrease the risk of bleeding during the procedure.

Some common thresholds for procedures

- 100 000 /µL—disseminated intravascular bleeding (DIC); bleeding in central nervous system; neurosurgery; ocular surgery
- 80 000 / µL—epidural anesthesia
- 50 000 / µL—active bleeding; most major surgeries; therapeutic endoscopic procedures; lumbar puncture in patient without hematological malignancy

- 20 000/ µL—diagnostic endoscopy; central line placement; bone marrow biopsy
- 10 000/ µL—lumbar puncture in patient with hematological malignancy

Prophylactic platelet transfusion

In patients without any bleeding risk, bleeding due to thrombocytopenia is unlikely to occur until endogenous platelet levels reach about **500 / µL**.

Patients at high risk of bleeding might start bleeding spontaneously with a platelet count between **10 000–50 000 / µL**, sometimes even at higher levels. In these patients you should consider giving platelets prophylactically when reaching these platelet counts.

Bone marrow suppression

A regular patient group in this high-risk category are patients with bone marrow suppression. If the bone marrow suppression is due to hematologic malignancies or cytotoxic chemotherapy, the threshold to give one unit of platelets prophylactically is generally **10 000–20 000 / µL**. However, if these patients have a fever or are septic, the threshold should be set higher. In one specific form of acute leukemia—**acute promyelocytic leukemia**—the threshold rises to **30 000–50 000 / µL**, due to the concomitant coagulation disorder.

Platelet disorders

Patients with platelet consumption disorders like immune thrombocytopenia (ITP), disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura (TTP), and hemolytic uremic syndrome (HUS), as well as patients with platelet function disorders like von Willebrand disease, should receive platelet transfusions only when they have major bleeding.

Reversing antiplatelet therapy

If patients on antiplatelet therapy need elective surgery, the individual risk of bleeding and thrombosis must be evaluated to decide whether cessation of antiplatelet therapy is necessary. If there is a significant bleeding risk, it is best to stop the antiplatelet therapy.

However, you need time to plan ahead. All of these decisions should be made on a case-by-case basis.

If patients on antiplatelet therapy need emergency surgery, platelet transfusions can be given to reverse antiplatelet activity. However, it is not clear whether this common procedure is actually effective, as current clinical data is variable. Performing laboratory platelet function testing can assist you in making decisions about when and how many platelet units are needed in these situations.

ESTABLISHING WHEN TO ORDER FRESH FROZEN PLASMA

Fresh frozen plasma (FFP) is the *all-rounder* of plasma products, as it contains all coagulation factors. However, FFPs are not the solution for just any bleeding problem, nor for correcting abnormal lab results.

There are different kinds of plasma products, which are commonly referred to as fresh frozen plasma in the clinical routine.

These include

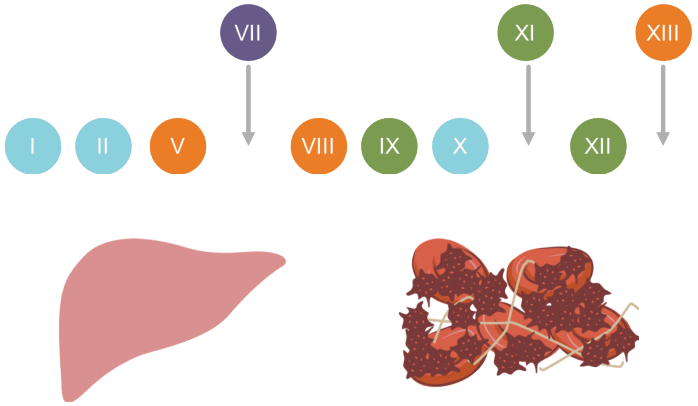
- Plasma frozen within 24 hours after phlebotomy (PF24)
- Solvent / detergent plasma (SD-plasma)
- Cryoprecipitate-poor plasma

In general, the transfusion service will decide which one to use.

Indications for FFP transfusion

The transfusion of fresh frozen plasma is only indicated in bleeding patients.

The most frequent indication is to replace deficiencies of multiple coagulation factors. This is often the case in patients whose production of coagulation factor is impaired, such as those with liver disease, and in patients who consume their coagulation factors, for example in disseminated intravascular coagulation (DIC).

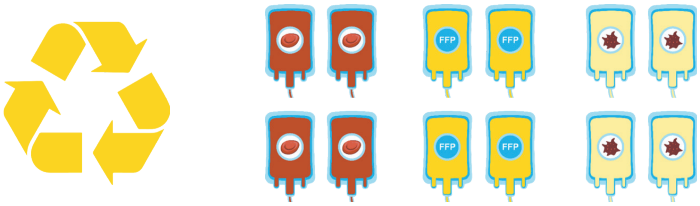


FFPs are also indicated to replace deficiencies of specific coagulation factors when specific concentrates for these factors are not available, for example, replacing factor XI, factor V, Protein C or Protein S.

You can also use FFPs to help treat major bleeding associated with warfarin anticoagulation or Vitamin K deficiency, but only if no prothrombin complex concentrate (PCC) is available.

Prothrombin complex concentrate (PCC)—a plasma product which contains all the vitamin K-dependent coagulation factors—is the main plasma product indicated in these two situations and should be used when available.

Other indications for FFPs include plasma exchange in thrombotic thrombocytopenic purpura (TTP), and massive transfusions.



When is FFP tranfusion not indicated?

Plasma products should not be used to correct only minimally elevated INR of 1.6 or lower, as a volume expander, or as a source of proteins or nutrients.

COPING WITH CRITICALLY ILL PATIENTS

Most critically ill patients should be transfused following the same rules as non-critical patients. However, there are a few exceptions you should remember, to help you provide the best medical care.

Anemia

In critically ill patients, anemia can be caused by bleeding, hemodilution, or frequent blood sampling.

Restrictive transfusion thresholds

A restrictive transfusion strategy was shown to be either favorable, or at least similar, compared to the liberal approach in most critically ill, non-bleeding patients in intensive care—including patients with sepsis.

Liberal transfusion thresholds

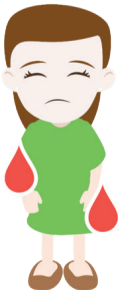
Patients with acute hemorrhage, acute coronary syndrome, neurological injuries or severe hypoxemia generally benefit from a more liberal transfusion strategy.

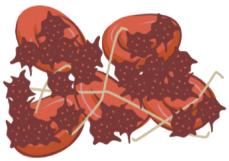
Thrombocytopenia

Thrombocytopenia is common in intensive care, especially in patients with disseminated intravascular coagulation (DIC) or sepsis.

Disseminated intravascular coagulation

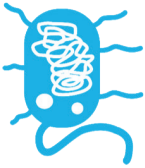
In bleeding patients with disseminated intravascular coagulation, the platelet count should be maintained at more than 50 000 / µL.





Severe sepsis

Platelet transfusion should only be performed in bleeding, critically ill patients, with one exception—patients in severe sepsis. These patients should maintain a platelet count of 20 000 / µL or more, even if they are not actively bleeding.

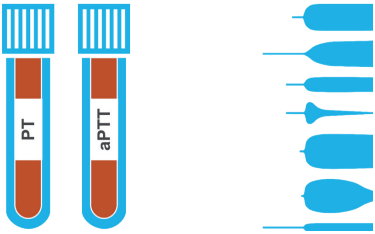


Antiplatelet therapy

In bleeding patients on antiplatelet drugs, platelet transfusion is also indicated. However, there is no specific platelet count that you should aim for. After the administration of one single donor platelet unit, it is safest to reassess the patient's bleeding status, or perform laboratory platelet function testing, to decide whether more units are needed to help stop the bleeding.

Abnormal coagulation

Fresh frozen plasma is an option to treat abnormal coagulation in bleeding patients. A basic coagulation lab panel, as well as global coagulation tests like thromboelastography (TEG) or thromboelastometry (ROTEM), can help you identify patients in need of FFPs.



Dosage

The minimum dose of FFPs is 10–15 mL / kg, but dosage should generally be guided by the results of your coagulation testing.

MANAGING SURGICAL PATIENTS

Blood products are expensive and finite, and transfusion therapy bears certain risks for the patient. Thus, the optimal use of blood products should be a priority. Since patients who undergo elective surgical procedures have the benefit of time, they should be managed according to Patient Blood Management guidelines.

You can make use of Patient Blood Management strategies before, during, and after surgery.

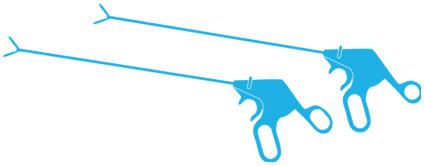
Before surgery

If a patient presents with anemia before surgery, their anemia should first be managed by treating the underlying cause, and not by increasing the hemoglobin level with blood transfusion.

In patients on antiplatelet or anticoagulant therapy, bridging strategies (changing to short-acting anticoagulants like low molecular weight heparin) must be addressed early enough to decrease the risk of bleeding during the procedure.

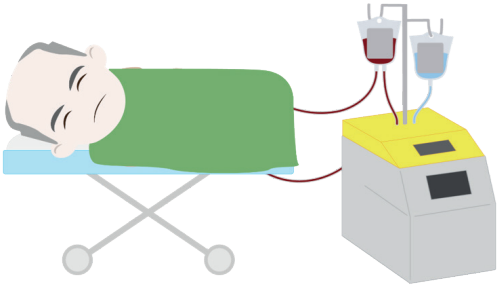
During surgery

Surgical techniques that minimize blood loss, like laparoscopy, should be favored.



Bleeding can be further reduced by using antifibrinolytic agents like tranexamic acid, or tissue sealants.

Another option is to conserve blood, for example with cell salvage procedures. Here, blood that was suctioned is processed at the bedside to be re-infused into the same patient.



After surgery

Minimizing the frequency and volume of blood sampling, as well as managing the patient's coagulation—if necessary therapeutically—will avoid blood loss and unnecessary use of blood products after surgery.

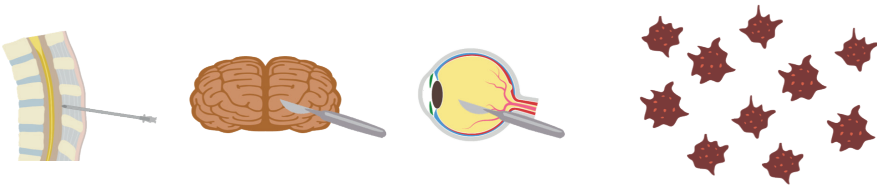
Transfusion thresholds

Restrictive transfusion thresholds should be used at all times in surgical patients. Red blood cell transfusion should be considered if hemoglobin is below 8 g / dL and is certainly indicated below 7 g / dL. Higher thresholds might be necessary if the clinical condition warrants.

7–8 g / dL

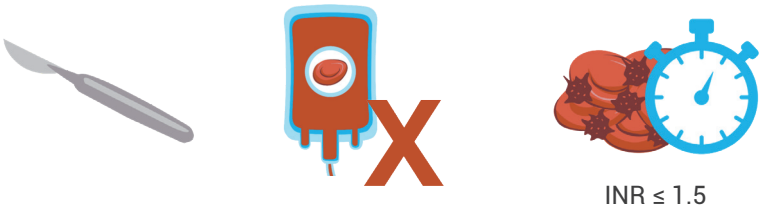
Most invasive surgeries can be performed without any prior platelet transfusion, as long as platelet levels are above 50 000 / µL. However, epidural anesthesia, neurosurgery, and ocular surgery are best performed with higher platelet concentrations of 80 000–100 000 / µL.

50 000 / µL



80 000–100 000 / µL

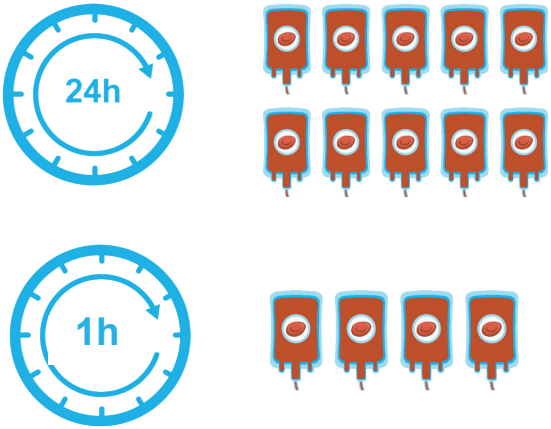
Most surgeries can also be performed without any prior fresh frozen plasma administration in patients with an INR of up to 1.5. However, decisions on how to deal with coagulation abnormalities should definitely be made individually, on a case-by-case basis.



INR ≤ 1.5

HANDLING MASSIVE TRANSFUSION

The amount of blood that must be lost to actually meet the criteria for massive blood loss is variable. One definition is replacement of blood volume in 24 hours. Another definition says massive blood loss occurs when 4 units of RBCs are used within 1 hour.



Whichever definition is used, these are patients suffering from life-threatening, uncontrolled hemorrhage, accompanied by hemostatic and metabolic complications. These patients need volume replacement to maintain hemodynamic stability, red blood cells to maintain tissue oxygenation, as well as fresh frozen plasma and platelets to regulate coagulation.

Massive transfusion protocol

Institutional massive transfusion protocols (or major hemorrhage protocols) describe how processes at the bedside, communication with the lab, and transfusion strategies should be carried out in these situations.

There are two different approaches for deciding how many blood products the bleeding patient needs.

Goal-directed therapy

Fixed ratio therapy

Goal-directed therapy

In goal-directed therapy, the number of blood products required is determined by monitoring lab markers, ideally in a point-of-care setting.

The following parameters should be monitored

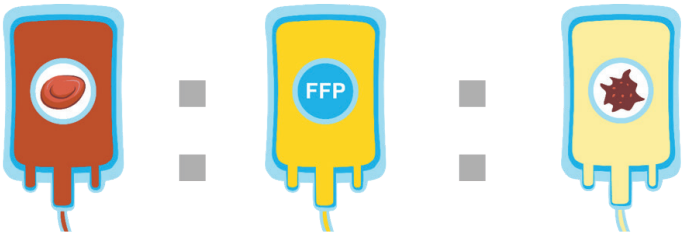
- Hemoglobin
- Platelet count
- Prothrombin time (PT)
- Activated partial thromboplastin time (aPTT)
- Fibrinogen
- Whole blood coagulation (e.g., thromboelastography)
- Arterial blood gas
- Body temperature

The results of these tests should guide replacement therapy, and help you determine how many products should be transfused to keep the patient stable.

Depending on the protocol, monitoring is repeated regularly, for example every 30–60 minutes or after administration of every 5–7 units of red blood cells.

Fixed ratio therapy

Fixed ratios of blood products are often preferred in trauma patients with massive bleeding. Studies have shown that a 1:1:1 approach is best. So, one unit of RBC, plus one unit of FFPs, plus one unit of single donor platelets.



In trauma patients with major bleeding, antifibrinolytic therapy with tranexamic acid is recommended, and best applied early after injury.

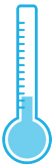
If fibrinogen levels are critically low (below 1 g / L) cryoprecipitate or fibrinogen concentrate should be administered.

Whichever transfusion strategy you choose, always try to avoid over-transfusion and volume overload in order to keep the dilutional effects at a minimum level.

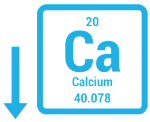
AVOIDING COMPLICATIONS IN MASSIVE TRANSFUSION

Aside from over-transfusion and coagulopathy due to dilutional effects, massive transfusion also presents other potential complications that need to be addressed.

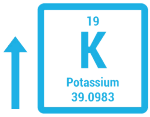
The most common complications are



Hypothermia



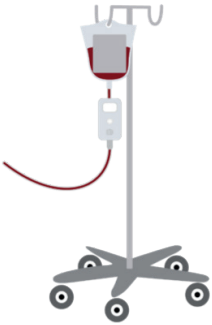
Hypocalcemia



Hyperkalemia

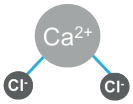
Hypothermia

Hypothermia develops as transfused blood components and fluids cool down the patient's body temperature. Hypothermia should be minimized by using in-line blood warming devices.

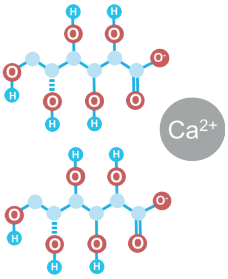


Hypocalcemia

Citrate is used as an anticoagulant in blood products. In massive transfusion, excessive binding of plasma calcium to citrate can lead to significant hypocalcemia. Patients with liver disease are especially at risk for developing post-transfusion hypocalcemia. If ionized calcium is low on blood gas analysis, it is best to supplement with calcium chloride or calcium gluconate.



Calcium chloride



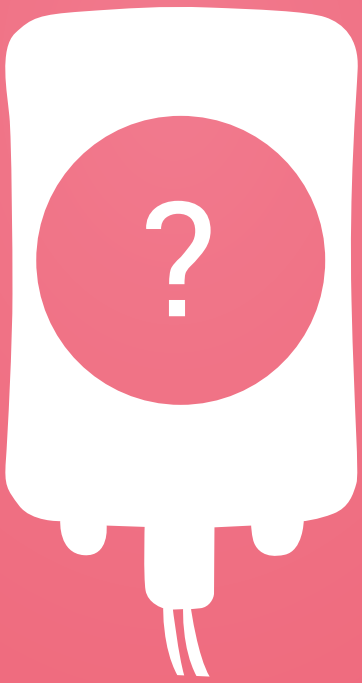
Calcium gluconate

Hyperkalemia

Hyperkalemia occurs as a consequence of potassium leakage out of red blood cells, due to blood storage or irradiation. Infants or patients with renal impairment are at especially high risk of developing hyperkalemia, since they struggle to cope with the sudden increase in potassium in rapid, large-volume transfusion. In these patients, you should use washed RBC units or RBC units that are less than ten days old to avoid hyperkalemia.

Chapter 3

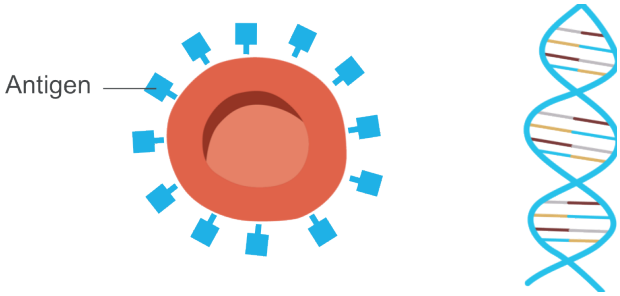
CHOOSING THE RIGHT PRODUCT



DEFINING BLOOD GROUPS

Blood group systems

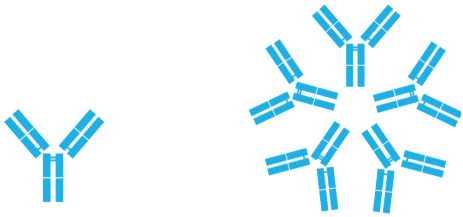
A blood group system is defined as a set of antigens expressed on red blood cells (RBCs) that are controlled by the same gene or cluster of genes. Over 30 blood group systems have been identified. There are many different blood group antigens expressed on the surface of every RBC.



When we determine an individual's blood group, we not only determine the **antigens** present on the red blood cell, but we also characterize the **antibodies** present in the individual's serum or plasma.

Alloantibodies

The immune system recognizes self and non-self molecules. To protect oneself from foreign intruders, the immune system produces antibodies that are directed against foreign antigens, such as those that are expressed on foreign blood cells. These antibodies are called alloantibodies. In Greek *allo* means foreign. Alloantibodies are typically either IgG or IgM molecules.



IgG IgM

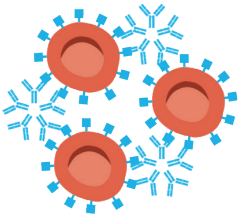
Alloantibodies against blood group antigens can be produced naturally, or through the process of sensitization, which is also called immunization.

Naturally Immunization

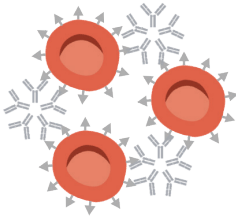
Naturally occurring alloantibodies

Naturally occurring antibodies are produced spontaneously, and do not require contact with a foreign antigen. These antibodies are produced in the first months of our lives.

The most prominent naturally occurring antibodies are antibodies directed against ABO blood group antigens: anti-A and anti-B antibodies. These antibodies are mainly of the IgM class. When these antibodies are mixed with red blood cells, carrying the respective antigen on their surface, agglutination (clumping) is seen macroscopically. For this reason, these antibodies are also called *agglutinins*. Agglutination is followed by hemolysis—rupture of the red blood cell.



Anti-A



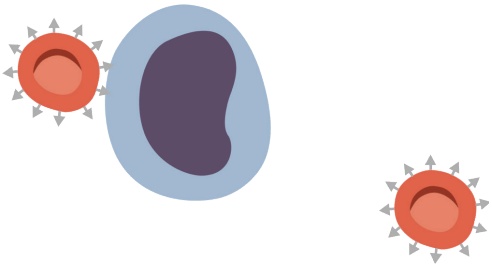
Anti-B

Other alloantibodies

All other alloantibodies against blood group antigens are only produced in response to sensitization / immunization.

First contact

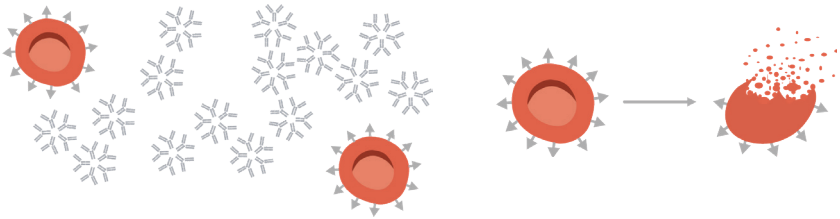
Immunization occurs when antigen-presenting immune cells first come into contact with foreign red blood cells—for example donor blood or the blood from a fetus.



The antigen-presenting cells then recognize that these RBCs carry foreign antigens and start an immune cascade that ends with the production of antibodies against these foreign antigens.

Second contact

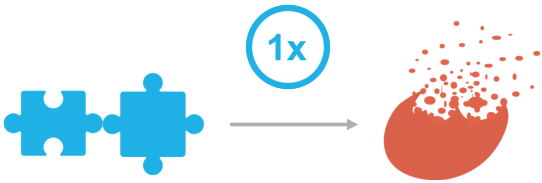
The next time similar foreign RBCs enter the circulation and are caught by the immune system, the production of antibodies is boosted, and the foreign RBCs are destroyed by hemolysis.



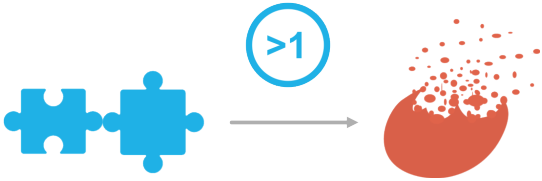
Timing of hemolytic reactions

It is important to understand that the timing of dangerous hemolytic reactions to incompatible blood products will be different between naturally occurring antibodies and antibodies produced after immunization.

Hemolysis will occur the **first time** a patient comes into contact with a blood product that has incompatible naturally occurring ABO blood group markers.

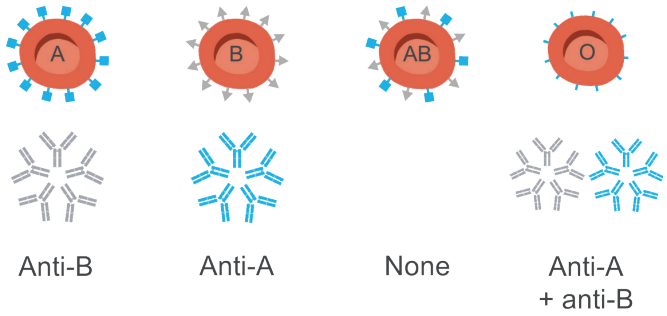


However, for all other blood groups, a patient must be exposed to the foreign RBCs **more than once** in order for a hemolytic reaction to occur.



REVIEWING THE ABO BLOOD GROUP

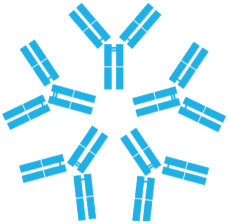
There are four major red blood cell phenotypes in the ABO blood group system: A, B, AB, and O. The most common phenotype is O, followed by A, B, and then AB.



The Austrian physician Karl Landsteiner discovered and named the antigens present on the red blood cell *A* and *B*. RBCs can carry only the A antigen (type A), only the B antigen (type B), both the A and B antigens (type AB) or neither the A or B antigens (type O). Landsteiner called this last option blood type *O* after the German word *ohne* which means *without*—so a blood type without the A or B antigens.

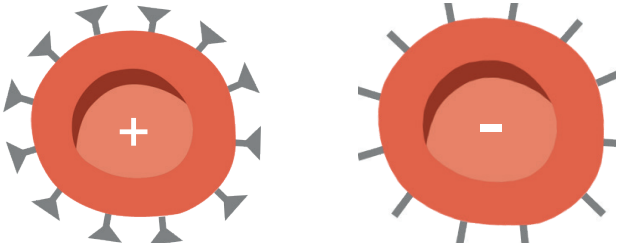
The naturally occurring antibodies anti-A and / or anti-B are found in an individual's blood if the corresponding antigen is missing from their RBCs. Anti-A and anti-B are IgM antibodies, and are produced within the first six months of life, as a response to the colonization of intestinal

bacteria that are similar in structure. Thus, there is no sensitization to foreign blood group antigens needed for their production. They are highly immunogenic and induce intravascular hemolysis if ABO-incompatible red blood cells are transfused.



EXAMINING THE RHESUS BLOOD GROUPS

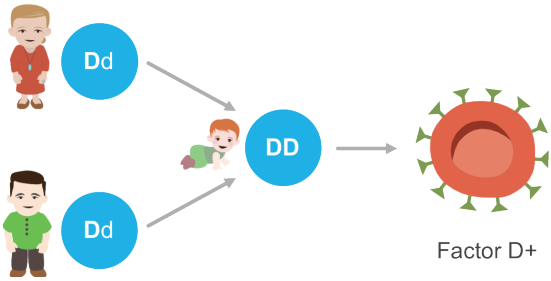
The Rhesus or Rh blood group system is a complex one. There are more than 45 serologically-defined antigens. The most common are Rhesus factors D, C, c, E, and e. Different styles can be used to denote the Rh blood type. The most common one states the antigens D, C, c, E, and e with either a plus (+) or a minus (–) next to them. A plus depicts the presence of the respective antigen, a minus indicates the absence of the antigen.



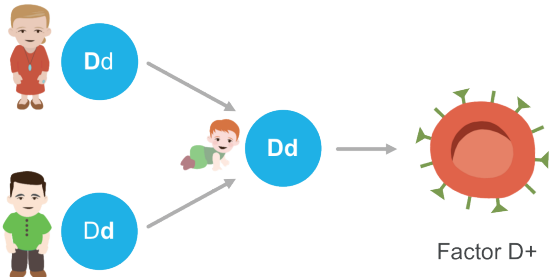
Rhesus D

Rhesus factor D is encoded by the RHD gene and is inherited in Mendelian fashion. Thus, every person carries two alleles—one inherited from each parent.

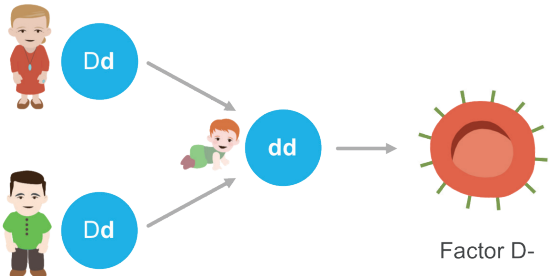
If both parents pass on the dominant allele (D), which codes for the D antigen, the genotype of their baby will be DD and phenotypically factor D will be expressed on the surface of the baby's red blood cells. Thus, the child will have Rhesus factor D positive (RhD+) blood type.



If one parent passes on the dominant D allele and the other passes on the recessive allele (d), which does not code for the D antigen, the child will have the genotype Dd. In this case, the D antigen is still expressed on the red blood cell surface. So again, the child will have Rhesus factor D positive (RhD+) blood type.

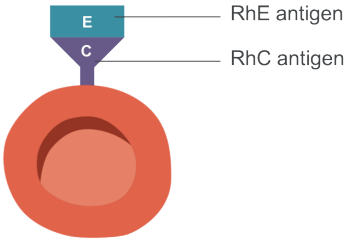


However, if both parents pass on the recessive allele (d), which does not produce the D antigen, this results in the child having the genotype dd. In this case, there is no factor D expressed on the red blood cell surface and the child will have a Rhesus factor D negative (RhD-) blood type.



Rhesus C, c, E, e

The Rhesus factors C, c, E, and e are encoded by the RHCE gene. The RHCE gene codes for a protein found on RBCs that contains two different antigens—RhC and RhE. There are two versions of the RhC antigen (C and c), and two versions of the RhE antigen (E and e).



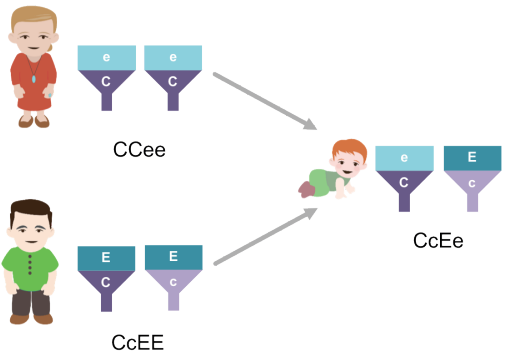
Since both antigens are present on the same peptide, these factors are inherited in combinations of two. Thus, there are four possible combinations—CE, Ce, cE, and ce.

Each parent passes on one of these combinations, so in the end the child has a genotype containing two copies of each antigen.

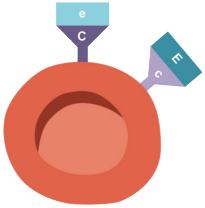
Example

If the Ce combination is inherited from the mother, and the cE combination is inherited from the father, then the child will have the genotype CcEe. The pairs C/c and E/e are autosomal codominant, which means that if a factor is part of the genotype, the respective antigen will be

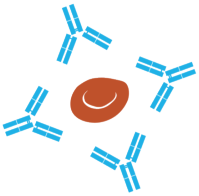
expressed. In this case, all four factors are present in the genotype and thus, all four factors will be expressed on the RBCs.



On the report we find *C+ c+ E+ e+*.



Alloantibodies against all Rhesus antigens are produced in response to immunization to foreign blood cells, which can occur after an incompatible blood transfusion, or a pregnancy where the fetal blood group is different from the mother's.



Immunization to foreign RBCs

Once immunization occurs, if a second stimulus is presented—either another incompatible transfusion, or a subsequent pregnancy—high levels of anti-Rh alloantibodies will be produced. Anti-Rh antibodies are immunogenic and can lead to significant hemolytic transfusion reactions, as well as hemolytic disease of the fetus and newborn.

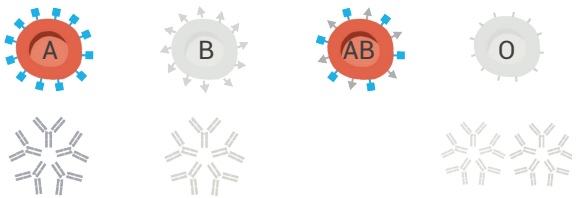
MASTERING
RED BLOOD CELL COMPATIBILITY

When choosing a compatible red blood cell (RBC) product for a patient, the essential question is, will the patient have antibodies against the donor's red blood cell antigens that could cause hemolysis?

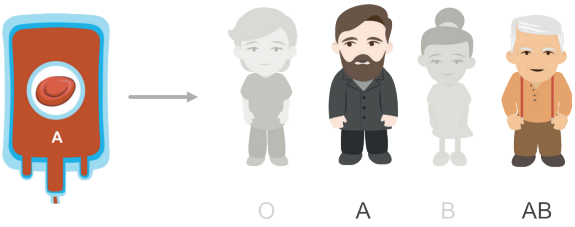
ABO compatibility

Donor blood group A

You want to avoid interactions between the A antigen on the donor RBCs and anti-A antibodies in the patient's plasma. Thus, type A blood can be transfused to all patients who do not carry anti-A antibodies in their plasma.

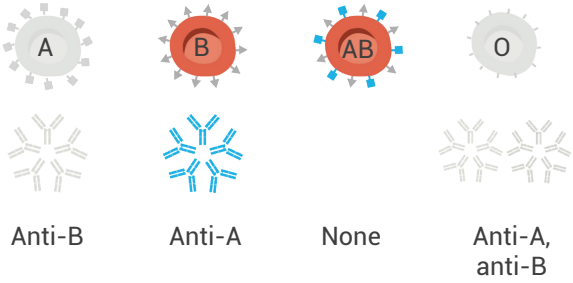


Consequently, group A donor blood can be transfused to patients with blood groups A or AB.

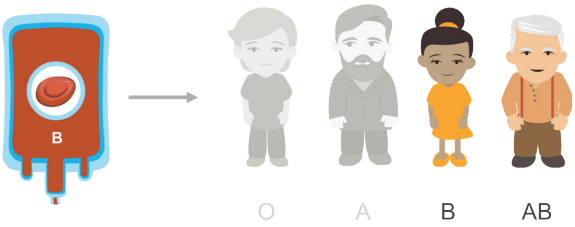


Donor blood group B

You want to avoid interactions between the B antigen on the donor RBCs and anti-B antibodies in the patient's plasma. Thus, B blood can be transfused to all patients without anti-B antibodies in their plasma.

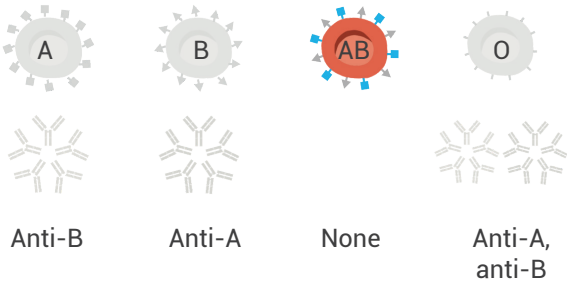


Consequently, group B donor blood can be transfused to patients with blood group B or AB.

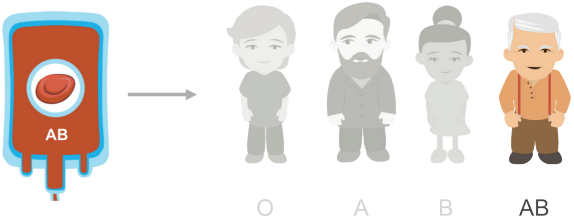


Donor blood group AB

You want to avoid interactions between the A and B antigens on the donor RBCs and anti-A or anti-B antibodies in the patient's plasma. Thus, AB blood can be transfused to all patients without anti-A or anti-B antibodies in their plasma.

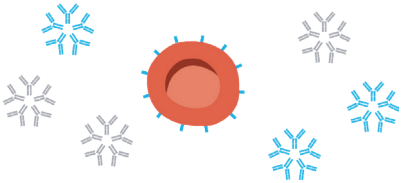


Consequently, group AB donor blood can only be transfused to patients with blood group AB.

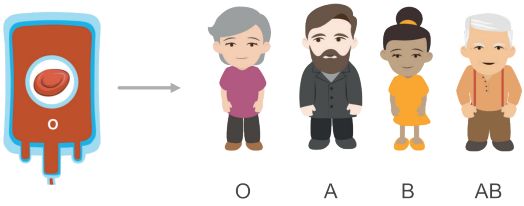


Donor blood group O

There are no A or B antigens on these donor red blood cells, so even if there are antibodies in the recipient's plasma, they won't have anything to bind to on these RBCs.



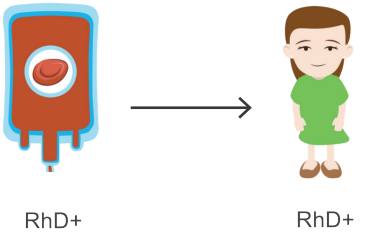
Consequently, blood group O donor blood can be transfused to patients of all ABO blood groups—O, A, B, and AB.

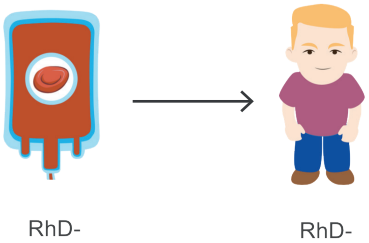


For this reason, group O is the universal donor blood group for red blood cells, and is used in life-threatening emergencies when there is no time to wait for blood typing.

Rhesus D compatibility

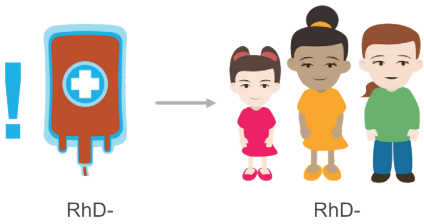
In general, transfused RBCs should be identical to the Rhesus D status of the patient, so a Rhesus D positive patient should receive Rhesus D positive blood, and a Rhesus D negative patient should receive Rhesus D negative blood.



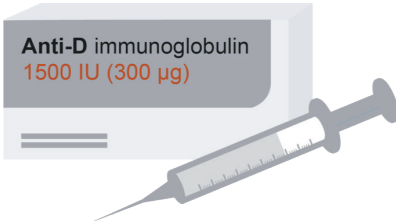


Due to a general shortage of D negative blood products, it is sometimes necessary to give D positive products to D negative patients. This is acceptable in selected and strictly indicated cases, since there is no immediate risk of an adverse transfusion reaction.

However, in girls or women who are Rhesus D negative, and who may become pregnant in the future, it is important that **only** Rhesus D negative blood products are used in order to avoid immunization and the potential development of hemolytic disease of the fetus and newborn in future pregnancies.



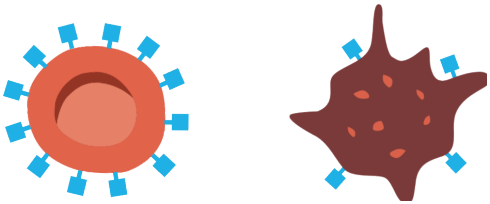
If it is absolutely unavoidable to give D positive products to a D negative female, the patient should be provided with anti-D immunoglobulin prophylaxis after the transfusion, to prevent immunization.



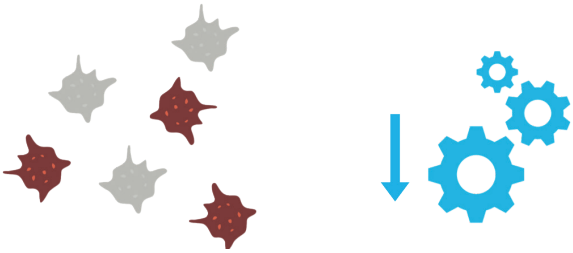
CONQUERING PLATELET COMPATIBILITY

ABO compatibility

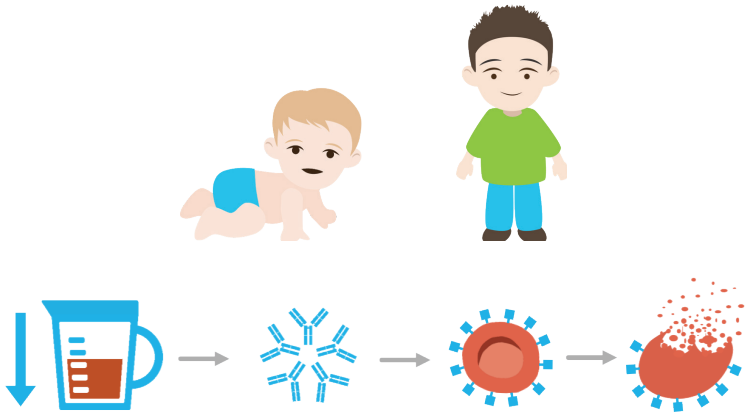
Platelets have the same ABO antigens on their surface as red blood cells, but at much lower levels. Therefore, platelets are immunogenic as well. However, the risk of immune reactions is much smaller than with red blood cells. For this reason, platelet transfusions should be ABO-identical, or at least ABO-compatible.



However, sometimes you might be provided with ABO-incompatible platelets by the transfusion bank. In most cases, you can safely transfuse these, since the number of antigens on the platelet surface is clinically insignificant. However, the survival rate of the platelets might be reduced, and the transfusion might be less effective.



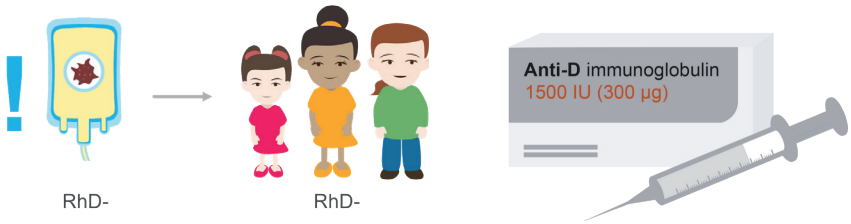
Platelet units also contain small amounts of plasma, which means that it is possible they could contain some anti-A or anti-B antibodies, depending on the blood type of the patient from whom they were derived. In general, this should be of no concern. However, in babies and small children, ABO incompatibility should be avoided, since due to their lower blood volume, the small amount of plasma antibodies in the product might be enough to attack their RBCs and cause clinically-significant hemolysis. For adults, the impact of this small amount of plasma is clinically insignificant.



Rhesus D compatiblity

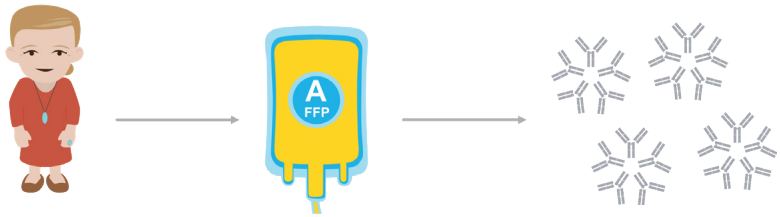
The Rhesus D antigen is expressed on platelets. Therefore, Rhesus D compatibility is important for platelet transfusions. As with red blood cells, it is sometimes necessary to give Rhesus D positive platelets to Rhesus D negative patients.

As with RBCs, it is important that girls and women with childbearing potential, who are Rhesus D negative, only be given Rhesus D negative platelets, to avoid immunization, which can lead to hemolytic disease of the fetus or newborn if they become pregnant in the future. If Rhesus D positive platelets must be given to a Rhesus D negative girl or young woman, a shot of anti-D immunoglobulin prophylaxis should be administered after the transfusion, to avoid immunization.



MASTERING PLASMA COMPATIBILITY

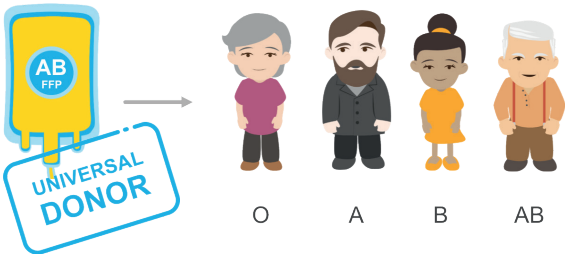
The key to understanding plasma compatibility is knowing that the label on plasma units always states the blood group of the donor. A label with A on it, means the donor had group A, and that means that there are anti-B antibodies in this pack. When we choose a plasma product we must avoid transfusing antibodies against the patient's own red blood cells!



ABO compatibility

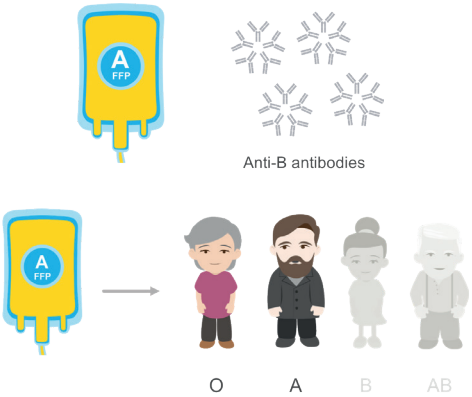
Donor plasma AB

Plasma from AB donors is the universal donor blood group for plasma transfusion, since it does not contain anti-A or anti-B agglutinins and can therefore be given to patients with any ABO blood type.



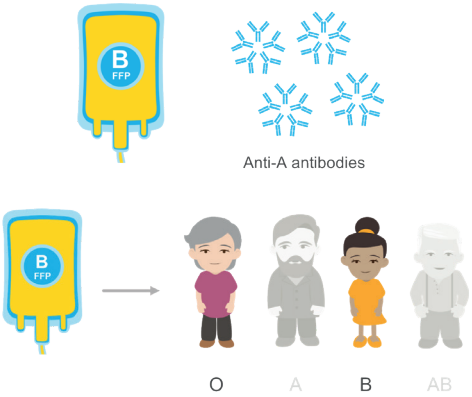
Donor plasma A

Plasma from donors with blood group A contains anti-B antibodies. Thus, it can only be given to patients whose red blood cells do not carry B antigens. Therefore, group A plasma can be given to patients with group A or O blood.



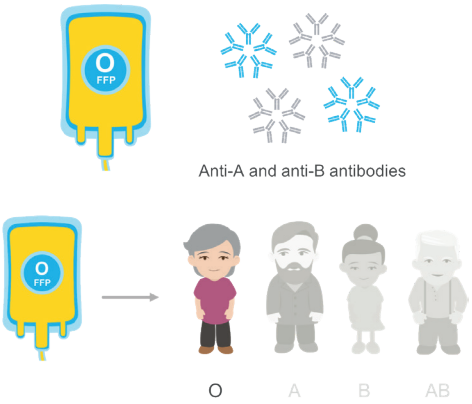
Donor plasma B

Plasma from donors with blood group B, on the other hand, contains anti-A antibodies. So, it can only be given to patients whose red blood cells do not contain A antigens. Group B plasma can be transfused to patients with group B or O blood.



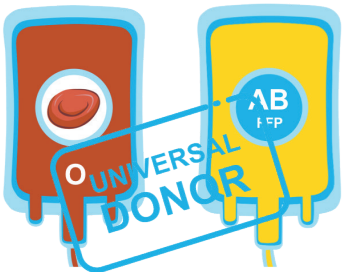
Donor plasma O

Plasma from group O donors contains both anti-A and anti-B antibodies. Thus, it can only be given to patients without A or B antigens on their RBCs. That only leaves patients with blood group O who can receive group O plasma.



Universal products

In the case of emergency transfusion, when there is no time to find out the patient's blood group first, the universal products you can more or less safely transfuse to any patient are RBC units of the blood group O and plasma units of the blood group AB.



Rhesus D compatibility

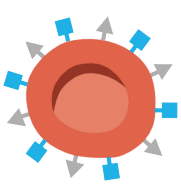
Remember, anti-RhD antibodies are not produced unless a person is sensitized to the RhD antigen. Therefore, Rhesus D compatibility is not an issue for plasma transfusions (because individuals with a previous sensitization are ineligible to donate blood products). In fact, plasma products do not even state the Rhesus D status on the label!

Chapter 4

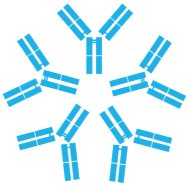
PRE-TRANSFUSION TESTING

GETTING TO KNOW BLOOD GROUP TYPING

In order to determine a patient's blood type, both the antigens expressed on the patient's red blood cells (RBCs), as well as the antibodies present in the patient's serum, must be determined.



Antigens



Antibodies

All typing techniques are based on the principle of antigen-antibody reactions, and agglutination. When plasma antibodies find the right antigens on red blood cells, the red blood cells agglutinate, or clump, which can be seen macroscopically. This principle is used in order to determine the blood type or antibody.

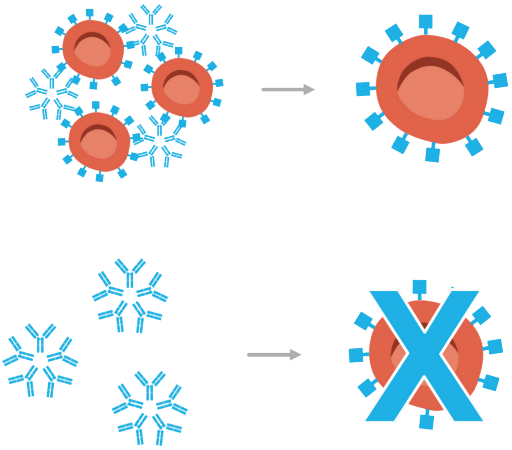
Two different approaches are used to determine the ABO blood group and Rhesus factor D: **forward and reverse typing**.

Forward typing

In forward typing, the presence of the A and B antigens is tested for on the surface of the patients RBCs.

The patient's RBCs are incubated with plasma reagents containing known antibodies: one reagent containing only anti-A, one containing only anti-B, one containing both anti-A and anti-B, and one reagent without either of the two antibodies, as a negative control.

After mixing the RBCs with the known antibody, agglutination indicates the presence of the specific antigen on the patient's RBCs. No agglutination indicates that the specific antigen is not present on the patient's RBCs. Forward typing is repeated with a different set of anti-A and anti-B antibodies to confirm the results.



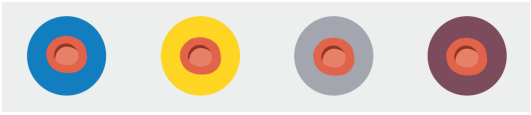
The same procedure applies for Factor D testing. The patient's RBCs are first mixed with a reagent containing anti-D antibodies, then with a reagent containing no anti-D antibodies and lastly, with a second anti-D antibody.

Example

First you place plasma reagents containing antibodies to the A or B antigen, reagent containing antibodies against both A and B, and lastly control reagent (containing no antibodies) on the slide.

Anti-A Anti-B Anti-A,B Control

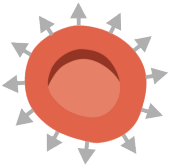
You then add RBCs from the patient and wait a couple of seconds for agglutination.



Anti-A Anti-B Anti-A,B Control

In this case, agglutination occurs when cells are mixed with the anti-B antibodies and the anti-AB antibodies, but not when mixed with the anti-A antibodies, or with no antibodies. Thus, the patient's RBCs must express the B antigen, but not the A antigen. This indicates the patient has type B blood.

Anti-A Anti-B Anti-A,B Control



Type B

Reverse typing

Reverse typing determines whether anti-A and / or anti-B agglutinins are present in the patient's plasma.

The patient's plasma is mixed with RBCs carrying only A antigens, only B antigens, or RBCs without A or B antigens (i.e., group O-wRBCs).

Agglutination indicates the presence of antibodies against the specific antigen present on the cells. No agglutination indicates that there are no antibodies against the specific RBC antigen present in the plasma.

Example

First you place RBCs containing A, B or no antigen (O) on the slide.

A B O

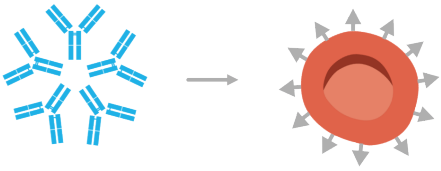
Then add the patient's plasma to test.

A B O

In this example, the patient's plasma agglutinates with RBCs carrying the A antigen, but not with RBCs carrying the B antigen and also not with the O-RBCs. Consequently, the patient must have anti-A antibodies in their plasma.

A B O

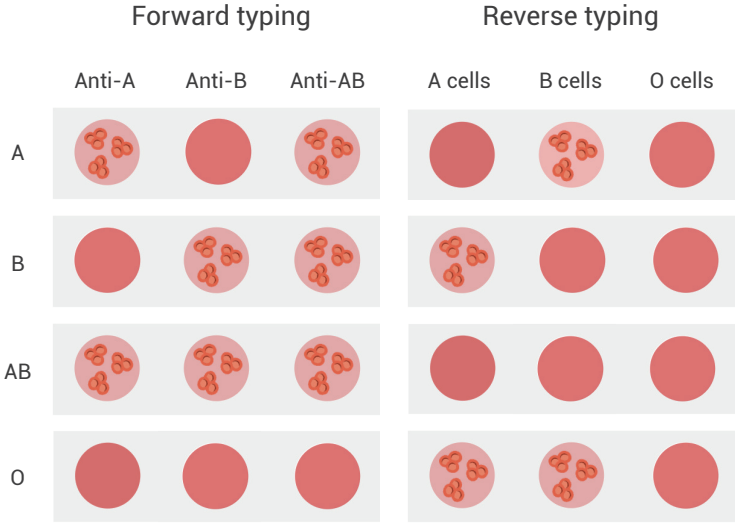
Since individuals only produce ABO antibodies against the antigens that are foreign to them, and not the ones their own cells express, this individual must have type B blood.



Anti-A Type B

The results of the forward and the reverse typing must be consistent. Otherwise, there must be some interference or blood sampling mistake. If they don't fit, further testing, and possibly a second blood sample, is obligatory.

Possible blood typing results

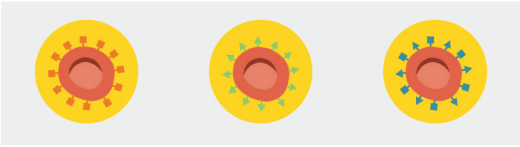


SCREENING FOR ALLOANTIBODIES

Whenever we test a patient's blood group, we also need to search for potential alloantibodies in the patient's plasma. This is obligatory. We do this by performing an antibody screen and identification.

Antibody screening

The antibody screen is the first, very rough glance at whether there are alloantibodies other than anti-A or anti-B in the patient's plasma. Three different types of reagent red blood cells are incubated with the patient's plasma. All RBCs are type O, but they each carry a variety of well-characterized antigens of other blood group systems.



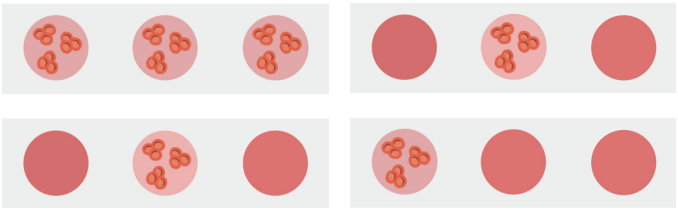
I II III

If agglutination occurs, there must be antibodies against these RBC antigens in the patient's plasma. To determine what specific antibodies have been found, the antibody identification test is performed next.

Antibody identification

Antibody identification works exactly like the antibody screening, but instead of using only three types of RBCs, ten to twelve different antigen profiles are used. Each type of red blood cell carries a certain antigen profile that is known to us, since the manufacturer provides a list showing the antigens on the test cells.

By evaluating the combinations of agglutination and non-agglutination using this evaluation list, we can identify which antigen(s) the patient's plasma antibodies are directed against.



After blood typing and antibody screen and identification, the clinician will be provided with a lab report stating the patient's ABO and Rhesus D blood group, as well as any specific alloantibodies that were identified in the antibody screen and identification. Together, these two results make the report an official blood group lab report.

CROSSMATCHING

If a patient needs blood, the lab must identify a compatible RBC unit based on the patient's blood group, antibody screen, and transfusion history. Avoiding incompatibility between the donor RBCs and recipient's plasma alloantibodies is essential, since this could lead to acute hemolysis.

After the blood typing and antibody screen have been performed, the lab staff selects a possible unit from the fridge, that is compatible with the patient's results. Next, they perform the crossmatch or compatibility testing.

Crossmatch

The goal of the crossmatch is to do one last safety check in order to uncover any incompatibilities or interferences that might have been missed in any prior testing.

To perform the crossmatch, the patient's plasma is mixed with the donor RBC product.

Negative crossmatch

If there is no agglutination detected, the crossmatch is negative. That means the patient can receive this product. The risk of hemolysis is extremely low.

Negative crossmatch

Positive crossmatch

If agglutination occurs, the crossmatch is positive. The patient's plasma must contain an alloantibody directed toward the donor RBCs, so this specific product **must not** be given to the patient.

Positive crossmatch

In rare cases, patients need to receive RBC units despite a positive crossmatch. For example, patients with hematological diseases, like myeloma, often have positive crossmatches that are a product of the underlying medical condition or certain monoclonal antibody therapies. In these cases, the positive crossmatch does not actually reflect the presence of alloantibodies to blood group systems. Therefore, it might still be safe to transfuse the patient with the tested product.

If you want more information on how to proceed in these cases, get in contact with the attending lab physician! Together you will find the best way to handle the situation.

Avoiding a booster effect

The booster effect occurs when the immune system comes into contact with foreign RBC antigens for the second time, and boosts antibody production, causing hemolysis and adverse transfusion reactions.

In cases where a patient had a positive antibody screen in the past and a specific alloantibody was identified, but the most recent antibody screen now shows a negative result for that particular alloantibody, we must avoid any booster effect. Consequently, even though the patient shows a negative antibody screen now, we must still act as if the screen was positive, and choose red blood cell units that lack the particular antigen the antibody was directed at.

PREPARING FOR PROCEDURES

The risk of bleeding associated with a particular procedure can help determine what tests are performed before the procedure itself. This allows us to be prepared for the possibility of transfusion, while still minimizing the use of blood products.

Crossmatching before procedures

Crossmatching is performed not only for instantly needed transfusions, but it can also be performed prophylactically, before surgery or invasive procedures when there is high risk of bleeding.

This allows for units that are compatible with the patient to be stored until they *might* be needed in the operation room. Since all tests are performed prior to the procedure, these blood units can then be released quickly if necessary.

Luckily for patients, there is often no use for these crossmatched, stored blood products. However, these products are *reserved* and cannot be used for other patients. Thus, the hospital must order more blood products than necessary, which is costly.

For this reason, some institutions chose to perform a special lab test protocol called a **Type and Screen**.

Type and Screen

Type and Screen is performed for patients who are scheduled to undergo a planned procedure or surgery with a very low risk of bleeding.

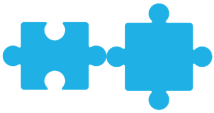
In Type and Screen protocols, blood group typing and antibody screening are the only tests that are performed before surgery. If these tests show no abnormalities, and the patient has no history of known alloantibodies or abnormal reactions to prior transfusions, no crossmatching is done prior to surgery.

Blood typing

Antibody screen

In the rare case of life-threatening bleeding during surgery, the patient quickly receives compatible but uncrossmatched RBCs, which presents a risk of a severe hemolytic transfusion reaction of less than 1%.

If the patient needs blood during surgery, but the situation is non-life-threatening, crossmatching can still be performed at that time.



Compatible

Uncrossmatched

HANDLING URGENT TRANSFUSIONS

If a patient needs blood urgently, otherwise they will die, there is a special protocol to follow in which uncrossmatched red blood cell units are transfused. This is also called **emergency release**.

First, get in contact with the lab and communicate clearly how urgent the transfusion is. Second, send one specimen of currently drawn blood to the lab right away.

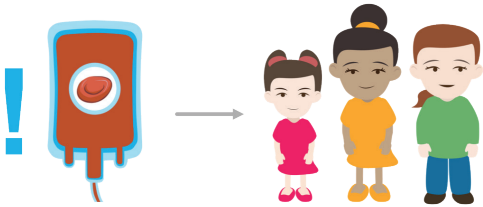
Depending on how urgent the situation is (i.e., how fast the patient needs blood) the lab will provide

- Group O, uncrossmatched blood units (if there is no time to complete any typing tests).

OR

- Blood type compatible, but uncrossmatched blood units (if the clinical situation allows for a quick blood typing evaluation, which typically takes 10–30 minutes).

Whether the released units are Rhesus D positive or negative will depend on availability and institutional policies. However, young girls and women of childbearing age should **always** receive Rhesus D negative blood until their Rhesus status is known.



RhD- Rh?

By following these rules, you will have chosen the blood type that has the least potential to do harm. However, using group O blood does not mean that the transfusion is completely safe. There are over thirty different blood groups, and the patient could still carry alloantibodies to other blood group antigens that could react with the transfused unit.

Following ABO mismatches, the most severe transfusion reactions are caused by alloantibodies against the Rhesus C/c, /E/e, Kell (K), Kidd (Jk), Duffy (Fy), Lutheran (Lu), and Ss blood group systems.

Normally you would uncover these alloantibodies in the antibody screen and eventually in the crossmatch. However, neither of these would be performed in this time-sensitive situation. Nevertheless, it is an urgent, life-threatening situation.

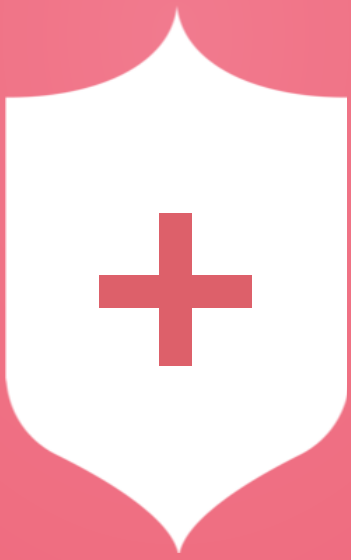
Although there is a chance your patient could develop a reaction to one of these other blood group antigens, the benefit of saving the patient's life by giving the blood transfusions will always be higher than the risks of adverse reactions due to this type of incompatibility.

There are two more things to remember before starting the transfusion

1. Take a blood sample before starting any transfusion. This allows the lab to type the patient's blood group, and to switch to group-specific, crossmatched blood as soon as possible. Furthermore, transfused uncrossmatched blood units can be retrospectively crossmatched with this sample.
2. Bedside ABO identity tests must be completed before performing emergency transfusions in countries where obligatory.

Chapter 5

SAFETY FIRST



PREPARING THE TOOLS

Three major steps that should be completed before starting the transfusion

1. Obtain informed consent from your patient
2. Complete all necessary documentation
3. Prepare tools you will need at bedside

Informed consent

In general, informed consent must be obtained in advance. However, in emergency settings, the consent can be obtained retrospectively.

The following topics regarding the transfusion are to be discussed with the patient

- Type of product(s) to be transfused
- Indication for transfusion
- Risks and benefits
- Possible alternatives to transfusion therapy
- Product administration process
- No donation of blood after transfusion

It is important that the patient has enough time to ask questions and consider their decision, and that the patient is provided with written information, such as the consent form itself.

For the clinician, it is important to make notes on the consent form, and to document what was talked about in the patient's clinical records as evidence for future legal inquiries.

Pre-transfusion documentation

Pre-transfusion documentation is important since it helps other care providers to follow the patient's treatment history, and also serves legal purposes.

The minimum that should be documented in the patient's clinical record

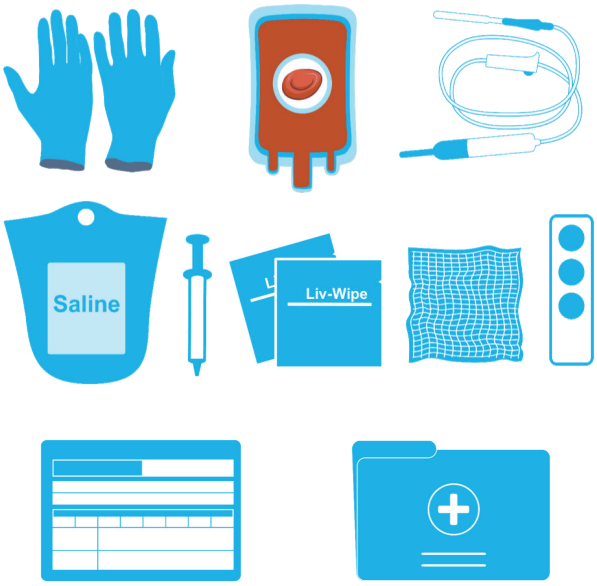
- The indication for transfusion
- The type and number of blood components to be transfused
- Confirmation that informed consent has been obtained
- Any special requirements for each component (i.e., irradiation of the product)

Preparing the tools

Assuming that a large 18- to 20-gauge IV catheter has already been placed, the following tools need to be prepared

- Gloves
- The ordered blood component unit
- The administration set containing an inline mesh filter
- 0.9% saline
- 5 mL syringe with saline
- Antiseptic wipes

- Gauze
- ABO identity bedside test (if legally required)
- The prescription
- The patient's clinical record



Saline is the **only** fluid you can co-administer with blood products. Five percent (5%) dextrose in water will cause hemolysis and Lactated Ringer's solution will cause clots.

PERFORMING PRE-TRANSFUSON BEDSIDE CHECKS

The final checks before starting the transfusion must be performed at the bedside, next to the patient. The clinician who performs the bedside checks should not be interrupted, since it is crucial to stay focused to avoid mix-ups. In some institutions, it is obligatory that two people perform the checks separately.

The pre-transfusion bedside check should always include

- Confirming patient identification
- Documenting vital signs
- Checking the blood product

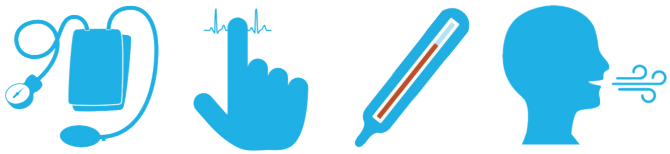
Patient identification

The patient must be identified to avoid mix-ups. The best technique is to have the patient actively state their full name and date of birth, then check the wrist band for the patient's name, date of birth, and the hospital identification (ID) number.

Vital signs

This includes checking and documenting

- Blood pressure
- Pulse
- Temperature
- Respiratory rate



Having a record of the patient's vital signs immediately before the transfusion will help to determine whether the patient experiences a transfusion reaction after the transfusion has been started.

Check the unit

This step seeks to confirm, once again, that the unit about to be transfused is really meant for this specific patient, and that the unit is flawless.

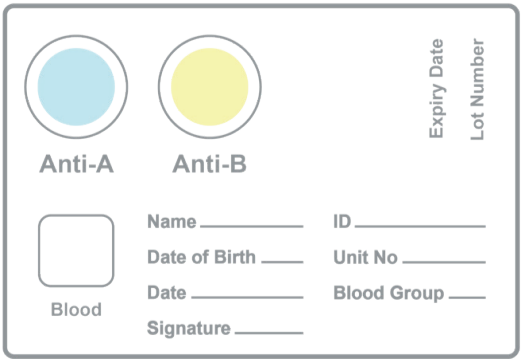
This includes checking for

- A match between blood group listed on pack, compatibility label, and patient's blood group
- A match between identification numbers on compatibility label and patient's wrist band
- Special requirements (i.e., irradiation or washing of the unit) if indicated

- Unit's expiration date
- Leakage
- Discoloration
- Clumping

COMPLETING THE ABO IDENTITY TEST

In some countries, the transfusing clinician is legally obliged to perform an ABO identity test at the bedside of the patient immediately before starting red blood cell transfusions. The purpose of this point-of-care blood typing test is to provide a final check, to confirm that the blood groups of the patient and the product are compatible.

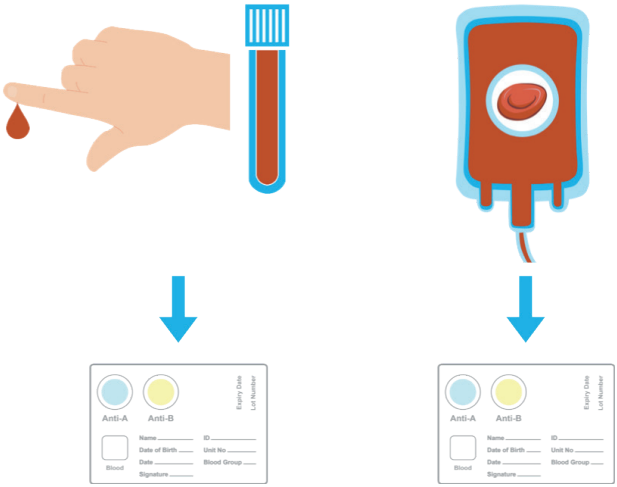


Tools

The following tools are needed

- Test card
- Vial of saline
- Antiseptic wipes
- Lancet
- Spatulas
- Gloves
- Gauze

The ABO identity test should be performed separately for the patient's blood and for the blood from the blood unit to be transfused. The blood sample from the patient can either come directly from a finger-prick, or from a vial of venous blood, which should be drawn immediately before performing the bedside test.

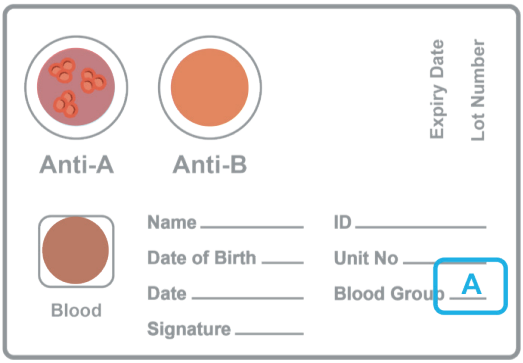


Test instructions

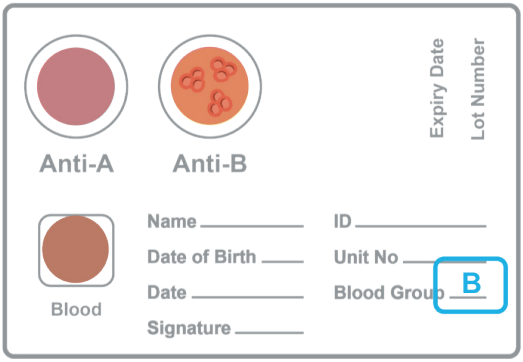
1. Put one drop of blood onto the anti-A spot, one drop onto the anti-B spot, and one drop onto the blood field.
2. Add one drop of saline to each field.
3. Mix the fluids on each field with a stick until the fluids appear dissolved.
4. Carefully wave the card horizontally in a circular motion for about 30–60 seconds.
5. Check each reaction field for agglutination: agglutination appears as clumping.
6. Document the results.

Agglutination is the result of antigen-antibody reactions. In this case, the patient's or product's red blood cell antigens found a reaction partner to agglutinate. The pattern of agglutination allows you to determine the blood type.

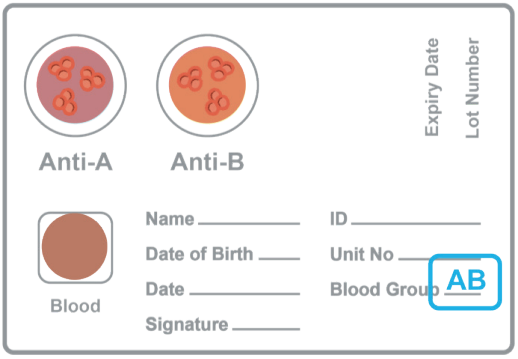
Blood group A



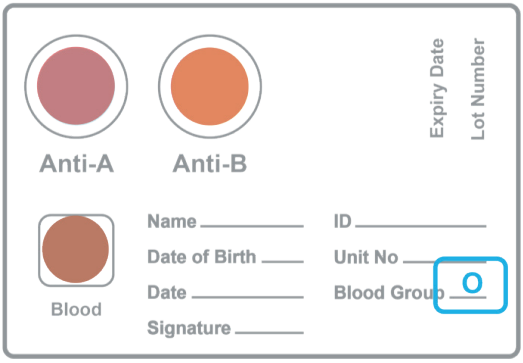
Blood group B



Blood group AB



Blood group O



The results and the lot number of the card should be documented in the patient's record.

Lastly, the results seen on the test card should match with the results on the patient's typing report, and the compatibility label on the bag. If there is any inconsistency, there must be a mix-up and you must restart the whole blood typing process from the beginning.

ADMINISTERING THE TRANSFUSION SAFELY

It is best to have one IV line set up specifically for blood components. Do not administer drugs or fluids other than 0.9% saline with the blood, as they may cause complications. If other fluids are necessary, use a different IV line!

Some transfusion policies recommend reusing tubing systems for more than one red blood cell (RBC) or plasma unit, as long as they are changed every couple of hours to avoid infection. However, I recommend using a new tubing set for every transfused unit. It's just safer for the patient.

For platelets, always use a separate tubing system and not one that was previously used for another type of component.

Transfusion procedure

1. Wash your hands.
2. Put on gloves.
3. Connect the tubing to the blood component bag by piercing the bag with the spike of the tubing system.
4. Hang the bag on an IV stand.
5. Fill the chamber by squeezing it.
6. Open the roller clamp and let the blood run through the tubing system all the way to the end of the tube.

7. Right before the blood reaches the end, close the roller clamp again.
8. Flush the IV line with saline using a 5 mL syringe.
9. Connect the blood tubing end with the patient's IV line.
10. Start the transfusion.

If you use saline priming, first connect one upper end of the Y tubing to the bag of saline, fill the chamber and wash the line through. Then, connect the other end of the Y tubing with the RBC unit, fill the chamber and let some blood go through the system as described above.

Transfusion rates

Common infusion rates for one unit

Sometimes, the recommended infusion rates cannot be met for various reasons. Generally, it is important that the transfusion of one unit not take longer than four hours, in order to reduce the risk of bacterial transmission.

Monitoring

Once the transfusion is running, the patient must be monitored.

For the first few minutes you should always go slow—open the clamp a little bit and let the blood flow slowly, so you can react quickly if you detect a potential transfusion reaction. You should definitely stay with your patient for the first 15 minutes.

Furthermore, encourage your patient to speak out loudly if they start feeling differently in any way.

If no reaction takes place within the first 15 minutes, you can increase the blood flow by opening the clamp a little more to achieve the recommended transfusion rate.

It is wise to check on your patient regularly during and after the transfusion, since one third of transfusion reactions occur more than 30 minutes after the transfusion starts and sometimes many hours later.

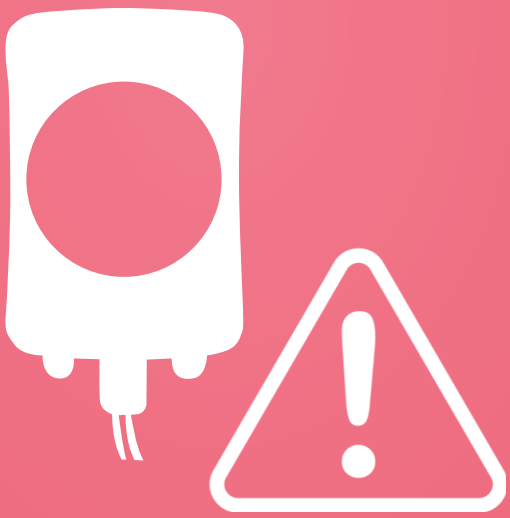
Documentation

The following data should be documented in the patient's clinical record

- Component's donation number
- Date of transfusion
- Type and number of transfused units
- Start time of transfusion
- Stop time of transfusion
- Administering practitioner

Chapter 6

HANDLING COMPLICATIONS



CONSIDERING RISKS AND COMPLICATIONS

Blood transfusion therapy has become a very safe procedure thanks to donor selection and infectious disease screening, pathogen inactivation techniques, as well as guidelines and standard operating procedures outlining how to safely transfuse blood components. However, potentially life-threatening complications still occur.

There are signs and symptoms that should raise the suspicion for transfusion reactions, if they occur within a certain timeframe after the administration of a blood component.

Signs and symptoms include

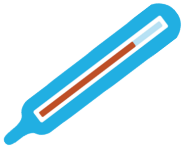
- Fever (a rise of at least 1°C from baseline)
- Flank pain
- Hemolytic (dark) urine
- Respiratory distress
- Hypotension or hypertension
- Skin rash
- Angioedema

Using these symptoms, we can distinguish life-threatening, severe transfusion reactions from rather mild reactions.

Mild transfusion reactions

Mild transfusion reactions include mild allergic reactions (also called hives) and febrile nonhemolytic reactions, which is the official diagnosis for transfusion-related fever without concomitant hemolysis.

Mild allergic reactions



Febrile nonhemolytic reactions

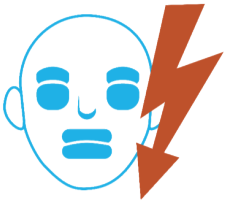
Severe transfusion reactions

The most important severe transfusion reactions are acute hemolytic reactions, transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), anaphylactic shock, sepsis, and graft-versus-host disease.

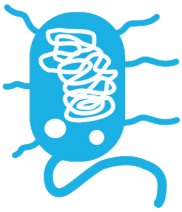
Hemolytic reactions

Lung injury

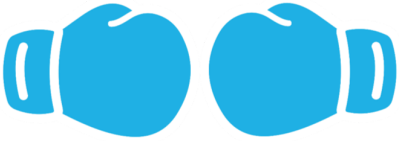
Circulatory overload



Anaphylactic shock



Sepsis



Graft-versus-host disease

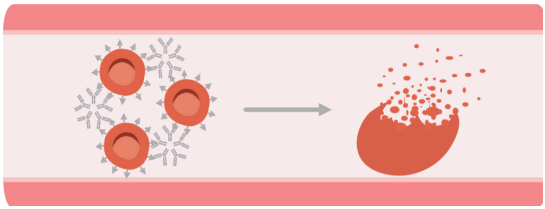
Mild transfusion reactions are the most common transfusion reactions followed by transfusion-associated circulatory overload (TACO) and transfusion-related acute lung injury (TRALI).

RECOGNIZING ACUTE HEMOLYTIC TRANSFUSION REACTION

A severe transfusion reaction is considered to be *acute* if it occurs within the first 24 hours after starting the transfusion.

24 hours

Each new symptom, or any deterioration in the patient's condition, in that period of time is suspicious and should be taken seriously. If you suspect the patient is having a reaction, the first step is to stop the transfusion and then workup the differentials. The first reaction you should think of is **acute hemolytic transfusion reaction**.

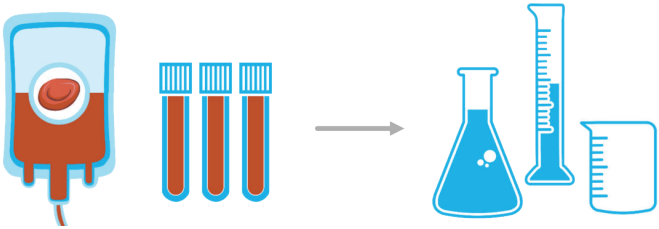


Acute hemolytic transfusion reaction is a rare complication caused by incompatible blood transfusion leading to intravascular hemolysis.

Signs and symptoms include

- Fever and chills (> 1°C from baseline)
- Hives
- Flank or back pain
- Hemolytic (dark) urine
- Hypotension or hypertension
- Abnormal bleeding

An important step in the workup for hemolytic transfusion reaction is to send the remaining blood product and new blood samples, obtained from the patient, back to the lab. The lab staff will then check for errors in pre-transfusion testing, and will test for hemolysis and bleeding abnormalities that should be treated.



IDENTIFYING OTHER SEVERE TRANSFUSION REACTIONS

Aside from hemolytic reactions, there are also other types of acute transfusion reactions that you should be aware of.

Transfusion-related acute lung injury (TRALI)

TRALI develops after factors in the blood product, for example donor anti-leukocyte antibodies (anti-HLA antibodies) cause the activation of neutrophils in the recipient's lung tissue.

Signs and symptoms present during or within 6 hours after beginning the transfusion

- Acute respiratory distress and hypoxia
- Fever and chills
- Hypotension

Pulmonary infiltrates on a chest x-ray, along with hypoxemia, confirm the diagnosis.

When TRALI is confirmed, the transfusion service may need to recall all other blood products derived from that donor, so it is important to inform them of this diagnosis.

Transfusion-associated circulatory overload (TACO)

TACO develops as a consequence of volume excess, typically after transfusion of large volumes in a short period of time. Patients with underlying heart or renal disease, as well as very young or very old patients, are at special risk.

Symptoms present during or up to 6 hours after beginning the transfusion. Clinically, TACO presents with

- Acute respiratory distress and hypoxia
- Rales and wheezing
- Hypertension
- Jugular venous distension

TACO is characterized by pulmonary edema, which can be seen in a chest x-ray.

The biomarkers BNP or NT-proBNP, which are typically elevated in ventricular dysfunction, might also be elevated in TACO. However, the sensitivity and specificity of these natriuretic peptides are not good enough to base the diagnosis of TACO solely on these lab markers.

Anaphylactic transfusion reaction

An anaphylactic shock related to transfusion is very rare and is caused by the transfusion of factors that the recipient is allergic to.

An anaphylactic reaction is typically characterized by a rapid onset of

- Acute dyspnea with hypoxemia (typically with stridor)
- Hypotension
- Angioedema (not obligatory)

There is no specific diagnostic workup that will help you define the diagnosis in the acute setting. However, the symptoms of anaphylaxis are very characteristic, so you can typically base your diagnosis on the presence of these symptoms in the acute setting.

Transfusion-transmitted bacterial infection / sepsis

Symptoms suspicious of contamination of the blood product typically include

- Fever and chills (> 39°C or > 2°C above baseline)
- Tachycardia
- Hypotension or hypertension

The onset of symptoms typically occurs within the first 5 hours after transfusion.

If you suspect sepsis, the remaining blood product should be sent to the pathology department for gram staining and culture, and the blood service should be informed.

MANAGING SEVERE TRANSFUSION REACTIONS

When a patient shows signs of an acute severe transfusion reaction, it will not immediately be clear what the cause of their symptoms is.

Steps the clinician should take

1. Stop the transfusion immediately
2. Call for medical assistance
3. Assess your patient using the ABC algorithm
    - Airway
    - Breathing
    - Circulation
4. Start chest compressions if no signs of circulation
5. Check that IV access stays patent by giving fluid therapy
6. Monitor body temperature, oxygenation saturation, blood pressure, heart rate, and urinary output
7. Make a quick clinical assessment
8. Check the blood component
    - compare compatibility label on product with patient's identification number (ID)
    - Check component for any signs of leakage, discoloration or bubbles

If a specific transfusion reaction is suspected, further testing should be initiated.

The transfusion service should be informed about

- *Why* the patient received the transfusion
- *What* the symptoms are
- *When* the transfusion was started
- *When* the symptoms began to appear

The transfusion service will help you find the diagnosis, determine what blood samples are needed for further investigations and what documents to fill out, and they will guide you on how to proceed if the patient is still in need of further transfusion therapy.

DEALING WITH MILD TRANSFUSION REACTIONS

Mild allergic transfusion reaction

Mild allergic transfusion reaction is the most common transfusion reaction.

It is characterized by mild symptoms such as

- Hives (urticaria)
- Itching
- No change in vital signs

Hypotension Dyspnea Angioedema

There are no systemic symptoms like hypotension, dyspnea or angioedema, all of which would indicate a systemic anaphylactic reaction.

If a patient shows signs of a mild allergic reaction, it is best to stop the transfusion and wait to see whether the symptoms improve. Antihistamines can also be administered. If the symptoms wane, the transfusion can slowly be continued. However, the patient should be monitored for the remainder of the transfusion.

Febrile nonhemolytic transfusion reaction (FNHTR)

Febrile nonhemolytic transfusion reaction is common. It is generally caused by leukocytes present in the blood product producing cytokines like interleukin 6 or 8. Prestorage leukoreduction of the blood product significantly decreases the probability of this complication.

Symptoms typically appear 1–6 hours after beginning the transfusion, and include

- Unexplained fever and chills
- Rigors
- Myalgia

The diagnosis of febrile nonhemolytic transfusion reaction is made only by excluding other transfusion reactions.

FNHTR can further be divided into mild and moderate. In the mild form, temperature rises up to 38°C or above, but still < 2°C above the pre-transfusion baseline. If the temperature rises to > 2°C above the pre-transfusion baseline, the reaction is considered moderate.

In **mild** cases, the transfusion might be stopped. If symptoms wane and the transfusion is still indicated, the transfusion can be started again—but slow it down a bit. Again, monitoring the patient is indicated.

In **moderate** cases, the transfusion should always be stopped. If it is still necessary to continue with the transfusion, it is best to order a new blood product rather than continuing with the old one.

Mild reactions are more common than severe ones. However, all transfusion reactions must be taken seriously as they can be fatal. Always stay safe, and when in doubt, talk to your transfusion lab and ask them for their opinion!

SPOTTING DELAYED TRANSFUSION REACTIONS

Delayed transfusion reactions occur more than 24 hours after the blood component was given.

> 24 hours

Delayed hemolytic transfusion reaction

Delayed hemolytic transfusion reactions occur days to weeks after transfusion.

The following findings suggest this type of delayed reaction

- Hemolytic anemia
- Jaundice
- Splenomegaly
- Renal impairment

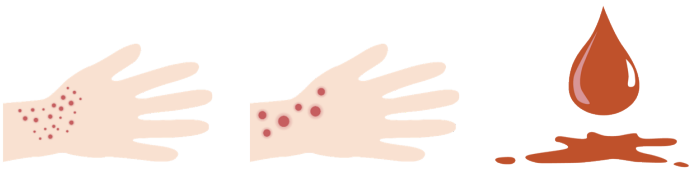
Often, the patient may be asymptomatic.

The diagnosis is made using laboratory tests, like the direct antiglobulin test (DAT) and an antibody screen, which identify the culprit antibodies, and can be used to prevent similar reactions in the future.

Post-transfusion purpura

Post-transfusion purpura generally occurs about 5–10 days after the blood transfusion. It is extremely rare, and almost always affects women.

This reaction occurs when antibodies against a specific antigen (human platelet antigen-1a), which are present in the recipient, attack the transfused platelets. These antibodies are extremely rare. Interestingly, they then destroy not only the transfused platelets, but also the recipient's own platelets. Consequently, the recipient develops significant, potentially life-threatening thrombocytopenia leading to petechiae, purpura or even active bleeding.



Petechiae Purpura Active bleeding

Transfusion-associated graft-versus-host disease

Transfusion-associated graft-versus-host disease occurs anywhere from 4–30 days after the transfusion. It has been described after the transfusion of red blood cells and platelets, and is almost always fatal.

Pathophysiologically, T-lymphocytes in the blood product attack the recipient's antigen-presenting cells and tissues, which leads to damage to the bone marrow, liver, gastrointestinal tract, and skin.

Symptoms include

- Fever
- Abdominal pain
- Profuse diarrhea
- Vomiting
- Skin rash

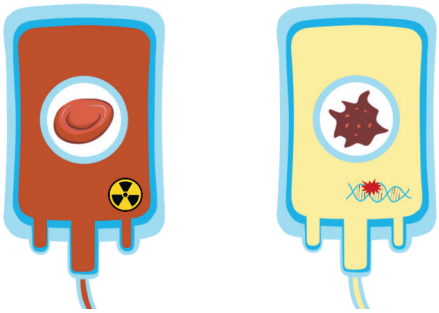
In the lab, you see pancytopenia (due to the bone marrow depression), abnormal liver function tests, and abnormal electrolyte levels (due to the diarrhea).

Patients at risk are those with impaired immune systems, including

- Immunodeficient patients
- Stem cell transplant recipients
- Patients receiving certain chemotherapy drugs
- Fetuses

Unfortunately, the diagnosis of graft-versus-host disease is commonly delayed, since the symptoms are often attributed to the underlying disease itself. The diagnosis is made by biopsy of the affected skin, and, eventually, HLA testing of the circulating lymphocytes.

Thus, in patients at risk for graft-versus-host disease, the use of irradiated red blood cells or nucleic acid-targeted pathogen-inactivated platelets is indicated to prevent this dangerous transfusion reaction.



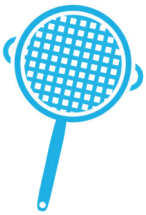
PREVENTING COMPLICATIONS

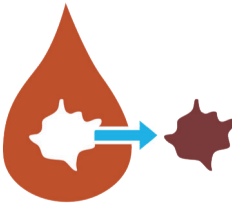
The most important way to prevent transfusion complications is to ensure pre-transfusion patient identification. By properly confirming identification, we can do our best to ensure compatibility, and dangerous hemolytic transfusion reactions can be avoided.

The risk of complications can be further decreased by ordering components that have undergone modifications before administration.

Leukoreduction

There is a small amount of donor leukocytes left in all red blood cell (RBC) units. These leukocytes can lead to mild or serious adverse transfusion reactions, such as febrile nonhemolytic transfusion reaction.
In many developed countries, universal leukoreduction by filtering or apheresis of RBC units is already in place. In other countries leukoreduction is only performed in selected cases.



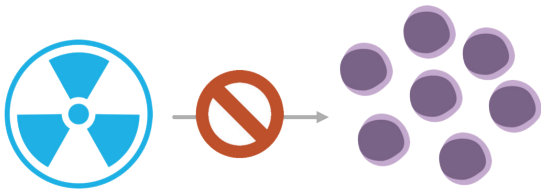


Indications for selected leukoreduction include

- Chronically transfused patients
- Transplant patients and potential transplant patients
- Patients with previous febrile nonhemolytic transfusion reactions
- Patients undergoing cardiac surgery

Irradiation

Red blood cells and platelets can be irradiated in order to decrease the risk of transfusion reactions. Irradiation of blood products with at least 25 gray (Gy) inhibits the proliferation of lymphocytes, which prevents graft-versus-host disease.



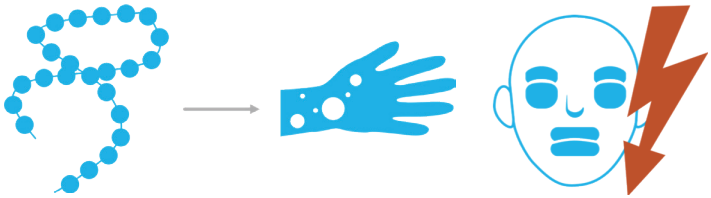
≥ 25 Gy

Indications for RBC or platelet irradiation include

- Immunodeficient or immunocompromised patients
- Transplant patients and potential transplant patients
- Fetuses and premature low birthweight neonates
- Recipients of blood products from relatives
- Recipients of blood products from HLA-matched donors

Washing

RBC units can contain small amounts of plasma. Proteins in the plasma can cause allergic reactions, either mild (e.g., rash or hives) or severe (e.g., anaphylactic shock). To reduce the risk of allergic reactions, components can be washed by the lab immediately before transfusion.



Indications for RBC washing include

- Severe or recurrent allergic reactions to previous transfusions
- Immunoglobulin A deficiency

Since washing also reduces the amount of transfused potassium, washing is also an option in patients at risk for developing hyperkalemia, such as newborns or patients with severe renal impairment.

Premedication

Some protocols attempt to reduce the risk of transfusion reactions by giving medications, such as antihistamines, steroids or antipyretics, prior to the transfusion.

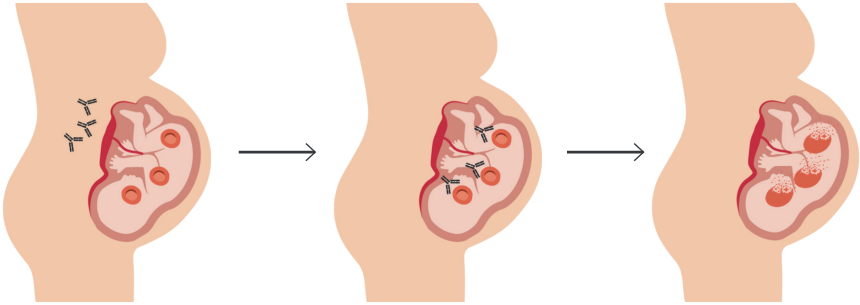
However, there is no evidence that this strategy reduces the incidence of these complications and should therefore not be encouraged.

Chapter 7

SPECIAL SITUATIONS

SCREENING FOR HEMOLYTIC DISEASE OF THE FETUS AND NEWBORN

Hemolytic disease of the fetus and newborn (HDNF) occurs when there is incompatibility between the maternal and fetal blood type. This causes maternal alloantibodies directed against fetal antigens to pass through the placenta and attack fetal red blood cells, causing hemolysis. Since only IgG antibodies can pass the placenta, only IgG antibodies can cause HDNF.



For the mother to produce IgG alloantibodies, it is generally necessary for her immune system to become sensitized by foreign red blood cells before the pregnancy.

This can happen in one of three ways

Previous pregnancy

Blood transfusion

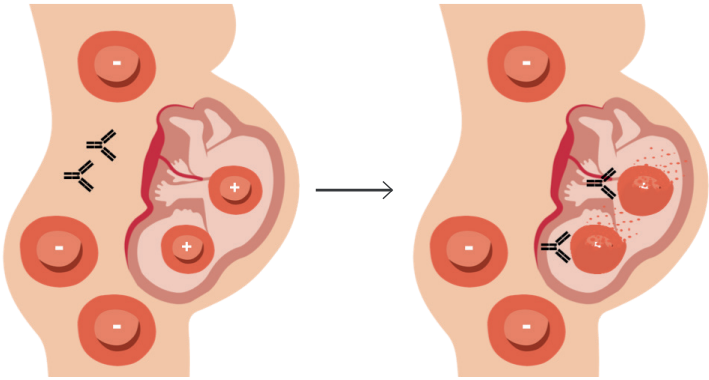
Needle sharing

How does pregnancy lead to immunization?

During pregnancy, small amounts of fetal blood pass into the mother's circulation. This is known as fetomaternal bleeding. If the fetal blood type is incompatible with the mother's, those cells can stimulate an immune reaction leading to the production of antibodies against the fetal antigens.

Rhesus D incompatibility

The most common incompatibility resulting in hemolytic disease is Rhesus D incompatibility. In this case, the mother is Rhesus D negative and the child Rhesus D positive. Consequently, the mother produces IgG antibodies against the foreign fetal D antigen. This is generally of no clinical consequence to mother or baby during this first pregnancy. However, if the mother later becomes pregnant with another D positive child, these antibodies will then cross the placenta and attack the fetal red blood cells, leading to hemolysis.

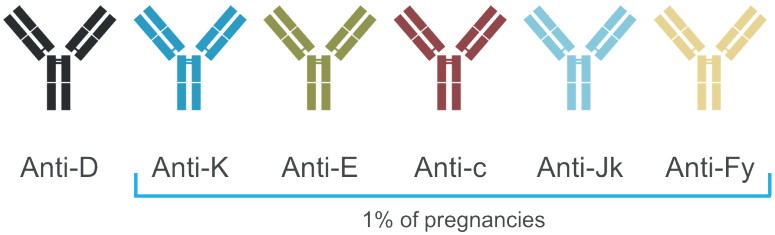


ABO incompatibility

ABO incompatibility between the mother and fetus can also have clinical consequences. Naturally occurring anti-A and anti-B antibodies are mainly IgM, so they do not cross the placenta. However, the mother may carry IgG ABO antibodies, especially if she was exposed to foreign ABO antigens in a previous pregnancy. These IgG antibodies can cross the placenta and cause hemolysis of fetal red blood cells.

Severe anemia is very rare in this situation. Normally, the newborn develops only mild anemia, or no anemia at all. However, they may show concomitant hyperbilirubinemia and jaundice, which is treated efficiently with phototherapy in most cases.

Other dangerous alloantibodies that can induce HDFN are anti-Kell (anti-K), anti-E, anti-c, anti-Kidd (anti-Jk), and anti-Duffy antibodies (anti-Fy).



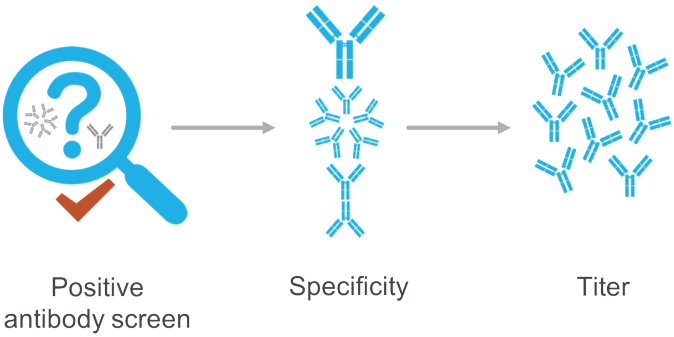
Antenatal screening

Antenatal screening programs have been widely implemented to prevent, or at least diagnose, and treat HDFN. Every pregnant woman should be screened on their first prenatal visit.

The following tests should be ordered

- ABO blood group
- Rhesus blood group
- Antibody screen

In patients with a positive antibody screen, the antibody specificity (i.e., the type of antibody), as well as the amount of antibody (i.e., the antibody titer) should be determined by the lab.



If the antibody titer is above a critical threshold further testing is necessary

- Fetal antigen testing—to identify the fetal blood group in order to evaluate the risk of HDFN
- Middle cerebral artery (MCA) Doppler ultrasound—to detect fetal anemia

Once the antibody titer is above the critical threshold, there is no need to repeat antibody testing, since the antibody titer does not correlate with the severity of the disease. Close follow-ups with MCA Doppler examinations should be planned throughout the pregnancy.

On the other hand, if the maternal antibody titer is below this critical threshold, antibody titers should be repeatedly monitored throughout the pregnancy in order to detect a possible rise in antibody titer early enough to act on it.

In any case, pregnant women with relevant antibody titers should always be referred to a specialist to ensure they receive the best medical care.

PREVENTING RHESUS DISEASE

Rhesus disease can occur when a Rhesus negative mother carries a Rhesus positive fetus. It first requires the Rhesus negative mother to become sensitized / immunized by a past exposure to Rhesus positive red blood cells, either in a previous pregnancy, through a blood transfusion, or rarely through needle sharing. If the woman subsequently becomes pregnant with another Rhesus positive child, small amounts of fetal RBCs enter the mother's circulation and boosts anti-D IgG antibody production. These IgG antibodies then cross the placenta and lead to hemolysis and anemia in the fetus (and occasionally the newborn).

The most severe form of Rhesus disease is called **hydrops fetalis**. Here, the fetus develops heart failure with multiple effusions and edema, which is fatal to the fetus.

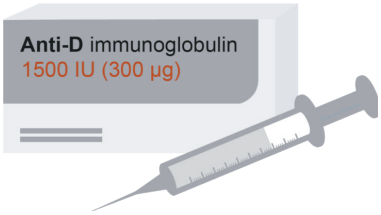
Rhesus disease screening programs

Many countries have implemented programs to prevent Rhesus disease by preventing sensitization of the mother's immune system. The program starts with screening all pregnant women for their Rhesus antigen and antibody status, at their first prenatal visit, as part of their blood group testing.

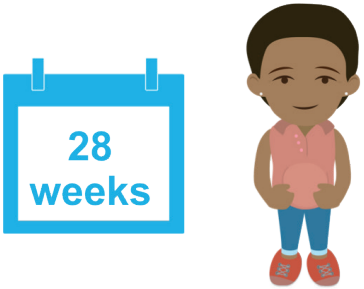
Any Rhesus negative woman who carries a Rhesus positive child bears the risk of becoming sensitized; therefore, all Rhesus negative mothers receive an anti-D immunoglobulin prophylaxis to prevent immunization. Basically, these prophylactic anti-D antibodies bind to red blood

cells with D-antigens, (i.e., the fetal RBCs) and induce increased clearance of the fetal RBCs without activating the mother's adaptive immune system. This minimizes the chance of developing hemolytic disease of the fetus and newborn in subsequent pregnancies.

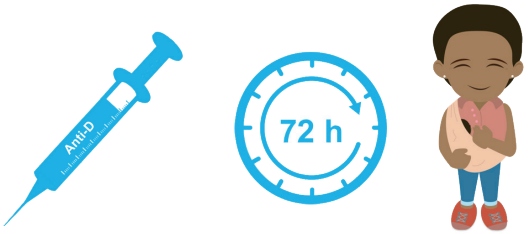
A single dose of the anti-D immunoglobulin (1500 IU or 300 ug) contains enough anti-D to suppress 30 mL of fetal whole blood. That should be enough for normal amounts of fetomaternal bleeding. The prophylaxis can be administered either intramuscularly or intravenously, depending on the preparation.



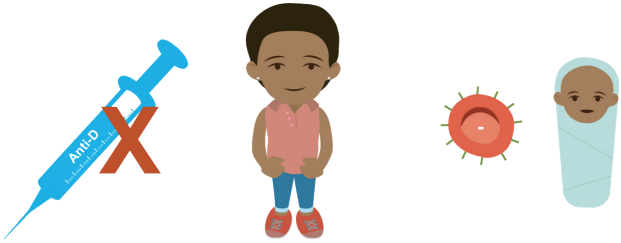
The first shot is given at 28 weeks of gestation.



The second shot is administered after birth, and is **only** given to Rhesus negative mothers whose newborn tests Rhesus positive in a simple cord blood examination. In this case, anti-D prophylaxis should be administered to the mother within 72 hours after giving birth.



If the baby turns out to be Rhesus negative, there is no need for prophylaxis, as there is no danger of sensitization and Rhesus D disease.



Additional anti-D prophylaxis shots

An additional shot of anti-D prophylaxis might be given to Rhesus negative mothers in situations that present a high risk of increased fetomaternal bleeding.

These situations include

- Abortion or threatened abortion
- Fetal death
- Ectopic pregnancy
- Invasive inutero procedures
- External cephalic version
- Antenatal vaginal bleeding
- Abdominal trauma
- Partial molar pregnancies

In most situations, one single dose (300 ug) of anti-D immunoglobulin will be enough to prevent immunization. When fetomaternal bleeding of more than 30 mL of fetal whole blood is suspected, special laboratory tests can estimate the extent of bleeding and determine the adequate dosage.

No need for anti-D prophylaxis

There is no need for anti-D prophylaxis in

- Rhesus D positive mothers
- Mothers who were already sensitized from past pregnancies or transfusions
- Rhesus negative mothers who certainly carry a Rhesus negative fetus

The most modern and safest way to determine the fetal Rhesus status is by performing fetal cell-free DNA testing.

DIAGNOSING AUTOIMMUNE HEMOLYSIS

Patients with hemolysis often present with symptoms of hemolytic anemia such as

- Paleness
- Fatigue
- Tachycardia

If anemia is only mild, there might be no specific symptoms at all.

Laboratory findings

The most important laboratory findings that can help you diagnose hemolysis include

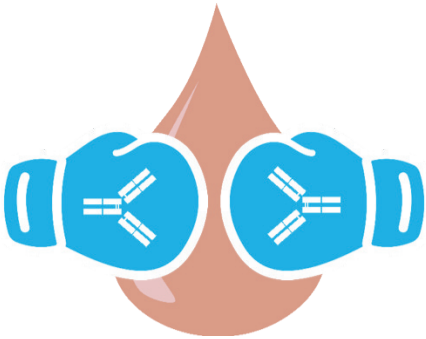
- Elevated lactate dehydrogenase (LDH)
- Elevated bilirubin
- Reticulocytosis
- Decreased haptoglobin
- Elevated free hemoglobin and hemoglobinuria (in intravascular hemolysis)

Immune-mediated hemolysis is mainly caused by four pathologies

- Autoimmune hemolytic anemia (AIHA)
- Drug-induced autoimmune hemolytic anemia

- Hemolytic transfusion reaction following incompatible blood transfusion
- Hemolytic disease of the fetus and newborn

If your patient's laboratory results suggest hemolytic anemia, you should immediately consider the most common cause of hemolytic anemia in adults: **autoimmune hemolytic anemia**.



Pathophysiology

In autoimmune hemolysis, antibodies that are directed against the individual's own red blood cell antigens (**autoantibodies**) attack the individual's RBCs causing hemolysis. The loss of functional red blood cells leads to anemia. These autoantibodies can be of different immunoglobulin classes: IgG, IgM or IgA. In some cases the complement system is also activated.

Causes

Approximately half of the cases of autoimmune hemolysis are idiopathic, meaning no overt cause can be determined. The other 50% result from secondary causes.

Idiopathic

Secondary

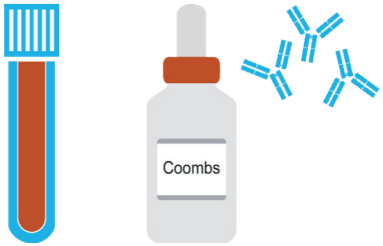
Diseases or conditions that are known to induce autoimmune hemolysis

- Neoplasms (especially lymphoproliferative disorders like lymphoma or chronic lymphocytic leukemia)
- Autoimmune diseases (e.g., systemic lupus, rheumatoid arthritis or inflammatory bowel diseases)
- Infections (e.g., mycoplasma, viral pneumonia or infectious mononucleosis)
- Drugs (e.g., penicillin, diclofenac or methyldopa)

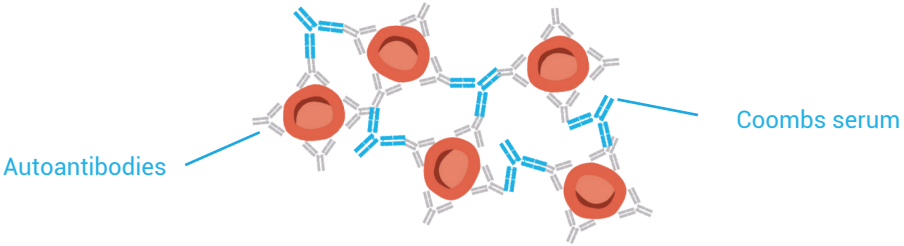
Direct antiglobulin test (DAT)

To determine whether the hemolysis is of autoimmune nature, the transfusion lab performs the direct antiglobulin test (DAT). Basically, the DAT can verify that the patient's red blood cells have already been attacked by antibodies that cause hemolysis.

To perform this test, the patient's RBCs are mixed with antiglobulin antibodies (i.e., antibodies that bind to IgG antibodies). This mixture is known as Coombs serum.



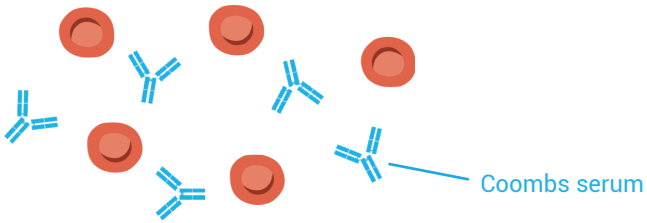
If the patient's RBCs are already covered with IgG antibodies, the antiglobulin antibodies (Coombs serum) will bind to the IgGs on the RBC surface and cause agglutination, which can be seen macroscopically. In this case, the direct antiglobulin test is positive. This result confirms the presence of autoimmune hemolysis.



Positive DAT

The lab can then go on to further determine the specificity of the autoantibodies, and whether the complement pathway is activated. These results, plus a proper medical history, help to narrow down the cause of the autoimmune process and lead the way to the best treatment option.

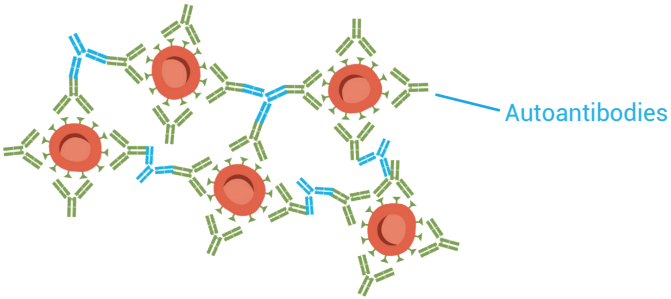
If there are no autoantibodies on the patient's RBCs, the antiglobulin serum has nothing to bind to, so there will be no agglutination. The direct antiglobulin test is negative. There must be a non-autoimmune reason for hemolysis.



Negative DAT

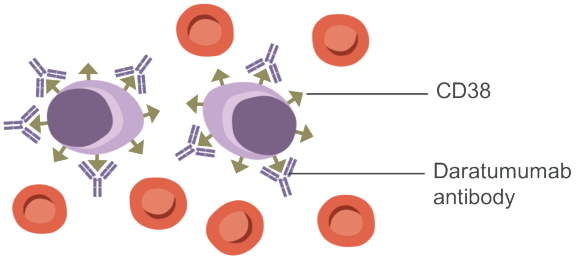
A positive DAT will not only indicate autoimmune hemolytic disease, but will also show recent hemolysis caused by the incompatibility of red blood cell antigens and antibodies, such as would occur following a hemolytic transfusion reaction or hemolytic disease of the newborn.

In these two cases, RBCs might be covered with IgG antibodies as well; however, these would be alloantibodies, instead of autoantibodies. The DAT will induce agglutination of these RBCs in the same way, so in these situations, the DAT helps you to demonstrate that hemolysis is ongoing.



CONSIDERING DARATUMUMAB

Daratumumab, a monoclonal antibody, is an established treatment option in relapsed or refractory multiple myeloma. Daratumumab is directed against the antigen CD38, which is highly expressed on myeloma cells.



However, CD38 is also weakly expressed on red blood cells. Therefore, the presence of daratumumab in a patient's serum can influence the results of pre-transfusion testing. It interferes with reagent and donor blood cells used in antibody screening, as well as in crossmatching, and may also affect the results of a direct antiglobulin test (DAT).

Two major problems arise from this interference

1. Daratumumab-induced agglutination can mask the presence of clinically relevant alloantibodies, which in turn might induce serious transfusion reactions.
2. Performing the procedures required to eliminate these interferences lead to delays in issuing RBC units, which might harm the patient. Communication between the clinicians and the transfusion lab staff is essential in this situation.

Recommendations

Current recommendations provide guidance on how to deal with interference from daratumumab.

Before therapy

Experts advise performing an array of tests on the myeloma patient's blood samples **before** starting daratumumab therapy.

These tests include

- Blood typing with an extended RBC phenotype or genotype
- Antibody screen
- Direct antiglobulin test (DAT)

The patient should also be provided with an alert card that states they are a daratumumab patient. This card should be presented to every healthcare provider prior to any treatment.

During therapy

If the patient needs blood transfusions during therapy, the lab must be informed, before the transfusion, that the patient was administered daratumumab.

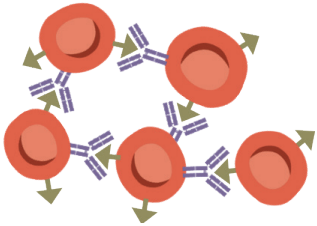
The lab staff will then treat both the test and donor cells with a special chemical called Dithiothreitol (DTT), which destroys CD38 on the cells. This should eliminate any interferences made by daratumumab.

However, this is a time-consuming and labor-intensive procedure, so it is best to plan the patient's visit or transfusion setting as early as possible, to avoid delays.

Another option is to order blood units that are matched not only according to the ABO and Rhesus blood group, but also other blood groups, in order to avoid any immunization. However, this level of matching takes time, depends on the availability of specifically matched blood products, and is more expensive.

After therapy

Since antibody screens and compatibility testing might show daratumumab-induced agglutination for up to six months after discontinuation of daratumumab therapy, it is important to inform the lab staff that the patient had been previously treated with daratumumab in this time period.

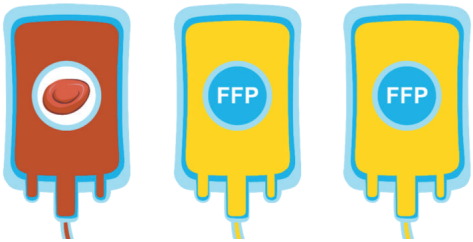


Chapter 8

PRACTICING YOUR SKILLS

ASSESSING AN ACUTE TRANSFUSION REACTION

On Nora's first night shift as a resident in the ICU, she gets the order to administer one red blood cell (RBC) unit and two units of fresh frozen plasma (FFP) to Mr Doe.



Mr Doe is a 78-year-old patient who came out of surgery today. He has lost a lot of blood and his coagulation assessment showed abnormalities. However, his vital signs are stable.

About four hours after starting the transfusion, Nora is called to examine Mr Doe. He has trouble breathing and is hypoxic (oxygen saturation 85%). He is tachycardic (pulse 101 beats / minute) and his blood pressure is high (150/95 mmHg). His temperature is 36.4°C. On auscultation, there is no wheezing, but Nora hears decent bibasilar rales.
Mr Doe's leading symptom is acute respiratory distress.

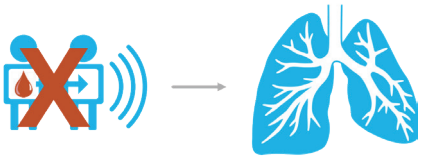
Respiratory distress with hypoxemia is suggestive of three severe acute transfusion reactions

Anaphylaxis

Transfusion-related acute lung injury

Transfusion-associated circulatory overload

Furthermore, there are non-transfusion-related causes of respiratory distress, like pneumothorax.



Anaphylactic transfusion reactions are usually accompanied by stridor, angioedema and / or hypotension. This does not fit Mr Doe's profile. Therefore, in this case, we should consider TRALI, TACO, and non-transfusion-related causes.

After providing Mr Doe with oxygen, Nora orders additional tests to better differentiate between these differentials.

- A chest x-ray is performed.
- Nora would wish to have an echo done, but there is no doctor available who is capable of performing an echo.
- A blood sample is also sent to the lab for NT-proBNP testing.

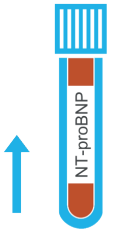
Test results

Chest x-ray

The chest x-ray shows pulmonary edema. There is no sign of infiltration and no pneumothorax.

Lab results

NT-proBNP levels are clearly elevated, at 3500 ng / mL.

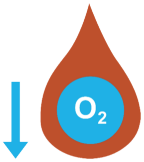


3500 ng / mL

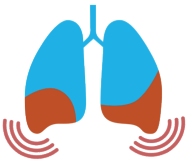
Diagnosis

Since there is no sign of pneumothorax on the chest x-ray we are left with the two differentials—TRALI and TACO. Both present with respiratory distress with hypoxemia and both can lead to pulmonary edema, which is indicated by the rales in auscultation. Both occur within the first six hours after transfusion.

Respiratory distress



Hypoxemia



Bibasilar rales

What differs is that TRALI is characterized by bilateral infiltration on the chest x-ray.

Bilateral infiltration

TACO, on the other hand, is characterized by signs and symptoms associated with heart failure: pulmonary edema, elevation in NT-proBNP or BNP levels, and hypertension.

Heart failure

Pulmonary edema

Elevated NT-proBNP

Hypertension

Taken together, Nora diagnoses **transfusion-associated circulatory overload (TACO)** and starts diuretic therapy intravenously to mobilize Mr Doe's excess fluid, of course with oxygen support. Soon, Mr Doe feels better, and his pulmonary edema recedes.

Furthermore, Nora notifies the lab of the transfusion reaction, since the lab must make a report for hemovigilance.

To avoid further problems, unnecessary transfusion should be avoided in Mr Doe's case. However, if he needs further blood components in the future, it is important to cut down on the volume given and to avoid fast transfusion rates.

MANAGING A PRE-SURGICAL PATIENT

Nora is spending the day at the pre-admission clinic. The next patient she sees is Max, a 70-year-old male, who is scheduled for a unilateral hip replacement in four weeks. The only medications Max takes are statins for his hyperlipidemia. Besides that, and an appendectomy in his youth, his medical record is blunt.

As part of the pre-admission clinic protocol, Nora orders a complete blood count (CBC) and a full iron status, among other tests.

Test results

RBC count: 3.4 million cells / µL (reference range 4.5–5.5)

Hemoglobin: 10.2 g / dL (reference range 13.5–17.5)

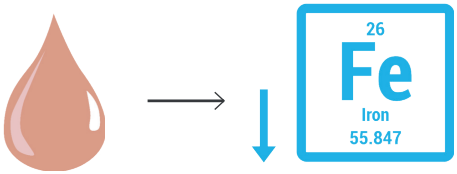
Hematocrit: 31% (reference range 40–54)

Mean corpuscular volume (MCV): 70 fL (reference range 80–96)

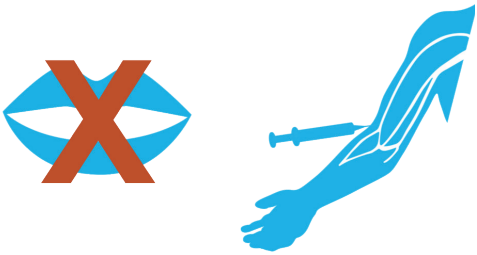
Ferritin: 15 ng / mL (reference range 23–336)

Diagnosis

With decreases in hemoglobin and MCV, Max has microcytic anemia. The most common cause of microcytic anemia, especially in older age, is iron deficiency. Looking at Max's low ferritin, we can confirm that Max has an iron deficiency anemia.

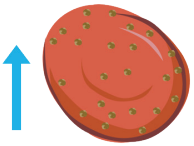


Since Max is having an elective hip arthroplasty in several weeks, there is enough time to restore his iron levels and treat his anemia before undergoing a surgery that presents a high risk of bleeding. Thus, the next step should be to start iron supplementation. Since Max does not tolerate oral iron well, Nora chooses to treat him with intravenous iron.

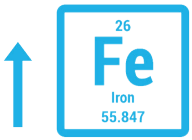


Surgery

On Max's lab report the day before surgery his hemoglobin has risen to 14 g / dL and his ferritin levels are at 120 ng / mL, both of which are within the normal range. Max is now ready for surgery.



14 g / dL



120 ng / mL

After surgery

After Max's hip replacement, the surgeons tell Nora that there has been a lot of bleeding, but they were able to stop it and the replacement went as planned.

As part of his post-operative assessment, Nora runs a CBC and she sees that Max's hemoglobin has dropped to 9.9 g / dL, so he is anemic again. On a follow up the same day, there is no change in hemoglobin levels. Max is doing well and is already slowly mobilized.

Since Max's hemoglobin levels are stable and he has no serious comorbidities, he is definitely the right patient to choose a restrictive transfusion threshold of 7–8 g / dL. Thus, he does not need a blood transfusion as long as he tolerates the drop in hemoglobin well.

Since the previous iron deficiency was treated, Max's red blood cell count should rise in the next couple of weeks. However, at his next checkup his blood count should be checked just to make sure.

TREATING A PREGNANT PATIENT

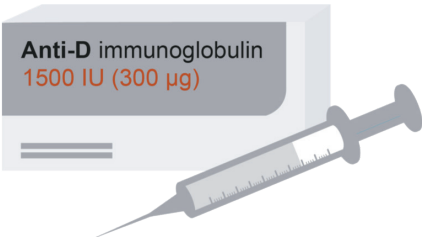
Our patient, Donna, is a 26-year-old female and is pregnant with her first child. She's in her first trimester, without any complications.

Her gynecologist orders a Type and Screen.

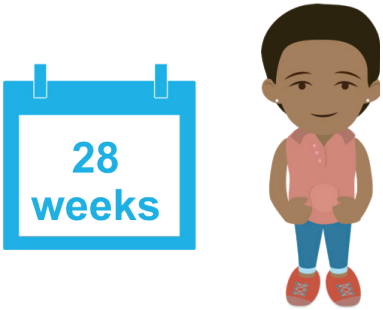
Donna's lab report states

- Blood group: A
- Rhesus D: negative
- Antibody screen: negative

Since Donna is Rhesus D negative, she must receive anti-D immunoglobulin prophylaxis during her pregnancy. This reduces the chance of developing Rhesus D disease in future pregnancies.

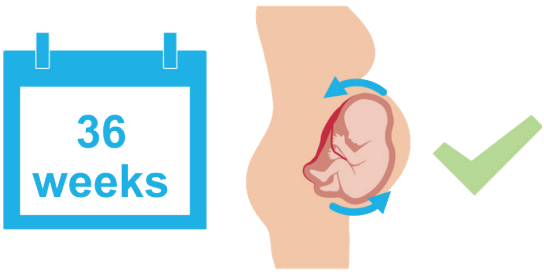


She should receive the first shot of anti-D immunoglobulin in the 28th week of gestation.

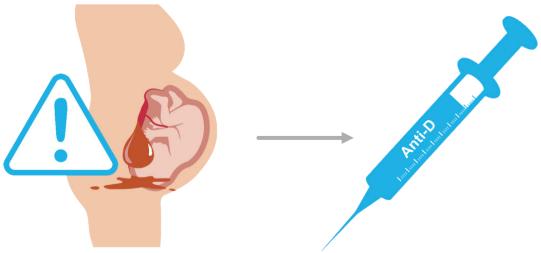


First shot

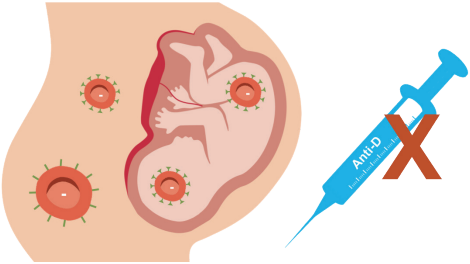
At 36 weeks of gestation, Donna's fetus is in breech position. Since Donna would like to have a vaginal birth, her gynecologist and Donna decide on performing an external cephalic version. The external cephalic version is successful.



After completing the external cephalic version, Donna should receive an additional shot of single dose anti-D prophylaxis, since this procedure increased her risk of fetomaternal bleeding.



After a successful external cephalic version, Donna goes on to deliver a healthy baby boy five days after her due date. The baby's blood type turns out to be A negative—just like his mother's. In Donna's case there is no need for another shot of anti-D, since her baby is Rhesus D negative and thus, there is no danger of Rhesus D disease.



FURTHER READING

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