Provincial Blood Coordinating Program

Bloody Good News

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Newfoundland Labrador

How the Blood Bank Chooses the Best Red Blood Cells for Transfusions

The Type & Screen is a blood bank test ordered as part of pre-transfusion testing. The 'type' part of the Type & Screen refers to ABO blood type and Rh factor.

There is an Rh blood group system but the Rh factor in the 'type' only refers to whether the patient does or does not have the 'D' antigen. Those who have D antigen are Rh positive; those who do not have the D antigen are Rh negative.

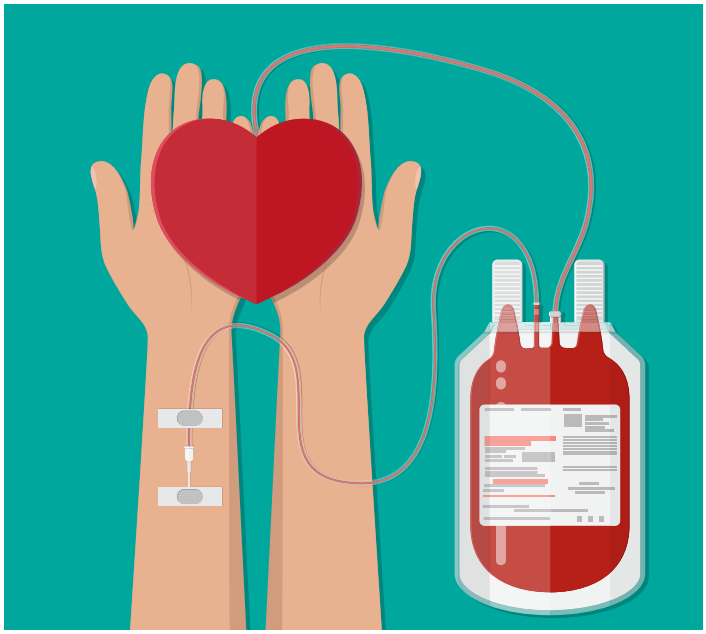
The ABO blood group system is the most well-known, important blood type system in transfusion medicine.

This chart summarizes some key information about the ABO system.

Blood Group	Antibodies	Antigens	Can Donate to	Can Receive from
AB	-	A,B	AB	AB, A,B,0
A	Anti-B	A	A,AB	A,0
B	Anti-A	B	B,AB	B,0
0	Anti-A, Anti-B	-	A,B,AB	0

Red blood cell antigens are genetically determined proteins found on the surface of red blood cells. When foreign red blood cell antigens are introduced into circulation, such as by a blood transfusion, they elicit an immune response. As a result of exposure to antigens, antibodies against the foreign antigens are produced.

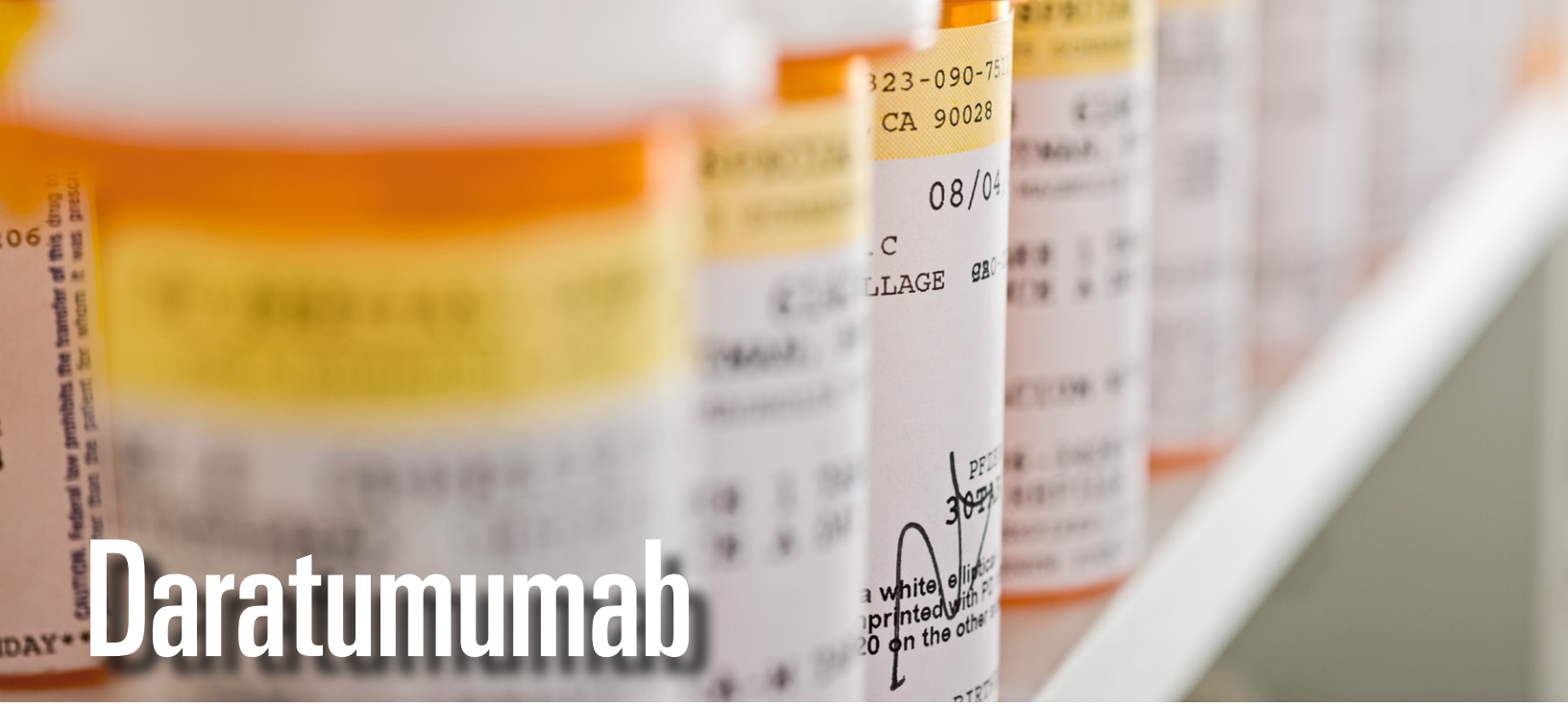
Understanding the ABO system provides an excellent base knowledge for understanding antigens and antibodies. For example, the reason why a person with type A blood group cannot receive a red cell transfusion from a person with type B is because the anti-B already circulating in the type A person would destroy the type B red cells by hemolysis.



Matching the ABO and Rh type of a recipient with ABO and Rh compatible blood is only part of the process when the blood bank is determining the most suitable blood for a recipient to get.

The 'screen' part of the Type & Screen refers to the blood bank test to detect irregular antibodies. This tests the patient's plasma with 'screening' red cells that have a number of common antigens on them. If the red cells 'clump' or agglutinate that means there may be antibodies in the patient's plasma. Following a positive 'screen', a similar process is performed with other panels of red cells with known surface antigens. This will narrow down the possible antibody or combination of antibodies that may be present on the patient's red blood cells.

Once the antibody is identified, a phenotype is performed on the patient for the corresponding antigen. Antigen phenotyping is a blood bank test to confirm the presence or absence of an antigen on red cells. If a patient requiring a transfusion has an antibody, the red cell unit selected for transfusion must lack the corresponding antigen. The blood bank can then release the best red cells for the patient.



Daratumumab

Daratumumab (DARA) is a drug that was approved in June 2016 by Health Canada for one application: third-line multiple myeloma treatment. Much wider use of the cancer drug is anticipated soon, as trials are showing that it is very effective.

Despite the benefits, there is a drawback associated with the use of DARA; when a patient is receiving the drug, antibody testing for transfusion is subject to erratic false-positive results. As a result the blood bank laboratory cannot release crossmatch compatible red cells until the false-positive can be resolved.

When a patient requires or may require units of red blood cells for transfusion a blood type, antibody screen and crossmatch are performed. The patient's ABO/Rh type is not affected by the DARA; however the antibody screen, a test for 'unexpected' antibodies in the patient's plasma, reacts as all positive.

The false-positive result is caused by the DARA binding to the CD38 protein on reagent red cells used for antibody screening, which is the same behavior an irregular antibody would display. The patient receiving DARA would now appear to possibly have an irregular antibody, triggering the blood bank to do a complete antibody investigation.

Blood bank technologists have algorithms for dealing with unexpected test results. The steps to follow in the antibody identification depend on the patient's transfusion history. At the end of the antibody identification a crossmatch is performed. The crossmatch will show up as *incompatible* for a patient on DARA.

The blood bank's investigation of any DARA patients would require less time and effort if advised the patient is on this drug before pre-transfusion testing is initiated. There are several options once the blood bank is aware the patient is receiving DARA. One is to perform antibody screen and identification using Dithiothreitol (DTT) treated reagent red blood cells. DTT treatment of reagent red blood cells prior to addition of patient's serum eliminates DARA interference and allows detection of antibodies with the exception of antibodies to Kell system antigens. DTT treatment destroys the Kell system antigens, therefore Kell negative units should be provided unless the patient is known to be K positive. Other antigens are denatured by DTT. Therefore antibodies against these antigens are also not detected when DTT treated reagent cells are used.

Ideally, before a patient is started on DARA, the blood bank could obtain a pre-DARA blood sample. The blood bank could then test the patient for any known antibodies prior to DARA interference. Other blood bank tests, phenotyping or genotyping, could also be performed to provide the patient with the red blood cells that are most similar to the patient to lower the possibility of the patient forming antibodies that will be masked by DARA in the future. A patient's samples will behave this way up to six months after DARA treatment is complete.

INR Correction in Those Individuals on Oral Anticoagulants

Elevated international normalized ratio (INR) correction is often incorrectly treated or over treated in some individuals receiving oral anticoagulant therapy. Certain factors need to be determined before outlining a plan to correct an elevated INR. The care provider must know which anticoagulant the patient is receiving, know the INR value, and have information on the patient's condition and general plan of care. Of particular importance is whether the patient is actively bleeding, and if the plan of care involves invasive procedures.

Half-life is the amount of time it takes for a drug concentration in the bloodstream to be reduced by one-half. The half-life of different anticoagulants varies. The mean half-life of warfarin, a vitamin K antagonist, is 40 hours. In cases where the INR is elevated but there is no bleeding present and/or surgery is non-emergent, that is, it can be delayed at least 6-12 hours, simply decreasing the dose or withholding the dose of the vitamin K antagonist and/or administering vitamin K therapy may be sufficient to decrease the INR to an acceptable level.

If the patient is actively bleeding or requiring emergency surgery (less than 6 hours) rapid reversal of the INR will be required. It is in these situations that Prothrombin Complex Concentrates (PCCs) should be utilized. PCCs contain clotting factors II, VII, IX, and X. Co-administration of a dose of vitamin K (10 mg IV) is strongly recommended if the INR reversal is required for longer than 6 hours (the half-life of PCCs). Early recognition of individuals who require INR correction followed by early administration of intravenous vitamin K may actually decrease the need for PCC administration.

Newer oral anticoagulants (direct oral anticoagulants or DOACs) such as apixaban, rivaroxaban, and dabigatran initially gained favor amongst both prescribers and patients because they do not require INR monitoring to measure effectiveness (no adjusting of doses required based on blood work), onset of action is more rapid, bridging therapy is not required, and half-lives are shorter so that their effect decreases more quickly (than warfarin) when the drug is discontinued. However, a disadvantage of these newer anticoagulants is that presently there is no proven antidote for reversal with the exception of Praxbind which immediately reverses the anticoagulant effect of dabigatran.

The half-life of DOACs is 8-15 hours in those with normal renal function so the best option presently is to provide supportive care while waiting for the anticoagulant effect of the drug to diminish. Those with minor bleeding may just require withholding the anticoagulant for a dose or two. In those with major bleeding or requiring emergent surgical care supportive measures such as procedures to control the source of bleeding, volume replacement, correction of other coagulopathies caused by the bleeding, and use of other blood products, such as recombinant factor VII and PCCs may be beneficial. Consultation with a hematologist or transfusion medicine expert may be necessary.

Case Study 25

A 74 year old female with chronic anemia, admitted with chest discomfort to rule out pneumonia. One unit of RBCs was ordered to be transfused. The patient had low grade temp 37.8-38.0 over the previous 24 hours. The patient displayed chills and rigors pre-transfusion.

Temperature pre transfusion was 37.5°C; at 15 minute check was 38.3°C.

Pulse pre 90; at 15 minute check 108

Respiration pre 20; at 15 minute check 22

BP pre 118/68; at 15 minute check 122/70

Transfusion was stopped and antipyretics were given. The remainder of unit returned to blood bank and discarded.

What kind of transfusion reaction did the recipient experience?

Answer on back page.

IVIG Doesn't Grow on Trees

The old saying of "money doesn't grow on trees" can be applied to many aspects of transfusion medicine. Canada's supply of blood components and products presently are provided by Canadian Blood Services (CBS) and Héma-Québec (Quebec only). Most blood components and products come from voluntary donors throughout Canada. The ebbs and flows of supply and demand cannot always be predicted and since the supply comes from a natural resource, people, there is only so much available at any given time. The uncertainty of the supply when combined with increasing demand globally is definitely a cause for concern.

Within the last year, the first paid plasma collection clinic opened up in Saskatoon, SK. Plasma is collected from paid donors and sent to a commercial plant for processing. The for-profit company provides payment in the form of a $25 gift card in exchange for plasma. The practise of paying for plasma has led to much debate globally. Many proponents of the paid plasma clinic propose that it is hypocritical to refuse to pay Canadian donors when much of the plasma used to produce products used by Canadians is from paid donors from the US and Europe. Critics of paid plasma clinics feel that the safety of the donor pool will be jeopardized if some form of payment is involved because it gives individuals a reason not to be truthful on the screening questionnaire as compared to a voluntary donation.

Each year over the last two decades intravenous immune globulin (IVIG) use has grown significantly globally. Canada is amongst the three top users per capita of IVIG in the world. Newfoundland and Labrador, along with the other Atlantic Provinces has formed the Atlantic Blood Utilization Strategy (ABUS). A key focus of this group is to develop and implement strategies to ensure appropriate ordering and utilization of IVIG. Conditions being treated with IVIG are subgrouped into three different categories:

- **Labeled (L):** The manufacturer may 'advertise' the use of the product for listed medical conditions;
- **Unlabeled indicated (UL-I):** Although the manufacturer cannot 'advertise' the use for the medical condition(s), there is some evidence to support its use;
- **Unlabeled not indicated (UL-N):** There is no evidence to support the use of IVIG or evidence exists that shows it to be ineffective

More stringent regulations are required to ensure that IVIG is not being used for those conditions with no evidence to support use, that is, the unlabeled-not indicated conditions. In essence those individuals are being given treatment with potential side effects with no evidence that it will be of any benefit to them. This does not reflect best practice. For the unlabeled-indicated conditions, there is some evidence to support use. In this group, individuals should be monitored at regular intervals to see if in fact the treatment is impacting them positively. If no evidence of effect, treatment should be discontinued. The focus should be on finding alternative treatments for these conditions. Again, it is a treatment with side effects, with limitations to supply, and is expensive, so many countries are implementing stringent evidence–based regulations to ensure IVIG is used only for those approved labeled conditions and for those unlabeled-indicated for which evidence has shown effectiveness. Measures must be in place to ensure that if new labeled conditions arise, that the supply will be there to meet the demand.

Case Study 25 Answer: This was not a transfusion reaction. Temperature did not rise greater than 1°C and symptoms were not caused by transfusion.

We want to hear from you to help us improve Bloody Good News! Please complete the survey at: www.surveymonkey.com/r/QGKQ557

In the next issue... Hereditary Angioedema

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