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Module Description and Purpose

This learning module is designed to assist nurses in understanding acute adverse transfusion reactions.

What exactly does Adverse Transfusion Reaction mean?

- **Adverse** - 1. Contrary in purpose or effect, opposite.
- 2. Harmful to one’s interest; unfortunate
- **Transfusion** - A transfer of blood from one person to another
- **Reaction** - An opposed or return action

A patient receives blood products to get better, not to become increasingly ill or in some cases expire. Since Dr. Karl Landsteiner’s ground breaking discovery of the ABO blood grouping in 1900, blood transfusions have become a standard medical option. Each year developments happen that make receiving blood products safer.

Unfortunately, there is still risk involved in receiving blood products. To make things more complicated, patients are also aware of this.

What can the nurse do? The desired goal is to have confidence but not to be complacent, to be aware without being obsessive. Knowledge and experience will help the nurse achieve this. While it will be up to the nurse to gain experience, the following material will help to provide the knowledge.

Objectives of the Module

At the completion of the Acute Transfusion Reactions Module the nurse will:

- Have the knowledge and ability to recognize and manage Acute Transfusion Reactions:
  - Identify symptoms of different types of acute transfusion reactions.
  - Administer treatment for different types of acute transfusion reactions.
  - Manage acute adverse transfusion reactions in a variety of environments.

Module Requirements

To complete this module, the learner will:

1. Study the module information.
2. Complete the quizzes at the end of each section of the module.
3. Record learning for Continuing Competency Program using the Record of Professional Activity form or other organized manner.
**Blood Products**

Blood is essential for life. It is an important science breakthrough that can be transfused from donors to patients.

What happens to that unit of whole blood once it is donated? It is separated into its different components which are:

![Composition of blood](image)

- **Plasma (45-55%)**
  - Transport nutrients to tissue
  - Transports waste to organs to be excreted
  - Humoral (i.e. Immunoglobulins) immunity
  - Coagulation proteins
  - Controls fluid volume

- **Cellular (45-55%)**
  - Red Blood Cells (RBC)
    - primary function transportation of oxygen to tissues
  - White Blood Cells (WBC) or leukocytes
    - primary function cellular immunity
  - Platelets (PLT)
    - primary function initiating coagulation

To maximize usage from each unit of whole blood, it is separated into three parts, each having different therapeutic applications:

1) Red Blood Cells (RBC)
2) Platelets (PLT)
3) Plasma

The most common use of donated blood is the use of RBCs that has had most of its plasma removed. RBC transfusions are used in the treatment of anemia.

Plasma, the liquid portion of blood, will also contain some platelets and WBCs. This portion of plasma with platelets can be used for the treatment of thrombocytopenia.

If the plasma is not to be used for a platelet transfusion, it can be utilized for many different applications. Freezing preserves the coagulation proteins in plasma and it can be used to replace these proteins. Plasma can also be processed to form products such as albumin, rhogam or immunoglobulin.
One component of blood that is not used and is in fact removed is the White Blood Cells (WBCs) or leukocytes. WBCs transfusions have been found to have no therapeutic value. In fact, when units of blood are collected, filters are used to reduce the amount of WBCs in all of the above mentioned products. These blood products will have the initials “LR” (Leukocyte Reduced), on them. WBCs present in blood products may also be responsible for causing transfusion reactions.

The bottom line is this, if the therapeutic agent comes from human blood, it is a blood product and has risk of causing an adverse reaction when given to the patient.

**Exercise:**

1. Units of RBC are used for treating what?

2. Why are RBC referred to as packed cells?

3. What is the remaining plasma used for?
Classification of Adverse Transfusion Reactions (ATR)

Classifying transfusion reactions is the first step to understanding them. Reactions can be grouped by how quickly they occur and by the triggering mechanism.

An acute adverse transfusion reaction is defined as one that occurs within 24 hours of the initiation of the transfusion. Reactions occurring more than 24 hours after the beginning of the infusion are a delayed adverse transfusion reaction.

If the cause of the reaction is due to an immunological mechanism, it is referred to as an immunological adverse transfusion reaction. Any other cause is referred to as a non-immunological adverse transfusion reaction.

The following flowchart can be used for reference:

![Flowchart for classifying Adverse Transfusion Reaction](image)

Immunology Review

Fifty percent of Adverse Transfusion Reactions are due to an immunologic mechanism. The word ‘immunity’ was originally a legal term used in late Middle English law derived from the Latin word immunise-free from liability, protected from the law. Medically, immunity is protection of the body from disease. Immunology is the branch of medicine that studies the body’s immune system.

So what happens when a foreign substance enters your body, for example, when someone accidentally sneezes in your face? Despite your best efforts of wiping the viral loaded saliva off, some of the virus will enter your body through your nose and/or mouth.
Once the virus is introduced into the body, the immune system will become activated.

So are viruses the only thing that can activate an immune response? No, bacteria, chemicals, even food (i.e. fish or peanuts) can do this. Any particle that causes an immune response is referred to as an **antigen**.

When an antigen enters the body, properly functioning WBCs will recognize them as foreign and begin the process of removing and destroying them. Some will try to destroy the antigen by engulfing it or releasing toxic chemicals that damage the antigen’s effectiveness, while other WBCs will begin to produce antibodies (also known as immunoglobulins), proteins that coat the antigen to increase the rate of removal from the body by activating even more WBCs to eliminate it. Once the antigen is removed, then WBCs will turn off the immune response.
How does this apply to transfusion medicine?

Whenever a blood product is transfused, the patient’s immune system will either recognize it as familiar and not become activated, or recognize it as foreign and try to remove it from the body, resulting in an adverse immunological transfusion reaction.

**Exercise:**

Define the following medical terms

1. Immunity-

2. Antigen-

3. Antibodies-
Immunology and Transfusion Medicine

It’s ironic that studying something as complex as the immune system began with one simple question, why do blood transfusions kill some patients, but not others?

In 1900, Dr. Karl Landsteiner investigated this problem. He took blood from different people and began experimenting with it. Now going back to figure 1, what is blood made up of?

After separating the plasma from the cells, Landsteiner then mixed the plasma of one patient with the cells of another. He then observed the following reactions and cells.

<table>
<thead>
<tr>
<th></th>
<th>Patient #1 Plasma</th>
<th>Patient #2 Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient #1 Cells</strong></td>
<td>No reaction</td>
<td>Reaction (Cells form clump)</td>
</tr>
<tr>
<td><strong>Patient #2 Cells</strong></td>
<td>Reaction (Cells form clump)</td>
<td>No reaction</td>
</tr>
<tr>
<td><strong>Patient #3 Cells</strong></td>
<td>No reaction</td>
<td>No reaction</td>
</tr>
</tbody>
</table>

From this table we see that some cells will react with other plasma, while others will not. Landsteiner determined that there was something on the red cells that reacted with the plasma. Not all blood was the same type. Looking at his data:

<table>
<thead>
<tr>
<th></th>
<th>Patient #1 Plasma</th>
<th>Patient #2 Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient #1 Cells</strong></td>
<td>No reaction</td>
<td>Reaction (Cells form clump)</td>
</tr>
<tr>
<td><strong>Patient #2 Cells</strong></td>
<td>Reaction (Cells form clump)</td>
<td>No reaction</td>
</tr>
<tr>
<td><strong>Patient #3 Cells</strong></td>
<td>No reaction</td>
<td>No reaction</td>
</tr>
</tbody>
</table>

Landsteiner decided that since Patient #3 cells had zero reactions, it would be Type 0. Since mixing Type O cells with the plasma of other patients did not cause a reaction,
Landsteiner believed that Type O blood could be transfused to any one without a reaction. However, Type O plasma had a factor in it that caused it to react with red cells of other patients. Therefore, Type O red cells did not cause a reaction with the other plasma, but type O plasma would react with any red blood cells that were not type O.

<table>
<thead>
<tr>
<th></th>
<th>Patient #1 Plasma</th>
<th>Patient #2 Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient #1 Cells</td>
<td>No reaction</td>
<td>Reaction (Cells form clump)</td>
</tr>
<tr>
<td>Patient #2 Cells</td>
<td>Reaction (Cells form clump)</td>
<td>No reaction</td>
</tr>
<tr>
<td>Type O Cells</td>
<td>No reaction</td>
<td>No reaction</td>
</tr>
</tbody>
</table>

The next thing Landsteiner noticed was that the two remaining blood groups reacted with each other when mixed together. Something on the Red Blood Cells reacted with the Plasma. Landsteiner called the factor on the Red Blood cells antigens and the factor in the plasma antibodies. Of the two remaining blood groups, one was called type A, the other type B. The following table summarizes Landsteiner’s data:

<table>
<thead>
<tr>
<th></th>
<th>Type A Plasma (Anti-B)</th>
<th>Type B Plasma (Anti-A)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type A Cells</td>
<td>No reaction</td>
<td>Reaction (Cells form clump)</td>
</tr>
<tr>
<td>(A Antigen on RBC)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type B Cells</td>
<td>Reaction (Cells form clump)</td>
<td>No reaction</td>
</tr>
<tr>
<td>(B Antigen on RBC)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type O Cells</td>
<td>No reaction</td>
<td>No reaction</td>
</tr>
<tr>
<td>(neither A or B antigen)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In 1902, a fourth blood type was discovered. Here are the reactions. Try to determine what this blood group is:

<table>
<thead>
<tr>
<th></th>
<th>Plasma of newly discovered blood group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type A Cells</td>
<td>No reaction</td>
</tr>
<tr>
<td>(A Antigen on RBC)</td>
<td></td>
</tr>
<tr>
<td>Type B Cells</td>
<td>No reaction</td>
</tr>
<tr>
<td>(B Antigen on RBC)</td>
<td></td>
</tr>
<tr>
<td>Type O Cells</td>
<td>No reaction</td>
</tr>
<tr>
<td>(neither A or B antigen)</td>
<td></td>
</tr>
</tbody>
</table>

What antibodies are present? None, there is no reaction with any of the RBCs. What about the antigens on the RBCs?

<table>
<thead>
<tr>
<th></th>
<th>Cells of newly discovered blood group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type A Plasma (Anti-B)</td>
<td>Reaction</td>
</tr>
<tr>
<td>Type B Plasma (Anti-A)</td>
<td>Reaction</td>
</tr>
<tr>
<td>Type O Plasma (Anti-A and Anti-B)</td>
<td>Reaction</td>
</tr>
</tbody>
</table>
What antigens are present? It reacts with Anti-A, so there are A antigens on the RBCs. It also reacts with anti-B so there are B antigens on the cells as well.

Congratulations, you have just discovered the fourth blood group in the ABO system, Type AB. The lack of antibodies in the plasma means that this patient can receive any RBCs based on the ABO grouping. What about plasma? If a Type AB patient needed Plasma, what blood group can they receive?

To answer that question we have to remember what is present in plasma, antibodies, and what are present on the patient’s RBCs, antigens. Type AB blood has both A and B antigens, so any plasma that has anti A and/or Anti B in it will react with the patient’s RBCs. What blood group has no anti A or B in it?

Group AB. So while group AB can receive any type of RBCs, it can only receive AB plasma. While group O blood can only receive group O blood cells, it can receive any type of plasma.

In 1907, the first blood transfusion using ABO matched blood was successfully performed at Mount Sinai Hospital in New York City. Unfortunately, as more transfusions were performed, it was discovered that the assumption there were only four blood groups, A, B, AB and O, was flawed. It was soon discovered that there were many blood groups and more testing was required before blood could be safely transfused.

From our review of immunology, the following conclusions can be made:

- An antigen is a foreign substance that enters the body and causes a pathological process.

- WBCs will then initiate the immune response to eliminate the antigen, which includes the production of antibodies.

- An immune adverse transfusion reaction occurs because of an interaction between an antibody and an antigen.

- RBCs have antigens that can initiate an immune response.
Symptoms of an ATR

Due to the patient’s condition, it has been decided that a transfusion of blood products must be performed. Before the transfusion begins, it is important to obtain baseline vital signs of the patient within one hour of beginning the transfusion. After verifying the intended recipient is receiving the correct blood products, transfusion is initiated and the following signs and symptoms are monitored:

1) Temperature - Has it risen (>1° C above 37° C)? Does the patient feel cold?
2) Blood pressure - Has it increased or decreased?
3) Breathe sounds – Is there an increase or decrease?
4) Any complaints of pain in chest, flank or back pain?
5) Color - Has the patient developed jaundice?
6) Skin appearance - Flushing, rash or urticaria?
7) Urine output and color - Decreased and/or become darker?
8) Abdominal status - Stomach pain and/or nausea?
9) Abnormal bleeding – i.e. at the IV site?
10) Mental state - Anxiety, drowsy, calm or does the patient have a sense of “impending doom”?

To compound matters, many of the above symptoms could be due to the patient’s anxiety reaction to the news they need a blood transfusion. The fear of complications from having a transfusion (i.e. HIV infection, adverse reaction) can lead to anxiety.

Another problem is that some symptoms of an ATR do not occur during or immediately after the transfusion. Symptoms can occur up to 24 hours after the start of the transfusion.

Finally, patients who are unconscious (i.e. patients suffering head trauma, post-operative patients under anesthesia) will not be able to tell the healthcare worker they are having a transfusion reaction.

So what are the steps that healthcare providers take if the patient appears to be having an ATR?

Four step approach to dealing with an ATR

1. **If an adverse reaction is suspected, stop the transfusion while keeping the vein open with Normal Saline.** If it is later determined that the blood product is safe and a reaction was not occurring, continue the blood transfusion as ordered.

2. **Recheck all the clerical data.** This is dull and tedious but absolutely necessary. Clerical errors are one of the main causes of serious transfusion reactions. Consider the following scenario:
Mr. John Smith (Patient A), DOB: 05/10/1976 is “A” Positive and was to receive one unit of packed RBCs. Mr. Jonathan Smith (Patient B), DOB: 10/05/1976 is “B” Positive and is to receive one unit of fresh frozen plasma. The healthcare provider for Mr. Smith (Patient A) accidentally began a transfusion of group B plasma and, the patient had a fatal reaction.

This patient has been a victim of a negligent clerical error. What about Mr. Smith (Patient B)? Instead of receiving one unit of group B plasma, he might accidentally receive one unit of group A packed cells which could also cause a severe transfusion reaction.

3. **Contact the attending physician immediately.** The patient may have had a similar mild reaction in the past and all that is required for treatment is acetaminophen and antihistamines. But, it may be serious enough to require step four?

4. **Contact the transfusion medicine department of the lab for directions on starting an investigation into a possible transfusion reaction.** If the lab decides that a transfusion reaction investigation is to be done, the tubing should be removed, clamped and returned with the original blood product to the lab along with all the important data (i.e. patient name, amount of product transfused, and symptoms) documented. Blood specimens will also need to be recollected for further testing.

Exercise:

1. There are ten things monitored that are indicative that an ATR may be occurring. List three:

2. What are the four steps that must be followed if the patient is suspected of having an ATR?

3. What blood component is not used for a therapeutic transfusion?
**Adverse Immunological Transfusion Reactions (AITR)**

As mentioned earlier, acute adverse transfusion reactions are divided into two categories, immunological and non-immunological.

There are four types of adverse immunological transfusion reactions: Haemolytic, Non-Hemolytic Febrile, Allergic and Transfusion Related Acute Lung Injury (TRALI).

**Acute Immunologic Haemolytic Transfusion Reaction (AIHTR)**

Hemolytic is the term used to describe the destruction of red blood cells. In an acute immunologic haemolytic transfusion reaction, the destruction of the transfused RBC is due to an immunologic mechanism.

Before Landsteiner’s discovery of the ABO blood grouping, this was probably what caused the majority of transfusion related fatalities.

**Symptoms**

- Chills
- Fever
- Hemoglobinuria
- Hypotension
- Renal Failure
- Oozing from IV sites (usually due to Disseminated Intravascular Coagulation (DIC))
- Back pain
- Pain along the infusion vessel (venous or arterial)

**Pathophysiology**

So what happens in an AIHTR, for instance when a patient who is Group O is being transfused with Group A RBCs? In this case the anti-A present in the patient’s plasma will react with the A antigens on the surface of the RBCs initiating an immune response.

WBCs are not the only thing activated. A group of proteins that enhance the destruction of antigens called the “complement system” are also involved. They are called this because they “complement” the antibody’s action by attacking the antigen’s surface forming holes in it, causing it to break up and be destroyed.

Two of the proteins in this system, C3a and C5a, are the ones that contribute to an AHTR. They cause the release of histamine and serotonin from mast cells, resulting in vasodilatation and smooth muscle contraction (especially bronchial). Other cells will also be stimulated to produce chemicals to help with the immune response, such as cytokines, leukotrienes, free radicals and nitric oxide; or to increase vasodilatation. Since this reaction is similar to that seen in an anaphylactic reaction, C3a and C5a are referred to as anaphylatoxins.
The severity of the reaction depends on how much incompatible blood was transfused. A small amount will result in a reaction that is self-limiting, stopping once the entire antigen has been removed. A larger volume transfused will result in more anaphylatoxins being formed resulting in wheezing, flushing, gastrointestinal symptoms, chest pain and tightness in the chest.

The antigen/antibody complex also activates the coagulation system. To explain how, a quick review of the body’s coagulation system is in order. In a healthy individual who has suffered damage to a vessel wall, the coagulation system is activated to prevent blood loss and to begin healing. It involves a cellular component in the form of platelets and calcium, and a liquid portion made up of proteins called coagulation factors found in the plasma.

Unfortunately, the nomenclature of these clotting factors can be confusing. Logically, if Factor I was the clotting factor that started the clotting sequence, it should be the first coagulation factor to be activated. But in fact, it is the last. That’s because the naming of the coagulation factors is based on when they were discovered.

What causes the activation of the coagulation system? There are two ways damaged blood vessels activate the coagulation system, either the intrinsic system or the extrinsic system.

The stimulus that activates the intrinsic coagulation system is the damaged vessel surface, which converts Factor XII to Factor XIIa resulting in clot formation. The extrinsic system is activated by ‘Tissue Factor’, a protein released from the damaged endothelial cells lining the vessel wall. Its action is to convert Factor VII to Factor VIIa.

The following flow chart illustrates the sequence of events in each system:
The antigen/antibody complex will activate both the intrinsic and extrinsic pathways of coagulation. It does this by converting Factor XII (Hageman’s Factor) into Factor XIIa, starting the intrinsic pathway. Factor XIIa will also convert kinin into bradykinin, resulting in increased vascular permeability that will cause vasodilation and hypotension. Complement activated by the Antigen/Antibody complex will cause WBCs and Endothelial cells to express tissue factor, resulting in activation of the extrinsic system. An activated extrinsic factor can also result in the patient developing Disseminated Intravascular Coagulation (DIC).

DIC is a life threatening condition. Once the extrinsic pathway has been activated, platelets and coagulation factors begin forming small thrombi (micro-thrombi). While these small thrombi will have no effect in the larger blood vessels, once they circulate through the microvasculature of major organs, they block circulation, resulting in tissue death. The organ responsible for filtering the blood, the kidney, is especially vulnerable to micro-thrombi blocking blood circulation, leading to kidney failure. Since DIC also causes the increased consumption of platelets and coagulation factors, resulting in a significant decrease in them, there will also be bleeding, especially at IV sites and any breaks in the skins (i.e. wounds, surgical incisions, etc.).

**Treatment**

Since it only takes as little as 10 mL of incompatible blood to start an AIHTR, the sooner the transfusion is stopped, the better. The unit of blood should be sent to the lab for further testing, as well as a post transfusion blood specimen.

The IV should be kept open to ensure continuous saline infusion for the following reasons:

- Treats hypotension
- Ensures adequate renal blood flow, the goal being to maintain a urine flow rate of >1mL/kg/hour
- Maintain venous access if additional therapy is required

By itself saline infusion may not be sufficient to treat AIHTR. There is also the potential of overload for the patient with low urinary output.

Administration of dopamine hydrochloric acid (1-5 μg/Lg/minute) will improve renal blood flow. It does this by increasing both cardiac muscle strength and renal vasodilatation. However, the healthcare provider should be aware that the use of dopamine to treat acute renal failure is controversial since there have been no studies on whether it actually prevents kidney failure.

Diuretics such as furosemide (40-80 mg IV for adults, 1-2 mg/kg for pediatric patients) will help promote urine output as well enhance renal cortical blood flow.
The above steps are important to maintain urine output. If there hasn’t been any improvement in output after a litre of Normal Saline has been infused, this is a sign that acute tubular necrosis is starting, which can lead to pulmonary edema.

**Prevention**

Now that the ABO blood grouping is known, these kinds of transfusion reactions should not be occurring, correct?

Unfortunately not.

Knowing about different blood groups is not enough. It’s been said that the devil is in the details, and in this case it is very true. The majority of immunologic haemolytic transfusion reactions are due to some level of clerical error.

Studies have shown that wrong patient transfusions due to clerical errors occur between 1:6000 to 1:12,000 patients. AIHTR due to mistakes in performing the ABO/Rh testing was between 1:6000 to 1:20,000 patients. Finally, the chance of dying from an AIHTR is 1:500,000 to 1:1,000,000 patients.

Let’s refer back to Step 2 of the four step approach to dealing with an adverse transfusion reaction, “recheck all the clerical data”. This cannot be stressed enough. Truly an ounce of prevention can save a life.

**Exercise:**

1. What is the Complement System?

2. Which Complement proteins contribute to an AIHTR?

3. Why are C3a and C5a referred to as “anaphylatoxins”?
4. How does an AIHTR activate the coagulation system?

5. What does D.I.C. stand for?

6. Why is dopamine hydrochloric acid administered to treat an AIHTR?
**Febrile Non-Hemolytic Transfusion Reactions (FNHTR)**

What happens if the patient’s temperature increases after the transfusion, but other important symptoms (i.e. hemolysis) are absent, is there still cause for concern?

Yes, because an increase in temperature can also be due to other adverse transfusion reactions such as sepsis or TRALI. Or it can be due to a Febrile Non-Hemolytic Transfusion Reactions (FNHTR)

**Symptoms**

So what are the symptoms? The main one is an unexplained increase in temperature of > 1°C above 37°C, that can be accompanied by shaking, chills, an increase in the respiration rate, blood pressure changes, and anxiety.

These symptoms mimic those of other reactions such as AHTR. When they occur, not only does it cause anxiety for the patient, but also anxiety for the healthcare provider who has to determine if the reaction is either a FNHTR, or something more life threatening.

The lack of hemolysis occurring is what differentiates an FNHTR from an acute immunological haemolytic transfusion reaction. The absence of pulmonary edema will eliminate TRALI. If there is no dyspnea present, then the reaction is not septic.

**Pathophysiology**

So what causes a NHFTR? There are two main causes.

One mechanism is similar to AHTR, an antigen-antibody reaction. Antigens on WBCs and platelets called Human Leukocyte Antigen (HLA) are what stimulate the immune response.

Another mechanism is that naturally occurring chemicals produced as a result of an immune response, called cytokines, are slowly released into the small amount of plasma of stored red blood cells while refrigerated. Once the unit is transfused into the patient, those cytokines in that plasma begin to circulate in the patient resulting in a NHFTR.

**Treatment**

Once it has been determined that the reaction is a FNHTR, how is treated?

1) Check the identification of the patient and the unit of blood
2) Stop the transfusion and maintain IV access
3) Contact the physician
The usual course of treatment is the administration of anti-pyretics such as acetaminophen. The transfusion medicine department should still be contacted and the unit of blood should be discontinued and sent to the lab for further investigation if required.

There is one situation when a unit of blood should not be discontinued. If the patient has an extremely rare blood group, the unit should not be discarded until the medical director of the transfusion medicine department has been consulted on whether the transfusion is to continue or not.

**Prevention**

An immune response to WBCs and/or platelets present in the transfused product is believed to be the main cause of FNHTR. The rate of occurrence is 1:300 units of transfused RBCs, and 1:10 units of transfused platelets.

Use of blood products that have been leukocyte reduced, have helped reduce the incidence of FNHTR. For blood that has not been leukocyte reduced, a blood filter can be connected to the IV tubing to help remove most of the WBCs.

Filtering out WBCs still might not be enough to prevent patients from suffering from FNHTR. The following procedures have been tried to decrease the risk of FNHTR:

- Using the following medications
  - Acetaminophen
  - Corticosteroids
  - Demerol
- Use of the following modified blood products
  - Fresh components (<5 days old)
  - Plasma depleted products
  - Washed RBCs

These procedures are unproven, and are up to the discretion of the physician.

Once again it cannot be stressed that before the decision to treat a FNHTR can be made; all other reactions must be ruled out.

**Exercise:**

1. What is FNHTR?
2. Name three symptoms of a FNHTR:

3. Name one other type of adverse transfusion reaction that has these symptoms?

4. What are the two causes of a NHFTR?

5. How can NHFTR be prevented?
Allergic Transfusion Reactions (ALTR)

An allergic reaction is an immune response that involves a class of antibodies called IgE and white blood cells known as eosinophils and basophils (also known as mast cells).

Allergens are antigens that cause an allergic reaction. They do this by binding to the surface of mast cells causing them to release their cellular contents, including histamine. Histamine is a powerful vasodilator which is responsible for the symptoms of an allergic reaction. The effect of histamine will be urticaria, or hives, resulting in the formation of wheals that are itchy or may be stinging. Swelling around the lips and eyes (angioedema) may also occur.

**Symptoms**

Allergic transfusion reactions with hives and/or angioedema will usually occur within seconds or minutes of the beginning of the transfusion. Severe anaphylactic reactions can also occur, resulting in severe hypotension, shock and unconsciousness. Respiratory symptoms include dyspnea, wheezing and stridor (a high pitched wheezing from blockage of the throat or voice box). There can even be gastrointestinal problems that include vomiting, stomach pain and diarrhea. Tachycardia, arrhythmia or cardiac arrests are also possible.

**Treatment**

As with all adverse transfusion reactions the first steps to treat an allergic transfusion reaction are:

- Stop the transfusion and recheck patient identification and product information
- Immediately contact the physician
- Contact Transfusion Medicine

As always it is important to maintain IV access with .09% saline. Hives can be treated with 25-50 mg of Diphenhydramine. Anaphylactic reactions should be treated by:

- Epinephrine
- Corticosteroids
- Diphenhydramine
- Vasopressors
- Ventilation if required
- Supportive Care

Patients who are deficient in Immunoglobulin A (IgA) are especially prone to anaphylactic transfusion reactions. This condition is present in ~ 1:700 people of European descent, with a small percentage of these patients forming IgE antibodies against IgA. The strength of the allergic reaction depends on how severe the patient’s IgA deficiency is. Total IgA deficiency may result in an anaphylactic reaction. Patients
with low levels of IgA may only suffer minor allergic reactions. For patients who have an allergy to IgA who require a blood transfusion, washed blood products or blood products from IgA deficient donors can be used.

**Exercise:**

1. What class of antibodies are responsible for allergic reaction?

2. What chemical is released by mast cells that cause an allergic reaction?

3. What are three symptoms of a severe anaphylactic reaction?

4. Patients deficient in what immunoglobulin are especially prone to anaphylactic reactions?

5. For patients deficient in this immunoglobulin, what products can be transfused to them?
Transfusion Related Acute Lung Injury (TRALI)

Before we discuss TRALI, we should briefly review Acute Lung Injury (ALI). ALI is defined as acute hypoxemia having a PaO$_2$/FiO$_2$ ratio of $\leq 300$ Hg with a frontal chest x-ray showing bilateral pulmonary edema. It can be caused by sepsis, trauma, near drowning and blood transfusions.

**Symptoms**

Symptoms include dyspnea, hypoxemia, fever, hypotension and pulmonary edema, and usually occur within 6 hours of transfusion. These symptoms may resolve in 24-72 hours. A high percentage (72%) of patients having a TRALI transfusion reaction will require mechanical ventilation. Eight to ten percent of TRALI reactions are fatal, making it possibly the most common cause of transfusion related fatalities. One hundred percent of all patients having a TRALI reaction will require oxygen support.

**Diagnosis**

Diagnosing TRALI requires a chest x-ray and an arterial blood gas sample.

A chest x-ray showing bilateral pulmonary edema is diagnostic of TRALI. The arterial blood gas can be used to calculate the PaO$_2$/FiO$_2$ ratio. This ratio is an index of how efficient the arterial oxygenation is. It takes the PaO$_2$ measurement from the arterial blood measure and compares it to the amount of oxygen the patient is breathing.

If the patient is breathing room air which has a FiO$_2$ of 21% and the patient’s PaO$_2$ was 98 mm Hg, the PaO$_2$/FiO$_2$ ratio would be 98 mm Hg/0.21 = 460 mm Hg. If the patient had a PaO$_2$ of 80 and was on 100% oxygen, the ratio would be 80mm Hg/1 = 80. Since the ratio is less than 300 mm Hg the patient is probably suffering from ALI.

It is critical to differentiate TRALI from other adverse or allergic transfusion reactions because, although the main treatment is the same, there are additional steps to follow.

**Treatment**

The first steps to treat TRALI are:

1. Stop the transfusion and recheck patient identification and product information
2. Immediately contact the physician
3. Contact Transfusion Medicine
4. The main treatment for TRALI is supportive measures with oxygen
5. If necessary, mechanical ventilation.

It is important to note that steroid treatments have been found to be of no benefit and use of diuretics will actually exacerbate the symptoms.
**Pathophysiology**

Patients with TRALI suffer from pulmonary edema due to increased pulmonary capillary permeability. There are two theories as to why this happens.

The first theory is that an antibody in the blood product reacts with the white blood cells of the patient causing a massive inflammatory response in the lungs. The endothelial lining of the lungs is then damaged resulting in capillary leakage which causes pulmonary edema.

The second theory is that patients who have conditions where neutrophils are going to be in the lungs (i.e. infection) are at risk of developing TRALI. Biologically active substances present in the blood product are transfused activating the neutrophils. This will cause the inflammatory response that triggers TRALI.

Donor plasma is the source of the problem. Because the exact mechanism of TRALI is not fully understood, screening blood products that could cause TRALI is not possible. Because it is thought to be an immune mechanism against the HLA antigens on WBCs, units of fresh frozen plasma from men is preferred.

Why? It’s because it has been postulated that women who have been pregnant are at risk of developing HLA antibodies that might cause TRALI. The antibodies formed as a result of being exposed to the HLA antigens of their baby.

**Exercise:**

1. What does TRALI stand for?

2. What is the definition of an ALI (Acute Lung Injury)?

3. What two diagnostic procedures are used to identify a patient suffering from TRALI, and what do they indicate?
4. How is TRALI treated?

5. What is the cause of the pulmonary edema seen in TRALI?
**Non-Immunological Acute Transfusion Reactions (NIATR)**

It’s not enough that the blood products must be the perfect immunological match. While the immune system of both the donor and recipients are important internal factors to be aware of in preventing adverse transfusion reactions, external factors must also be considered.

There are six kinds of Non-Immunological Acute Transfusion Reactions (NIATR); Transfusion Associated Sepsis, Transfusion Associated Circulatory Overload (TACO), Non Immunological Hemolytic Transfusion Reaction, Air Embolus, Massive Transfusion and Bradykinin Mediated Hypotension.
Transfusion Associated Sepsis

Sepsis is an infection that has spread to tissues and/or the blood. While viral infections such as Hepatitis and Human Immunodeficiency Virus (HIV) can be caused by a blood transfusion, the complications from these infections can take days, weeks, months, even years to develop a delayed transfusion reaction. Bacterial infections can occur in less than 24 hours. The question then is how do blood products become contaminated with pathogenic bacteria?

There are three ways: during collection, during storage or during handling of the blood product.

If the donor’s skin hasn’t been properly cleaned before collection, some of the normal skin bacteria will enter the unit during collection. Or the donor may actually have bacteria in their blood and not be aware. Either way, bacteria will enter the unit of blood where it will find an environment perfect for unlimited growth.

Improperly stored units are also at risk of becoming contaminated. For example, a unit of blood that has a small amount of bacteria in it poses a small risk of sepsis to the patient, but if this unit is taken out of the fridge and kept out longer than 30 minutes, the bacteria will have a chance to grow exponentially and increase the risk of a septic transfusion reaction.

If the blood product is not handled aseptically, there is a greater chance of sepsis. A unit of blood that has been handled with aseptic technique will have less chance of being contaminated.

How common are acute transfusion reactions due to sepsis? Patients receiving 5 units of platelets have a 1:1000 chance of receiving a contaminated unit, while patients have a 1:50000 chance of receiving a unit of contaminated RBCs. Why do platelet transfusions have a higher risk of sepsis? In order for platelets to work, they have to be stored at room temperature, which increases the risk of bacterial growth in a contaminated unit.

Ten percent of transfusion related fatalities are due do bacterial sepsis.
Exercise:

1. What are the three ways blood can become bacterially contaminated?

2. Why do units of Platelets have a higher risk of causing sepsis?
**Symptoms**

The symptoms seen in a septic transfusion reaction include: rigors, fever, tachycardia, nausea, vomiting, dyspnea and DIC.

**Treatment**

As always, whenever an acute transfusion reaction is suspected; stop the transfusion, notify the physician and contact the transfusion medicine department.

The laboratory will need to contact the organization that provided the unit (i.e. Canadian Blood Services) to make sure that no other blood products from the donor have been transfused and quarantine any remaining units. The unit and tubing (clamped) should be sent for culture. Blood cultures should also be done on the patient. Broad spectrum antibiotics should be given and any supportive therapy required for other complications of sepsis (i.e. ventilation, fluid replacement, treatment for DIC).

**Transfusion Associated Circulatory Overload (TACO)**

Sometimes in the rush to treat chronic anemia we forget to look at the situation as a whole. A patient urgently needs a transfusion and in the zeal to replace the lost blood, it is forgotten that there are other factors making the patient ill that have to be considered during transfusion.

Transfusion Associated Circulatory Overload (TACO) usually occurs in patients with impaired cardiac function and/or those having a blood transfusion at an excessively high rate. TACO occurs in approximately 1:700 transfusions. Patients most at risk of developing TACO are:
- Perioperative older orthopaedic patients in a surgical setting
- Patients over 60
- Infants
- Patients with severe euvoletic anemia (anemia with a haemoglobin of <50 g/l)

**Symptoms**

The clinical presentation of TACO includes: dyspnea, orthopnea, cyanosis, tachycardia, increased venous pressure and hypertension
**Testing**

Not only are the symptoms of TACO similar to TRALI, these two reactions may also occur at the same time. The tests to differentiate them are:

<table>
<thead>
<tr>
<th>Test</th>
<th>TACO</th>
<th>TRALI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jugular Venous Pressure</td>
<td>Increased</td>
<td>Normal</td>
</tr>
<tr>
<td>Brain Natriuretic Peptide (BNP)</td>
<td>Increased</td>
<td>Normal</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td></td>
<td>Bilateral infiltration consistent with pulmonary edema</td>
</tr>
<tr>
<td>Treatment with diuretics</td>
<td>Improvement</td>
<td>No improvement</td>
</tr>
</tbody>
</table>

**Treatment**

As always the first three steps in acute transfusion reaction; stop the reaction, contact the physician and notify the lab. Supportive therapy including oxygen therapy and diuretics should be implemented. If TACO is the cause of the reaction, the transfusion can be restarted, but at a slower rate.

Prevention of TACO can be done by identifying patients at risk and then taking the following measures; transfusion over a longer period of time up to a maximum of 4 hours per unit, pre-emptive diuretics and avoid transfusing more than one unit at a time.

One alternative is to split the unit into smaller aliquots. This is especially beneficial for pediatric patients, allowing for the product to be gradually transfused without waste, and decreasing the amount of donors the patient is exposed to. Before performing this, the approval of the Transfusion Medical Department’s medical director is required.

**Exercise:**

1. What does TACO stand for?

2. Name two types of patients at risk of developing TACO
Non-Immunological Hemolytic Transfusion Reaction (NIHTR)

Red blood cells can still be destroyed in storage without involving the immune system. While this is not a true adverse reaction, the healthcare provider should be aware of it for two reasons. First of all, a unit of hemolyzed blood is useless. Since the RBCs are destroyed, there will be no therapeutic benefit, and the patient will be needlessly exposed to a donor that might be potentially infectious. Secondly, even though the patient is not having a hemolytic transfusion reaction, the sudden appearance of haemoglobin in their urine will make it appear that one is happening. Therefore, a lot of unnecessary testing and work will be done, as well as needless anxiety for both patient and staff. It should be noted that the cause of hemolysis should be identified so that the organization supplying the blood can ensure that there are no problems (i.e. improper collection, storage and delivery).

Temperature can affect the RBC unit. If units are kept in a conventional fridge and are accidentally frozen, then thawed, this will cause hemolysis. Sometimes, it is necessary to use warmers to bring blood to 37°C before transfusion. These warmers have to be properly maintained and calibrated to ensure that they are not warming the blood over 37°C, as this can also cause hemolysis.

Sometimes in an attempt to be efficient, IV solutions and medications are mixed with the unit of blood, which can cause hemolysis. It cannot be stressed enough that units of RBCs are to be transfused separately and that IV solutions and medications should not be added to RBC units. While not absolute, this would not be advisable practice. Very rare circumstances have occurred where it had to be done, but only under the approval of the Medical Director of the Transfusion Medicine Department.

Units taken out of storage that look suspiciously hemolyzed should not be transfused.

Exercise:

1. What are two causes of non-immunological hemolysis in RBC units?

2. When transfusing a unit of hemolyzed RBCs to a patient, what symptom can be mistaken for a true haemolytic reaction?
**Air Embolus**

When the venous system is exposed, there is risk of air entering the blood. If strict protocols are not followed, a central catheter can be a port for air entry while blood administration sets are being changed. The minimum volume of air for an embolus to be potentially fatal for an adult is 100 mL.

Symptoms of an air embolus are: cough, dyspnea, chest pain and shock. A diagnosis is made by an x-ray showing intravascular air.

Treatment is to immediately place the patient on their left side with the bed tilted so that the head is lower than the feet. This will displace the air bubbles from the pulmonary valves.

Air emboli can be prevented by inspection of equipment and adherence to strict policy and procedures for blood transfusion.

**Exercise:**

1. What is the minimum volume of air required for an air embolus?

2. What are two symptoms of an air embolus?

3. What is the diagnostic test of an air embolus?
Massive Transfusion

For patients whose bleeding is uncontrolled and have been transfused in less than 24 hours with the equivalent volume of blood in the human body (i.e. 6 units in the average sized adult), then that is referred to as a Massive Transfusion. While a Massive Transfusion may be necessary to save the patient, it is important to remember they can also harm a patient.

Hypothermia

Since units of RBCs are stored at 6° C, receiving multiple units has the potential of causing hypothermia. This can result in a decrease of:

- Platelet and coagulation factor function
- Myocardial function
- Hemoglobin release of oxygen to tissues
- Citrate metabolism

These blood transfusion reactions will cause dangerous side effects. Impaired clotting will only increase bleeding. Hemoglobin unable to release oxygen to the tissues is useless. No matter how much blood a body receives, a healthy heart is necessary to pump it through the body or blood becomes a useless liquid.

Using blood warming devices can help prevent the development of hypothermia as long as they do not cause hemolysis.

Cardiac symptoms associated with hypothermia will have the following ECG changes:

- Prolonged PR, QPS and QT
- T-wave inversion
- J (Osborne) Waves (a “hump-like” deflection between the QRS complex and the early part of the ST segment)

Statistically the increased risk of mortality from hypothermia is:

<table>
<thead>
<tr>
<th>Core Temperature</th>
<th>Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;34° Celsius</td>
<td>40%</td>
</tr>
<tr>
<td>&lt;33° Celsius</td>
<td>69%</td>
</tr>
<tr>
<td>&lt;32° Celsius</td>
<td>100%</td>
</tr>
</tbody>
</table>
**Impaired Hemostasis**

Fifty percent of massively transfused patients will develop an INR of >2.0 and 33% will develop thrombocytopenia (platelet count of <50). To compound matters there is also the risk of developing DIC as well.

Historically the approach to prevent bleeding was to transfuse one unit of Fresh Frozen Plasma (FFP) for every six units of RBCs. Recent evidence however, has shown that it is not the number of units transfused that determine whether FFP should be transfused, but lab monitoring of platelet count and coagulation factors.

**Citrate Toxicity**

Citrate is the main anticoagulant used in the storage of blood units to prevent them from clotting and works by binding with calcium, an electrolyte necessary for the coagulation of blood. The amount of citrate in one unit of transfused blood will not affect the patient’s calcium level. The amount of citrate from six or more units will not only bind with calcium, but magnesium as well. This action will result in hypocalcemia, hypomagnesia and metabolic acidosis formed by the bicarbonate metabolite of citrate.

Clinically the patient will present with: hypotension, narrow pulse pressure, elevated pulmonary artery pressure, tetany, paresthesia, arrhythmia, reduced ventricular function and increased neuromuscular excitability.

**Microaggregates**

During Massive Transfusion there is the possibility of microaggregates of platelets; fibrin and white blood cells forming that might not be removed by a standard 170μm blood filter. Filters less than 40μm are available, although use of them will impair the capability of rapid transfusion.

**Potassium**

Potassium is an electrolyte essential for muscle function. A Massive Transfusion can cause either increased potassium plasma levels (hyperkalemia) or decreased potassium plasma levels (hypokalemia).

1) **Hyperkalemia** - As units of packed cells sit in storage, potassium will slowly seep from the RBCs into the plasma, increasing level in the unit. While the amount of potassium in one unit will not affect the patient, six or more units would result in hyperkalemia.
**Hypokalemia** - Paradoxically, Massive Transfusion can also cause the potassium levels to drop to a critical level. For example, in this same unit of blood, the potassium from the RBCs can also shift into the plasma. When these potassium depleted cells are introduced to a new source of potassium (the patient), osmosis will occur with potassium in the plasma rapidly moving into the transfused RBCs.

**Metabolic Acidosis**

As the units of RBCs sit in storage, they will become slightly acidic in pH. Massive Transfusions can result in metabolic acidosis, a condition that can exacerbate in hypothermic patients from the build-up of lactic acid in the tissues.

**Volume Status and Myocardial Function**

The patient who is undergoing a Massive Transfusion (especially while still haemorrhaging) is vulnerable to the stress associated with extremes in intravascular volume (hypovolemic to hypervolemic) and myocardial depression.

Physical examination may not be enough to diagnose this, and invasive monitoring such as central venous pressure, pulmonary artery catheter and echocardiography may be required.

**Tips for Treating Patients Enduring Massive Transfusion**

Massive Transfusion can be extremely frightening, not only for the patient but also for the family members and the health care team. The patient has uncontrolled bleeding that requires immediate intervention of a multi-disciplinary team of doctors, nurses, diagnostic technologists and support staff.

The following suggestions will support successful outcomes during a Massive Transfusion:

- Monitor core temperature
- Prompt use of measures to prevent hypothermia, including use of a blood warmer for all IV fluids and blood components (do not to mix the two together)
- Use a SQ 40° Pall filter with blood tubing, minimizing the number of times blood tubing has to be changed (q4-q24hr, as opposed to q2-q4)
- Monitor hemoglobin
- Monitor platelet count (platelet transfusion for head injury patients with count of <100x10⁹/L, <50x10⁹/L with INR, 1.5 and fibrinogen of >1.0g/L in all other patients)
- Monitor coagulation factors (be aware only). If there are no clinical signs of coagulopathy, don’t transfuse FFP. Recombinant Factor VIIa activity has been shown to be successful for intractable bleeding
- Be aware of possibility of DIC
- Check acid base status
- Check calcium, magnesium, potassium and albumin

Exercise:

1. What is the definition of a Massive Transfusion?

2. List three possible complications that can occur during a Massive Transfusion
**Bradykinin Mediated Hypotension**

Angiotensin Converting Enzyme (ACE) is an enzyme that helps control extracellular volume and arterial vasoconstriction. ACE inhibitors are a class of drugs that are used for the treatment of hypertension.

ACE is also the main enzyme that degrades bradykinin, a peptide that causes blood vessels to enlarge, resulting in blood pressure lowering. A decrease in ACE will cause increased bradykinin levels which causes blood pressure to drop.

The majority of hypotensive reactions occur with platelet transfusions, with 50% of the patients on ACE inhibitors. The theory is that some blood products will have increased levels of bradykinin. Since patients on ACE inhibitors will not be able to break it down, the patient will become hypotensive. Other symptoms may include dyspnea, urticaria, nausea and vomiting.

If these symptoms occur, stop the transfusion, call the physician and contact the lab. Treat with supportive therapy (i.e. IV fluids), and try to differentiate from TRALI or an allergic reaction.

**Exercise:**

1. What does ACE stand for?

2. What is its function?

3. What is the theory of why patients on ACE inhibitors are at risk of developing hypotension after receiving a transfusion?
Acute Adverse Transfusion Reactions Flow Chart

- **Hives**
  - Yes
  - **Allergic Transfusion Reactions**
    - Also look for: severe hypotension, shock, unconsciousness, dyspnea, wheezing, gastrointestinal problems (i.e. vomiting, stomach pain and diarrhea), Tachycardia and arrhythmia
  - **No**
    - Yes
      - **Unexplained increase in temperature of ≥ 1°Celsius above 37°C.**
    - No
      - **Hemoglobinuria**
        - Yes
        - **Acute Immune Hemolytic Transfusion Reaction (HTR), also look for:** Chills, Fever, Hypotension, Renal Failure, Oozing from IV sites (usually due to DIC, Disseminated Intravascular Coagulation), Back pain, Pain along the infusion vessel (venous or arterial)
        - **No**
          - **Pulmonary Edema**
            - Yes
              - **Dyspnea**
                - Yes
                  - **TRALI (Transfusion Related Acute Lung Injury), also look for:** Dyspnea, Hypoxemia, Fever, Hypotension
                - No
                  - **Transfusion Associated Sepsis**
                    - Yes
                      - **Febrile Non Hemolytic Transfusion Reactions (FNHTR), also look for:** Shaking, Chills, Increase in respiration rate, Blood pressure changes, Anxiety
                    - No
                      - **Bradycardia Mediated Hypotension**
        - No
          - **Air Embolus**
          - **No**
            - **Hypotension**
              - Yes
                - **TACO (Transfusion Associated Circulatory Overload). Also look for:** Dyspnea, Cyanosis, Orthopnea, Tachycardia, Increased venous pressure and Hypertension
              - No
References
Clinical Guide to Transfusion, Canadian Blood Services, 2007 Canadian Blood Services
Technical Manual, AABB
**Exercise Answers**

**Blood Products**
1. Anemia

2. Because most of the plasma has been removed, and the majority of the volume is made up of RBCs

3. The portion of the plasma containing the platelets is removed and transfused to patients suffering from thrombocytopenia (an abnormal low level of platelets). There are several uses for the remaining plasma. One is to freeze it and use it for the coagulation proteins present in it. If it is not frozen, it is then pooled with other units of plasma and treated to purify and concentrate different proteins that have different therapeutic uses, such as albumin and IV immunoglobulin

**Immunology Review**
1. The body’s system that protects it from foreign particles

2. Particle in the body that is foreign

3. Proteins produced by WBCs to get rid of antigens

**Adverse Transfusion Reaction**
1. Temperature - Has it risen (≥1° C above 37° C)? Does the patient feel cold?
2. Blood Pressure - Has it increased or decreased?
3. Breathing - Has it increased or decreased?
4. Any complaints of pain in chest, flank or back pain?
5. Color - Has the patient developed jaundice?
6. Skin appearance - flushing, rash or urticaria?
7. Urine output and color - decreased and/or become darker?
8. Abdominal Status - stomach pain and/or nausea?
9. Abnormal Bleeding - i.e. at the IV site?
10. State of mind - anxiety, drowsy, fear, hysteria

2. If an ATR is suspected of occurring, stop the transfusion while keeping the line open with Normal Saline.

3. Recheck all the clerical data.

3. Contact the treating physician immediately. Note: it will be up the physician if the fourth step (Contact the transfusion medicine department of the lab for directions on starting an investigation into a possible transfusion reaction) will be done.

3. Leukocytes or White Blood Cells (WBCs)
Adverse Immunological Transfusion Reactions

1. It “complements” the antibody’s action by attacking the antigen’s surface and forming holes in it, causing it to break up and be destroyed

2. C3a and C5a

3. They cause the release of histamine and serotonin from mast cells, resulting in vasodilatation and smooth muscle contraction (especially bronchial)

4. It does this by converting Factor XII (Hageman’s Factor) into Factor XIIa, starting the intrinsic pathway. Factor XIIa will also convert kinin into bradykinin, resulting in increased vascular permeability that will cause vasodilation and hypotension. Complement activated by the antigen/antibody complex will cause WBCs and endothelial cells to express tissue factor, resulting in the extrinsic system to be activated.

5. Disseminated Intravascular Coagulation

6. It improves renal blood flow by increasing both cardiac muscle strength and renal vasodilatation

Febrile Non-Hemolytic Transfusion Reactions (FNHTR)

1. Febrile Non-Hemolytic Transfusion Reactions (FNHTR)

2. An unexplained increase in temperature of \(\geq 1^\circ\)Celcius above 37°C
   - Shaking
   - Chills
   - An increase in the respiration rate
   - Blood pressure changes
   - Anxiety

3. Acute Immunological Hemolytic, Septic or TRALI

4. Antibodies formed against the Human Leukocyte Antigens (HLA) on white blood cells
   - Cytokines present in the plasma of the stored unit

5. Leukocytes Reduced (LR). RBC units will have most of the WBCs removed which will reduce the amount of donor WBCs from being transfused into the patient.

Allergic Transfusion Reactions

1. IgE

2. Histamine
3. • Severe hypotension  
   • Shock  
   • Unconsciousness  
   • Dyspnea  
   • Wheezing  
   • Stridor (a high pitched wheezing from blockage of the throat or voice box)  
   • Gastrointestinal problems that include vomiting, stomach pain and diarrhea  
   • Tachycardia, arrhythmia or cardiac arrests are also possible

4. IgA

5. Washed blood products, or blood products from IgA deficient donors can be used

**TRALI (Transfusion Related Acute Lung Injury)**

1. Transfusion Related Acute Lung Injury

2. Acute hypoxemia having a PaO$_2$/FiO$_2$ ratio of $\leq$ 300 Hg with a frontal chest x-ray showing bilateral pulmonary edema. It can be caused by sepsis, trauma, near drowning and blood transfusions.

3. • Chest x-ray showing bilateral pulmonary edema  
   • Arterial blood gas showing a PaO$_2$/FiO$_2$ ratio of $\leq$ 300 Hg

4. Supportive with oxygen and if necessary, mechanical ventilation

5. Increased capillary permeability

**Non-Immunological Acute Transfusion Reactions**

1. a. Transfusion Associated Sepsis  
   b. Transfusion Associated Circulatory Overload (TACO)  
   c. Non Immunological Hemolytic Transfusion Reaction  
   d. Air Embolus  
   e. Massive Transfusion  
   f. Bradykinin Mediated Hypotension

**Transfusion Associated Sepsis**

1. 1. Improper collection  
   2. Improper storage  
   3. Improper handling

2. They have to be stored at room temperature, which increases the risk of bacterial growth in a contaminated unit.
Transfusion Associated Circulatory Overload (TACO)

1. Transfusion Associated Circulatory Overload

2. a. Perioperative older orthopaedic patients in surgical setting
   b. Patients over 60
   c. Infants or patients with severe euvoletic anemia (anemia with a haemoglobin of <50 g/l)

Non Immunological Hemolytic Transfusion Reaction

1. a. Temperature
   b. Mixing IV solutions in the unit of blood

2. The sudden appearance of haemoglobin in their urine

Air Embolus

1. 100 mL

2. 1. Cough
   2. Dyspnea
   3. Chest pain
   4. Shock

2. An x-ray showing intravascular air.

Massive Transfusion

1. When the volume of blood transfused in less than 24 hours is the equivalent of total blood volume

2. 1. Hypothermia
   2. Impaired Hemostasis
   3. Citrate Toxicity
   4. Microaggregates
   5. Hyper/Hypokalemia
   6. Metabolic Acidosis
   7. Volume Status
   8. Myocardial Function

Bradykinin Mediated Hypotension

1. Angiotensin Converting Enzyme

2. Helps control extracellular volume and arterial vasoconstriction by degradation of bradykinin

3. There is an increased level of bradykinin in the blood product. Patients on ACE inhibitors will not be able to degrade and will become hypotensive.