

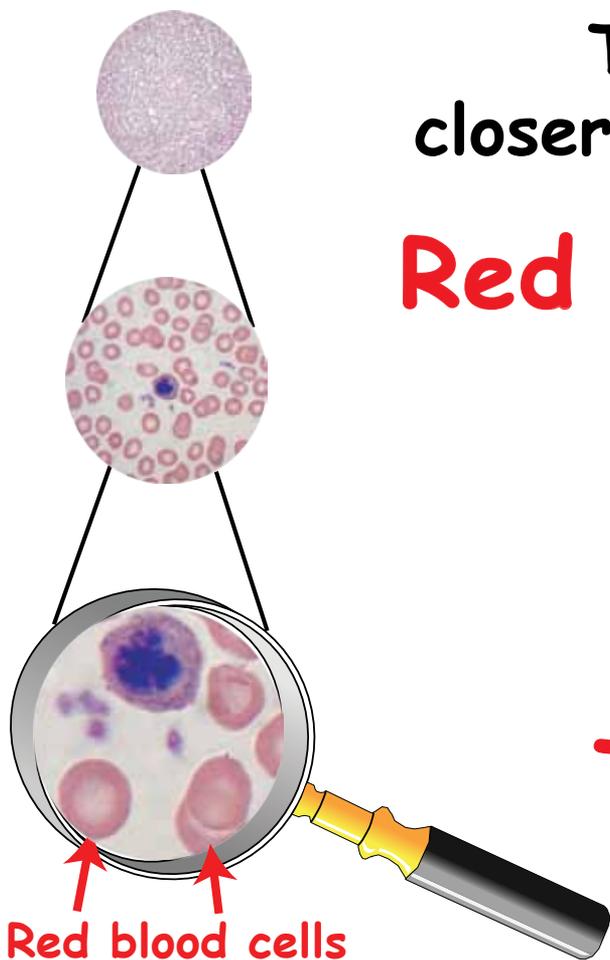
Bloodology II

Taking a
closer look at

**Red Blood
Cells**

and

**Blood
Types**



When the first attempts were made to transfuse blood, some people benefited from it, while others had violent reactions or even died.

The discovery that people have **different types of blood** explained the mystery.

Mother and baby being of different blood types also explained why some newborn babies died. Such dangers can now be anticipated and such deaths prevented.

How does the **immune system** respond to transfusions and pregnancy?

What are **red cell antigens** and **antibodies**? Why are they important?

What is a **blood type**? What does it mean to have **rare blood**? Why is there a frequent need for rare blood?

How do the blood types of parents determine the blood type of their children?

This pamphlet will explore these questions.



The Bloodology blood education pamphlet series

Bloodology II, 2nd Edition

Created by Robert Ratner
and Marion Reid

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We thank numerous colleagues for their suggestions.

For more information and/or for additional copies of this or other pamphlets in the *Bloodology* series, contact: 212-570-3037, rratner@nybloodcenter.org or visit www.nybloodcenter.org



Taking a closer look at blood

To the naked eye, blood looks like a red liquid, but it is actually made up of billions of red and white blood cells and platelets, in a yellow fluid called plasma.



Blood in centrifuge

The different components of blood can be separated by spinning blood in a centrifuge.

Plasma is the liquid in which blood cells “swim.” Plasma contains nutrients, clotting factors and other proteins as well as antibodies.

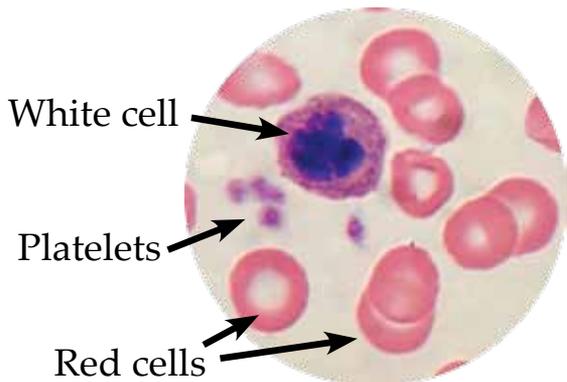
Platelets are small fragments of cells, which are vital for forming blood clots that stop bleeding.

White cells play a vital role in the immune response and in combating infections.

Red cells carry oxygen from the lungs to all parts of the body and exchange it for carbon dioxide, which it carries to the lungs. Red cells carry the “marker” antigens that distinguish one blood type from another and can trigger an immune response.



A view of blood with a microscope

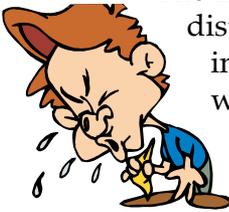


The Immune Response

How the body protects itself from invaders

The human body is in constant battle against viruses and bacteria. The body responds to foreign material with a complex series of events, called the **immune response**.

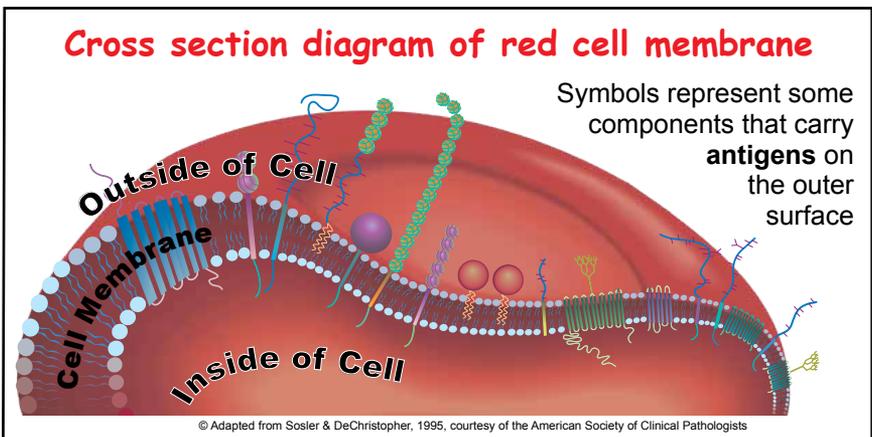
Along with millions of our own body's cells, millions of other organisms (types of bacteria, for example) reside within our bodies. Most are harmless or even beneficial for our bodies. The immune system has a sophisticated ability to distinguish "self" (our own cells and other organisms long "resident" in our bodies), from "non-self" (cells and organisms from the outside that could be potentially harmful).



The immune system generally makes the right distinctions – protecting us from harmful invaders, while allowing things we need (food, water, etc.) to enter our bodies. But sometimes the immune system reacts unnecessarily. Examples are allergies to a particular food, cats, or pollen.

Immune Response to Red Cells

Blood cells have an outer surface known as a **cell membrane** that restricts what can pass in and out of the cell. On the outer

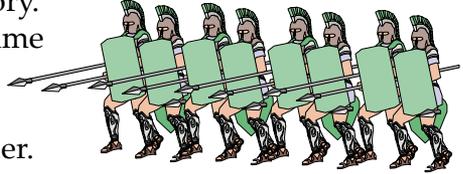


surface of the red cell membrane are molecular structures, called **antigens**, which “mark” a person's blood “type.”

When a patient receives a transfusion of blood carrying the *same* antigens as on his or her own red cells, the donor red cells are welcomed because the body does not recognize the transfused cells as foreign. But, red cells with a *different* combination of antigens may be treated as a hostile invader. The presence of a “non-self” antigen on the donor red cells triggers special white blood cells to make **antibodies** to attack the presumed hostile invaders.

The first time the immune system encounters a “non-self” antigen, white cells begin to manufacture antibodies against the antigen. This process is gradual and long lasting, providing the immune system with a “memory.”

Another encounter with the same antigen results in an army of antibodies quickly and massively attacking the invader.



Therefore, if a transfusion is needed, such potentially harmful reactions must be avoided. The patient's plasma is tested for antibodies. **Patients with particular antibodies can only safely receive blood that lacks the corresponding antigens.**

Blood testing

In 1901, Karl Landsteiner mixed blood from fellow scientists and observed that some combinations resulted in clumping and others did not. The large number of cells in the clumps makes them easily seen by the naked eye.

The presence of a specific antibody, interacting with an antigen, causes red cells to clump -- in a reaction known as **agglutination**. When an antibody is used to identify the blood type of red cells,



Red cells agglutinated



Red cells not agglutinated

clumping is a “positive” (+) test and indicates the presence of the antigen. When no clumping is observed, the test is “negative” (-), which indicates the absence of the antigen.

Based on the presence of antigens on a person's red cells, blood is categorized into different “types.” Type A blood, for example, refers to red cells that carry the A antigen.

Antibodies in the plasma are named by adding “anti-” to the name of the antigen with which it reacts. Thus, “anti-A” refers to the antibody that reacts with the A antigen.

The ABO blood types

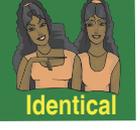
For decades, scientists knew of only the four basic ABO blood types familiar to many people: **type O** (containing neither the A nor B antigens), **type A** (containing the A antigen), **type B** (containing the B antigen) and **type AB** (containing both the A and B antigens). With rare exceptions, the blood of all people fit into one of these four types.

Testing red cells for A and B blood types				
Result of testing with Anti-A	Result of testing with Anti-B	Antigen(s) present on red cells	Blood type	Antibody in plasma
		No A or B	O	Anti-A and anti-B
		A antigen	A	Anti-B
		B antigen	B	Anti-A
		Both A and B	AB	None

ABO antigens are also found in plants and bacteria so people who lack A or B antigens are exposed to them even without previous exposure to blood, and will make antibodies.

Matching ABO type for red cell transfusions

While all patients can receive blood from donors with the same ABO blood type, some can also receive blood of certain other ABO blood types and is shown in the following chart.

		Blood type of PATIENT			
		O	A	B	AB
Blood type of DONOR	O	 Identical	 Compatible	 Compatible	 Compatible
	A	 Incompatible	 Identical	 Incompatible	 Compatible
	B	 Incompatible	 Incompatible	 Identical	 Compatible
	AB	 Incompatible	 Incompatible	 Incompatible	 Identical

As type O blood has neither A nor B antigens, a transfusion of type O blood can be safely transfused not only to type O patients, but also to type A, B, and AB patients. For this reason, **type O donors** are often called **Universal Blood Donors**.

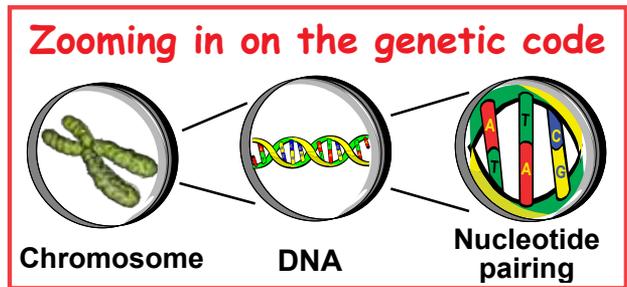
In contrast, type O *patients* have anti-A and anti-B in their plasma and therefore, they can **not** receive red cells from type A, B, or AB donors. Type O patients can only be safely transfused with type O red cells.

How blood types are inherited

Most cells have a nucleus containing pairs of **chromosomes**, which include **deoxyribonucleic acid (DNA)**. DNA has a pair of two complementary twisted strands of millions of **nucleotides**.

There are only four different types of nucleotides in each of the pairs of long DNA strands: adenosine (A), thymine (T), cytosine (C) and guanine (G). Adenosine is always paired with thymine and cytosine is always paired with guanine. There are literally billions of variations in the order these nucleotides can appear on the strands.

The order of nucleotides is the **genetic code** that guides the production of all proteins, including red cell antigens.



The order of these nucleotides define **genes** that provide instructions (inherited from the parents) guiding how the body develops and functions. Slight variations in the sequence of nucleotides in a particular area (**gene**) can lead to a person having different features, for example eye color or blood type.

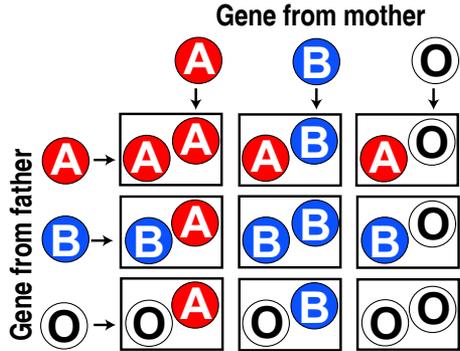
Some genes are **recessive**. A single recessive gene has no effect on its own. Only when inherited from **both** parents, with the presence of two recessive genes working together, can a recessive gene determine a feature of a person.

A **dominant** gene will determine a particular trait on its own, without a similar gene coming from the other parent.

The genetic makeup (**genotype**) can be different from the resulting observable characteristics (**phenotype**).

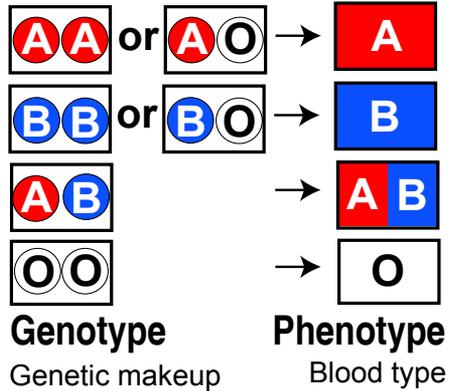
Many possible **genetic combinations (genotypes)** are possible from the pairing of genes from the mother and father.

The chart shows possible genetic combinations of A, B and O genes from parents to children (boxes).



Genotype and phenotype can be different:

Because a dominant gene “hides” the presence of a recessive gene, those with an identical physical characteristic (**phenotype**) can have a different genetic makeup (**genotype**). Chart to right shows this in the case of ABO blood types.



A child can have a different blood type than a parent

If mother is Type A **A**

Her genes could be either: **AA** or **AO**

For this example, assume that she only has one A allele:



And if father is Type B **B**

His genes could be either: **BB** or **BO**

For this example, assume that he only has one B allele:



Then, the child possibly is:

Genotype: **AO**
(genetic makeup)



Phenotype:
(resulting blood type)

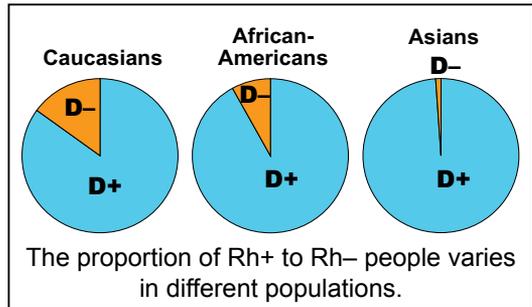


Child is Type: A or AB or B or O

The Rh blood types

In the 1940s, the first of another group of antigens was identified. Called "Rh" because it was first discovered in the blood of rhesus monkeys, the antigen was later named "D". Red cells agglutinated by anti-D are called "Rh-positive" (Rh+) and those not agglutinated by anti-D are called "Rh-negative" (Rh-).

Blood of patients and donors is also routinely tested and matched for ABO *and* Rh type. This is because Rh- patients readily produce anti-D if transfused with D+ blood. Over 50 different Rh antigens have now been identified.



Hemolytic disease of the newborn

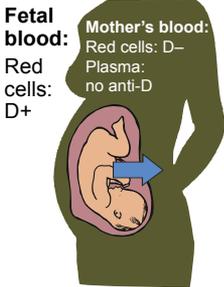
A fetus has its own blood circulation system, separate from that of the mother. The blood type of the fetus may be different from that of the mother. The **placenta** acts like a filter keeping the large red cells of the mother separate from those of the fetus, while allowing vital nutrients and antibodies to pass from the mother to the fetus.

Occasionally during childbirth or due to injury, a break occurs in the placenta allowing small amounts of the fetal red cells to enter the mother's blood. If the red cells of the fetus have an antigen, inherited from the father, that the mother's red cells lack, the antigen on the baby's red cells can trigger the production of the corresponding antibody in the mother's plasma.

Generally, the fetus of a *first* pregnancy is not affected because only a small amount of antibody is produced by the time the baby is born. However, if the mother becomes pregnant again and the fetal red cells carry the same antigen, the mother's immune response "memory" is activated. Large amounts of

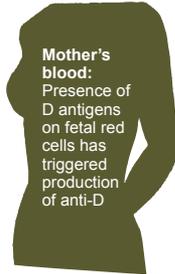
How hemolytic disease of the newborn develops (in case of anti-D)

First Pregnancy



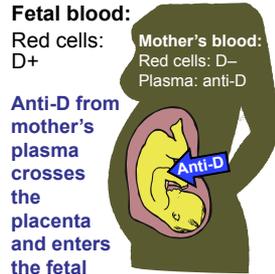
Healthy Fetus
Fetal red cells with D antigen can cross placenta and enter mother's blood.

After Pregnancy



Mother becomes "sensitized" to D, begins making anti-D

Subsequent Pregnancy with a D+ baby



FETUS IN DANGER
from reaction between D antigens on fetus and mother's anti-D

antibody are produced that can cross the placenta and react with the fetal red cell antigens, possibly threatening the life of the fetus. This is **hemolytic disease of the newborn**.

With identification of the blood type of the parents and the detection and identification of antibodies in the maternal plasma, this potentially deadly disease can now be anticipated and treated.

Matching ABO and Rh

The ABO and Rh type of a donor's red cells must be compatible with the ABO and Rh type of the patient. The percentage of the U.S. population with each type is given in the adjoining table.

Blood Type	Name	Occurrence
Type O Rh+	O +	38%
Type O Rh-	O -	7%
Type A Rh+	A +	34%
Type A Rh-	A -	6%
Type B Rh+	B +	9%
Type B Rh-	B -	2%
Type AB Rh+	AB +	3%
Type AB Rh-	AB -	1%

Discovery of more blood types

In 1945, the **Indirect Antiglobulin Test** was introduced, which led to the detection of many other red cell antibodies.

In addition to ABO and Rh, we now know that there are hundreds of other red cell antigens. Red cell antigens can occur in thousands of different combinations.

One of the first antibodies found by the indirect antiglobulin test was called "anti-Kell" (now known as "anti-K"). The name came from Mr. and Mrs. Kelleher, whose baby suffered from hemolytic disease of the newborn. Mrs. Kelleher's serum agglutinated D+ and D- red cells in the same proportion, indicating that an antibody other than anti-D was involved. Since then, another 25 different Kell antigens have been identified.

The next antibody was found in the plasma of Mr. Duffy, a hemophiliac (a person having a disorder where the blood lacks the ability to clot normally) who had received many blood transfusions. The antibody was named anti-Fy^a based on the last two letters of his name.

The Jk^a antigen, and the Kidd blood group system, was named after John Kidd, a baby with hemolytic disease of the newborn. New antibodies and thus new blood types continue to be identified. There are now over 250!

After many transfusions, a patient may accumulate a number of different antibodies

In a person who has not received a blood transfusion or been pregnant, the presence of antibodies other than anti-A or anti-B is rare. However, after transfusion or pregnancy about 2% of people develop antibodies. With each transfusion or pregnancy there is the possibility that additional, different antibodies may be formed.

Patients with certain diseases (such as sickle cell disease, thalassemia, or aplastic anemia) and certain treatments (such

as chemotherapy) require repeated transfusions. Because of the vast array of different combinations of antigens on red cells of various donors, receiving blood almost always introduces "non-self" antigen(s) and these antigens can trigger antibody production in the recipient's plasma. Once antibodies have been produced, a second exposure to blood with the triggering antigen may cause a transfusion reaction and harm to the patient.

With the addition of each new antibody to a patient's blood system, the ability to find donors with blood that can be safely transfused to these patients becomes more difficult. Potential donors whose red cells lack the necessary antigens can be rare. **Such patients require more and more precisely matched red cell transfusions.**

Patient testing and donor red cell selection

When a patient needs a transfusion, a sample of the patient's blood is tested to determine the ABO and Rh type to identify what type of donor blood can be transfused. The patient's plasma is also tested to detect red cell antibodies. If an antibody is detected, the blood sample is tested further to determine which antigen(s) it recognizes. The donor red cells selected for transfusion should lack the corresponding antigen(s), in order to prevent a transfusion reaction.



Testing of
blood samples
to identify
antigen

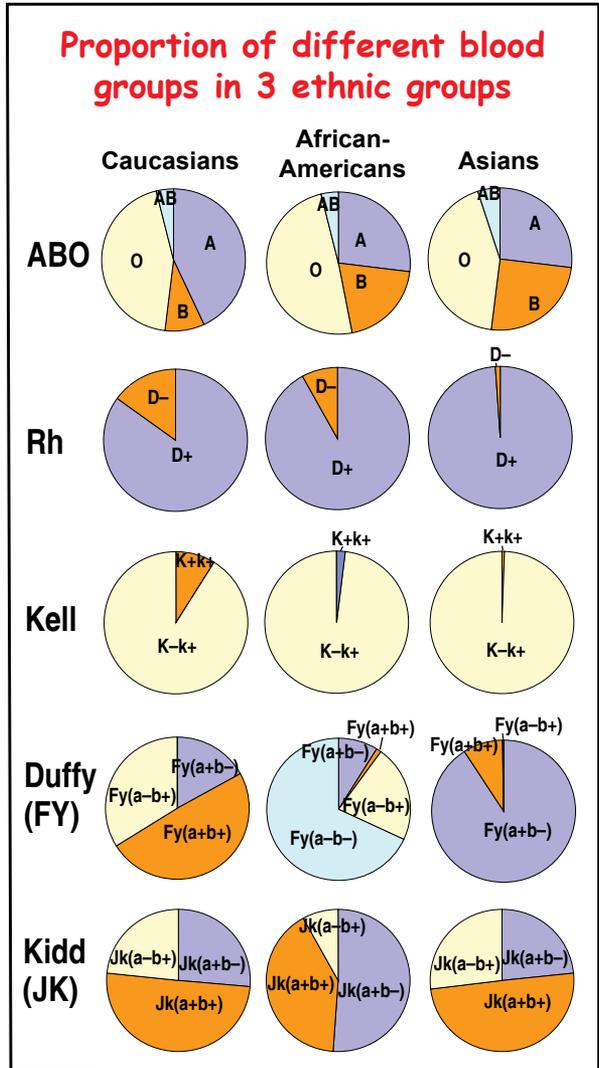
PRECISE MATCHING

and knowing where to look

The distribution of phenotypes in the five most important blood group systems (ABO, Rh, Kell, Duffy, and Kidd) in three populations is shown.

D- is rare in Asians; Fy(a-b-) is found in 68% of African Americans but is rare in Caucasians and Asians.

If a patient requires a transfusion with K-, Fy(a-), Jk(b-) red cells, this type of blood is most likely found in African Americans because this combination of absent antigens is found in 1 in 2 of them but only in 1 in 10 of Caucasians and less than 1 in 100 of Asians.



Thus, "rare" is a relative term because what is rare in one ethnic group can be common in another.

What makes blood "rare"?

"Rare" refers to how often the blood type is found, and *not* how often such blood is needed. Rare blood can be defined as being found in one person in 200, or is even less common.

Many donors needed for precise match

Let's use example of a patient with sickle cell disease who is type A Rh-positive and has anti-E, anti-K and anti-Jk^a antibodies requires transfusion of 3 units of blood.

15 Units of A Rh-positive blood available in hospital inventory



Test with anti-E



4 units are E+, thus unacceptable for patient

Test with anti-K



1 unit is K+, thus a total of 5 units unacceptable for patient

Test with anti-Jk^a



7 units are Jk(a+), thus a total of 12 units unacceptable for patient

Of 15 units of A Rh-positive, only 3 units were precisely matched and acceptable for this patient



Finding a donor with the needed rare blood type is like finding "a needle in a haystack."



The need for "rare" blood is not a rare event. - There is a **FREQUENT** need for rare blood!

You can help!

♥ **Become a blood donor** Whatever your blood type may be, your donation is truly a “gift of life.” Encourage friends and family to donate at least twice a year.

To donate, you should:

- Be between the ages of 16 and 76,
- Be in good health, and
- Weigh at least 110 lbs.

♥ **Sponsor a blood drive** at your job, school or community.

♥ **Encourage others to donate**

♥ **Help identify rare blood donors** Check the Donor Registration Form box indicating ethnic background when donating. This information allows us to focus testing in the ethnic population in which a needed “rare” type is most likely to be found.

If you have been identified as a rare blood donor, there is a much greater chance that your brothers and sisters may also have inherited the same rare type. Encourage them to donate blood and be tested to identify their blood type.

Donate Blood - Give the Gift of Life!

 **New York** *Blood Center*

For more information or to make an appointment, we invite you to call **1-800-933-BLOOD** or go to our website: **WWW.NYBLOODCENTER.ORG**.