

2. Blood group antigens are surface markers on the red blood cell membrane

Before the 1900s, it was thought that all blood was the same, a misunderstanding that led to frequently fatal transfusions of animal blood into humans and hazardous transfusions of blood between people. Human blood is not the same—people belong to different blood groups, depending upon the surface markers found on the red blood cell.

The cells that make up the body's tissues and organs are covered with surface markers, or antigens. Red blood cells are no different. This chapter will describe the types of red blood cell antigen and explain why they are so important in medicine today.

Antigens stimulate an immune response

An antigen is any substance to which the immune system can respond. For example, components of the bacterial cell wall can trigger severe and immediate attacks by neutrophils.

If the immune system encounters an antigen that is not found on the body's own cells, it will launch an attack against that antigen. Conversely, antigens that are found on the body's own cells are known as "self-antigens", and the immune system does not normally attack these.

The membrane of each red blood cell contains millions of antigens that are ignored by the immune system. However, when patients receive blood transfusions, their immune systems will attack any donor red blood cells that contain antigens that differ from their self-antigens. Therefore, ensuring that the antigens of transfused red blood cells match those of the patient's red blood cells is essential for a safe blood transfusion.

Red blood cell antigens can be sugars or proteins

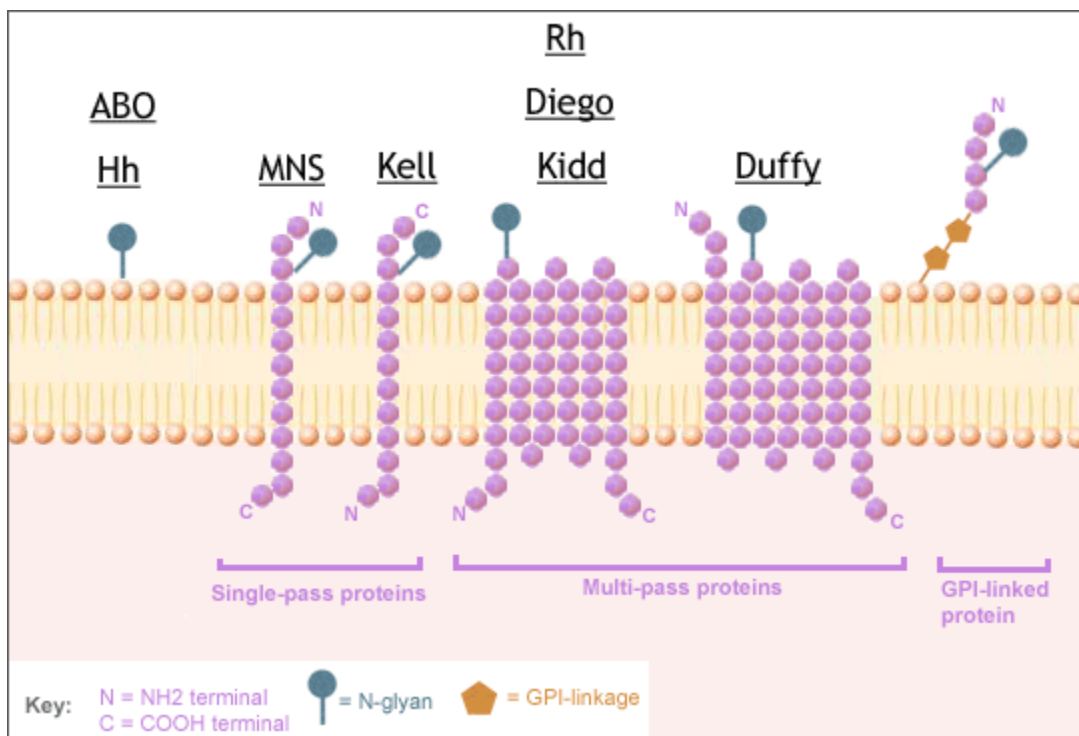
Blood group antigens are either sugars or proteins, and they are attached to various components in the red blood cell membrane.

For example, the antigens of the ABO blood group are sugars. They are produced by a series of reactions in which enzymes catalyze the transfer of sugar units. A person's DNA

determines the type of enzymes they have, and, therefore, the type of sugar antigens that end up on their red blood cells.

In contrast, the antigens of the Rh blood group are proteins. A person's DNA holds the information for producing the protein antigens. The RhD gene encodes the D antigen, which is a large protein on the red blood cell membrane. Some people have a version of the gene that does not produce D antigen, and therefore the RhD protein is absent from their red blood cells.

The figure below shows the red blood cell membrane and some of the blood group antigens attached to it. Aside from the sugar (glycan or carbohydrate) antigens, the red blood cell membrane contains three types of protein that carry blood group antigens: single-pass proteins, multi-pass proteins, and glycosylphosphatidylinositol (GPI)-linked proteins. Click on the blood groups to find out more about the antigens that define it.



Red blood cell antigens determine your blood group

The antigens expressed on the red blood cell determine an individual's blood group. The main two blood groups are called ABO (with blood types A, B, AB, and O) and Rh (with Rh D-positive or Rh D-negative blood types).

The functions of many of the blood group antigens are not known, and if they are missing from the red blood cell membrane, there is no ill effect. This suggests that if the blood group antigens used to have a function, e.g., one particular blood group antigen made red blood cells more resistant to invasion from a parasite, it is no longer relevant today.

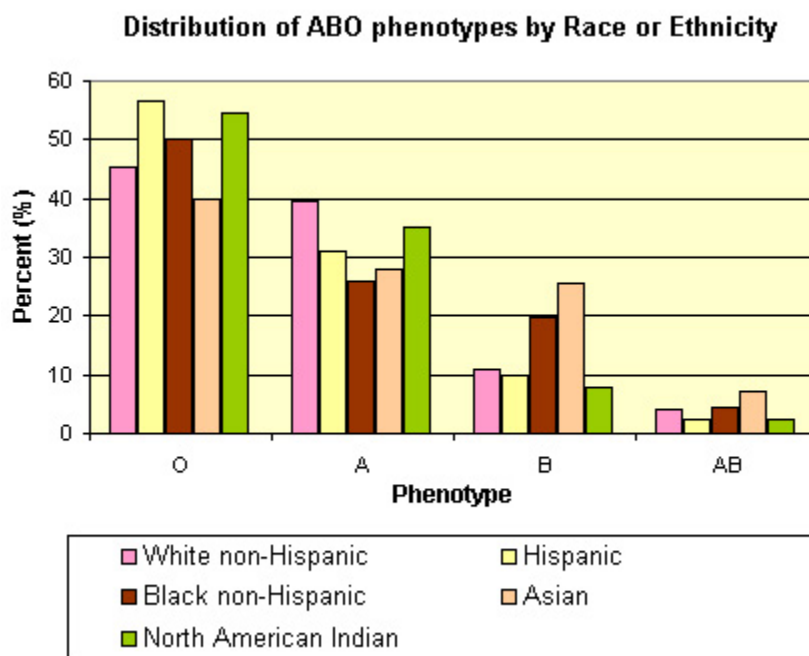
But the presence or absence of red blood cell antigens becomes extremely important when blood from different people mixes, e.g., when a patient receives a blood transfusion from a blood bank. This also happens when a mother becomes pregnant because during labor, a small amount of fetal blood enters her circulation. In these circumstances, exposure to the foreign antigens on the red blood cells can trigger immune reactions.

It is not possible to completely remove the danger of adverse reactions when blood from two people mix, but the danger can be minimized. Before a blood transfusion takes place, the blood to be donated must be "typed and cross matched" with the patient's blood to ensure immune compatibility (see [Chapter 3](#)). In pregnancy, the risk of the mother's immune system attacking the foreign antigens present on her fetus' red blood cells is prevented by giving the mother antibodies to cover fetal red blood cell antigens and removing them from the mother's circulation before her immune cells find them (see [Chapter 4](#)).

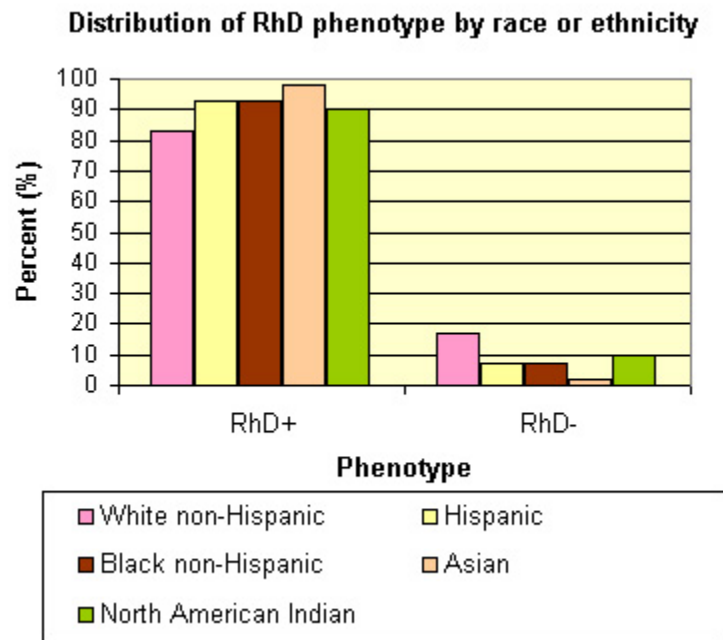
Blood groups differ around the world

The distribution of the four ABO blood types, A, B, AB, and O, varies in populations throughout the world. It is determined by the frequency of the three alleles of the ABO gene in different populations. Blood type O is the most common worldwide, followed by group A. Group B is less common, and group AB is the least common.

The frequencies of ABO and Rh type in the United States were recently examined by collecting data from blood donors over a 10 year period (1). The charts below summarize the findings for blood type and race:



The highest percentage of type O (57%) was found in Hispanic donors (a group that includes donors of Mexican, Puerto Rican, and Cuban descent). The next highest percentage of type O was found in North American Indian (55%) and black (50%) donors.



In all donors, the Rh D-positive (RhD+) blood type was more common than the Rh D-negative (RhD-) blood type. The highest percentage of RhD- was found in white donors (17.3%).

Blood type O: the Americas

People with blood type O are said to be "universal donors" because their blood is compatible with all ABO blood types. It is also the most common blood type in populations around the world, including the USA (1) and Western Europe (2, 3). Among indigenous populations of Central and South America, the frequency of O blood type is extremely high, approaching 100%. It is also high among Australian aborigines.

Blood Type A: Central and Eastern Europe

Type A is common in Central and Eastern Europe. In countries such as Austria, Denmark, Norway, and Switzerland, about 45-50% of the population have this blood type, whereas about 40% of Poles and Ukrainians do so.

The highest frequencies are found in small, unrelated populations. For example, about 80% of the Blackfoot Indians of Montana have blood type A.

Blood type B: Asia

Blood type B is relatively common in Chinese and Indians, being present in up to 25% of the population. It is less common in European countries and Americans of European origin, being found in about 10% of these populations.

Blood type AB is the least common

Blood type AB individuals are known as "universal receivers" because they can receive blood from any ABO type.

It is also the rarest of the blood groups. It is most common in Japan, regions of China, and in Koreans, being present in about 10% of these populations.

The classification of blood cell antigens

Traditionally, newly discovered red blood cell antigens were named alphabetically (e.g. ABO, MNS, P) or were named for the first person who produced antibody against them (e.g. Duffy, Diego). In 1980, The [International Society of Blood Transfusion \(ISBT\)](#) Working Party on Terminology for Red Cell Surface antigens was formed to create a standard for blood group terminology. Under this terminology, each blood group antigen has a number, and it belongs to a blood group system, a collection, or a series (4).

Blood groups

A blood group system contains antigens controlled by a single gene (or by multiple closely linked loci), and the system is genetically distinct. At the time of writing, there are 22 blood group systems, including the ABO, Rh, and Kell blood groups which contain antigens that can provoke the most severe transfusion reactions.

Each blood group antigen is assigned a six-digit number by the ISBT. The first three digits represent the blood group (e.g., ABO is 001, Rh is 004), and the last three identify the antigen in the order it was discovered. For example, for ABO, the A antigen was the first to be discovered and has the number 001.001 whereas the B antigen was next and is designated 001.002.

Collections

A collection contains antigens that are related in some way, e.g., by genetics or biochemistry, but they do not meet the criteria to form a blood group. Once a collection of antigens can be proven to be genetically distinct, they are given the status of a blood group. At the time of writing, there are six collections of antigens.

Series

Red cell antigens that do not fit into a blood group or a collection are sorted into two series: if they are rare (frequency of less than 1%), they are placed in the 700 series, if they

are common (frequency greater than 90%), they are placed in the 901 series. At the time of writing, there are 22 antigens in the 700 series and 11 antigens in the 901 series.

References

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