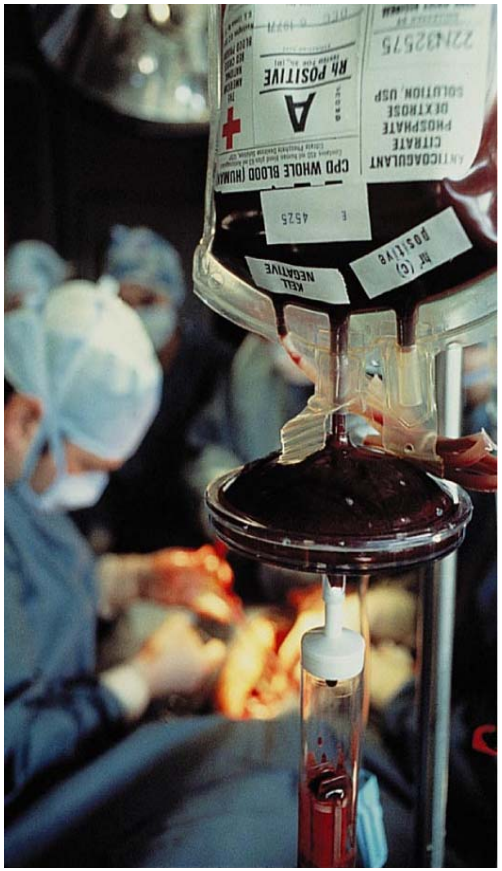
Blood Transfusions

Danil hammoudi.MD



- Whole blood transfusions are used:
  - When blood loss is substantial
  - In treating thrombocytopenia
- Packed red cells (cells with plasma removed) are used to treat anemia

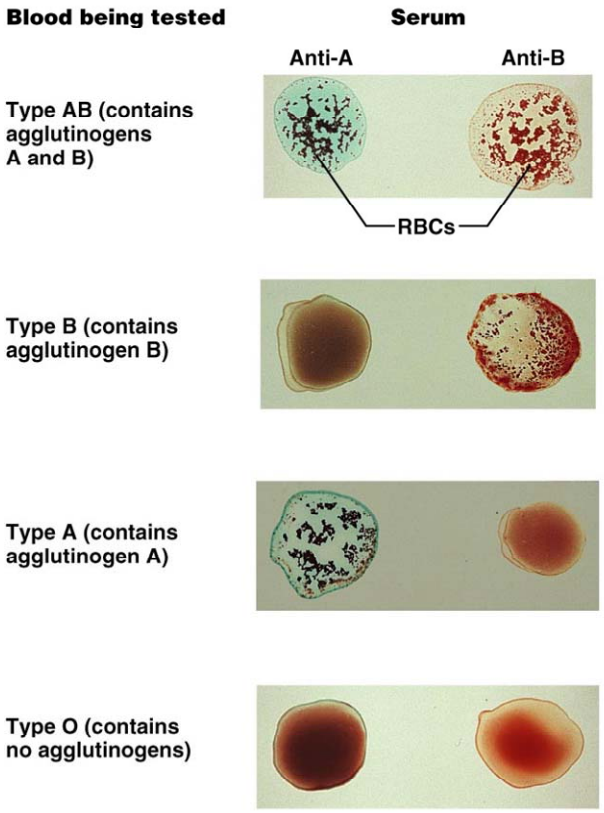
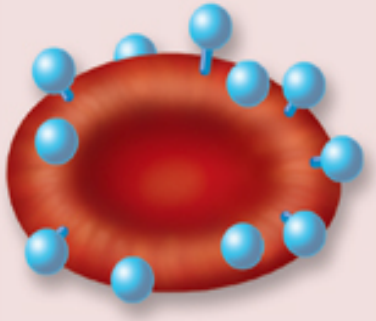
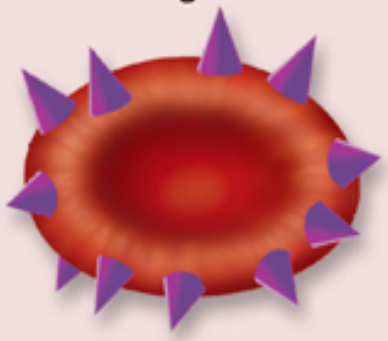
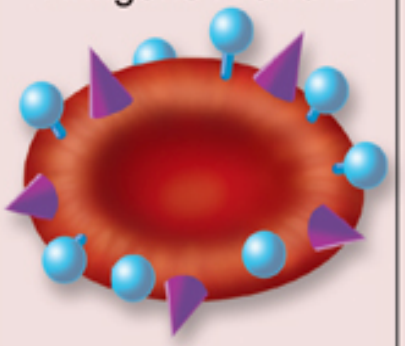


Figure 17.15

Human Blood Groups

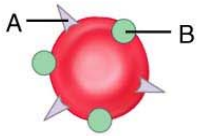
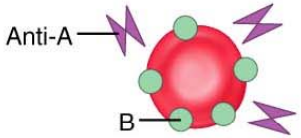
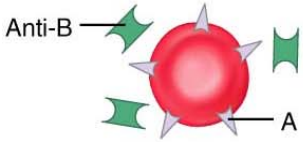
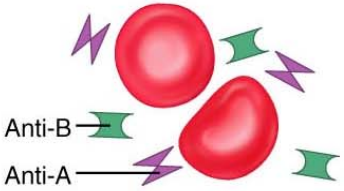
- RBC membranes have glycoprotein antigens on their external surfaces
- These antigens are:
  - Unique to the individual
  - Recognized as foreign if transfused into another individual
  - Promoters of agglutination and are referred to as agglutinogens
- Presence or absence of these antigens is used to classify blood groups

Erythrocytes	Antigen A 	Antigen B 	Antigens A and B 	Neither antigen A nor B 
Plasma	Anti-B antibodies 	Anti-A antibodies 	Neither anti-A nor anti-B antibodies	Both anti-A and anti-B antibodies 
Blood type	**Type A** Erythrocytes with type A surface antigens and plasma with anti-B antibodies	**Type B** Erythrocytes with type B surface antigens and plasma with anti-A antibodies	**Type AB** Erythrocytes with both type A and type B surface antigens, and plasma with neither anti-A nor anti-B antibodies	**Type O** Erythrocytes with neither type A nor type B surface antigens, but plasma with both anti-A and anti-B antibodies

Blood Groups

- Humans have 30 varieties of naturally occurring RBC antigens
- The antigens of the ABO and Rh blood groups cause vigorous transfusion reactions when they are improperly transfused
- Other blood groups (M, N, Dufy, Kell, and Lewis) are mainly used for legalities

TABLE 17.4 ABO Blood Groups

BLOOD GROUP	FREQUENCY (% U.S. POPULATION) WHITE	BLACK	ASIAN	NATIVE AMERICAN	RBC ANTIGENS (AGGLUTINOGENS)	ILLUSTRATION	PLASMA ANTIBODIES (AGGLUTININS)	BLOOD THAT CAN BE RECEIVED
AB	4	4	5	<1	A B		None	A, B, AB, O (Universal recipient)
B	11	20	27	4	B		Anti-A (a)	B, O
A	40	27	28	16	A		Anti-B (b)	A, O
O	45	49	40	79	None		Anti-A (a) Anti-B (b)	O (Universal donor)

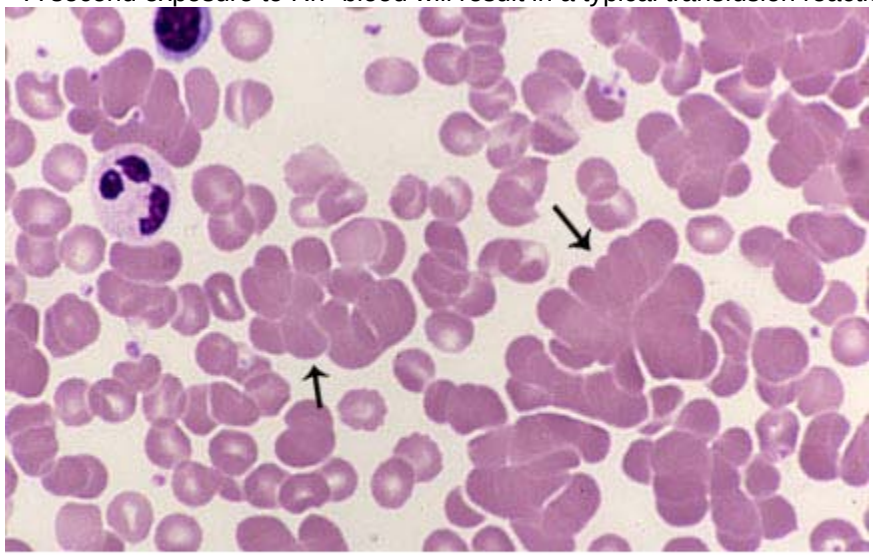
ABO Blood Groups

- The ABO blood groups consists of:
  - Two antigens (A and B) on the surface of the RBCs
  - Two antibodies in the plasma (anti-A and anti-B)
- ABO blood groups may have various types of antigens and preformed antibodies
- Agglutinogens and their corresponding antibodies cannot be mixed without serious hemolytic reactions

Rh Blood Groups

- There are eight different Rh agglutinogens, three of which (C, D, and E) are common
- Presence of the Rh agglutinogens on RBCs is indicated as Rh^+
- Anti-Rh antibodies are not spontaneously formed in Rh^- individuals

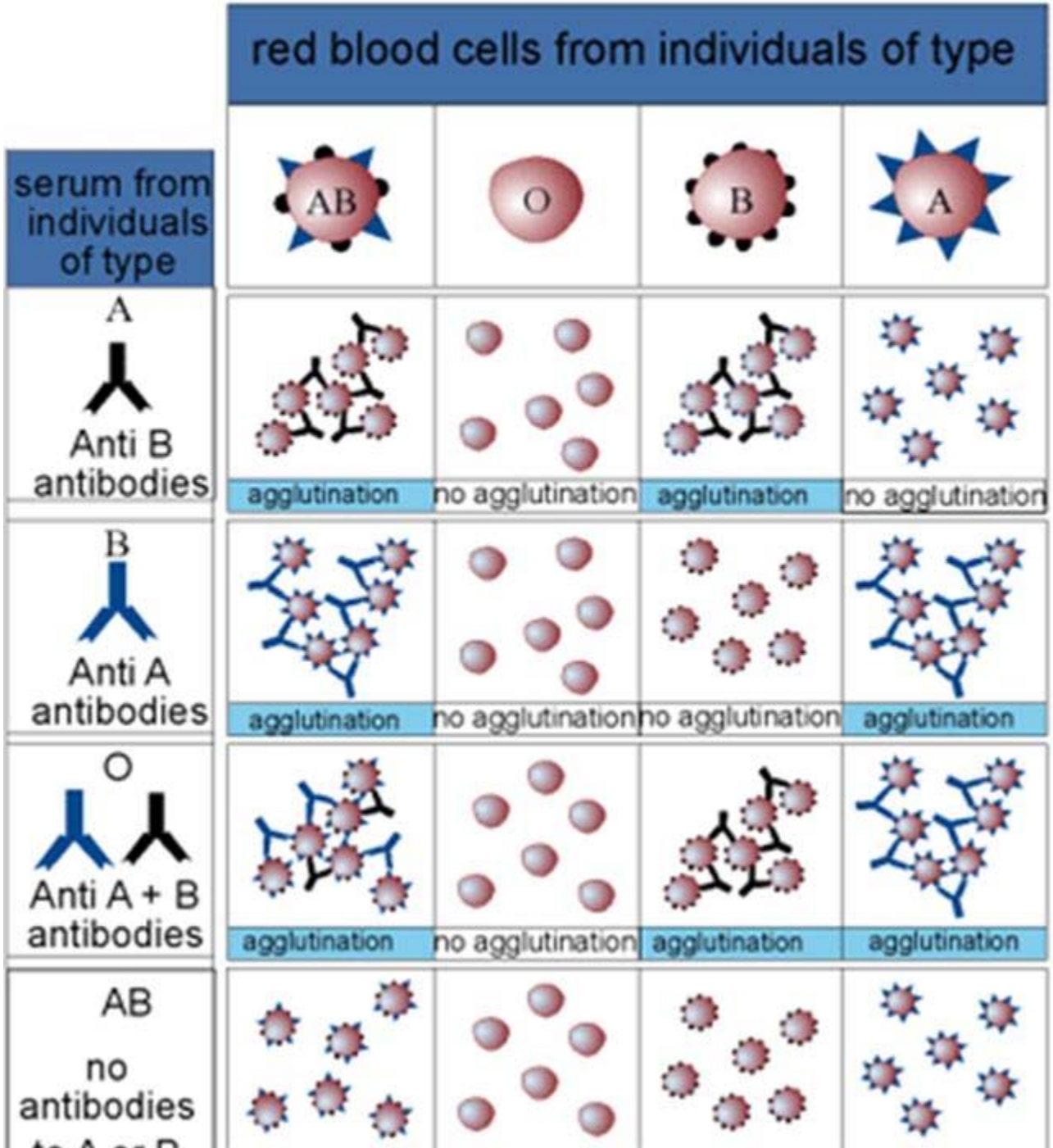
- However, if an Rh^- individual receives Rh^+ blood, anti-Rh antibodies form
- A second exposure to Rh^+ blood will result in a typical transfusion reaction

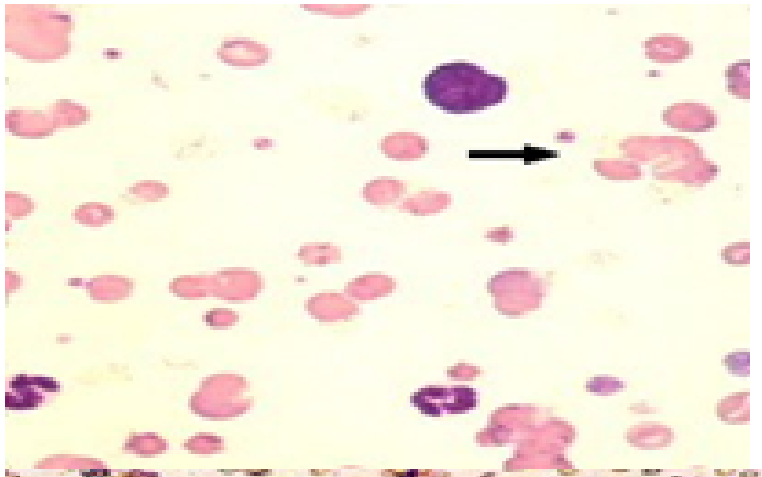


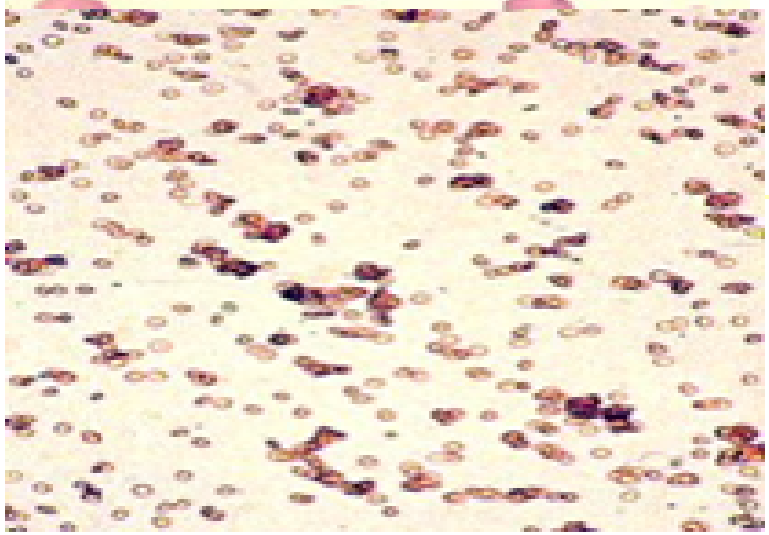
Source: Lichtman MA, Shafer MS, Felgar RE, Wang N:
Lichtman's Atlas of Hematology: http://www.accessmedicine.com

Blood type of cells	Genotype	Antibodies made by body	Reaction to added antibodies	
			Anti-A	Anti-B
A	I^AI^A or I^AI^O	Anti-B		
B	I^BI^B or I^BI^O	Anti-A		
AB	I^AI^B	Neither anti-A nor anti-B		
O	I^OI^O	Both anti-A and anti-B		

Hemagglutination







The observation of red blood cell agglutination (also referred to as autoagglutination) must be distinguished from rouleaux formation which is a physiological phenomenon. The presence of antibodies (usually IgM) on the surface of red blood cells is responsible for the phenomenon of autoagglutination. Agglutination can be observed during immune-mediated hemolytic anemia, but also during 'cryoglobulinemia' (a far more rare condition).

Agglutinating red blood cells resemble grapelike clusters whereas red blood cells in rouleaux formation resemble a stack of coins.
In order to clearly distinguish erythrocyte agglutination from rouleaux formation, a simple saline test can be performed.

Hemolytic Disease of the Newborn

- Hemolytic disease of the newborn $^{-}$ Rh^{+} antibodies of a sensitized Rh^{-} mother cross the placenta and attack and destroy the RBCs of an Rh^{+} baby
- Rh^{-} mother becomes sensitized when exposure to Rh^{+} blood causes her body to synthesize Rh^{+} antibodies

Hemolytic Disease of the Newborn

- The drug RhoGAM can prevent the Rh^{-} mother from becoming sensitized
- Treatment of hemolytic disease of the newborn involves pre-birth transfusions and exchange transfusions after birth

Transfusion Reactions

- Transfusion reactions occur when mismatched blood is infused

- Donor's cells are attacked by the recipient's plasma agglutinins causing:
  - Diminished oxygen-carrying capacity
  - Clumped cells that impede blood flow
  - Ruptured RBCs that release free hemoglobin into the bloodstream

Transfusion Reactions
- Circulating hemoglobin precipitates in the kidneys and causes renal failure

Blood Typing
- When serum containing anti-A or anti-B agglutinins is added to blood, agglutination will occur between the agglutinin and the corresponding agglutinogens
- Positive reactions indicate agglutination

Blood groups are created by molecules present on the surface of red blood cells (and often on other cells as well).

The ABO Blood Groups

The **ABO blood groups** were the first to be discovered (in 1900) and are the most important in assuring safe blood transfusions.

The table shows the four ABO phenotypes ("blood groups") present in the human population and the genotypes that give rise to them.

Blood Group	Antigens on RBCs	Antibodies in Serum	Genotypes
A	**A**	Anti-B	*AA* or *AO*
B	**B**	Anti-A	*BB* or *BO*
AB	**A** and **B**	Neither	*AB*
O	Neither	Anti-A and Anti-B	*OO*

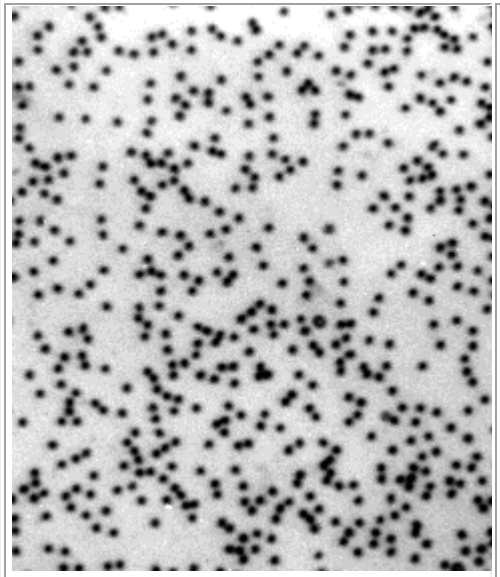
- When red blood cells carrying one or both antigens are exposed to the corresponding antibodies, they agglutinate; that is, clump together. People usually have antibodies against those red cell antigens that they lack.

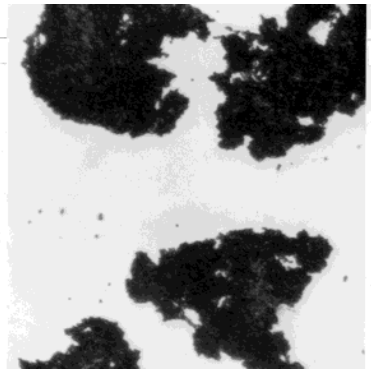
The Rh System

- Rh antigens are transmembrane proteins with loops exposed at the surface of red blood cells. They appear to be used for the transport of carbon dioxide and/or ammonia across the plasma membrane. They are named for the rhesus monkey in which they were first discovered.
- There are a number of Rh antigens. Red cells that are "Rh positive" express the one designated **D**. About 15% of the population have no RhD antigens and thus are "Rh negative".
- The major importance of the Rh system for human health is to avoid the danger of RhD incompatibility between mother and fetus.

- During birth, there is often a leakage of the baby's red blood cells into the mother's circulation. If the baby is Rh positive (having inherited the trait from its father) and the mother Rh-negative, these red cells will cause her to develop antibodies against the RhD antigen. The antibodies, usually of the IgG class, do not cause any problems for that child, but can cross the placenta and attack the red cells of a subsequent Rh^+ fetus. This destroys the red cells producing anemia and jaundice. The disease, called **erythroblastosis fetalis** or **hemolytic disease of the newborn**, may be so severe as to kill the fetus or even the newborn infant. It is an example of an antibody-mediated cytotoxicity disorder.
- Although certain other red cell antigens (in addition to Rh) sometimes cause problems for a fetus, an **ABO** incompatibility does not. Why is an Rh incompatibility so dangerous when ABO incompatibility is not?
- It turns out that most anti-A or anti-B antibodies are of the IgM class and these do **not** cross the placenta. In fact, an **Rh^-/type O** mother carrying an **Rh^+/type A, B, or AB** fetus is resistant to sensitization to the Rh antigen. Presumably her anti-A and anti-B antibodies destroy any fetal cells that enter her blood before they can elicit anti-Rh antibodies in her.
- This phenomenon has led to an extremely effective preventive measure to

- Human red blood cells before (left) and after (right) adding serum containing anti-A antibodies. The agglutination reaction reveals the presence of the A antigen on the surface of the cells.





- The antigens in the ABO system are O-linked glycoproteins with their sugar residues exposed at the cell surface. The terminal sugar determines whether the antigen is A or B.
- The critical principle to be followed is that transfused blood must not contain red cells that the **recipient's** antibodies can clump. Although theoretically it is possible to transfuse group O blood into any recipient, the antibodies in the donated plasma can damage the recipient's red cells. Thus, when possible, transfusions should be done with exactly-matched blood.
- In 2007, Danish and French investigators reported the properties of two bacterial glycosidases that specifically remove the sugars responsible for the A and B antigens. This discovery raises the possibility of being able to treat A, B, or AB blood with these enzymes and thus convert the blood to Group O, the "universal donor".
- Why do we have antibodies against red cell antigens that we lack? Bacteria living in our intestine, and probably some foods, express epitopes similar to those on A and B. We synthesize antibodies against these if we do not have the corresponding epitopes; that is, if our immune system sees them as "foreign" rather than "self".

avoid Rh sensitization. Shortly after each birth of an Rh^+ baby, the mother is given an injection of anti-Rh antibodies. The preparation is called **Rh immune globulin** (**RhIG**) or **Rhogam**. These passively acquired antibodies destroy any fetal cells that got into her circulation before they can elicit an active immune response in her.

- Rh immune globulin came into common use in the United States in 1968, and within a decade the incidence of Rh hemolytic disease became very low.

Other blood groups

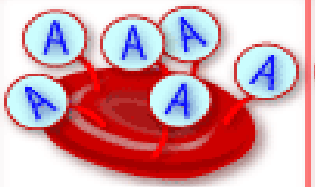
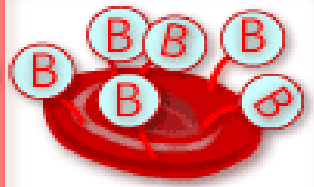
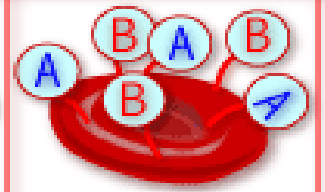
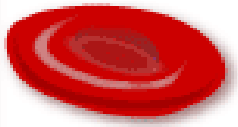
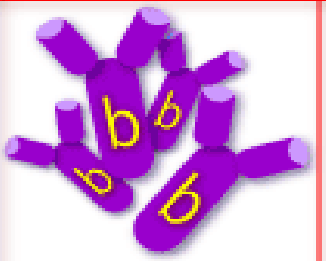
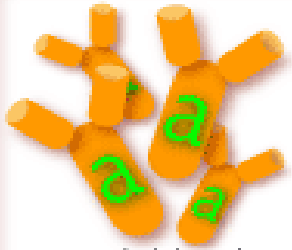
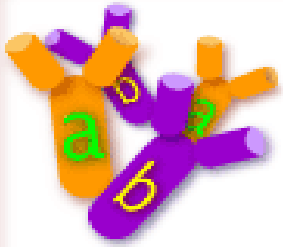
Several other blood group antigens have been identified in humans. Some examples: **MN** , Duffy, Lewis, Kell.

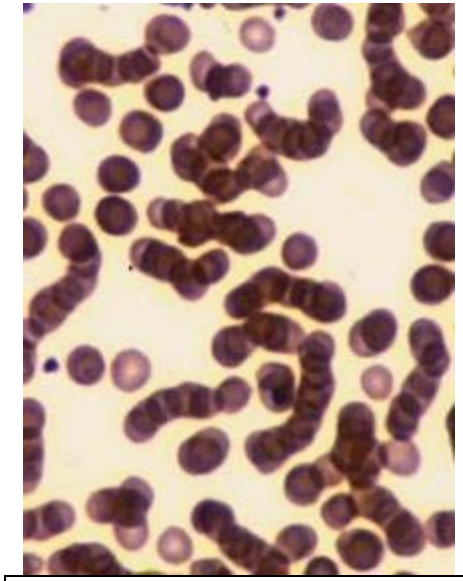
They, too, may sometimes cause

- transfusion reactions and even
- hemolytic disease of the newborn

in cases where there is no ABO or Rh incompatibility.

The ABO Blood System

Blood Type (genotype)	Type A (AA, AO)	Type B (BB, BO)	Type AB (AB)	Type O (OO)
Red Blood Cell Surface Proteins (phenotype)	 A agglutinogens only	 B agglutinogens only	 A and B agglutinogens	 No agglutinogens
Plasma Antibodies (phenotype)	 b agglutinin only	 a agglutinin only	NONE. No agglutinin	 a and b agglutinin



Blood Transfusions

In the United States, in 2001, some 15 million "units" (~475 ml) of blood were collected from blood donors.

- Some of these units ("whole blood") were transfused directly into patients (e.g., to replace blood lost by trauma or during surgery).
- Most were further fractionated into components, including:
    - RBCs. When refrigerated these can be used for up to 42 days.
    - platelets. These must be stored at room temperature and thus can be saved for only 5 days.
    - plasma. This can be frozen and stored for up to a year.

Ensuring the safety of donated blood

A variety of infectious agents can be present in blood.

- viruses (e.g., HIV-1, hepatitis B and C, HTLV, West Nile virus
- bacteria like the spirochete of syphilis
- protozoans like the agents of malaria and babesiosis
- **prions** (e.g., the agent of variant Crueutzfeldt-Jakob disease)

and could be transmitted to recipients. To minimize these risks,

- donors are questioned about their possible exposure to these agents;
- each unit of blood is tested for a variety of infectious agents.

Most of these tests are performed with enzyme immunoassays (EIA) and detect **antibodies** against the agents. However, it takes a period of time for the immune system to

produce antibodies following infection, and during this period ("window"), infectious virus is present in the blood. For this reason, blood is now also checked for the presence of the RNA of these RNA viruses:

- HIV-1
- hepatitis C
- West Nile virus

by the so-called **nucleic acid-amplification test** (NAT).

Thanks to all these precautions, the risk of acquiring an infection from any of these agents is vanishingly small. Despite this, some people — in anticipation of need — donate their own blood ("autologous blood donation") prior to surgery.

Blood Typing

Donated blood must also be tested for certain cell-surface antigens that might cause a dangerous transfusion reaction in an improperly-matched recipient.

Blood Substitutes

Years of research have gone into trying to avoid the problems of blood perishability and safety by developing blood substitutes. Most of these have focused on materials that will transport adequate amounts of oxygen to the tissues.

- Some are totally synthetic substances.
- Others are derivatives of hemoglobin.

Although some have reached clinical testing, none has as yet proved acceptable for routine use.

Plasma Volume Expanders

- When shock is imminent from low blood volume, volume must be replaced
- Plasma or plasma expanders can be administered
- Plasma expanders
  - Have osmotic properties that directly increase fluid volume
  - Are used when plasma is not available
  - Examples: purified human serum albumin, plasminate, and dextran
- Isotonic saline can also be used to replace lost blood volume

Diagnostic Blood Tests

- Laboratory examination of blood can assess an individual's state of health
- Microscopic examination:
  - Variations in size and shape of RBCs – predictions of anemias
  - Type and number of WBCs – diagnostic of various diseases
- Chemical analysis can provide a comprehensive picture of one's general health status in relation to normal values

Developmental Aspects

- Before birth, blood cell formation takes place in the fetal yolk sac, liver, and spleen
- By the seventh month, red bone marrow is the primary hematopoietic area
- Blood cells develop from mesenchymal cells called blood islands
- The fetus forms HbF, which has a higher affinity for oxygen than adult hemoglobin
- Age-related blood problems result from disorders of the heart, blood vessels, and the immune system
- Increased leukemias are thought to be due to the waning deficiency of the immune system
- Abnormal thrombus and embolus formation reflects the progress of atherosclerosis

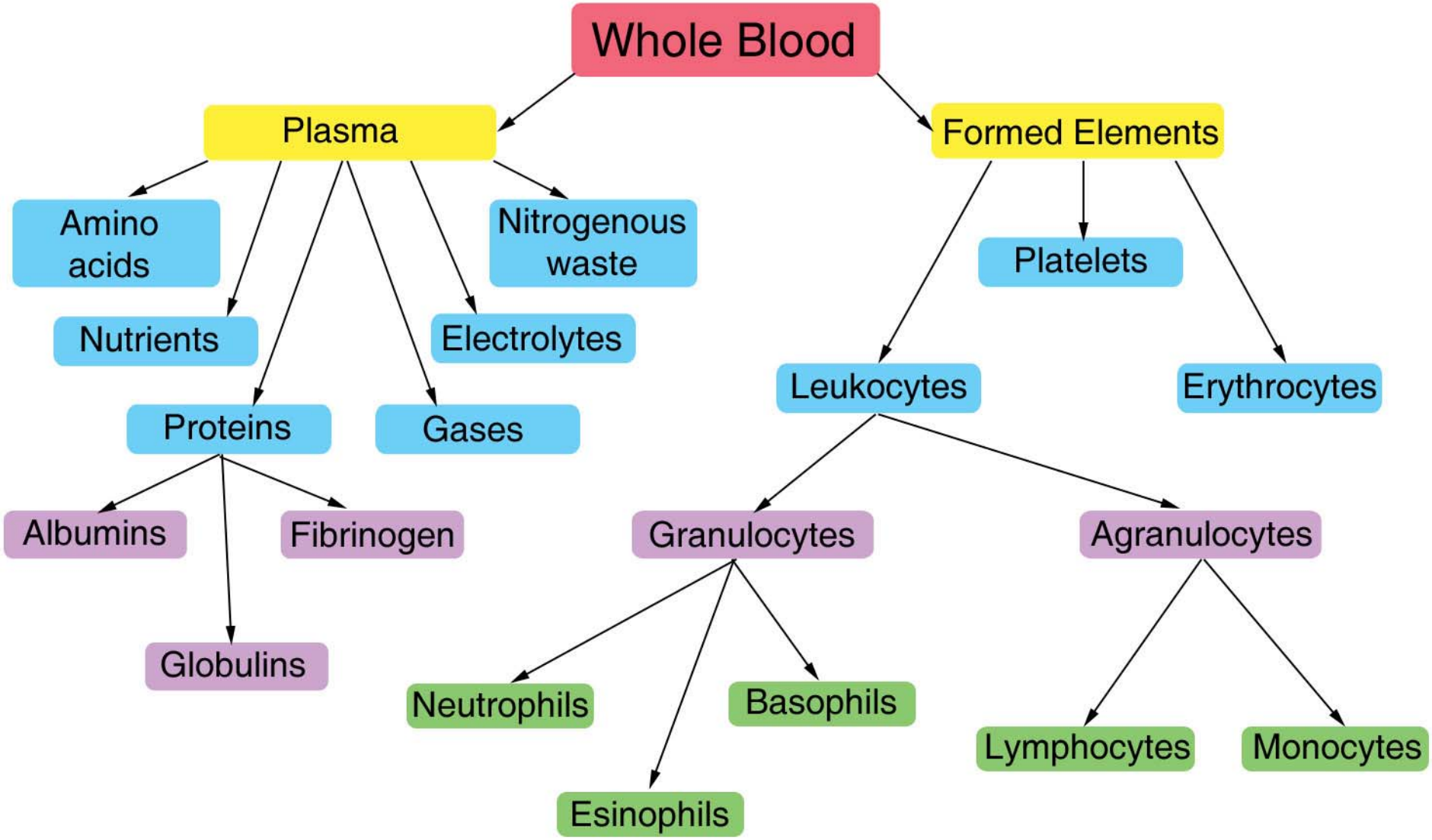
Aging changes in the blood

The properties of blood change as we grow older. It is thought that these changes might contribute to the increased incident of clot formation and atherosclerosis in older people. Some of the most prominent findings on these changes include:

1. Rise in fibrinogen
2. Rise in blood viscosity
3. Rise in plasma viscosity
4. Increased red blood cell rigidity
5. Increased formation of fibrin degradation products
6. Earlier activation of the coagulation system

- The increased level of plasma fibrinogen is thought to be due to either its rapid production or slower degradation.
- As age progresses, fibrinogen and plasma viscosity tend to be positively correlated, with the rise in plasma viscosity being largely attributed to the rise in fibrinogen.
- The viscosity of blood depends on factors such as shear rate, hematocrite, red cell deformability, plasma viscosity and red cell aggregation.
- Although there are many factors involved, hyperviscosity syndrome can be generated by a rise in only one factor.
- A state of hyperviscosity causes sluggish blood flow and reduced oxygen supply to the tissue.
- An age-dependent increase in various coagulation factors, a positive correlation with fibrinogen and a negative correlation with plasma albumin has also been found.
- Both platelet and red cell aggregation increase with age, with red cell aggregation appearing to be the primary factor responsible for a rise in blood viscosity at low shear rates.
- The decrease in red cell deformability (increase in rigidity) refers to its ability to deform under flow forces. Less deformable cells offer more resistance to flow in the microcirculation, which influences the delivery of oxygen to the tissues.

- Studies have found that older people have less fluid membranes in their red cells. Blood H+ has also been found to be positively correlated with age, making the blood slightly more acidic as we age.
- This results in a swelling of the cell, making the red cells less deformable.
- This sets up a cycle for further increase in blood viscosity and worsening of blood flow parameters.
- Since aging causes a reduction in total body water, blood volume decreases due to less fluid being present in the bloodstream.
- The number of red blood cells, and the corresponding hemoglobin and hematocrite levels, are reduced which contributes to fatigue in the individual.
- Most of the white blood cells stay at their original levels, although there is a decrease in lymphocyte number and ability to fight off bacteria, leading to a reduced ability to resist infection.
- Overall, the rise in fibrinogen is the most common and significant change in blood during aging because it contributes to a rise in plasma viscosity, red blood cell aggregation and a rise in blood viscosity at low shear rates.
- Increased age is associated with a state of hypercoagulation of blood, making older people more susceptible to clot formation and atherosclerosis.


Whole Blood
Plasma
Formed Elements
Amino acids
Nitrogenous waste
Nutrients
Electrolytes
Platelets
Leukocytes
Erythrocytes
Proteins
Gases
Albumins
Fibrinogen
Granulocytes
Agranulocytes
Globulins
Neutrophils
Basophils
Lymphocytes
Monocytes
Esinophils

References :

Atlas of Microscopic Anatomy: Section 4 - Blood Plate 4.52: White Blood Cells **Granulocytes Ronald A. Bergman, Ph.D., Adel K. Afifi, M.D., Paul M. Heidger, Jr., Ph.D.**

Marieb , media manager , human anatomy and physiology 5th edition

Ajmani RS, Rifkind JM. Hemorheological changes during human aging. Gerontology 1998; 44 (2): 111-120

Coagulation cascade [online]. 2003 [cited 2007 Sep 9]. Available from: URL: http://labtestsonline.org/ understanding/ analytes/ coag_cascade/ coagulation_cascade.html

Marieb EN. Human anatomy & physiology. 4th ed. Menlo Park, Calif.: Benjamin/Cummings; 1998.

Saladin KS. Anatomy and physiology - the unity of form and function. 3rd ed. New York: McGraw-Hill; 2004.

Sherwood L. Human physiology - from cells to systems. 5th ed. Belmont, Calif: Brooks/Cole; 2004.

Alex Munoz notes