Blood and Microcirculation; Lipid Profile

INTRODUCTION

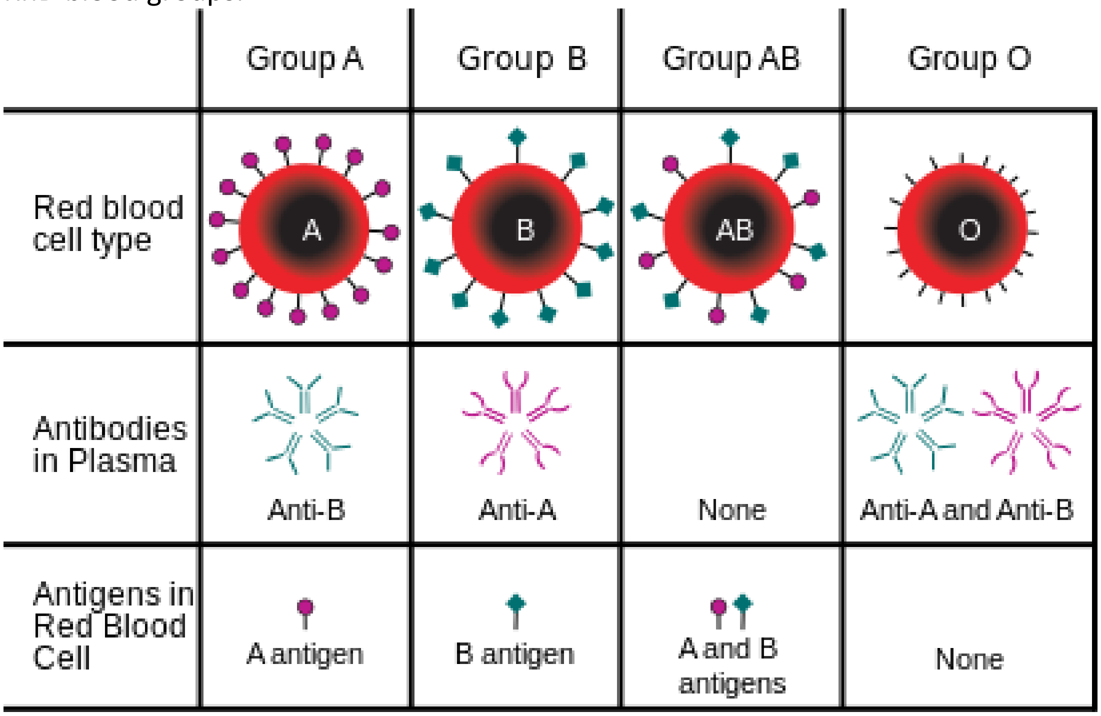
The composition of blood is best described as consisting of two parts; **formed elements** and **plasma**. Formed elements refers to cells, either erythrocytes (red blood cells) or leukocytes (white blood cells) and cell fragments call platelets. This blood lab will focus on erythrocytes. The major function of the erythrocyte is to transport oxygen from the lungs to the cells. To perform this function, they utilize the properties of a protein called hemoglobin. The ability to carry oxygen is directly correlated to the amount of hemoglobin per erythrocyte. The normal values of hemoglobin are around 14-16grams/100ml of blood (male = 13.5-18g/100ml; female = 12-16g/100ml). A decrease in either the red blood cell amount or hemoglobin reduces the oxygen carrying capacity of the body, resulting in fatigue and a condition called **anemia**. On the opposite spectrum is polycythemia, or an overabundance of red blood cells. The diagnosis of either condition is performed using a test known as the **hematocrit**, or the percentage of blood that is red blood cells. A normal hematocrit for men ranges from 45% to 55% while a normal hematocrit for women ranges from 35% to 45%. The discrepancy between men and women is the result of testosterone, while the range discrepancy is the result of training.

As already identified, the formed elements make up about half the blood. The other half is made up of a fluid mixture called plasma. The plasma component of blood is mostly water (92%) and other solutes (8%). The most abundant solutes are the proteins (albumin, globulins and fibrinogen) and NaCl. Fibrinogen is a major protein involved in clotting and can easily be separated out by allowing blood to clot and then centrifuging the clot to the bottom. The fluid left over (without the clotting factors) is called serum. Serum is used for diagnostic testing, blood typing and various forms of therapy because it still contains all the proteins, minus the cumbersome clotting proteins.

In addition to determining hematocrit, another commonly performed blood test is called the erythrocyte sedimentation rate (**ESR**). The ESR measured the rate of red blood cell settling that occurs over an hour. In other words, blood is collected in a tube, the tube is placed in the vertical position, and the red blood cells are allowed to settle in response to gravity. How far they settle is then measure from the top down and an ESR is calculated in mm. In healthy individuals red blood cells settle very little (2-5mm) because their surfaces contain negative charges that repel each other. However, in some disease conditions (myocardial infarction or heart attack, ruptured ectopic pregnancy, appendicitis), increased production of fibrinogen or antibodies can interact with the negative charge, reducing the repelling effect. With a reduced, overall negative charge, red blood cells stack or clump together forming a structure known at a rouleaux formation. This formation allows them to settle faster, resulting in an increased ESR. An increased ESR is also observed in anemia (ie., low iron, menstruating females, loss of bone marrow), simply because fewer cells mean that the normal levels of fibrinogen act like elevated levels, inhibiting more of the negative charge. A decreased ESR would result from anything that adds an additional force that repels the red blood cells apart even more. This could result from diseases that changed the shape of the red blood cell. The ESR is also used to track the progression of diseases such as sickle cell anemia, cancer or inflammatory diseases like rheumatoid arthritis.

Blood Typing

Red blood cells possess many glycoprotein cell surface molecules known as antigens. Surface antigens are organized into categories known as blood groups. There are probably more than 30 human blood group systems that are recognized by science. However, the two most important ones are the ABO and RhD blood groups.



ABO Blood Type	% of U.S. Population		
	White	Black	Asian
A	41	27	28
B	9	20	27
AB	3	4	5
O	47	49	40

ABO Blood Type Chart. This chart was downloaded from Wikimedia commons April of 2013; Author: Shahinsahar; License: Creative Commons Attribution-Share Alike 3.0 Unported license.

This figure above shows an ABO blood grouping chart. This chart shows the possible antigens that a red blood cell could contain in the ABO grouping. This chart also shows the antibodies that would be expected in the plasma of a person with a particular blood type. This chart does NOT show the RhD blood grouping. Keep in mind that each blood type in this chart could be Rh (-) or Rh (+). The table shows the relative amounts (%) of blood types per major ethnic groups in the US.

ABO Blood Group System

Through an arrangement known as the ABO blood group system, each erythrocyte in the human body may be classified into one of four different groups based upon the existence of antigens labeled “A” and “B”. Under this system, an individual possessing red blood cells with the type A antigen is said to have type A blood, whereas an individual possessing red blood cells with the type B antigen is said to have type B blood. The third ABO blood type is an example of genetic codominance, as it is possible for an individual to possess red blood cells incorporating both type A and type B antigens. An individual with this blood type is said to have type AB blood. Finally, an individual possessing red blood cells incorporating neither type A nor type B antigens is said to have type O blood. The ABO blood group system can be used to describe plasma antibodies as well as erythrocyte antigens. Type A plasma contains anti-B antibodies, type B plasma contains anti-A antibodies, type AB plasma contains neither antibody, and type O plasma contains both anti-A and anti-B antibodies.

The importance of blood typing becomes evident when a transfusion becomes necessary. Any condition that results in massive amounts of blood loss or that decreases the blood's ability to carry oxygen may necessitate a transfusion. If an individual receives, blood of a type incompatible with their own, agglutination may occur, potentially resulting in blood clots, kidney damage, and death.

For example, if an individual with type A blood receives a transfusion containing type B blood, anti-B antibodies within the bloodstream (of the recipient) will recognize and bind the foreign type B antigens (of the donor), thus initiating the process of agglutination. Hopefully it now makes sense why individuals with type AB blood are sometimes referred to as universal recipients and why individuals with type O blood are known as universal donors. Individuals with type AB blood can receive any type of blood because they possess neither anti-A nor anti-B antibodies. Thus, they are universal recipients. Individuals with type O blood can donate blood to an individual of any blood type because their erythrocytes possess neither type of surface antigen. Thus, no antibodies will react to these erythrocytes, and these individuals are universal donors. There is an exception to this universal donor rule, however. Although a recipient's antibodies will not react to type O erythrocytes, any antibodies within the donated type O blood will react to antigens on the recipient's blood cells. In order to avoid problems from donor antibodies, packed red blood cells are segregated from the donor antibodies prior to transfusion.

Although antibodies are typically only generated following exposure to a specific antigen, agglutination may occur upon initial exposure to an incompatible ABO blood type. Owing to this, scientists hypothesize that alternative means of antigen exposure likely exist through exposure to foods and bacteria.

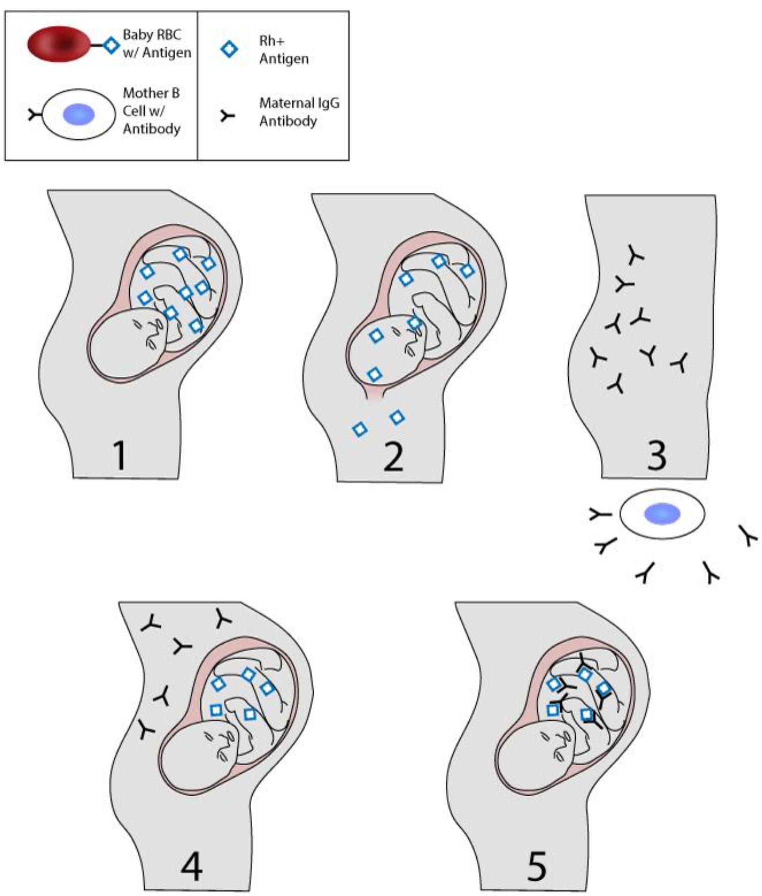
Rh Blood Group System

Another common group of surface antigens that coincides with the ABO blood group is known as the RhD blood group, which received its name based on its initial discovery in the rhesus monkey. The Rh blood group system includes a number of different surface antigens, the most important of which is known as the D antigen or Rhesus (Rh) factor. An individual is considered to be either Rh positive or Rh negative depending on the presence or absence of the D antigen. For instance, the blood type of an individual whose erythrocytes possess the A, B, and D surface antigens is AB positive (AB+). If that individual did not possess the D surface antigen, then they would be considered AB negative (AB-), which incidentally is the least abundant blood type. Around 85% of the world's population is Rh positive. Thus, for 85% of the population the presence or absence of the Rh factor is irrelevant to transfusions, as they have no anti RhD antibodies. However, it is critical that the other 15% of the population receive only erythrocytes lacking the RhD antigen, as the dangers of agglutination and hemolysis exist with regard to the Rh factor as well.

Rh sensitization, or the production of anti-Rh antibodies in Rh negative individuals, only occurs upon contact with Rh positive erythrocytes. There appears to be no alternative route of exposure such as one found in the ABO blood group system. Owing to this, it is possible that a Rh-negative individual may show very few negative effects from an initial incompatible Rh-positive transfusion. This is due to the fact that anti-Rh antibodies must build up gradually in the recipient's blood. However, should this same Rh-negative individual receive a second Rh positive blood transfusion, anti-Rh antibodies will already be present and agglutination and hemolysis will occur swiftly with devastating results.

Hemolytic Disease of the Newborn

The scenario mentioned above is highly unlikely to occur, as modern technology generally prevents individuals from receiving incompatible blood transfusions. A more applicable example of the dangers associated with Rh factor incompatibility is a condition known as hemolytic disease of the newborn (HDN). During pregnancy and especially during delivery, fetal blood may unintentionally cross the placenta into the mother's bloodstream. Should this unintentional transmission occur between a Rh-negative mother and a Rh-positive fetus, the maternal immune system will begin to produce anti-Rh antibodies capable of crossing the placenta and damaging the fetus.



Hemolytic Disease of the Newborn. Image created by BYU-I student Austin Dean Fall 2016

1. An infant with Rh antigens is found in the womb of a mother who has no Rh antigens. Also, having never yet been exposed to Rh antigens, this mother has no Rh antibodies either. Therefore, the infant is not attacked by the mother's Rh antigens.

2. During birth, maternal and infant blood is mixed and the infants Rh antigens are exposed to the mother's immune system.

3. After delivering the baby, the mother continues to produce antibodies and immune memory B-cells against future exposure to Rh antigen.

4-5. If the mother who is Rh (-) gets pregnant again with a Rh (+) fetus, then the mothers new load of Rh antibodies can cross the placenta and attack the fetus's Rh (+) red blood cells.

The image above explains how there is not significant harm to the first Rh positive child. However, following initial exposure to the Rh factor, a sensitized mother will be capable of reacting quickly to the presence of Rh factor in a future pregnancy. If left untreated, HDN can cause agglutination, hemolysis accompanied by excessive bilirubin accumulation, jaundice, and fetal death. Luckily, this condition can normally be prevented by the injection of a compound known as Rho (D) Immune Globin (RhoGAM). The RhoGAM injection contains donor anti-Rh antibodies that bind to any Rh positive fetal erythrocytes that cross into the mother's bloodstream, countering the stimulus for maternal sensitization. This will prevent the mother from forming immune memory cells and antibodies for the future. In a way, this injection "tricks" the mother's immune system into "believing" that Rh antigen has never been exposed to the mother and every pregnancy can be like the first one. In order to render the maternal production of antibodies unnecessary, this injection may be given multiple times during the later stages of pregnancy and even following delivery. Remember, and be able to explain that HDN is a condition of Rh (-) mothers who give birth to Rh (+) children). This incompatibility is only possible if the mother has Rh (-) blood type and the father has Rh (+) blood type. HDN does not generally occur as a result of ABO blood type incompatibilities because anti-A and anti-B antibodies do not readily cross the placenta.

Exercise 1. Hematocrit

Consider the following table of hematocrit values:

Hematocrit	46%	41%	51%	45%	27%	32%
SAMPLE	1	2	3	4	5	6

Questions: Exercise 1

1. Using the data in the table, match the sample with the correct blood donor from the list below.

A. healthy female, living at 5000 feet
B. healthy male, living at 200 feet
C. male with aplastic anemia
D. female with iron deficiency anemia
E. healthy female, living at 200 feet
F. healthy male, living at 5000 feet

Sample 1: ____________________ Support your answer:

Sample 2: ____________________ Support your answer:

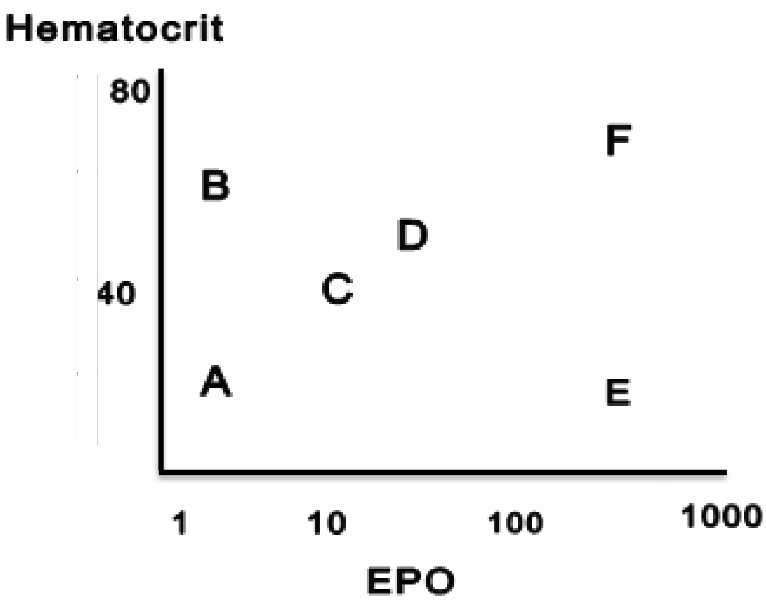
Sample 3: ____________________ Support your answer:

Sample 4: ____________________ Support your answer:

Sample 5: ____________________ Support your answer:

Sample 6: ____________________ Support your answer:

2. Would you predict diarrhea to show an elevated or a decreased hematocrit? Explain your answer:



3. The graph compares hematocrit to erythropoietin (EPO) levels. EPO is a hormone released by the kidneys that regulates red blood cell production. EPO is regulated by oxygen in typical negative feedback fashion. *Note: normal EPO levels are around 10.

Match and explain the following donors to the graph above:

Olympic Marathoner
Aplastic anemia
Renal disease
Secondary Polycythemia
Normal female
Blood transfusion

Exercise 2. Erythrocyte Sedimentation Rate (ESR)

Consider the following table of ESR values:

ESR Value	5mm/hr	15mm/hr	0mm/hr	30mm/hr	40mm/hr	3mm/hr
SAMPLE	1	2	3	4	5	6

Questions: Exercise 2

1. Match and explain the following donors to the table of values:

A. Menstruating female
B. Sickle cell anemia
C. Normal Healthy male
D. Myocardial infarction
E. iron deficiency anemia
F. angina pectoris

Sample 1: ___________________ Support your answer:

Sample 2: ___________________ Support your answer:

Sample 3: ___________________ Support your answer:

Sample 4: ___________________ Support your answer:

Sample 5: ___________________ Support your answer:

Sample 6: ___________________ Support your answer:

Exercise 3. Hemoglobin

Consider the following table of hemoglobin values:

Hemoglobin	16g/100ml	14g/100ml	8g/100ml	20g/100ml	22g/100ml
SAMPLE	1	2	3	4	5

1. Using the data in the table, match the sample with the correct blood donor from the list below.

A. healthy male
B. healthy female
C. female with iron deficiency anemia
D. Male with polycythemia
E. female Olympic athlete

Sample 1: ___________________ Support your answer:

Sample 2: ___________________ Support your answer:

Sample 3: ___________________ Support your answer:

Sample 4: ___________________ Support your answer:

Sample 5: ___________________ Support your answer:

Exercise 4. Blood Typing

https://educationalgames.nobelprize.org/educational/medicine/bloodtypinggame/

Click on the link above which will navigate you to a blood typing game found on nobelprize.org. Click on the link labeled "Play the Blood Typing Game". Feel free to try the mission based game. When you feel familiar with the concept complete the following table of values.

Exercise 4: Questions

1. Below is a table that lists all of the blood types across the top and vertically (Donor and Recipient). Place a "✓ or YES" if the transfusion can be performed and place an "X or No" if it cannot. Three of the table squares have been completed for you as examples. Go ahead and complete all of the rest of the table squares to complete your points for this question.

****Either print the table and use a pen or pencil and then photograph it (and add it to the word file you turn in), or recreate a table like this in the word file that you turn in. ****

Recipient	**Red Blood Cell Compatibility Table**							
	Donor							
	O-	O+	A-	A+	B-	B+	AB-	AB+
O-	Yes							
O+								
A-								
A+								
B-						No		
B+		Yes						
AB-								
AB+								

2. Why are there normally no problems with mother/fetus blood incompatibilities with the ABO blood antigens while there can be with the Rh antigens?

Exercise 5: HbA1c

Research via google and thumim what an HbA1c test is

Questions: Exercise 5

1. What is an HbA1c test and what can it determine?

2. What are normal values for HbA1c?

3. What is the most common pathology associated with regular testing of HbA1c?

Exercise 6: Problem Solving

Questions Exercise 6

1. A patient with which of the following conditions is likely to present with the highest erythrocyte sedimentation rate (ESR) as compared to normal?

A. Hyperthermia
B. Iron deficiency anemia
C. Polycythemia
D. Sickle cell anemia
E. Systemic Lupus erythematosus

2. Question 2. A 43-Year old Caucasian woman visits here doctor with complaints of feeling tired and short of breath on exertion, and the physician notes that the woman looks pale. The patient mentions that sometimes her feet feel tingly and numb for no known reason. When questioned about her diet, she states that she is a vegetarian, and has been trying to adopt the vegan lifestyle but is not always adherent. Her family history is unremarkable. A complete blood count is ordered and the results are as follows:
RBC: 2.05 x 10^6/ul
Hb: 8g/dl
Hct: 31%
RBC shape: Very Large

Based on the woman's history, physical, and lab data, what type of anemia is she most likely suffering from?
A. aplastic anemia
B. Iron deficiency anemia
C. Pernicious anemia
D. Sickle cell anemia

3. Which of the following conditions most likely leads to anemia but presents with a normal hematocrit and a normal hemoglobin concentration?

A. Acute hemorrhage
B. Aplastic anemia
C. Folate deficiency
D. Hemolysis
E. Iron Deficiency
F. Vitamin B_{12} deficiency

4. A 34-year-old female has noticed a marked decrease in energy over the last few months. She has an overall healthy lifestyle but usually drinks six beers per week, usually on weekends. Her physical exam does not present any abnormalities. Her laboratory blood results are as follows, with abnormal values indicated with an asterisk.

RBCsL 4.0 x 10^6/L*
Hb: 9.7 g/dl*
Hct: 29.9%
Serum iron: 29 µg/dl*
Transferrin: 450 mg/dl*
Serum ferritin: 10 ng/ml*
MCV: 83.2 fL
PT: 13 seconds
PTT: 28 seconds

What is the most likely diagnosis?

A. Acute bleeding
B. Anemia of chronic disease
C. Iron deficiency anemia
D. liver disease
E. Vitamin B12 deficiency
F. Vitamin K deficiency
G. Von Willebrand’s disease

5. A 25-uear-old woman gives birth to a baby that is her second child. The baby has pale skin and jaundice. The mother's blood type is AB negative and the father's blood type is A positive. Hemolytic disease of the newborn is suspected. Which of the following combinations of blood types could be likely explanations for this scenario if the diagnosis of hemolytic disease of the newborn is confirmed for the second child? (Mark all that are possible)

First child blood type	Second child blood type
A+ →	AB+
A- →	A+
B- →	AB-
AB- →	A-
B+ →	B+
AB+ →	B-
O+ →	O+
O- →	O-