SHEET NO. 9

Physiology

Hematolymphatic System

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Blood groups & blood transfusion

A blood type is a classification of blood, based on the presence and absence of antibodies and inherited antigenic substances on the surface of red blood cells.

The most well-known and medically important blood types are classified according to the ABO & Rhesus systems.

In blood typing, antigens on the surfaces of red blood cells (RBCs) are also known as **agglutinogens** (because they often cause blood cell agglutination) and the antibodies that react against them are also called **agglutinins**.

ABO system

According to the ABO system, red blood cells are classified into 4 classical groups: A, B, AB, and O.

1. Type A blood

People with type A blood will have the A antigen on the surface of their red cells. As a result, anti-A antibodies will not be produced by them because they would cause the destruction of their own blood. However, if B type blood is injected into their systems, anti-B antibodies in their plasma will recognize it as alien and burst or agglutinate the introduced red cells to cleanse the blood of alien protein.

2. Type B blood

People with type B blood will have B antigen & anti-A antibodies

3. Type O blood

Individuals with type O blood don't have A & B antigens. Therefore, their blood normally will not be rejected when it is given to others with different ABO types.

4. Type AB blood

Those who have type AB blood do not produce A & B antibodies. Their blood does not discriminate against any other ABO type. Consequently, they are universal receivers for transfusions, but their blood will be agglutinated when given to people with every other type because they produce both kinds of antigens.

- These antigens are also present in other tissues such as the salivary glands, the kidneys, the liver, the lungs, the semen, the intestine and the amniotic fluid.

- These antibodies are not usually found in the plasma of newborn babies (at birth), as they only start to appear gradually between the 2^{nd} and 8^{th} month after birth, probably in response to antigens (A &/or B) taken in from food of animal origin, especially meat, and in some bacteria in the environment.

Rhesus system

The Rh system is described based on the presence or absence of the rhesus antigen (D) on the surface of RBCs.

- If present, the individual is described as D^+ or Rh^+
- If absent, the individual is described as D^- or Rh^-

Rh→ means positive.

rh→ means negative.

■ 85% of Europeans, (90-95) % of Arabs and Africans, 98% of Asians are Rh+ or D+ meaning that they:

1) have D antigens on their RBCs. 2) don't have antibodies against them in their plasma

■ 15% of Europeans don't have the D antigen on their RBCs surfaces. Also, they do not have antibodies against the D antigen in their plasma, **unless** they've been exposed to D antigens.

■ Rhesus antigens:

There are at least 3 sets of alternative antigens in the Rh system:

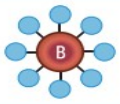
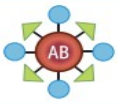
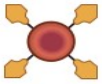
D or d / C or c / E or e

*However, D is a strong antigen and therefore clinically more important than the others. In blood banks, Rh grouping is performed with anti-D serum.

Other blood groups

The surface of the RBCs doesn't only contain the ABO & Rh antigens, it also contains many other series of genetically determined glycoproteins and glycolipids that act as blood group antigens. They appear early in life and remain unchanged throughout life. More than 100 blood antigens have been described out of which at least 15 well-defined RBC group systems exist in most racial groups. Of these, only two are of major importance in clinical medicine: The ABO and rhesus (RH) systems. **Other blood group systems include MM, MN, NN, PP, Pp, kell, Lewis, kid, Lutheran, Duffy, and others**.

Blood groups

	ABO classification				Rh classification	
	A	B	AB	O	Rh⊕	Rh⊖
RBC type						
Group antigens on RBC surface	A	B	A & B	None	Rh (D)	None
Antibodies in plasma	Anti-B 	Anti-A 	None	Anti-A Anti-B 	None	Anti-D 
Clinical relevance Compatible RBC types to receive	A, O	B, O	AB, A, B, O	O	Rh⊕, Rh⊖	Rh⊖
Compatible RBC types to donate to	A, AB	B, AB	AB	A, B, AB, O	Rh⊕	Rh⊕, Rh⊖

Inheritance of classical blood groups

■ The inheritance of the A and B antigens is dictated by the A and B genes. The O gene doesn't produce any demonstrable red cell antigen. This is the reason why group A genotype can be AA (homozygous) or AO (Heterozygous). Similarly, for group B, the possible genotype is BB or BO, while for blood group O, the only possible genotype is OO. Group Ab has both A and B genes, and the only possible genotype is AB. Knowing these genotypes is useful in working out the probable blood group of an offspring based on the knowledge of the blood genotypes of the father and mother. It is also helpful in sorting out the disputed parentage of the child.

REMEMBER: The term "genotype" can refer to the two alleles inherited for a particular gene. while the term 'pheno' in "phenotype" refers to 'observe' and thus phenotype is used to indicate the observable characteristics in organisms like their heights and colors.

■ Again, Both A and B alleles are dominant over O. As a result, individuals who have an AO genotype will have an A phenotype. People who are type O have OO genotypes. In other words, they inherited a recessive O allele from both parents. The A and B alleles are codominant. Therefore, if an A is inherited from one parent and a B from the other, the phenotype will be AB. Agglutination tests will show that these individuals have the characteristics of both type A and type B blood.

Parents alleles	A	B	O
A	AA (A type)	AB (AB type)	AO (A type)
B	AB (AB type)	BB (B type)	BO (B type)
O	AO (A type)	BO (B type)	OO (O type)

■ Individuals who are homozygous dominant (DD) or heterozygous (Dd) are Rh+. Those who are homozygous recessive (dd) are Rh- (i.e., they do not have any Rh antigens)

Example: RhRh (father) x rhrh (mother) → Rhrh (fetus)

Now, if a woman is Rh-negative (just like in the previous example), and is pregnant, and the fetus is Rh-positive; then when some RBCs from the fetus pass into the maternal blood (which is possible during the delivery), then the mother is going to produce D antibodies as they recognize D antigen as a foreign antigen. Later, in recurring pregnancy with Rh positive babies, Rh antibodies attack the Rh-positive baby's blood cells, causing **Rh disease.**

Question الدكتور حكي رح يجي سؤال زي هيك بس مش بهاي الصيغة المباشرة

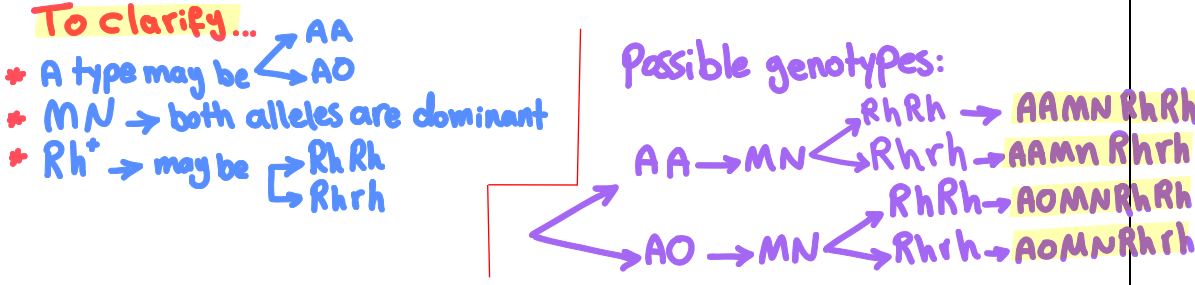
Someone has an AMNRh$^+$ phenotype. What is the possible genotype ?

AAMNRhRh

AAMNRhrh

AOMNRhRh

AOMNRhrh



Note: Regarding the following two tables, Dr. Saleem just read them and said that in all races blood group **O is the most common type** and that there is a variation in the Rh Blood groups.

The racial distribution of blood groups by % in the United States:

	A	B	AB	O	Rh+	Rh-
whites	41	10 1/0	4	45	85	15
Blacks	28	20 2/0	5	47	90	10
Chinese	28	23 2/3	13	36	99	1
Indians	3	0	0	97	100	0

The racial distribution of blood groups by percentage in Jordan among 300 students:

A	B	AB	O	Rh+	Rh-
39	14	9	39	97	3

Hemolytic diseases of newborns (HDN)

They are blood problems in newborn babies, their major cause is an incompatibility of the Rh blood group between the mother and fetus.

Pregnancies at risk of HDN are those in which an Rh-negative mother becomes pregnant with an Rh-positive child (the child inherited the D antigen from the father).

There are 3 conditions in which (Rh-) mother can develop Antibodies against Rh+ antigens:

1. Blood transfusion before marriage from Rh+ person: if the (Rh-) mother received blood from an Rh+ donor the mother's immune system would develop Antibodies against Rh+
2. Leakage of a small amount of fetus blood into the maternal circulation (Placental hemorrhage)
3. During delivery, some of the fetal blood is squeezed back to the maternal blood

IN EACH ONE OF THESE 3 PREVIOUS CONDITIONS THE MOTHER WILL DEVELOP ANTIBODIES AGAINST D ANTIGEN, AND IF THESE ANTIBODIES PASS TO THE FETAL BLOOD AGLUTINATION WILL OCCURS AND ONE OF THESE HEMOLYTIC DISEASES MAY OCCUR:

Mild disease (Erythroblastosis Fetalis)	kernicterus/moderate disease (Icterus Gravis neonatorum)	severe disease (Hydrops Fetalis)
Once the mother's immune system develops antibodies against Rh antigens these antibodies can pass into the fetal blood causing Mild Hemolysis of the RBCs of the fetus. This newborn baby can be rescued by giving him Rh- blood, **but not from his mother**, Because the mother's blood contains antibodies that will further attack the RBCs of the fetus. Why not Rh+? because the fetus has antibodies aginast Rh antigen	A rare kind of preventable brain damage disease that can happen in newborns, the infant is born at term either jaundiced or will develop jaundice within 24 hours. There may be severe neurological lesions involving the basal ganglia in which the bile pigments are deposited, because bilirubin crosses the BBB if it rises to critical levels	The hemolysis is severe, the infant may die in the uterus or develop severe anemia, jaundice, and edema which leads to death within a few hours

Example: A mother is pregnant with her first baby and "her blood group is O-, the father's blood group is O+", she didn't receive any kind of blood transfusion, and let's suppose that the baby is O+…

Some of the baby's blood will leak into the mother's circulation and her immune system will recognize it as a foreign antigen, and anti-D antibodies will develop. However, the mother's antibodies can't attack the antigens at the first time of exposure, In other words, the maternal

anti-D that is formed at the time of first exposure cannot cross the placenta" but the mother becomes sensitized". Subsequent pregnancies (with Rh+ babies), or repeated encounters with the Rh antigen stimulate the rapid production of anti-D, which can be transported across the placenta and enter the fetal circulation.

- **How to prevent these diseases?**

These diseases can be prevented by giving an Rh- mother Human Gamma Globulins against Rh+ erythrocytes within 72 hours after she has delivered an Rh+ infant,

- **How do they work?**

These Gamma Globulins bind to the antigenic sites on any Rh-positive erythrocytes that might have entered into the mother's blood **during delivery**, preventing Rh+ antigens from inducing antibody synthesis by the mother

~ All the previous diseases are caused by Rh incompatibility

Is ABO blood types incompatibilities will cause hemolytic diseases in newborns?

Theoretically, the answer may be yes it causes problems, **but actually, it usually does not**.

For example, a woman with blood type (O) has natural antibodies for blood types A and B, if her fetus is of type A or B, there won't be any clinical manifestations, this is because:

1. Fetal erythrocytes do not express (A) and (B) antigens strongly.
2. Maternal natural antibodies are of the IgM type which does not cross the placenta easily.

BLOOD TRANSFUSION

■ Blood transfusion is the process of transferring blood into one's circulation either the whole blood's "whole components" or some products of it.

So, we can use technological machines that isolate blood components to provide the patient specifically with what he/she is deprived of.

■ The indications for blood transfusion:

- Restoring Blood Volume, in hemorrhage.
- Providing red blood cells, in anemias.
- increasing blood coagulability in hemorrhagic diseases, Like hemophilia and purpura.
- replacing infant's blood with Rh- blood, in Erythroblastosis fetalis.
- supplying antibodies to raise the general resistance of the body.
- providing White blood cells.

■ Donors and recipients:

*Blood type (O) can donate to every blood type, since it has no antigens, but it has natural antibodies for antigen (A) and antigen (B), and we call it "**GENERAL DONOR**"

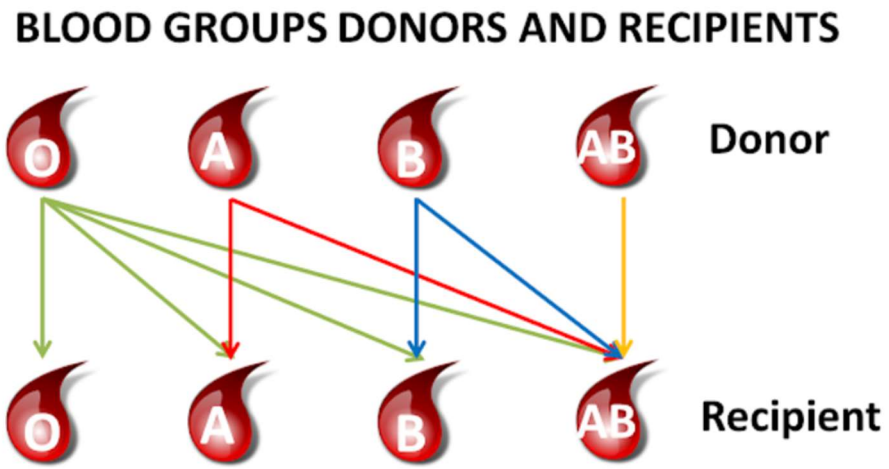
*Blood type (AB) can receive from all blood types, since it has antigens of both (A) and (B) and no antibodies for these blood groups, and we call it "**GENERAL RECIPIENT**"

■ When the (O) blood group donates to another blood group, the antibodies present in (O) blood group are diluted in the blood of the recipient, but the recipient can't tolerate more than 1L which is around 2-3 bags, **why**?

Because antibodies of the (O) group will attack the recipient's blood type and agglutination occurs

So, the term "general" donor OR recipient isn't accurate since there are limitations in the amount you are donating or receiving.

*There are no limitations if the patient receives blood from his own blood group like O to O.



■ Complications of blood transfusion

Early complications:

1. Hemolytic reactions; immediate or delayed.
2. Reactions due to infected blood ➔Allergic reactions to white cells, Platelets, or proteins
3. Circulatory overload
4. Air embolism
5. Citrate toxicity, Hyperkaliemia and Clotting abnormalities (after massive transfusion)

Late complications:

1. Transmission of diseases e.g. hepatitis, malaria, syphilis, and AIDS.
2. Transfusional iron overload
3. Immune sensitization, e.g. to the rhesus D antigen

■ Blood Storage and Use

When blood is withdrawn, we must do the following points:

1. The blood should be tested, grouped, and cross-matched: determining whether the donor's blood is compatible with the recipient's blood or not.
2. Addition of ACD (Acid Citrate dextrose), an anticoagulant
3. Storage at a temperature of 4°C
4. Take into consideration the timing of when the blood is transfused
   • If there is no time for the first procedure, then donate the (O, Rh-) because it's compatible with all blood groups.
   • In extreme emergencies, we donate (O, Rh+) blood type.

■ Blood transfusion is used for donations of RBCs, but not WBCs and platelets, because white blood cells and platelets have a short half-life, so for WBCs and platelets, we need fresh blood samples to transfuse.

■ Blood stored for 14 days shows 80% survival of RBCs in the recipient's blood 24 hours after the transfusion, then the survived RBCs are destroyed at a rate of 1% per day.