- **Immunohaematology:** a branch of immunology that deals with the immunologic properties of blood.

    - The red blood cells have on their surface hundreds of antigens and according to the antigen on their surface we can define some blood group systems. We have many blood group systems which are 20 in numbers, and only two out of these 20 are important which are **ABO blood group and Rhesus blood group**.
    - Other blood group systems include the MSN system and lewis and Kel groups.

❖ ABO BLOOD GROUP:

○ General principles:

✓ IN THE RED BLOOD CELLS we have a gene code for a carbohydrate chain that attach to RBC called H chain. In addition to the gene that code for H chain, there is another two genes code for two TRANSFEREASE which are N-acetylglocuamine and Galactose.

✓ If you have the gene that code for **N-acetylglocuamine** attach to H chain in your red blood cell then you are **blood group A**, however, if you have the gene that code for **Galactose** then you are **blood group B**. IF you have **both transferases** (N-acetylglocuamine attach to some H chains and other H chains with Galactose) then you are **AB blood group.** If you have **only H chain** (no transferases) then you're **O blood group.**

✓ Note that ABO blood group is not only present in RBC but it can be available in other cells such as endothelial cells.

✓ IF there is **no H chain** then you can't add the two transferases (N-Acetylglucoamine and Galactose) and this phenotype called **Pompei blood group** (there's no A or B antigen). This group is very rare.

✓ This group is sometimes considered like group O, it's called Oh blood type.

- Since these antigens are **carbohydrate**" T-independent", the antibody that is produced is **IgM**.

- How to produce these antibodies?
  - Let say you are O blood group and you don't have antigen A and antigen B then you are likely to develop antibodies against A and B because they are recognized as foreign bodies.

  - Note that when babies are born, they don't have antibodies against A and B.

  - They are **only acquired after birth**, probably due to exposure to similar carbohydrate antigens in the blood.

  - These antigens probably arise from some types of bacteria or the normal flora from the GI tract

  - So the antibodies are not present at birth, but they usually appear six months after it.

  - They are considered **naturally arising antibodies** due to the fact that the primary source of the antigens is the normal flora , not a foreign bacteria or foreign blood cells

  - These IgM antibodies (anti A and anti B) are known as **IsoHemaglutinins**

This table illustrates antibodies and antigens produced in each group.

bombay GROUP	Anti A	Anti B	ANTI H
A	A Antigen	Anti B	H Antigen
B	Anti A	B Antigen	H Antigen
AB	A Antigen	B Antigen	H Antigen
O	Anti A	Anti B	H Antigen

Rhesus antigen:

- ✓ The Rhesus antigen actually has five antigenic determinants
- ✓ C and c (capital and small) antigens
- ✓ E and e antigens
- ✓ D antigen (no small d) which is the most important (the real Rhesus antigen)
- ✓ The other 4 are not significant
- ✓ There are two genes code for these determinants. One gene code for D antigen and another one code for two Varity of antigen CE which are (CE and ce).

If you have D antigen then you are **RH +ve**
If you don't have D antigen then you are **RH –ve**

- 85% of people are RH +ve and 15% are RH-ve.

As for the ABO groups:

50 – 60% of the population are O group (the most common)

20-25 % A group

10% B group

And only 5 % are AB group (the least common)

Blood transfusions:

The Isohemaglutinins cause agglutinations and lysis of the RBCs, which might lead to problems in blood transfusions.

So if you transfer blood from an incompatible donor, this will lead to agglutination and then complement activation and lysis, which might cause DIC (disseminated intravascular coagulation), shock and death in some cases (50% of cases are fatal).

O-ve carriers are considered **universal donors**, as they have no antigens on their Rbcs, can donate blood to any group.

AB+ve carriers are considered **universal recipients** as they have all the antigens and no antibodies.

- **The first step in blood transfusions** is to withdraw a sample of the recipient **RBCs** and react with different known serums (a serum that contains anti A, and other that contain Anti B and so on ..), then you check for agglutination to determine the blood type (checking the **antigens**).

- This process is called **blood typing**.

- **The second step** is to take the **serum** of the recipient and react it with known RBCs to check for **antibodies** and thus confirm the first typing.

Don't forget that there are secondary blood groups antigens (like Rh, Msn ,Xkand Kel etc..), but you only check for them if the patient had previous blood transfusions, because his serum might have Antibodies against these groups due to exposure in the previous transfusions.

How to detect these antibodies?

We react the serum of the recipient with a known Rbcs (type O), and then we perform a **Coomb's test** because the antibodies against these groups are IgGs not IgM so no agglutination will appear, unless you add an anti IgG.

- This process is called **blood screening**

Remember: the Isohemaglutinins for ABO groups are naturally arising antibodies, you produce them without previous exposure and thus you have to check them in the first time.

IgG are as dangerous as the IgMs , because they also can cause Hemolysis and complement activation, although they can't cause agglutination.

Now, after the typing and the screening we have to do a **cross-match** between the donor and the recipient to be extra sure, we take the serum of the recipient and we mix it with the RBCs of the Donor, if there is no agglutination then it's okay to transfuse.

The main cause for incompatible transfers is clinical mistakes, either in the lab (mixing in the samples or the reports) or due to nurses (e.g: mixing of blood tubes)

What are the symptoms of a faulty transfusion?

1. Hemolysis and complement activation
2. Fever
3. Shivering
4. Kidney failure
5. DIC
6. Shock and death (50% of cases)

Sometimes there is a delayed hemolytic reaction (7 or 8 days after the **first transfusion**), in this case there is nothing wrong with the procedure but the recipient started to produce antibodies against the secondary groups (MSN,Kell) after exposure and these antibodies started to attack.

This reaction is not serious nor is it common, as usually the number of antibodies produced is not that high.

Other complications are the **febrile reactions** (mostly fever), some say that these reactions arise because the donor white blood cells will release interleukin-1, or because of the antigen antibody reaction between the recipient antibodies and the HLA molecules on the donor WBC

These reactions will only happen if the recipient has anti HLA antibodies, either due to a previous transfer or in females who had multiple pregnancies.

If there are a high number of these anti HLA antibodies, they might activate the complement system in the lungs and lead to acute lung injury, due to the high number of anaphlatoxins and complement proteins in the lungs.

Another complication may arise if the recipient has an Ig-A deficiency, because he might produce antibodies to the Ig As in the donor's serum and induce a severe anaphylactic reaction. (1 in 700 people)

So the best thing to do in case of IgA deficiency is to only transfer the RBCs without the serum.

Also there is an increased risk of infection, that's why the blood has to be screened for possible pathogens before transfusions, like HIV, Hepatitis B and C, Syphilis, and Cytomegalovirus(this virus only affects the immunosuppressed individuals ,it is found in 50% of the public) .

- <u>Now let's move to the Rh incompatibility</u>

First of all the IgG antibodies are produced against the D antigen only (no antibodies against The C or the E)

These antibodies do not occur naturally and the patient has to be immunized, either by exposure due to previous mistaken blood transfusion or multiple pregnancies.

The mother can be exposed to the antigen during the delivery of the first Rh +ve child as the placenta rupture from the uterus and causing mixing of the blood and the mother will produce IgGs against the Rh antigen

In the second pregnancy of another rh +ve child these antibodies will cross the placenta into the fetal circulation, and destroy the RBCs of the fetus (hemolysis)

So the fetus will become anemic, and it might progress to complete heart failure and death.

This condition is known as Hydrops fetalis which will lead to miscarriage of the baby.

In other cases the baby survive and is born alive, but he will have severe hemolytic anemia, heart failure and jaundice (called hemolytic disease of the newborn HDN)

Remember that jaundice is common in any newborns (physiological jaundice) and it usually appear 1 day or more after delivery, but in case of HDN the baby will be born with jaundice immediately after birth because of the severe hemolysis that has already happened during pregnancy (high amount of bilirubin in the blood).

The increased bilirubin might accumulate in the central nervous system, especially in the basal ganglia which might lead to severe brain damage (depending on the amount)

This bilirubin is classified as direct bilirubin (as it comes directly from the hemoglobin after the hemolysis of the Rbcs)

The treatment of this disease is by exchange transfusion (you exchange the fetus blood with a compatible type gradually).

We can prevent this condition by giving any Rh -ve pregnant woman an injection of anti-D antibodies within 72 hours of delivery to prevent her immune system itself from being activated to produce similar antibodies against the Rh antigen (Rh immunization).

How do these injected antibodies work? There are two possible explanations:

1. these antibodies will collect and clear all the antigens in the mother blood very quickly, thus preventing her from mounting an immune response against the rh antigen
2. The antibodies will bind to the antigen and form immune complexes, these complexes will bind with a B-cell that is reactive to the D antigen (through the Fc receptor on the b-cell), and these cells will undergo antibody feedback which will lead to immediate inactivation of the B-lymphocyte.

The second explanation is more feasible.

Some people recommend that the injection should be given after 28 weeks of pregnancy.

Not every woman who is Rh-ve will become reactive to the fetus rh+ve blood as sometimes the amount of mixed blood is not sufficient to produce an immune response.

Statistically, immune reaction happens in only 20% of Rh incompatible pregnancies.

The percentage is much lower (2-3%) in case the mother and the baby have different ABO blood groups.

For example; if the mother is A –ve and the baby is B+ve, the fetal blood in the mother circulation will be immediately cleared by the anti B antibodies before the immune system can produce IgGs against the Rh antigen, thus reducing the possibility of Rh disease.

"The difference between a successful person and others is not a lack of strength, not a lack of knowledge, but rather a lack of will." ***Vince Lombardi***

Done by Ebraheem Alabdali

Notes from the correction team: Sheet 19:

Page 7: 3rd paragraph from the botto: "but at the same time the proteins in the antiserum will…", by proteins here we mean both the antibodies of the horse as well as other proteins found in the antiserum.