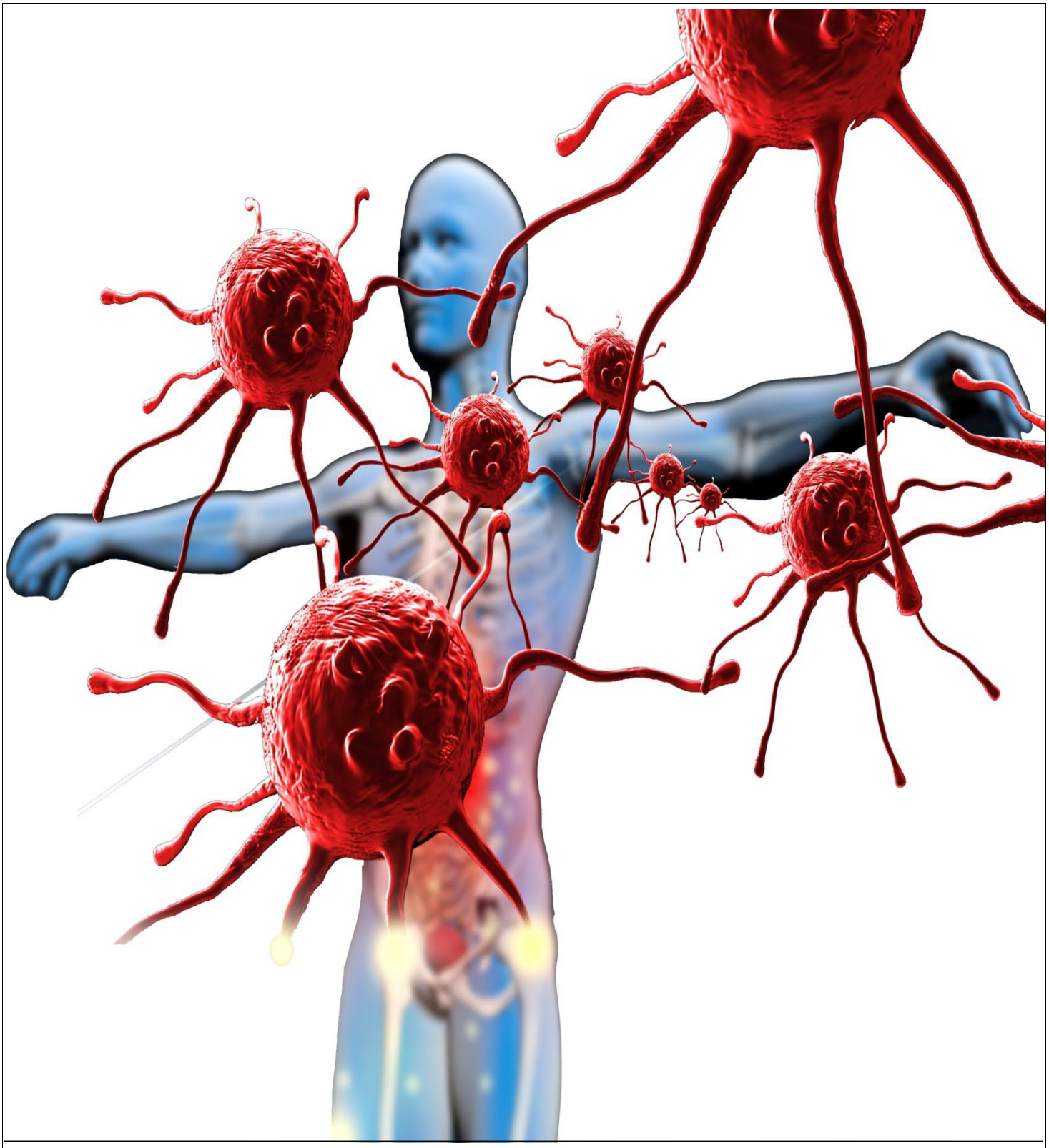

IMMUNOLOGY

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#17

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Immunohematology

This sheet includes

- ABO BLOOD GROUP
- Rhesus blood group
- Steps of Blood transfusion
- Complication of blood transfusion

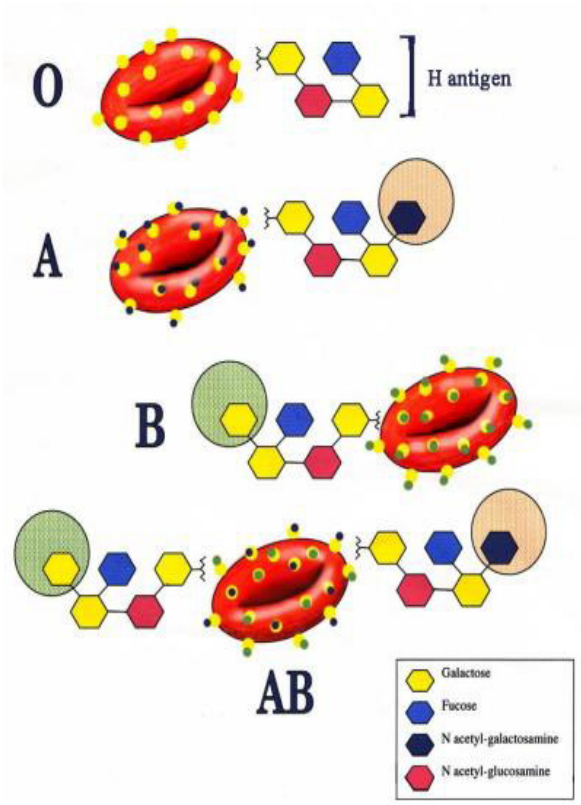
➢ The red blood cells have on their surface hundreds of antigens and according to the antigen on their surface we can define some blood group systems. We have many blood group systems that are designated according to these antigens, but only two of them are important which are **ABO blood** group and **Rhesus blood** group

ABO BLOOD GROUP

➢ -IN THE RED BLOOD CELLS we have a gene coding for a carbohydrate chain that attaches to the RBC called **H chain**
This H chain has the following characteristics :

- It's a polysaccharide chain that is a **precursor** to **each** of the ABO blood group antigen so it is found on all RBCs .
- It is a carbohydrate sequence and there is a fucose"hexose sugar "moiety at the end added by fucose transferase enzyme
- Depending upon a person's ABO blood type, the H antigen is converted into either the A antigen, B antigen, or both. If a person has group O blood, the H antigen remains unmodified.

- The conversion of H antigen to A or B antigen is dependent on transferase enzymes :
  1- **A transferase enzyme** : which adds **N-acetylgalactosamine** to the H chain forming **A blood type** .
  2- **B transferase enzyme** : which adds **galactose** to the H chain forming **B blood type**



- ABO system **transferases** are enzymes with **glycosyl transferase** activity which in humans are encoded by the ABO gene .

- The A and B alleles of the ABO gene express enzymes with glycosyltransferase activities that differ adding either N-acetyl galactosamine or galactose to the H antigen, converting it into the A or B antigen respectively

- {If you have the gene that encodes a **N-acetylgalactosamine** transferase enzyme (A transferase) that bonds N-acetylgalactosamine to the end of the H chain in your red blood cell then you are **type A blood group**, however, if you have the gene that encodes **Galactose transferase enzyme (B transferase)** then you are **type B blood group** .IF you have **both transferases** (N-acetylgalactosamine attach to some H chains and other H chains with Galactose) then you are type **AB blood group**. If you have **only H chain (no transferases**) then you're type **O blood** group}

- In rare cases some people might have a mutation in **fucose transferase** because of that they can't add fucose to the terminal part of the H-chain consequently they can't add neither NAGA nor galactose this phenotype is called **Bombay blood group**

- **BOMBAY blood group**
  - ✓ **There is no H chain (because there is no fucose)**
  - ✓ **There's no A or B antigen**
  - ✓ **This group is very rare.**

Student question : can the Bombay blood group be considered a universal donor ?

Yes it can because it doesn't have both A And B antigen (like O blood type) but unlike O blood type it has anti A and Anti B and **Anti H antibodies** so they can only receive blood from another Bombay blood type .

❖ GENERAL NOTES:

- People who have the antigen (either A or B) are tolerant to them and they don't produce antibodies against them .

- People who lack A or B antigen will most likely produce antibodies against the antigen he lacks (Anti A or Anti B) but 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.These **IgM** antibodies (anti A and anti B) are known as "**Isohaemagglutinins"**

- Isohaemagglutinins 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. It is believed that these antibodies develop after exposure to some normal flora in GIT who**

have sugars similar to Galactose or N-acetylgalactosamine, so we can develop antibodies against them according to the ABO antigen that you lack.

To be more clear (not from the doctor) : if you are B- blood type then you normally have galactose on your RBC but you don't have N-acetylgalactoseamine so when you produce antibodies against normal flora you produce them against NAGA because you don't have it so you will end up with Anti-A antibodies of the IgM type

- **If you are O blood type, you have anti A and anti B**
- **If you are AB, you don't have neither anti A nor anti B**
- **This is important for blood transfusion because we cannot transfuse blood between people with incompatible blood . for example transfusion of blood from A to O causes Anti A antibodies in O recipient to attack the A antigen in the blood of the donor which leads to agglutination and hemolysis which can lead to death .**
- The Isohemaglutinins cause agglutinations and lysis of the RBCs when they attack their antigens,and 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.
- **O -ve** carriers are considered **universal donors**, as they have no antigens on their RBCs so they can donate blood to any group.
- **AB +ve** carriers are considered **universal recipients** as they have all the antigens and no antibodies.

➢ Notice that

- ✓ When babies are born, they **don't** have antibodies against A and B even if they are O blood group because they need to be exposed to their normal flora first .

- ✓ Isohaemagglutininsare 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 .

- ✓ The ABO antibodies are not present at birth, but they usually appear 2 or 3 months after it.

- ➢ ABO blood group is important for blood transfusion and organs transplantation. ABO blood group is not only present on RBC but can also be present on other cells such as endothelial cells.

- ➢ A and B antigens can be present on the endothelial cells, so if you have anti A or B that it doesn't only attack the RBCs only, but can also attack the transplanted organs because the antigens are presented on them leading to transplant rejection .

❖ Rhesus blood group

- ✓ The Rhesus antigen actually has **five antigenic** determinants.

- ✓ The main antigens are D, C, E, c and e, which are encoded by two adjacent gene loci on chromosome 1 , **the RHD gene** which encodes the **RhD protein** with the **D antigen**, and the **RHCE gene** which encodes **the RhCE protein with the C, E, c and e** antigens.

- ✓ There is no d antigen. Lowercase "d" indicates the absence of the D antigen

- ✓ { You can either have the gene that produces D antigen or the gene is absent and there is no Antigen at all (d)
  The RHD gene is dominant so a person is considered to be RhD positive whenever this gene is present, even though the gene may have been inherited from one parent. Conversely, a person will be RhD negative if no RHD gene is inherited }

- ✓ If you have D antigen then you are RH +ve

- ✓ If you don't have D antigen then you are RH –ve
  - ➢ [Rh positive and Rh negative refer to the D antigen only]
  - ➢ D antigen which is the most important (the real Rhesus antigen). The other 4 are not significant.

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

❖ GENERAL Notes:

- ✓ **Rhesus** antigens are **proteins** and the antibodies that are produced against them are **IgG antibodies .**
- ✓ **ABO** antigens are **carbohydrates** (sugars), and the antibodies that are produced against them are IgM **antibodies.**

- ✓ **A mother who is Rh +ve and a father who is Rh +ve can have an Rh negative child ,this occurs when mother and father have D antigen that presents at one chromosome and absent on the other chromosome. If the child inherits the two chromosomes that lack D antigen, then the child is Rh –ve so it is possible to have an RH negative child from two RH positive parents .**

❖ Rh incompatibility

- ✓ -IgG antibodies are produced against the D antigen
- ✓ These antibodies **do not occur naturally** and the person has to be immunized, either by exposure due to previous mistaken blood transfusion or multiple pregnancies.
- ✓ **A mother who is Rh-negative** 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 causes hemolysis of the RBCs of the fetus {this means the mother has become sensitized and her antibodies may cross the placenta and attack the baby's blood.}
- ✓ This will occur at each pregnancy of Rh +ve baby.
- ✓ The fetus will become anemic, and it might progress to complete heart failure and death.
- ✓ **Rhesus incompatibility doesn't affect the first baby**.

(RH IMMUNIZATION).

- ➢ We can prevent this condition by giving any Rh -ve pregnant woman an injection of **anti-D antibodies** .
- ➢ The injection should be given after 28 weeks of pregnancy and before delivery, also within 72 hours after delivery.
- ➢ There are two possible mechanisms of action

- 1-ANTI D 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.

Incompatibility of newborns is highly associated with D antigen .But; sometimes you find women with **type O blood can be associated with incompatibility**. Usually, Anti A and Anti B are IgM in these women {with type O blood group} and they cannot cross the placenta ,so there is no possibility of hemolytic disease to occurs in newborns. In Few cases, **women with type O blood group can produce Anti A and Anti B which are IgG varieties and this type of Antibodies can cross the placenta and cause the hemolytic disease of newborns.**

In addition to the ABO antigens and Rhesus antigens, many other antigens are expressed on the red blood cell surface membrane. For example, an individual can be AB RhD positive, and at the same time M and N positive (**MNS system**), K positive (**Kell system**), and Lea or Leb positive (**Lewis system**).

Steps of Blood transfusion

✓ **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 or other that contain Anti B), then you check for **agglutination** to determine the **blood type** (checking the antigens).

✓ {If the sample reacts with anti A ->Type A blood
If it doesn't react at all ->Type O blood}

- 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**.

✓ This process is called "**Reverse typing** "

✓ **The Third step** is to take a sample of the recipient and donor RBCs and react them with anti D immunoglobulin, if there is agglutination, it is Rh+ and if there is no agglutination, it is Rh-

- In case of Rh - , sometimes the number of D antigens is few{**weak D reactant** :they are Rh+ but there is a few number of D antigens }, so they escape from agglutination .Here we **should confirm** our result by adding anti-immunoglobulin {anti IgG: combs test}, if there is agglutination, it is Rh+.We perform a Comb's test because the antibodies against these groups are IgGs not IgM, so no agglutination will appear, unless you add an anti IgG .

- {**Every blood test that gives Rh - result ,SHOULD be confirmed by anti –immunoglobulin test because sometimes they are not really Rh- }**

- Don't forget that there are **secondary blood groups antigens** (like MNS ,and Kel etc..), but you only check for them if the patient had a previous blood transfusion, 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 known RBCs {type O blood groups} [note: we choose type O to avoid the presence of any ABO antigens]

✓ In this step we check about unexpected antibodies

➢ TO sum up

Secondary antigens have IgGs which are produced after previous exposure to the antigens {after first blood transfusion} unlike antibodies of ABO antigens which are **NATURAL and Rh antibodies which are produced after certain cases of pregnancy** , So if there is **no previous experience of blood transfusion,** no need to check them.

➢ 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 of the secondary antigens** are dangerous, because they can cause Hemolysis and complement activation, although they **can't cause agglutination. You check them if there is previous blood transfusion because they are not produced without previous exposure.**

- **The transfused blood can be the whole blood, or packed cells {without serum} or certain products like factor 8 for hemophilia.**

- **In blood transfusion ,we should take care about all of the previous steps and make sure that ,there is no interaction between the transfused RBCs and the serum of the recipient.**

- **If we transfuse the whole blood, could the opposite reaction happen? { interaction between RBCs of the recipient and the serum of the donor }**

- **Example : type AB blood group recipient who receives blood from O donor ,it's okay ,although the O donor has both ANTI A and ANTI B in his serum and the recipient has Both antigens .This is because the donor serum get diluted , so the effect of his antibodies is negligible .We should take care in case of HUGE amount of blood transfusion, because the chance of the opposite agglutination increases and the best way to avoid this agglutination is to transfuse RBCs only {packed cells}.**

✓ 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.

Complications of blood transfusion

1) ABO INCOMPATIBILITY

➢ The **main cause** for incompatibility are **clinical mistakes**, either in the lab (mixing in the samples or the reports) or due to nurses (mixing of blood tubes) .

➢ What are the symptoms of a faulty transfusion {cross match **ABO incompatibility}?**

1. Hemolysis and complement activation
2. Fever, nausea, sweating, and vomiting.
3. Shivering
4. **Kidney failure** and other organs failure
5. DIC

6. Shock and death.

- These symptoms will appear very quickly after transfusion approximately after 3 hours.

2) FEBRILE REACTION

- A type of transfusion reaction that **is associated with fever.**

- This reaction arises because the **donor white blood cells** will release interleukin-1 and IL6 that work on the hypothalamus of the recipient . This is not serious because antipyretics can relieve the effects of the interleukins.

3) ACUTE LUNG INJURY REACTIONS:

- The antigen antibody reaction between the recipient antibodies and the HLA molecules on the donor WBCs.

These reactions will only happen if the recipient has anti HLA antibodies, if there are a high number of these anti HLA antibodies, they might activate the complement system in the lungs and lead to pulmonary EDEMA, due to the huge amount of anaphylatoxins and complement proteins in the lungs.

4) ALLERGIC REACTIONS

- Another complication may arise if the recipient has an Ig-A deficiency [The most common type of deficiency" 1in 700"]
- The recipients who have an IgA deficiency, their bodies mistakenly recognize the IgA as foreign body and produce antibodies [IgE] against the IgAs in the donor's serum and induce a severe **anaphylactic reaction**.
- The best thing to do in case of IgA deficiency is to transfer the RBCs alone without the plasma

5) INFECTION

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 {CMV}.

Cytomegalovirus

- It is very wide spread.
- Most people are positive for CMV.
- Most of the transfused blood is positive for CMV.
- In cases of immunodiffient and CMV negative person, youshould not give him blood that is positive for CMV.

يعطيكم العافية

انبثاقا من وليد اللحظات الراهنة , وعنونة لعبارات مستقبلية قادمة

كل ما أود ايصاله هو اياك أن تكتفي ب" قليلك المشمع بالقناعة" طالما المزيد في نطاق المباح , فليست القناعة هي تجمدك عن السعي مدعيا أنك اكتفيت وانما هي سعيك الدائم مع اكتفائك بما قدر لك في كل مرحلة على انه نصيبك منها ز