Lec. 9 , physiology

(Slides + Record).

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* Classic Blood Groups :

A	B	AB	O
AA or AO	BB or BO	AB	OO

← Phenotypes (A, B, AB, O)

← Genotypes (AA or AO, BB or BO, AB, OO)

* minor Blood Groups :

MM , MN , NN , PP , Pp , others

* Rhesus Blood Groups :

Rh (positive)	rh (negative)
(85% of Europeans) (There is Antigen, But no antibody)	15% (No antigen, No antibody)
RhRh or Rhrh	rhrh

← phenotypes (Rh (positive), rh (negative))

← Genotypes (RhRh or Rhrh, rhrh)

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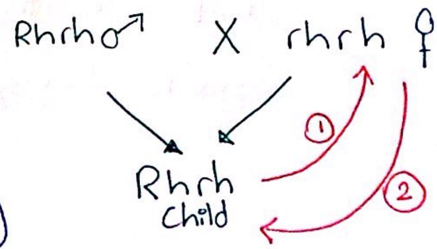
* If an Rh positive ♂ (G: Rhrh) gets married to a woman who is Rh negative and she gets pregnant with an Rh positive child :

① It is possible that some of the RBCs of the fetus pass to the maternal Blood.
⇒ the mother develops Antibodies.

② The antibodies developed in the mother might Pass to the fetal Blood (that contains the Antigens)
⇒ Antigens + Antibodies ⤳ Agglutination.
which means hemolysis , and the Baby will be in danger. → severity of hemolysis



Hemolytic diseases of the newborn because the incompatibility of Rh blood groups:

Three conditions in which the mother may develop antibodies:

A. Blood transfusion before marriage by blood from Rh+ person. ⇒ the mother will either develop antibodies (more dangerous) or develop sensitivity to produce antibodies.

B. leakage during pregnancy of small amount of fetal blood (Rh+) into maternal circulation (placental hemorrhage).

يمكن سببه infection or inflammation in the placenta.

→ if the Developed Antibodies pass to the fetus, he will be in danger.

الخطورة أكثر في الاستمرارات الأولى

C. during delivery, same blood squeezed back to maternal blood.

* Hemolysis has degrees.

In these conditions one of the followings hemolytic diseases may occur:

A. erythroblastosis fetalis (mild disease): small amount of RBC,s leak into mother circulation, some mothers develop antibodies against D antigens. These antibodies pass to fetal blood & cause mild hemolysis of the RBC,s of the fetus.

This newborn baby can be rescued by giving him (Rh-) blood, but not from his mother.

مشان ما يكون فيه
لا Antigen
و لا Antibody
فما تحدث أي مشكلة
(مع ان الطفل مع امه +)
ولكن صار عنده
Antibodies
(بالإضافة للAntigen
التي أصلا عنده

B. Icterus graves neonatorum (kernicterus) (moderate disease): the infant is born at term, is jaundiced, or becomes so within 24 hours, there may be severe neurological lesions involving the basal ganglia in which the bile pigments deposited.

↳ might become mentally retarded.

C. Hydrops fetalis (severe disease). The hemolysis is severe, the infant may die in uterus or may develop severe anemia, Jaundice & edema; dies within few hours.

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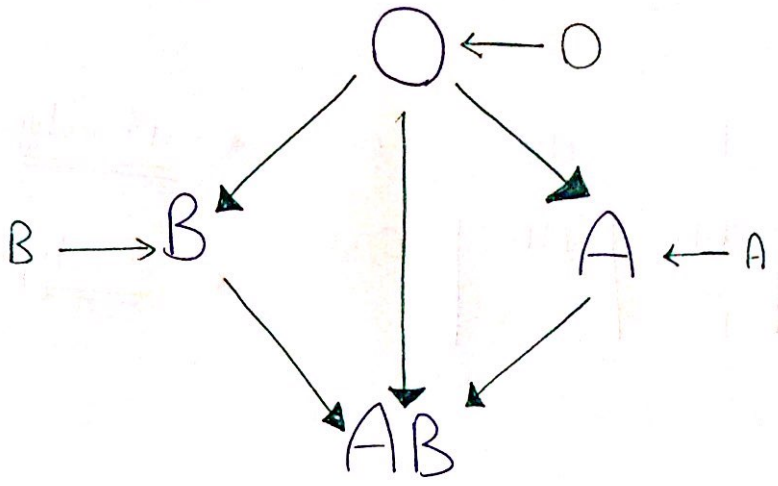
Fortunately, this disease can be prevented by giving an Rh-negative mother human gamma globulin against Rh-positive erythrocytes within 72 h after she has delivered an Rh-positive infant. These antibodies bind to the antigenic sites on any Rh-positive erythrocytes that might have entered the mother's blood during delivery and prevent them from inducing antibody synthesis by the mother. The administered antibodies are eventually catabolized.

General Donor



General Recipient

* Is O always a General Donor (And AB always a general Rec.?)?

No, there are conditions.

Example : O given to AB

O: Antibodies ✓, Antigens ✗

AB: Antibodies ✗, Antigens ✓

Agglutination occurs, but it's very minor
(Because the Antibodies get diluted in the 5L Blood of the Recipient)
& the Body can deal with it

* one or two bags of transfused Blood would be okay.
(~~xxx~~ 3 in extreme cases)

But more than that is not allowed Because

severe hemolysis will occur causing Death.

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You may be wondering whether ABO incompatibilities are also a cause of hemolytic disease of the newborn. For example, a woman with type O blood has natural antibodies to both the A and B antigens. If her fetus is type A or B, this theoretically should cause a problem. Fortunately, it usually does not, partly (1) because the A and B antigens are not strongly expressed in fetal erythrocytes and (2) partly because the natural antibodies are of the IgM type, which do not readily cross the placenta. IgG

Blood Transfusion

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Indications of blood transfusion:

1. to restore the Blood Volume, e.g. in haemorrhage.
2. to provide Red Blood Cells, e.g. anaemias.
3. to increase Blood Coagulability in haemorrhagic diseases, (we donate Coagulation Factors). e.g. haemophilia & purpura.
4. to replace infant's blood with Rh.-ve blood in erythroblastosis foetalis.
5. to supply antibodies to raise the general resistance of the body.
6. to provide White Blood Cells, e.g. in leucopenia (= decreased W.B.Cs).
7. to supply plasma proteins in hypoproteinaemia.

* زمان، اذا الشخص احتاج clotting Fs or WBC. or platelets كنا نضطر نعمل دم كامل (بكل محتوياته) بس حالياً، ممكن انو نفصل المكونات

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Complications of Blood Transfusion

Early	Late
① Haemolytic reactions immediate delayed.	① Transmission of disease e.g. hepatitis, malaria, syphilis, AIDS.
② Reactions due to infected blood	② Transfusional iron overload
③ Allergic reactions to white cells, Platelets or proteins	③ Immune sensitisation, e.g. to rhesus D antigen
④ Circulatory overload	
⑤ Air embolism	
⑥ Citrate toxicity	
⑦ Hyperkalaemia (↑ K^+ → Affects the ventricles)	
⑧ Clotting abnormalities (after massive transfusion	

7)

Blood transfusion

Blood for transfusion can be kept for several weeks if it is collected from donors under aseptic conditions into sterile plastic packs containing a suitable preservative solution, and it is stored at 4°C. A commonly used preservative, citrate–phosphate–dextrose (CPD) solution, provides citrate as anticoagulant and glucose (dextrose) as metabolic substrate for the red cells. Adequate numbers (i.e. not less than 70%) of red cells remain viable after transfusion when previously stored in CPD solution for 3–4 weeks at 4°C. Adding adenine to the solution can increase this period to 5 weeks.

* when a person Donates Blood, we should ① test it (infections مشان ال)
② Group it (A, B, --)
③ Cross matching tests

* The Blood stored should be Anti-coagulated, and stored at 4°C.
we add an anticoagulant ⟶ ACD
Acid Citrate Dextrose
(the best Anticoagulant)

اذا مريض إجا، وما في وقت للفحوصات
وهو بحاجة لدم
~~ORh~~ نعطيه ⟸
Orh (negative)

واذا ما في، في الحالات القصوى
نعطي ORh (+)
إما يعيش أو يموت

أحسن خيار دائماً هو إعطاء ~~[illegible]~~ فصيلة الدم نفس

لو أقل، بيأثر على غشاء ال RBC
لو أعلى، بخرب الدم

"لما تحط" ,89 (يتجمد) That's why we put Blood on the ice (not in the ice)

(2) During storage at 4°C, the red cells show a progressive decrease in content of adenosine triphosphate and 2,3-BPG, while with decreased activity of the Na^+–K^+ pump, the cells gradually lose K^+ to the surrounding plasma and gain Na^+ from it. The concentration of K^+ in the plasma may reach values as high as 30 mmol L^{-1} after storage of blood for 4 weeks. The pH of the plasma also decreases with time of storage and its concentration of ammonia rises. These changes can make stored blood dangerous for transfusion in certain patients, e.g. those with renal or hepatic failure. The decline in Na^+–K^+ pump activity makes some red cells spherocytic, with loss of deformability. These effects may be irreversible and after transfusion the abnormal red cells are destroyed very rapidly by macrophages in the spleen and elsewhere. Other constituents of blood do not withstand prolonged storage. Granulocytes begin to lose their phagocytic capacity within 6 h of collection and they are functionally inert after 24 h. Platelets lose their haemostatic effect (p. 310) within 48 h at 4°C, while the labile coagulation factors, V and VIII (p. 314), also rapidly deteriorate in chilled blood.

* hyperkalemia in plasma.
* cells swell and become oval, shorter, fatter, & hemolyse easily especially if storage exceeds 2 weeks.

(3) Before donated blood is made available for issue from a blood-bank, the ABO and rhesus groups of the cells are determined and commonly the serum is screened for atypical antibodies. Serological tests are also done for syphilis, hepatitis and human immunodeficiency virus (HIV). Before transfusion, the ABO and rhesus groups of the patient's red cells are determined, the serum is checked for unexpected antibodies and red cells from the donor are tested against the patient's serum by **cross-matching** tests (compatibility tests). These cross-matching tests are essential for checking that there has been no error in ABO grouping of donor and recipient, and for ensuring that the recipient's serum does not contain naturally occurring or immune antibodies active against the donor's cells.

* Cross matching test:-

2 steps

(1) RBCs from the Donor + Plasma from the Rec.

(2) Plasma from the Donor + RBCs from the Rec.

⇒ If no reactions occur, things are Good.

By this method, we can exclude any incompatibility (in major or minor Blood Groups, or other Problems).

* If we need to donate WBCs or platelets, we need fresh days.

(WBCs خلال ساعات)

Because the half-lifes of major cells is hours (ex: neutrophils)

Transfusion of whole blood is sometimes necessary but, over recent years, the use of cell-separator machines and large-scale production of plasma constituents have made it increasingly possible to transfuse specific components of blood which the patient lacks. Thus **red-cell concentrates**, often resuspended in a small volume of electrolyte solution, are used to restore the haemoglobin concentration in an anaemic patient in whom the plasma volume may already be expanded. **Platelet concentrates** are of use in patients with severe thrombocytopenia (p. 317). A variety of plasma fractions is also available to supply coagulation factors, e.g. **cryoprecipitate**, which is rich in factor VIII and fibrinogen, and for expanding plasma volume, e.g. **stable plasma protein solution**. A useful source of antibodies against common viruses is **pooled normal immunoglobulin** and various specific immunoglobulins are also available, e.g. anti-D and antibodies against tetanus, hepatitis B and diphtheria.

* Donation of Plasma

plasma: stored in Blood → months

If dried → Years.

* if we donate Blood that was stored for 2 weeks:

if we measure (the Donated RBCs) in the next day, we'll find that 80% of these RBCs are functioning and every day, 1% will undergo hemolysis

في طريقة to label them.

Platelets → Aggregation 5 steps (Lec. 8)

RBCs → Agglutination

→ Antibodies bind to Antigens.

(Antibodies have receptors (Range: 1-10) & can bind RBCs)

??

However much care is taken in cross-matching and administering blood, transfusion carries definite risks of unpleasant or even fatal complications. Major red-cell incompatibility can lead to lethal intravascular haemolysis or delayed extravascular breakdown of donor cells. Transfusion of blood contaminated with bacteria can cause profound shock with hyperpyrexia, while allergic reactions to transfused white cells, platelets and plasma proteins can also be severe. Circulatory overload, air embolism and changes in plasma electrolyte concentrations (e.g. hyperkalaemia) may occur and there may be direct transmission of disease, e.g. HIV and cytomegalovirus infections, hepatitis and malaria.

* True Or False: (الأجوبة مش أكيدة مشان ما كانو واضحين بالريكورد)

(1) After Blood has been stored for 3 weeks, at least 70% of the transfused RBCs will be retained in the circulation 24 hours after transfusion. True

النسبة غير أكيدة (ما كانت واضحة بالريكورد)

(2) Donor Blood is usually collected into heparin that acts as an anticoagulant. False (we use ACD)

(3) Antibodies are often absent from the serum of O-Grouped babies.

True (Antibodies are absent in the new born babies. But antigens don't change from Birth to death) ~~xxxxx~~

↓ Genetically Determined

(4) About Von Willebrands Disease (Lec 8):-

a) it is inherited as sex-linked disease False (somatic)

b) Bleeding time is usually Normal False

(Note: Bleeding time depends on vasoconstriction and clotting)

c) Factor VIII activity measured by clotting essay is low. True

d) Factor VIII related Antigen is usually normal. False

e) platelet function is Abnormal. True