University of Basrah
Al-Zahraa Medical College

Ministry of higher Education
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REPRODUCTIVE BLOCK

Lecture

Duration : 1 hour

RH isoimmunization

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GYNAECOLOGY 20th
EDITION by Ten Teachers

Learning Objectives (LO)

1- Rhesus isoimmunization .
2- The aetiology of rhesus disease .
3- Potential sensitizing events for rhesus disease .
4- Prevalence of rhesus disease
5- Preventing rhesus isoimmunization .
6- Signs of fetal anaemia .
7- The management of rhesus disease in a sensitized woman
8- Treatment options of sensitized mother .

LO 1
Rhesus isoimmunization

- **Blood groups are defined in two ways:**

First, there is the ABO group, allowing four different permutations of blood group (O, A, B, AB). Second, there is the rhesus system, which consists of C, D and E antigens.

- **The importance of these blood group systems is that a mismatch between the fetus and mother can mean that when fetal red cells pass across to the maternal circulation, sensitization of the maternal immune system to these fetal 'foreign' red blood cells may occur and subsequently give rise to haemolytic disease of the fetus and newborn (HDFN).**

LO 2

The aetiology of rhesus disease

- **The rhesus system comprises at least 40 antigens, the most clinically important of which are C, D and E. They are coded on two adjacent genes that sit within chromosome one. One gene codes for antigen polypeptides C/c and E/e while the other codes for the D polypeptide (rhesus antigen) .**

- **In practice , only anti-D and anti-c regularly cause HDFN and anti-D is much more common than anti-c.**

- **Occurrence of HDFN as a result of rhesus isoimmunization involves three key stages . Firstly, a rhesus-negative mother must conceive a baby who has inherited the rhesus-positive phenotype from the father. Secondly, fetal cells must gain access to the maternal circulation in a sufficient volume to provoke a maternal antibody response. Finally, maternal antibodies must cross the placenta and cause immune destruction of red cells in the fetus .**

- **Rhesus disease does not affect a first pregnancy as the primary response is usually weak and consists primarily of immunoglobulin (Ig) M antibodies that do not cross the placenta. However, in a subsequent pregnancy with a rhesus-positive baby, rhesus-positive red cells pass from the baby to the maternal circulation and cause maternal re-sensitization .**

- **this time of IgG antibodies that can cross the placenta to the fetal circulation. If these antibodies are present in sufficient quantities, fetal haemolysis may occur, leading to such severe anaemia that the fetus may die unless a transfusion is performed.**

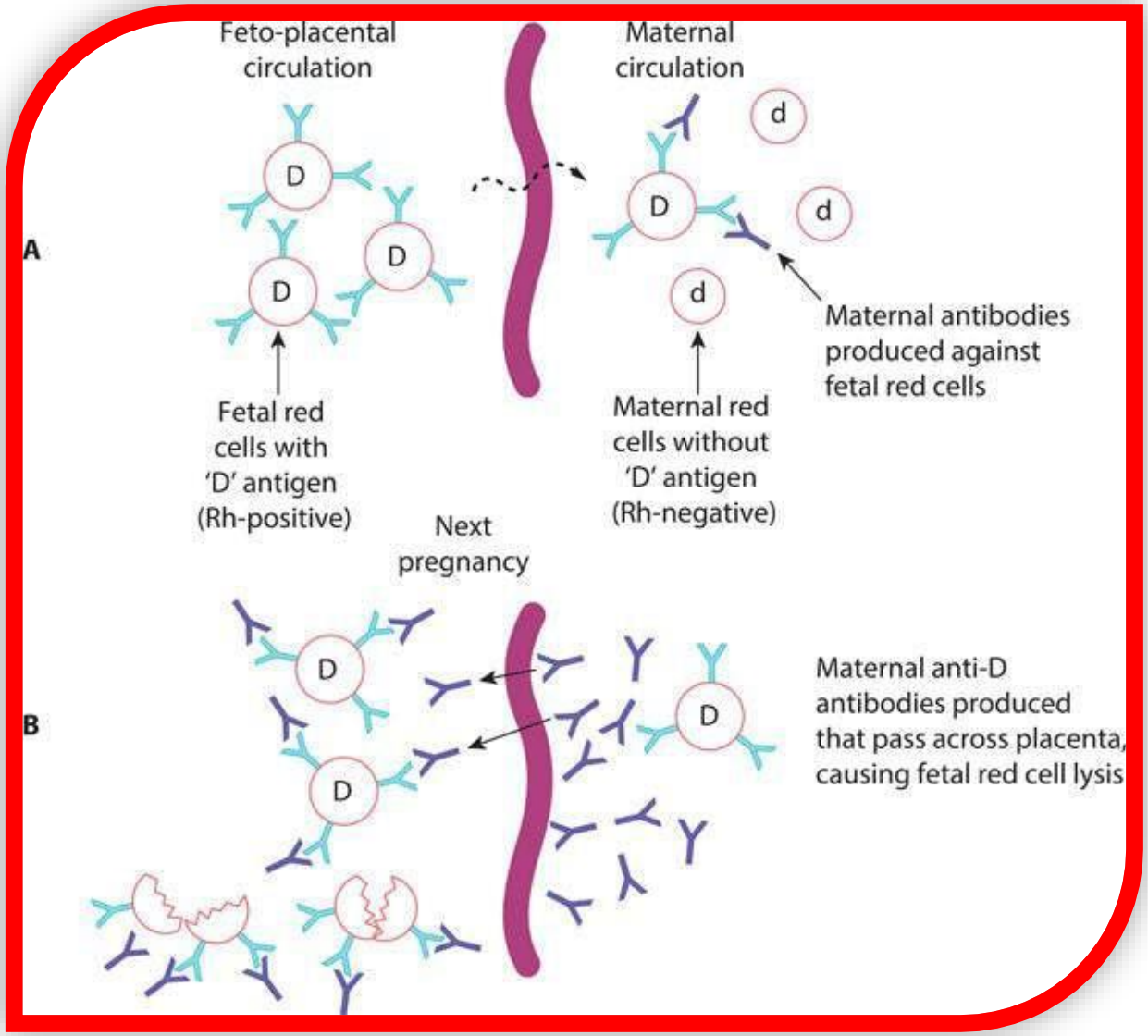
LO 3
Potential sensitizing events for rhesus disease

- **Miscarriage.**
- **Termination of pregnancy.**
- **Antepartum haemorrhage.**
- **Invasive prenatal testing (chorion villus sampling, amniocentesis and cordocentesis).**
- **Delivery.**

LO 4
Prevalence of rhesus disease

- **The prevalence of D-rhesus negativity is 15% in the UK Caucasian population .**
- **Rhesus disease is commonest in countries where anti-D prophylaxis is not widespread, such as the Middle East and Russia.**

The mechanism of rhesus sensitization (A) and fetal red cell destruction (B)



LO 5
Preventing rhesus isoimmunization

- **The process of isoimmunization can be prevented by the intramuscular administration of anti-D immunoglobulins to a mother.**
- **It is normal practice to administer anti-D as soon as possible after any potential sensitizing events that may cause feto-maternal haemorrhage and preferably within 72 hours of exposure to fetal red cells.**
- **some protection may still be offered if anti-D Ig is given up to 10 days after the sensitizing event.**
- **Current UK guidelines suggest that all rhesus-negative pregnant women who have not been previously sensitized should be offered routine antenatal prophylaxis with anti-D, either with a single dose regimen at around 28 weeks or a two-dose regimen given at 28 and 34 weeks' gestation.**

- **The exact dose is determined by the gestation at which sensitization has occurred and the size of the feto-maternal hemorrhage. A Keilhauer test of maternal blood determines the proportion of fetal cells present in the maternal sample. It relies on the ability of fetal red blood cells to resist denaturation by alcohol or acid and it allows calculation of the size of the feto-maternal transfusion and the amount of extra anti-D Ig required.**

LO 6
Signs of fetal anaemia

- **clinical and ultrasound features of fetal anaemia do not usually become evident unless fetal haemoglobin is more than 5 g/dl less than the mean for gestation. Usually, features are not obvious unless the fetal haemoglobin is less than 6 g/dl.**
- **Polyhydramnios.**
- **Enlarged fetal heart.**
- **Ascites and pericardial effusions.**
- **Hyperdynamic fetal circulation (can be detected by Doppler ultrasound by measuring increased velocities in the middle cerebral artery or aorta).**
- **Reduced fetal movements.**
- **Abnormal CTG with reduced variability, eventually a ‘sinusoidal’ trace.**

LO 7
The management of rhesus disease in a sensitized woman

- **In a sensitized woman, if the father is D-rhesus positive or unknown, standard management involves monitoring antibody levels every 2–4 weeks from booking.**
- **Antibody levels or quantity can be described using the titer or by using IU (international units) as a standard quantification method.**
- **The titer simply refers to the number of times a sample has been diluted before the amount of antibody becomes undetectable; titre of 2, 4, 8, 16, 32, 64, 128, etc. Each time a sample is tested it should be checked in parallel with the previous sample to ensure the detection of significant changes in the antibody level.**
- **If antibody levels rise, the baby should be examined for signs of anemia.**

middle cerebral artery (MCA) Dopplers

- (peak velocity measurement) have been shown to correlate reliably with fetal anaemia.A fetus with a raised peak MCA velocity has a high probability of anaemia.

LO 8

Treatment options include delivery or fetal blood transfusion.

- Delivery of the fetus is an option if the fetus is sufficiently mature .Delivery must take place in a unit where adequate neonatal support and expertise is available, and generally delivery should not be before 36–37 weeks' gestation unless there are specific reasons such as special difficulty with fetal transfusion.
- Fetal blood transfusion is life saving in a severely anaemic fetus that is too premature for delivery. The aim is to restore haemoglobin levels, reversing or preventing hydrops or death.

Routes of administration include:

- **Into the umbilical vein at the point of the cord insertion (ideally through the placenta and not through the amniotic sac).**
- **Into the intrahepatic vein.**
- **Into the peritoneal cavity (not as effective but some blood is absorbed and this may be the only option, for example in early gestations).**
- **Into the fetal heart.**

Transfused blood is:

- RhD negative.
- Crossmatched with a maternal sample.
- Densely packed (haemoglobin usually around 30 g/l) so that small volumes are used.
- White cell depleted and irradiated.
- Screened for infection including cytomegalovirus (CMV

- **At delivery If the baby is known to be anaemic or has had multiple transfusions, a neonatologist must be present at delivery.**
- **Blood must therefore always be ready for the delivery.**
- **All babies born to rhesus negative Women should have cord blood taken at delivery for blood count;blood group&indirect Coombs test.**

THANK YOU