Obstetrics and Gynecology
Rh isoimmunization

University Of Fallujah
College Of Medicine

Lecture : 8

Stage : 4th Year

Lecturer : Assistant Professor/ Rasha shakir

Department: obstetrics and Gynecology

Date: 2|12|2025

Learning objectives

1. How to follow up Rh negative in pregnancy.
2. Understanding the managements og Rh isoimmunization in both sensitized and non sensitized female.
3. Know the pathophysiology behind Rh isoimmunization.
4. Know the pathophysiological changes and managements of ABO incompatibility.

Rhesus iso-immunization and ABO incompatibility

Blood group is defined in two ways:

ABO group: four different blood group (O, A, B, AB).

The rhesus system: which consists of C, D, E, c, d, e antigens.

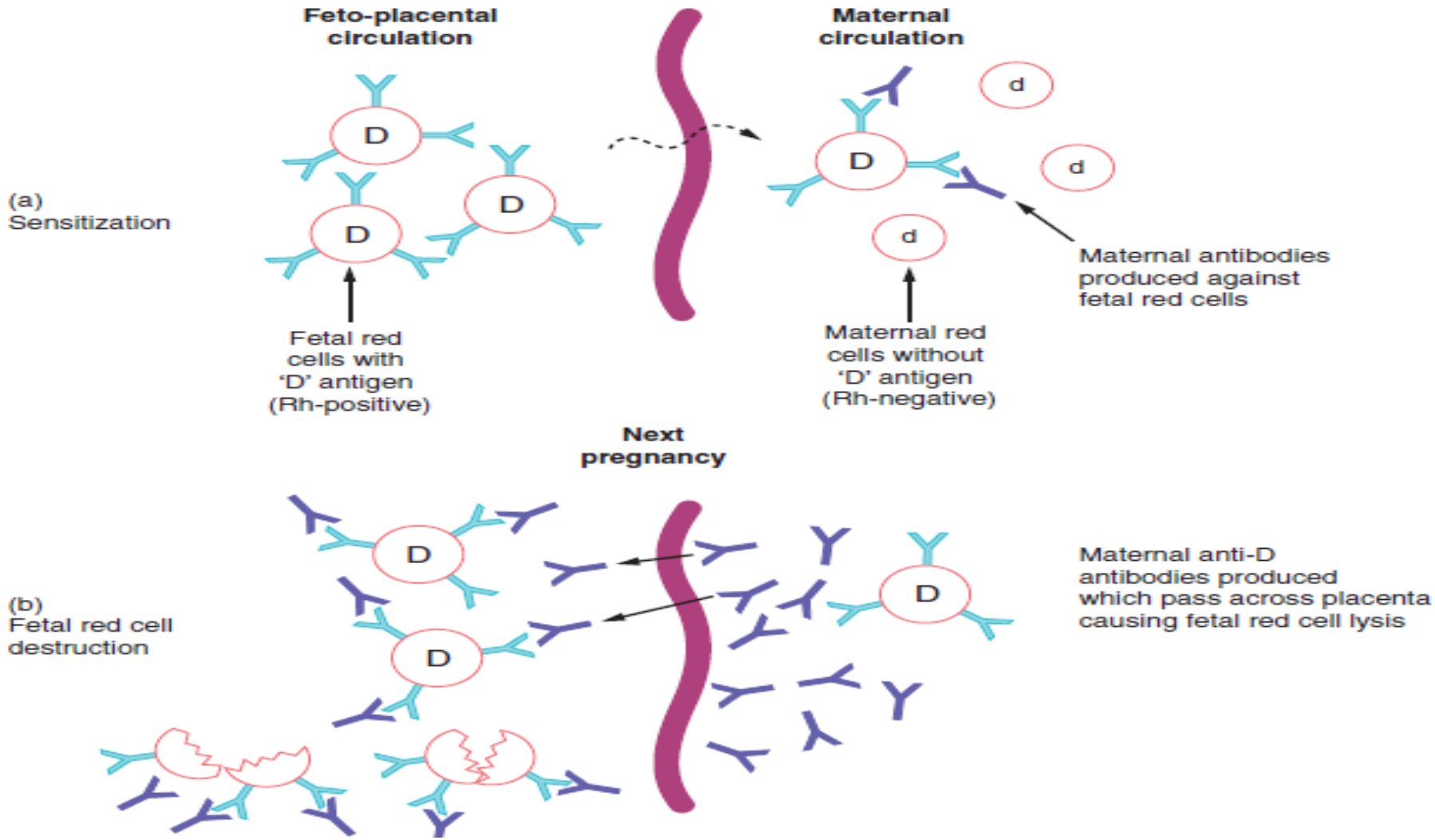
The Rhesus system

- The Rhesus system is coded on two adjacent genes (on chromosome number one). One gene codes for antigen polypeptides C/c and E/e while the other codes for the D polypeptide. little d antigen has not been identified so it may be that women who are D negative lack the antigen altogether, as opposed to those with little c and little e, where c is the allelic antigen of C and e is the allelic antigen of E.

- Antigen expression is usually dominant, whereas those who have a negative phenotype are either homozygous for the recessive allele or have a deletion of that gene.
- A person who lacks the D antigen on the surface of the red blood cells is regarded as being “RhD-negative,” and an individual with the D antigen is considered to be “RhD-positive.”

Rhesus iso-immunization:

- is an immunologic disorder that occurs in a pregnant, Rh-negative woman who is carrying Rh-positive fetus (the father should be RH positive). The fetal cells cross the placental barrier into the maternal circulation to produce antibodies to the Rh antigen, which then cross the placenta into the fetal circulation and attack fetal Rh-positive red cells, resulting in their destruction in the spleen and eventually haemolysis of fetal red cell. If the hemolysis is untreated, it will result in severe extramedullary hematopoiesis, and the progressive development of in utero heart failure and hydrops fetalis.


Feto-placental circulation
Maternal circulation
(a)
Sensitization
D
D
D
d
d
d
Fetal red cells with 'D' antigen (Rh-positive)
Maternal red cells without 'D' antigen (Rh-negative)
Maternal antibodies produced against fetal red cells
Next pregnancy
(b)
Fetal red cell destruction
D
D
D
Maternal anti-D antibodies produced which pass across placenta causing fetal red cell lysis

- Rhesus disease does not affect a first pregnancy as the primary response is usually weak and consists primarily of IgM antibodies that do not cross the placenta because of their large molecular weight. Thereafter IgG antibodies are produced and these can cross the placenta because of their small molecular weight, so in a subsequent pregnancy, when maternal resensitization occurs, the IgG antibodies cross from the mother to the fetal circulation. If these antibodies are present in sufficient quantities, fetal haemolysis may occur.

Potential sensitizing events for Rhesus disease

The fetal and maternal circulations are normally separated by the placental barrier. Most cases of sensitization are caused by a placental leak of fetal red blood cells into the maternal circulation (fetomaternal hemorrhage) during pregnancy, most common sensitizing events include:

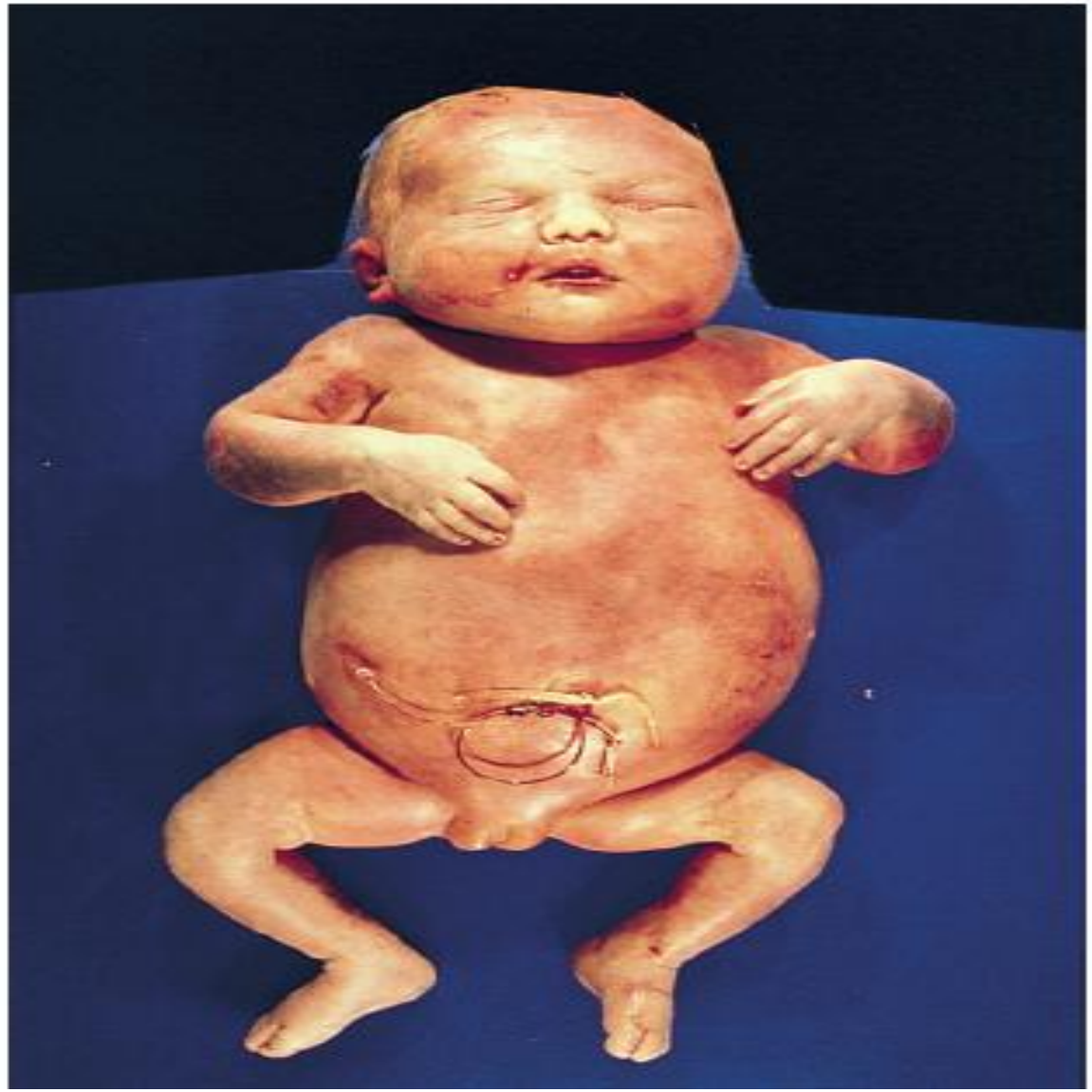
- Delivery
- Miscarriage
- Termination of pregnancy
- Antepartum haemorrhage
- Invasive prenatal testing (chorion villus sampling, amniocentesis and cordocentesis)

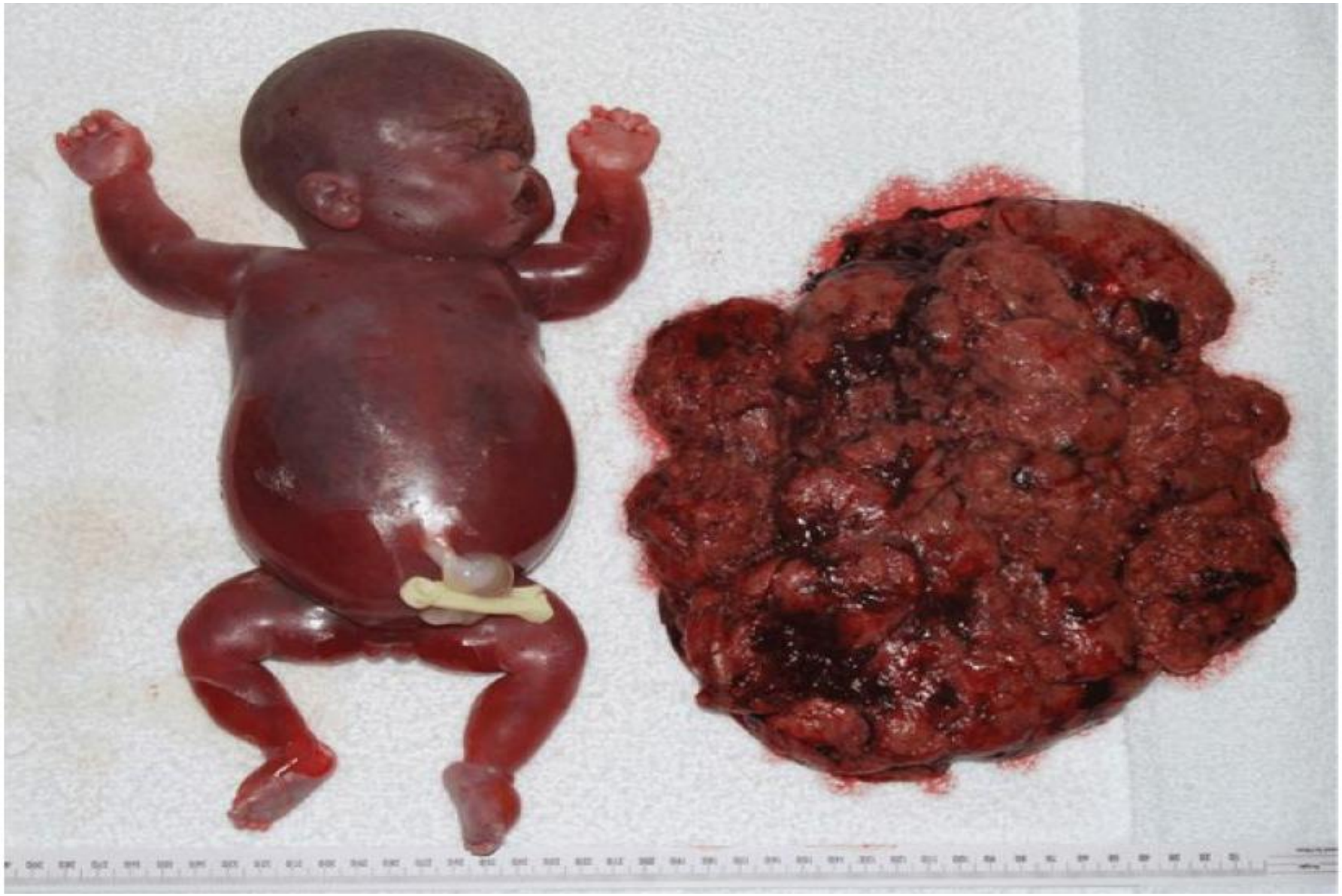
hydrops fetalis:

the older term erythroblastosis fetalis. Clinical and ultrasound features of fetal anaemia do not usually not obvious unless the fetal haemoglobin is less than 6 g/dL. In the setting of Rh alloimmunization hydrops fetalis

it is characterized by the presence of:

- fetal ascites, pericardial effusion, pleural effusion, subcutaneous edema.
- polyhydramnios.
- Hyperdynamic fetal circulation (can be detected by Doppler ultrasound by measuring increased velocities in the middle cerebral artery).
- Reduced fetal movements and abnormal CTG with reduced variability.
- early ultrasonic signs are an increase in the size and thickness of the placenta and fetal hepatomegaly





Prevalence of Rhesus disease

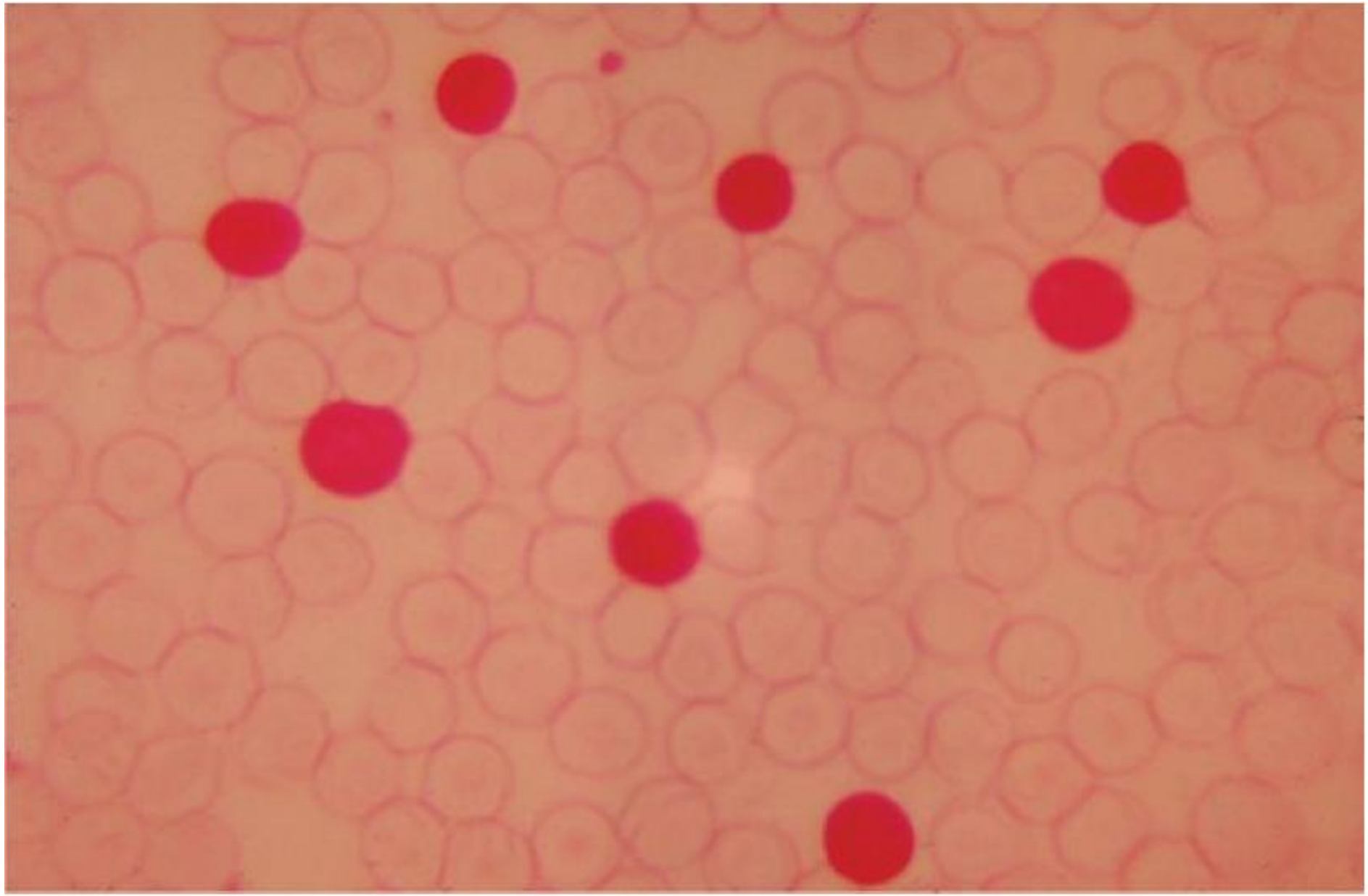
The prevalence of D Rhesus negativity is 15 per cent in the Caucasian population, but lower in all other ethnic groups. Rhesus disease is most common in countries where anti-D prophylaxis is not widespread.

Preventing Rhesus iso-immunization

- The process of iso-immunization can be prevented by the intramuscular administration of anti-D immunoglobulins to a mother, preferably within 72 hours of delivery or exposure to fetal red cells.
- Anti-D is given only as prophylaxis and is useless once sensitization has occurred.

- Anti-D immunoglobulins will distract any circulating rhesus-positive cells before an immune response is excited in the mother.
- The exact dose of the anti D is determined by the gestation at which sensitization has occurred and the size of the fetomaternal haemorrhage. In the first trimester of pregnancy, because the volume of fetal blood is so small, it is unlikely that sensitization would occur, and a ‘standard’ dose of anti-D is given. In the second and third trimesters, fetal blood volume is greater a larger dose is given.

A Kleihauer test: is a test of maternal blood to determine the proportion of fetal cells present and hence the dose of anti D required. It is dependent on the fact that adult hemoglobin is more readily eluted through the cell membrane in the presence of acid or alcohol than is fetal hemoglobin which resist denaturation by alcohol or acid.



the anti D prophylaxis during pregnancy without sensitizing event:

Rhesus-negative women are routinely given a single dose of anti-D at 28 weeks or two dose at 28 and 34 weeks. This is based on the finding that a small number of Rhesus negative women become sensitized during pregnancy despite the administration of anti-D at delivery and without a clinically obvious sensitizing event.

The management of Rhesus disease in a sensitized woman

- Once a woman who is D Rhesus negative has been sensitized to the D Rhesus antigen, the anti-D will ever be of benefit and in a subsequent pregnancy, close surveillance is required. Rhesus disease gets worse with successive pregnancies.

- If the father is RhD-positive, his Rh genotype should be determined using polymerase chain reaction. If he is homozygous for the D antigen, the fetus will be RhD-positive and potentially affected. In this case, the pregnancy must be monitored closely for hemolytic disease. If the father is heterozygous, the fetus has a 50% chance of being RhD-positive, indicating the need for fetal RhD genotyping. If it is not possible to test the D antigen status and zygosity of the father, it must be assumed that he is D antigen–positive.

- In a sensitized woman, with RH positive father, management involves monitoring antibody titre every 2–4 weeks from booking.
- If the antibody titre < 4 IU/mL haemolytic disease is unlikely, 4–15 IU/mL there is a moderate risk of haemolysis, >15 IU/mL High risk of haemolysis (hydrops fetalis).

- If antibody levels rise, the baby should be examined for signs of anaemia. In the past, the bilirubin concentration of amniotic fluid was determined to give an indirect measure of fetal haemolysis. This involved an invasive procedure with the attendant risks of miscarriage/preterm labour and further boosting of the alloimmune response. In the last decade, middle cerebral artery (MCA) Dopplers (peak velocity measurement) have been shown to correlate reliably with fetal anaemia and it is non-invasive assessment.

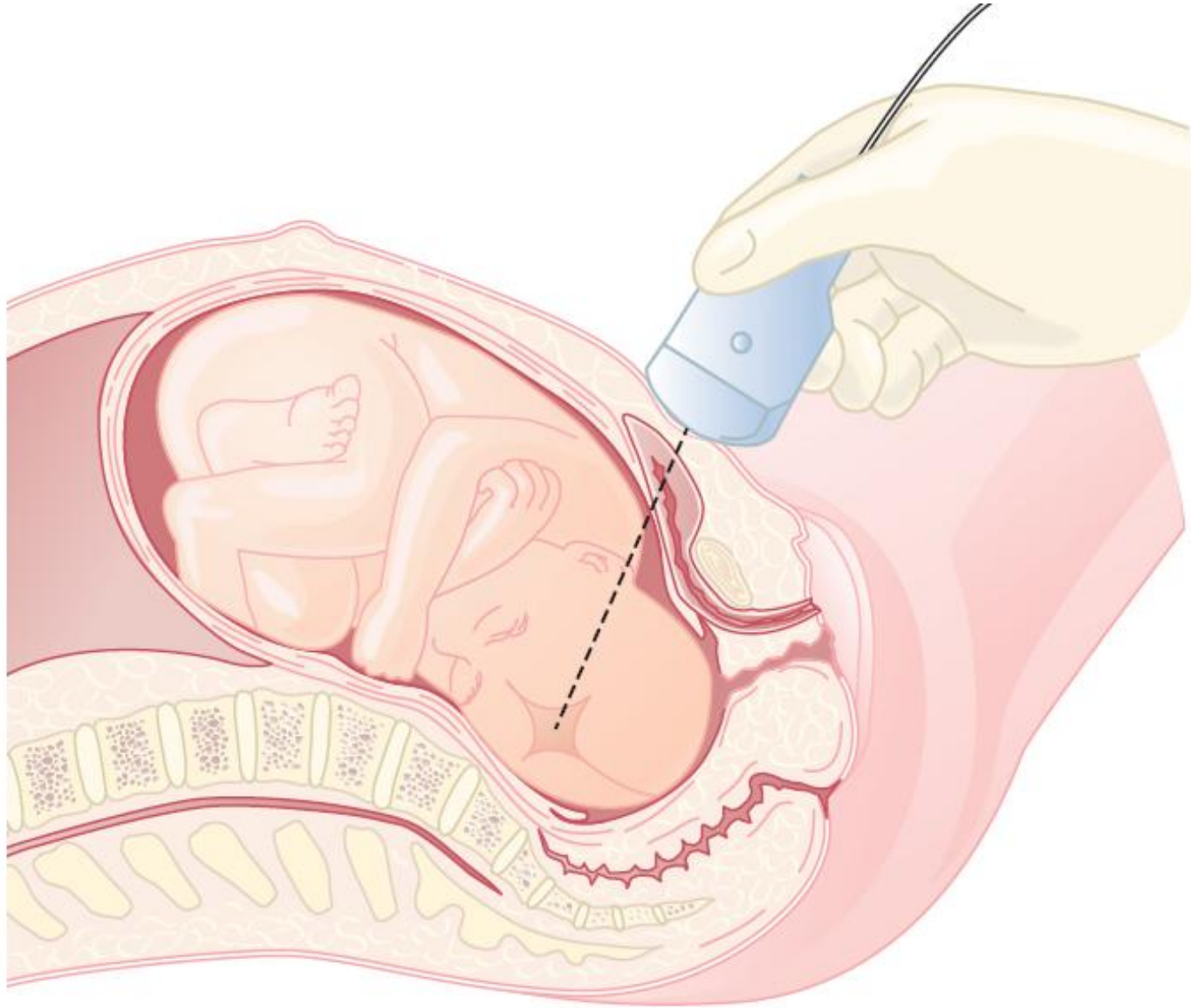


FIGURE 15-3 Obtaining a middle cerebral artery Doppler peak systolic velocity.

- A fetus with raised MCA Dopplers has a high probability of anaemia. Treatment options include delivery or fetal blood transfusion. Delivery of the fetus is an option if the fetus is sufficiently mature.

- **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. Blood can be transfused into a fetus in various ways including the umbilical vein, 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 low gestations); and lastly into the fetal heart. Transfused blood should be RhD negative, crossmatched with a maternal sample, densely packed (Hb usually around 30 g/L) so that small volumes are used; white cell depleted, irradiated; and screened for infection including CMV.

ABO

- ABO blood group iso-immunization may occur when the mother is blood group O and the baby is blood group A or B.
- Anti-A and anti-B antibodies are present in the maternal circulation naturally, in this situation, anti-A or anti-B antibodies may pass to the fetal circulation, causing fetal haemolysis and anaemia.

- ABO incompatibility may occur in a first pregnancy. However, most anti-A and anti-B are mainly IgM and do not cross the placenta. In addition, A and B antigens are not fully developed in the fetus. Therefore, ABO incompatibility generally causes only mild haemolytic disease of the baby and its severity does not increase with subsequent pregnancy, but may sometimes explain unexpected jaundice in an otherwise healthy term infant.