HEMOLYTIC DISEASE OF NEWBORN

PREPARED BY:

LAU SHOW XUAN (101841)

NUR IZZATUL AKMAL (101276)

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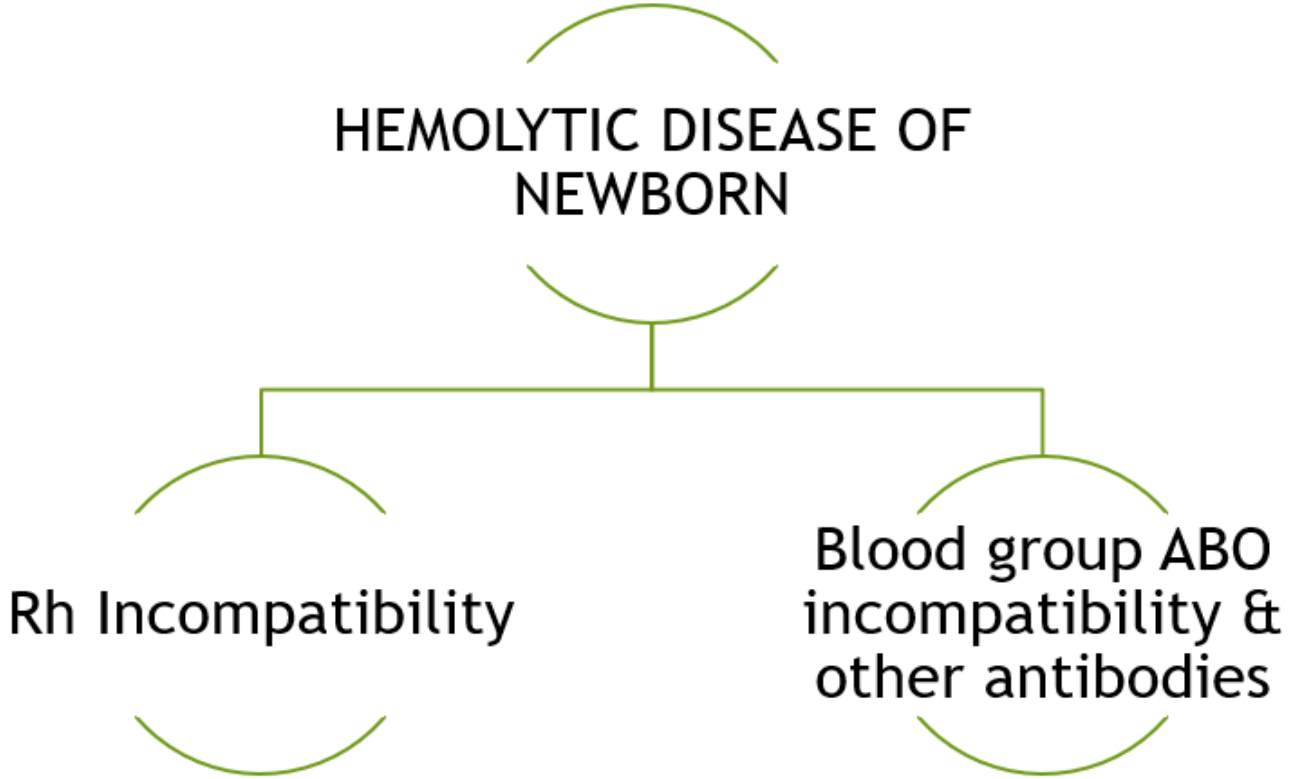
1. INTRODUCTION

- Hemolytic disease of newborn (HDN) is the destruction of newborn red blood cells (RBCs) by antibodies produced by mother.
- HDN is caused by the transplacental passage of maternal antibodies against paternal RBC antigens of the newborn.
- The maternal IgG antibody is transported across the placenta and coated the fetal RBCs which lead to the RBCs destructions by fetal spleen.
- The fetal bone marrow will then respond by increasing the erythropoiesis and releasing the newly produced RBCs which lead to the term “erythroblastosis fetalis”.
- HDN is characterized by an increased rate of RBCs destruction and causing the anemia and jaundice of newborn infant.

2. TYPES OF HEMOLYTIC DISEASE OF NEWBORN



3. PATHOGENESIS OF HDN

3.1 Rh incompatibility

3.2 Blood group ABO incompatibility and other antibodies

3.1 Rh incompatibility

- Rh antigenic determinants are genetically transmitted from each parent, determine Rh type, and direct the production of a number of blood group factors (C, c, D, d, E and e).

- Each factor can elicit a specific antibody response under suitable conditions; 90% are due to D antigen and the remainder to C or E.

- When a mother with Rh-negative blood becomes pregnant with Rh-positive baby which is inherited from Rh-positive father entered the maternal circulation during pregnancy, either with spontaneous or induced abortion, or at delivery - antibody formation against D antigen may be induced in the unsensitized Rh-negative recipient mother.

- Once sensitization has taken place, considerably smaller doses of antigen can stimulate an increase in antibody titer.

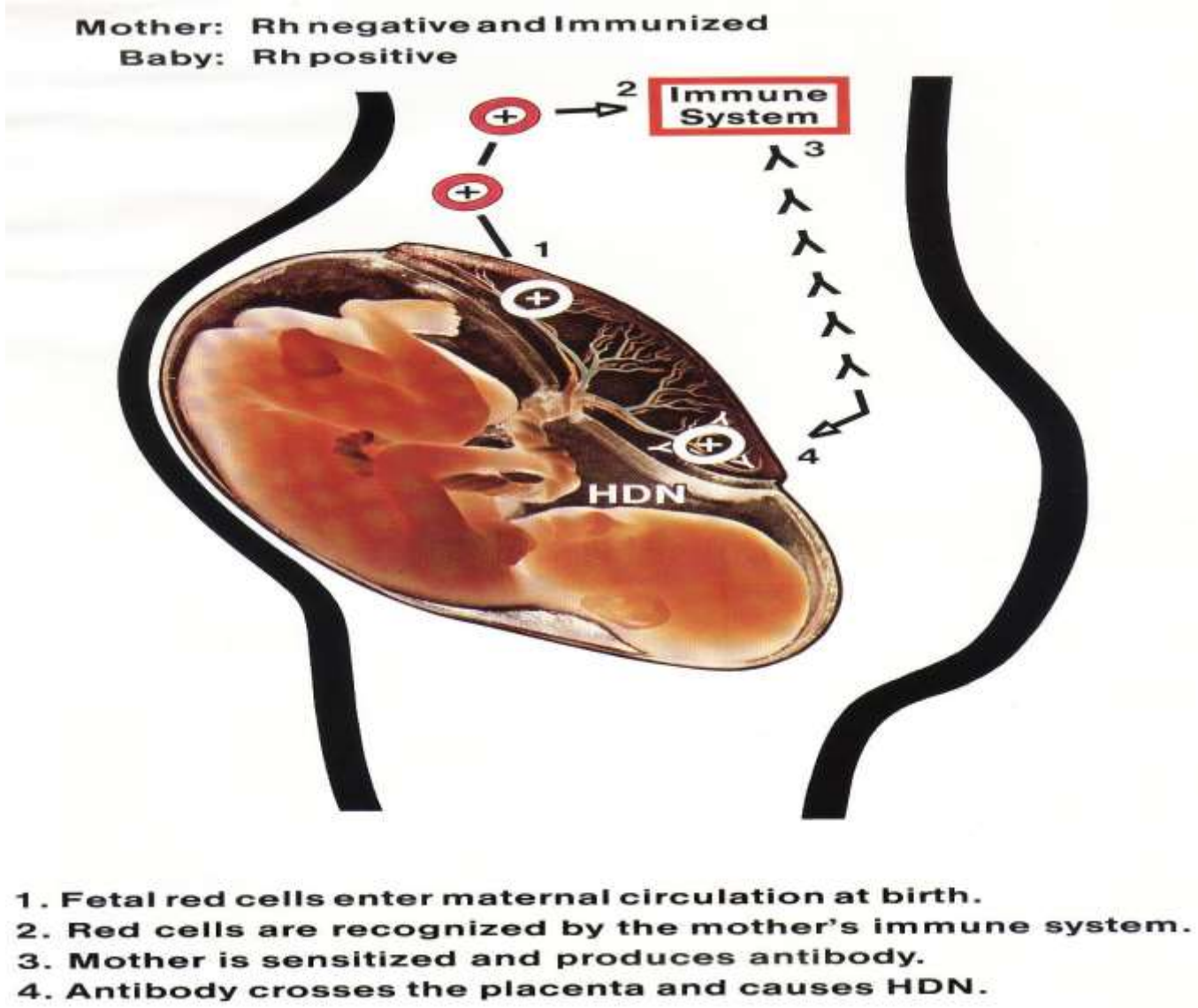


Figure 1: Mechanism of transplacental passage of maternal antibodies against paternal RBC antigens of the newborn.

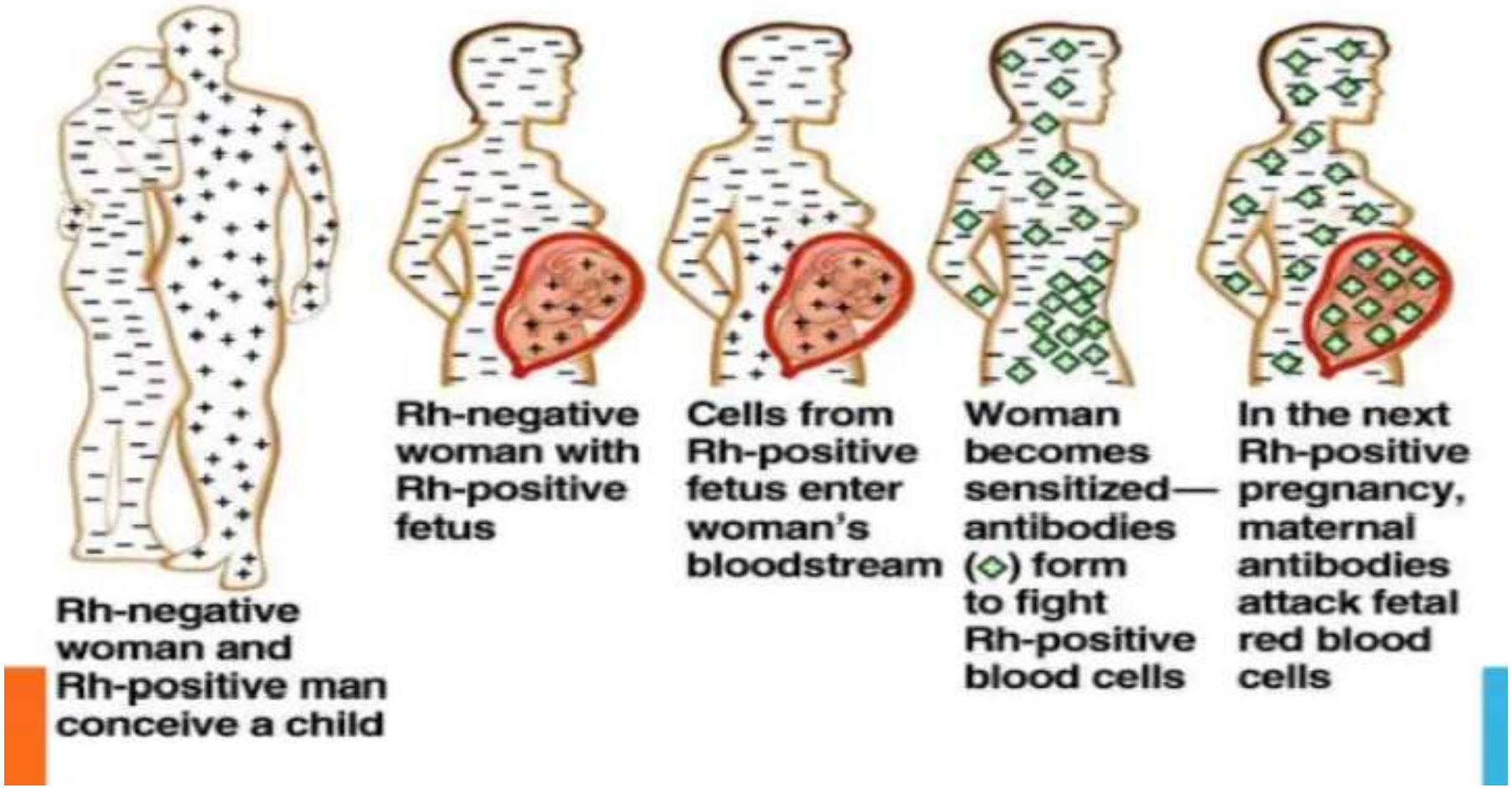


Figure 2: Pathophysiology of HDN

- Under normal circumstances, the process if alloimmunization has no effect on fetus during the first pregnancy with Rh positive fetus, because the Rh sensitization is unlikely to occur before the onset of labour in a first pregnancy.

- However, the increased risk of fetal blood being transferred to the maternal circulation during placental separation, maternal antibody produced is stimulated.

- During a subsequent pregnancy with Rh positive fetus, these previously formed maternal antibodies to Rh positive blood cells enters the fetal circulation, where they attached to and destroy the fetal erythrocytes.

- Multiple gestations, abruption placenta, placenta previa, manual removal of placenta and caesarean delivery increase the risk of transplacental haemorrhage and subsequent alloimmunization.

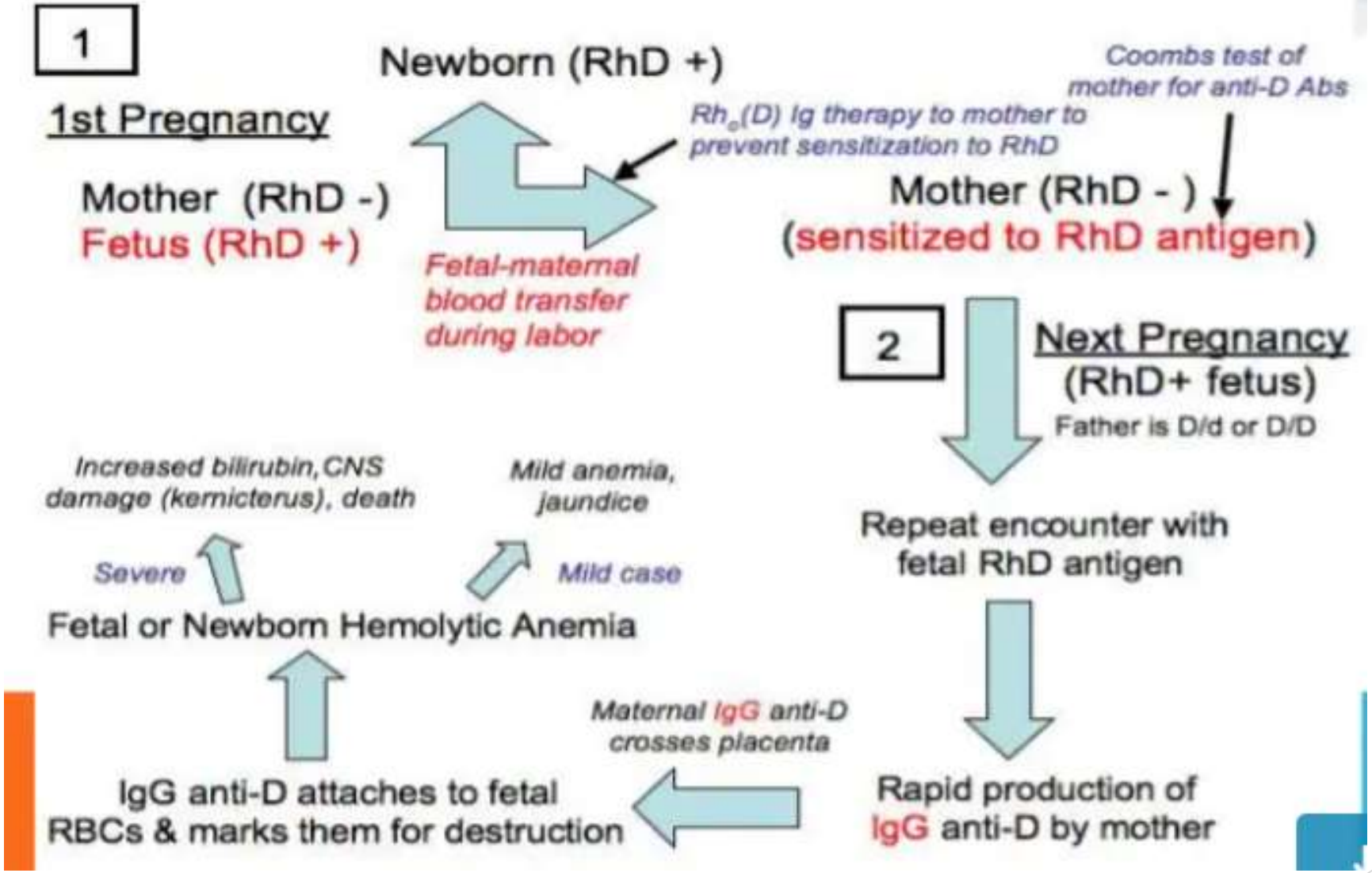


Figure 3: Mechanism of HDN for first and subsequent pregnancy.

3. PATHOGENESIS OF HDN

3.1 Rh incompatibility

3.2 Blood group ABO incompatibility and other antibodies

3.2 Blood group ABO incompatibility and other antibodies

ABO incompatibility

- The most common cause of HDN after Rh incompatibility.
- Milder disease than Rh incompatibility
- Usually the mother is type O and the infant is type A or B.
- Naturally occurring A, B IgG antibodies in typ O mother are then transported across the placenta and bind to fetal RBCs which expressed A or B antigens cause the destruction of RBCs.
- The hemolytic effect of ABO incompatibility is minimal probably due to still poorly developed of fetal ABO antigens.
- The disease is not necessarily associated with positive direct coombs test (DAT) or positive anti-A, anti-B, anti-AB during elution test although in severe disease the DAT is nearly always positive.

Other antibodies- Kell antibody

- Kell antibodies (Anti-K) found in 1/1000 pregnant women
- Anti-K usually IgG therefore it is among the antibodies that can transport across the placenta and bind to the fetal RBCs causing HDN during pregnancy.
- It can cause severe HDN when immunization is due to previous pregnancy.
- Anti-K can cause lower concentration of amniotic fluid bilirubin than anti-D HDN
- Lower levels of reticulocytes, bilirubin, erythroblasts in anti-K newborn compared to anti-D associates cases.

4. CLINICAL MANIFESTATIONS

The severity of disease varies from the degree of agglutination and destruction of fetal red cells, the four major clinical symptoms for the haemolytic disease of newborn including:

1. **Hydrops fetalis**

- The most serious form of Rh haemolytic disease
- Abnormal accumulation of fluid with ascites, pleural and pericardial effusions

2. **Congenital anemia of newborn**

- The destructed RBCs are removed from fetal circulation by macrophages of the spleen and liver which lead to anemia, limits the ability of the blood to carry oxygen to baby's organs and tissues.

3. **Hepatosplenomegaly**

- Due to the haemolysis, the fetal bone marrow and other haematopoietic tissues in the spleen and liver increase the amount of RBCs production, causing the enlargement of organ.

4. **Hyperbilirubinemia**

- As the RBCs break down, the bilirubin is formed and accumulated in the bod tissues and fluid result in jaundice.
- The unconjugated bilirubin increasing and crossing the blood brain barrier and causing kernicterus.

5. LABORATORY FINDINGS

- **Biochemical test:**

A. Progressive severe hyperbilirubinemia or prolonged hyperbilirubinemia (neonatal bilirubin is generally between 3 and 5 mg/dL).

B. Hypoglycemia: due to islet cell hyperplasia and hyperinsulinism, release of metabolic byproducts such as glutathione from lysed RBCs.

C. LDH : increase

D. Haptoglobin : decrease

- **Hematology test (FBC):**

A. Hemoglobin: low (depends on the severity of disease)
B. MCV, MCH, MCHC: normal or increase
C. Platelets: normal to decrease
D. Neutropenia
E. Increase nucleated RBCs, reticulocytosis (6%-40%), polychromasia, anisocytosis, spherocytes and cell fragmentation

- **Blood banking test:**

A. Direct coombs test: positive (newborn)
B. Antibodies screening test : positive (mother)
C. Antibodies identification : positive anti-K

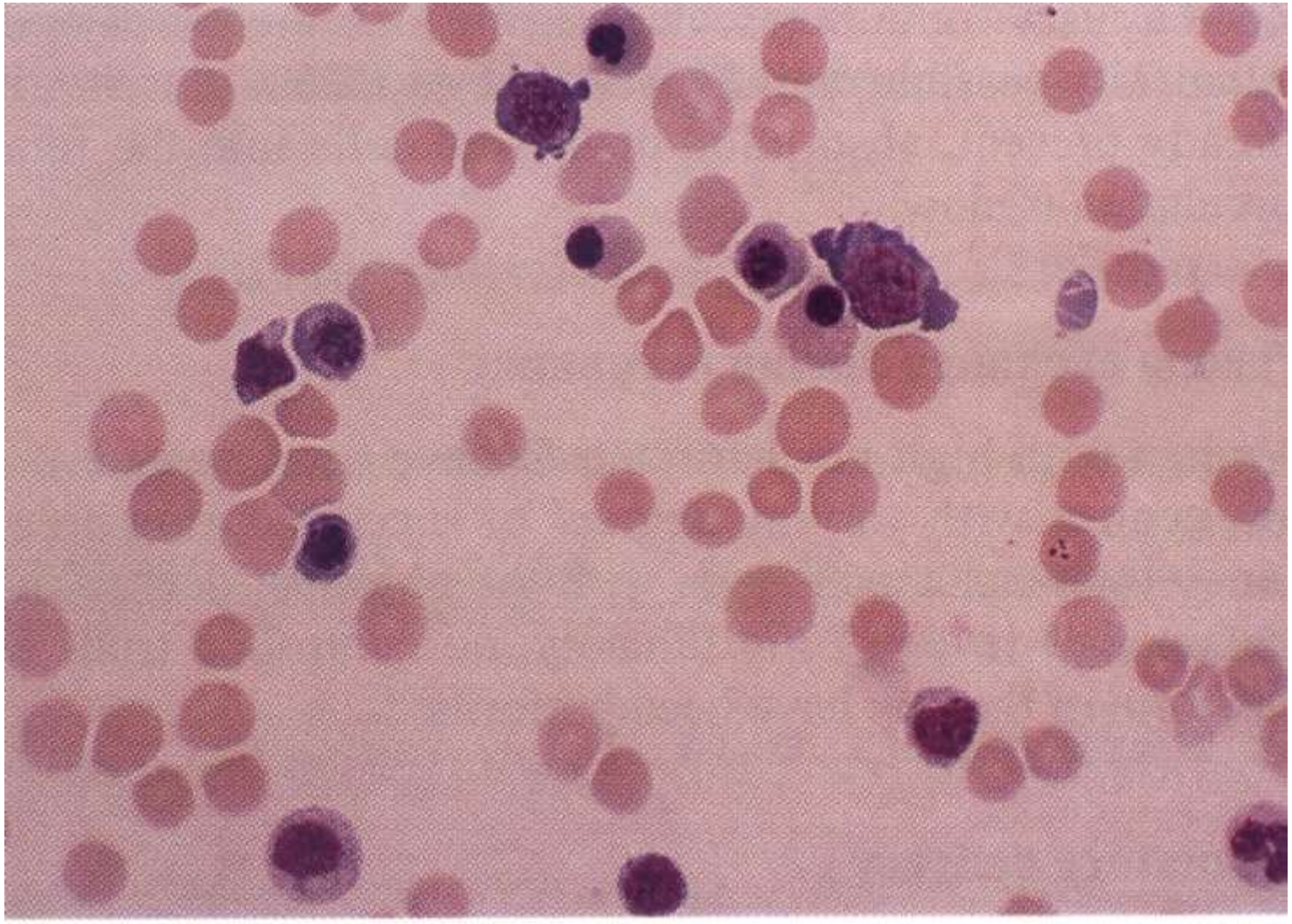
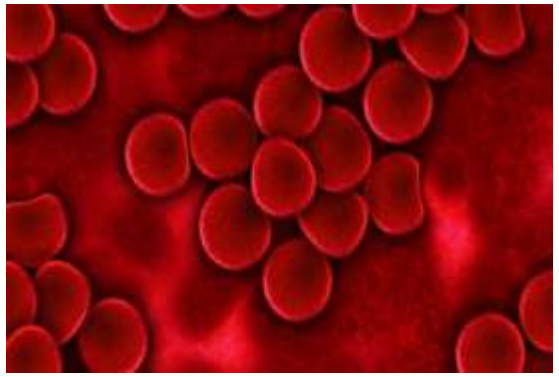


Figure 4: Blood film of a fetus affected by HDN showing polychromasia and increased number of normoblasts and reticulocytes.

LABORATORY FINDINGS

Peripheral blood film shows significant amount of nucleated red cells, polychromasia and anisopoikilocytosis.



high reading for the fetal serum bilirubin and nucleated red cells but with low reading for fetal heamoglobin.

positive DAT due to the mother's antibody sensitized on the fetus red cells.

6. DIAGNOSIS

- In Rh-negative women, a history of previous transfusions, abortion, or pregnancy should suggest the possibility of sensitization.
- Expectant parents' blood types should be tested for potential incompatibility, antibodies identification for positive antibodies' mother and the maternal titer of IgG antibodies to D antigen should be assayed at 12-16, 28-32, and 36 week.
- Ultrasonographically guided trans-abdominal aspiration of amniotic fluid may be performed as early as 18-20 week of gestation.
- Amniocentesis and cordocentesis can also be used for early detection of HDN.

7. TREATMENT AND MANAGEMENT

For mother (Antenatal)

Rh negative mothers which pregnant with a Rh positive infant are given:

- Rh immunoglobulin (RhIG)- to prevent sensitization to D antigen and protects against the effects of early transplacental hemorrhage.
  - at 28 weeks during pregnancy
  - At 34 weeks during pregnancy
- Close monitoring of fetus as reflected by Rh titers,amniocentesis and sonography results.

For mother (Postnatal)

Rh negative mothers with Rh positive infant:

- Injection of RhoGAM must be given within 72 hours of delivery of the newborn.

For fetus before birth (Antenatal)

- Intrauterine transfusion (IUT)
  - Blood are infused into abdominal cavity of fetus and then absorbed into fetal circulation
  - In IUT, a needle is passed through the mother's abdomen and into the abdomen of fetus by the aided of ultrasound image to determine the position of the fetus and placenta.
  - Can be done as early as 17 weeks

- Early induction of labour when
  - Pulmonary maturity
  - Fetal distress is present
  - 35 to 37 weeks of gestation have passed.

For newborn after birth (Postnatal)

The treatment is depends on the severity of disease:

- Phototherapy - for hyperbilirunemia
- Transfusion with compatible packed RBCs - for newborn anaemia
- Exchange transfusion -for newborn who has a high risk of rapid development of severe anaemia (Hgb:≤10g/dl) or hyperbilirubinemia (bilirubin:≥5mg/dl) suggest severe haemolysis.

For newborn with anti K-HDN

- No correlation between antibody titer and degree of inhibition
- Newborn with Kell HDN requires less phototherapy and exchange transfusions
- Because of the destruction of red cell precursors, treatment with erythropoietin maybe more effective in newborn with anti-K HDN than Rh HDN.

8. CONCLUSION

- Hemolytic disease of newborn occurs when IgG antibodies produced by the mothers against the corresponding antigen which is absent in mother, and crosses the placenta and destroy the RBCs of the fetus.

- Proper early management of HDN will save the lives of a child and future pregnancies.

9. REFERENCES

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