Erythroblastosis Fetalis

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INTRODUCTION

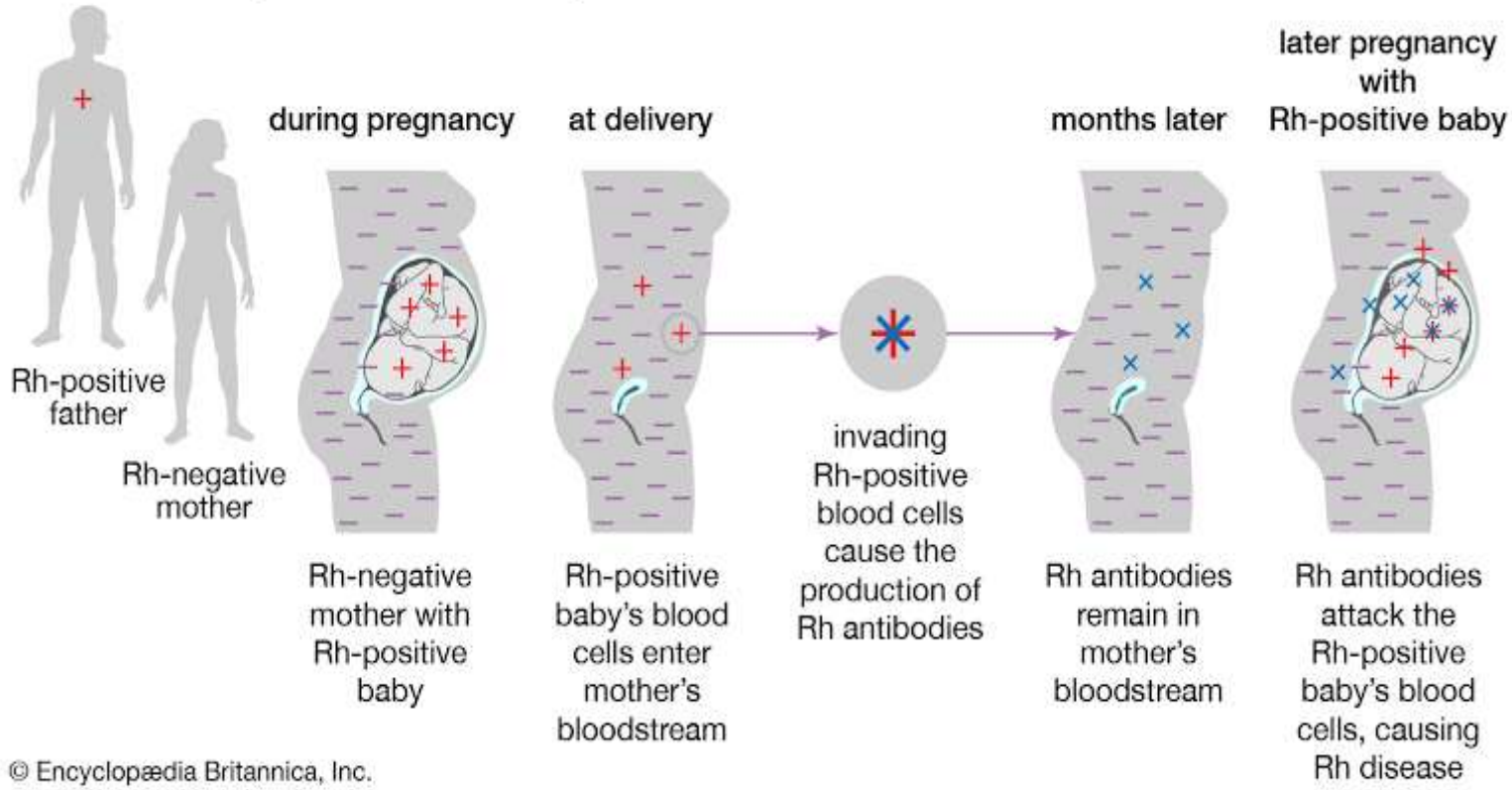
- **Erythroblastosis fetalis** is hemolytic anemia in fetus, in which the red blood cells (erythrocytes) of a fetus are destroyed in a maternal immune reaction resulting from a blood group incompatibility between the fetus and its mother.
- It is TYPE II hypersensitivity reaction, where antibody is directed against antigen on cells (such as circulating red blood cells) or extracellular materials (basement membrane). The resulting Ag-Ab complexes activate complement (via the classic pathway), leading to cell lysis or extracellular tissue damage.
- In Erythroblastosis fetalis: maternal IgG crosses the placenta and attaches to fetal RBC's.

- Two blood group systems, Rh and ABO, primarily are associated with erythroblastosis fetalis. The Rh system is responsible for the most severe form of the disease, which can occur when an Rh-negative woman (a woman whose blood cells lack the Rh factor) conceives an Rh-positive fetus. Sensitization of the mother's immune system (immunization) occurs when fetal red blood cells that carry the Rh factor (an antigen in this context) cross the placental barrier and enter the mother's bloodstream. They stimulate the production of antibodies, some of which pass across the placenta into fetal circulation and lyse, or break apart, the red blood cells of the fetus (hemolysis).

- It is rare for a mother to become sensitized during the course of her first Rh-positive pregnancybecause the amount of fetal Rh antigen that enters maternal circulation is insufficient to cause sensitization; usually only during labour will exposure be significant. However, because Rh sensitivity is likely to develop during labour, the risk of the disease developing in subsequent Rh-positive (containing D antigens) pregnancies increases. The risk can be reduced if the mother receives injections of Rh immunoglobulin, which destroys fetal red blood cells in her bloodstream, during her first pregnancy. The fetus also is protected from Rh hemolytic disease if an ABO blood group incompatibility exists concurrently; protection is conferred by ABO antibodies, which destroy fetal blood cells in the maternal circulation before the mother develops Rh sensitivity. Fetal-maternal incompatibilities within the ABO blood group alone are more common than those of the Rh type, but the immune reaction is usually much less severe, unless the fetus is type A and the mother type O.

- The severity of erythroblastosis fetalis varies depending on the degree of hemolysis. Symptoms include anemia, with the presence of many immature red blood cells (erythroblasts) in the circulation; jaundice, resulting from a buildup of bilirubin (a breakdown product of hemoglobinfrom red blood cells); and an enlarged liver and spleen. In its mildest form, the disease manifests only as slight anemia with no other complications; in its most extreme form, the fetus dies in utero. Hydrops fetalis, which is characterized by extreme edema (abnormal accumulation of serous fluid) and congestive heart failure, is the most severe form of the disease in newborns. Usually the infant dies, unless an exchange transfusion in which the Rh-positive blood of the infant is replaced by Rh-negative blood is successful. A complication of erythroblastosis fetalis is kernicterus, which is caused by deposition of bilirubin in the brain. Hearing loss, mental retardation, or death may result. Nevertheless, many procedures are available to avert these consequences. If it is determined that the fetus is at risk for erythroblastosis fetalis, amniocentesis can be used to measure bilirubin concentrations and predict the severity of the disease. If levels are elevated, intrauterine transfusions of Rh-negative blood can be given until premature delivery can be induced. These measures, together with the use of Rh immunoglobulin, have almost eliminated the incidence of erythroblastosis fetalis in developed countries.

How Rh hemolytic disease develops



- During a first pregnancy with an Rh^+ child, there are usually few problems related to the blood type disparity.
- With the first pregnancy, the mother will be exposed to the D protein(Antigen due to Rh+ factor) for the first time. During the pregnancy itself, little fetal blood makes it into the mother's system and there is generally no problem. However, at labor and delivery, there is significant exposure of the mother's system and the fetal blood. This exposure will cause the mother to make antibodies directed against the D protein. Since the baby has been born by the time this occurs to any major extent, neither mother or child are affected adversely.

- With the second pregnancy, the mother's body had already started making antibodies and has a memory cell for those antibodies in "storage". A nice thing about the immune system is that the second time we are exposed to a foreign protein, the immune response is much more sensitive (i.e. it takes less exposure), much stronger (more antibodies will be produced) and much quicker. With the second pregnancy, the little bit of fetal blood that enters the maternal system is sufficient to produce an immune response (since the Mom's immune system has memory cells in storage), and antibodies to the D protein begin to attack the fetal RBC's. This results in *erythroblastosis fetalis.*

Treatment

- Erythroblastosis fetalis can be prevented by injecting the mother with a substance called "rho-gam" (the antibodies against the D protein) after each exposure. This appears to work by "fooling" the mother's immune system into believing that a memory cell for the Anti-D has already been created. Therefore, the next time the mother is exposed to the D antigen, her body does not have the memory cell available to start rapidly producing the antibodies and it behaves as if this were the first exposure. As noted above, this must be repeated with each exposure (pregnancy).

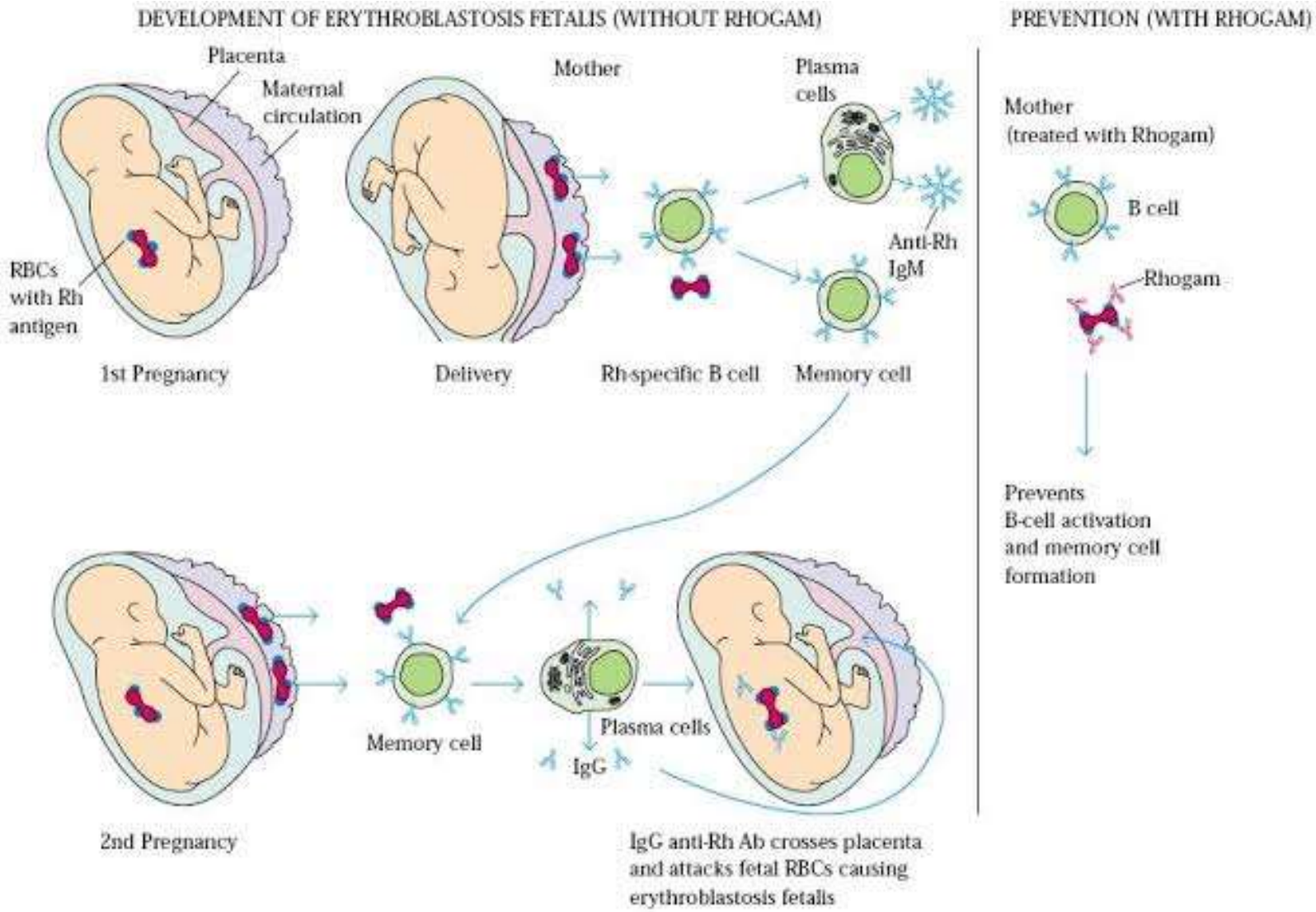


FIGURE 16-14 Development of erythroblastosis fetalis (hemolytic disease of the newborn) caused when an Rh^- mother carries an Rh^+ fetus (*left*), and effect of treatment with anti-Rh antibody, or Rhogam (*right*).

SYNOPSIS

- Erythroblastosis fetalis is the destruction of an Rh+ infant's erythrocytes by maternal antibodies against the D protein.
- Unless the Rh- mother has received a transfusion in the past, the first Rh+ baby born is safe because the mother is typically exposed to significant fetal blood during delivery.
- Once exposed, the mother generates antibodies against the D protein.
- Future pregnancies in which the fetus is Rh+ are complicated by the fetal hemolysis produced by maternal antibodies against the D protein.
- If the neonate requires transfusions, Rh- blood is given. The Rh+ fetus does not recognize the absence of the D protein and the maternal antibodies find nothing to react with. Thus, the oxygen carrying capacity of the infant is preserved.
- Rho-gam (anti-D) prevents the mother from developing the memory cells and allow future pregnancies to proceed normally. It is injected after each exposure to the Rh protein.
- Similar reactions (but resulting from different antigens) produces hemolytic disease of the newborn

THANK YOU