

## Erythroblastosis fetalis produced by Kell immunization: dental findings

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### Abstract

*Erythroblastosis fetalis is a severe hemolytic disease in the newborn that originates in utero because of a maternal-fetal blood incompatibility. An unusual case of erythroblastosis fetalis caused by an irregular antibody of the Kell blood group is presented. The dental findings are compared to those found with Rh(D) incompatibility.*

### Introduction

Erythroblastosis fetalis is a term used to describe the hemolytic anemia of newborns caused by a blood incompatibility between the mother and fetus. The immunological basis of the disease was recognized following red cell agglutination studies (Levine et al. 1941). The dental findings include developmental enamel defects of varying degree. This paper reports an unusual type of blood incompatibility resulting in severe erythroblastosis fetalis, and the dental findings.

### Clinical Manifestations

Erythroblastosis fetalis results from hemolysis of fetal red cells due to a maternal-fetal antibody-antigen reaction. The most common cause is an Rh(D) incompatibility. Since the development of anti-Rh(D) immunoglobulin in the mid-1960s, erythroblastosis fetalis generally has been prevented (Beal 1979; Dornan 1982). However, other types of blood antibodies, called "irregular" antibodies, cause the same destruction of red cells as the Rh(D) antibodies (Giblett 1964). The Kell System is the most potent irregular antibody, although it is relatively rare (Giblett 1964, Smith et al. 1967; Pepperell et al. 1977).

The pathogenesis of anti-Kell erythroblastosis fetalis is identical to that caused by anti-Rh(D) (Schellong et al. 1976). In utero, the maternal antibodies coat the fetal red cells and cause hemolysis. The fetus develops anemia with a resultant increase in the bilirubin content of the amniotic fluid (Bowman 1986). The fetus compensates with extramedullary erythropoiesis, particularly by the

liver, spleen and kidneys (Bowman 1984). Hence, the term erythroblastosis fetalis is used to describe this condition.

The newborn with severe disease appears pale and anemic, and presents with hepatosplenomegaly, edema, and ascites (Bowman 1984). Shortly after birth, jaundice occurs as a result of the high bilirubin levels. Based on this varied clinical picture, erythroblastosis fetalis also is known as icterus gravis neonatorum, anemia of the newborn, generalized edema of the newborn, hydrops fetalis, and hemolytic disease of the newborn (Phibbs 1987). The occurrence rate is 1:100 births, although the majority are considered mild to moderate (Giblett 1964).

In the past, there was a high correlation of neurologic damage in children with erythroblastosis fetalis. The primary cause was the neurotoxic effects of untreated jaundice, referred to as kernicterus (Watson 1955). These children often have cerebral palsy, with or without mental retardation. Currently, aggressive medical treatment to control bilirubin levels in the newborn has reduced the extent of the bilirubin encephalopathy (Klemperer 1984).

Enamel defects may include hypoplasia limited to the primary dentition, or may affect the cusps of the permanent first molars (Gibson and Conchie 1964). The extent of the dental disturbance coincides with the timing of the metabolic disturbance (Gibson and Conchie 1964). Approximately 15% of the children present with teeth that are discolored due to the incorporation of biliverdin, the by-product of bilirubin, which causes jaundice (Forrester and Miller 1955; Bevis 1956). The discoloration may range from yellow to deep shades of green (Watson 1955). The degree of the enamel defects and discoloration may be mild, moderate, or severe, and are not interdependent (Watson 1955; Perlstein and Massler 1956).

## Case Report

A 3-1/2-year-old, white male with a prenatal diagnosis of erythroblastosis fetalis due to Kell incompatibility presented to the University of Detroit School of Dentistry for a dental evaluation. The child was the product of a 33-week pregnancy, complicated by a positive Coombs test and high Kell antibody titers. The mother was Kell positive as a result of fetal-maternal transplacental hemorrhage, and a mixing of blood from her third pregnancy. The three previous children were all Kell negative and in good health.

Starting at the 20th week of pregnancy, serial amniocenteses were performed every other week. At the 26th, 27th, and 28th weeks, fetal blood sampling, and intrauterine intraperitoneal fresh-packed red-blood-cell transfusions were completed with O-negative blood. The child was delivered at the 33rd week by Cesarean section and weighed 2.05 kg. Clinically, he presented with signs of severe hemolytic disease and prematurity. He was anemic, with hepatosplenomegaly and edema. He had severe jaundice caused by the high bilirubin counts. At 1 week old, he was given a blood transfusion to control the jaundice. Due to the prematurity, his ventilations were assisted by a respirator for six weeks. To prevent infection, he received gentamicin sulfate (an aminoglycoside antibiotic), and to relieve the edema, he received the diuretic furosemide. He had a patent ductus arteriosus, which closed by six weeks.

The child's current medical problems include bronchopulmonary dysplasia (BPD) and bilateral high frequency deafness. He is not taking any medications, and is enrolled in a speech therapy program. He presented within normal limits for height and weight, with normal intelligence and coordination. His speech is delayed, and he wears bilateral hearing aids.

The dental examinations revealed a primary dentition, intact except for the maxillary right primary central incisor, which had been extracted due to trauma when the child was 2 years old. The dentition had generalized spacing and a flush terminal plane. No caries was noted. There was enamel hypoplasia as follows (Figs 1 and 2):

1. Maxillary incisors — Thinning of the incisal one-third and yellow color
2. Canines — "Ring" defect of cusp tip
3. First molars — Occlusal-buccal one-third
4. Second molars — Cusp tips
5. Mandibular incisors — Thinning of incisal two-thirds
6. Canines — "Ring" defect of cusp tip
7. First molars — Occlusal table
8. Second molars — Cusp tips and occlusal table.



Fig 1. Neonatal line on mandibular primary incisors.

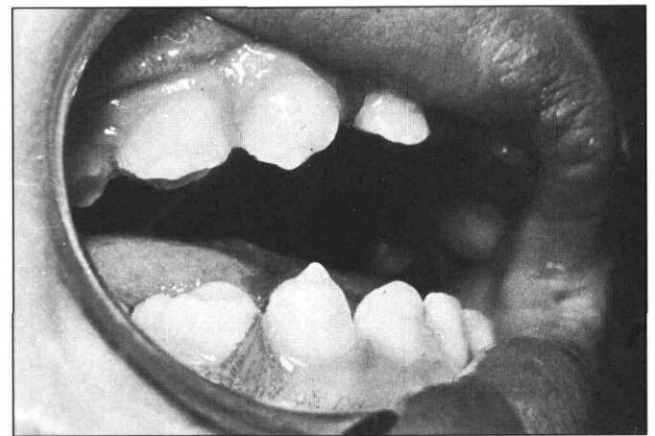


Fig 2. Enamel hypoplasia with "ring" defect on the primary maxillary and mandibular canines.

## Discussion

There are at least 21 blood groups that represent unrelated chromosomal loci, such as ABO, MNSs, P, Rh(D), Lutheran, Kell, and Kidd (Giblett 1987). In the ABO system, there are three alleles called A, B, and O, while in the Kell system, one gene is known as K (Kell) and its allele is k (Cellano). In the general white population, 9% are Kell positive, and 98% are heterozygous (Kk) (Race and Sanger 1968). The Kell system was first identified in 1946 when it produced an unexpected positive Coombs test (Coombs et al. 1946).

The antibodies produced by the maternal immune system are G immunoglobulins (IgG), which are able to cross the placenta and affect fetal blood. Maternal antibodies are Kell positive, and the fetus is Kell negative (Caine and Mueller-Heubach 1982). Kell is responsible for 0.48% of hemolytic disease in the newborn, where Rh(D) incompatibility is the cause of 82% of cases (Giblett 1964). The majority of Kell immunization is caused by the mother receiving a blood transfusion, which sensitizes her (Wenk et al. 1985). A less common

cause occurs at parturition, when "foreign" antigen crosses the placental barrier and enters the maternal circulation. The second exposure to the antigen in subsequent pregnancies results in an antibody formation which threatens the fetus, as occurred in this patient (Dornan 1982; Bowman 1984).

The medical management of the pregnant patient is similar to the treatment of Rh(D) (Caine and Mueller-Heubach 1986). Since the amniotic fluid contains the bilirubin by-product of the hemolysis, direct fetal sampling will indicate the need for prenatal transfusions. Transfusions begin at the 26th week and correspond to the rising levels of maternal antibody. Blood transfusions are used to prevent hyperbilirubinemia and resultant neurotoxicity or death from the complications of the severe anemia (Bowman 1984). Exchange transfusions after birth also control the level of bilirubin by removing any Kell-antibody-coated red cells before they are hemolyzed (Phibbs 1987).

Once the newborn is delivered, ascites may restrict lung expansion. Many infants develop cardiorespiratory distress because of their prematurity. As in this patient, ventilations are assisted with a respirator (Phibbs 1987). A long-term consequence of the respirator is the development of bronchial pulmonary dysplasia, which should resolve over time (Wilson and Mikity 1960).

During the neonatal period, the medications this patient received may have been the cause of his hearing impairment. Diuretics are known to have increased the ototoxic potential of the aminoglycoside antibiotic (Barnhart 1989). However, hearing impairment has been noted as a complication of severe jaundice and erythroblastosis fetalis (Johnsen and Freiesleben 1952). The patient presented with normal intelligence, and no signs of bilirubin encephalopathy. The blood transfusions were effective in removing any antibody-coated red cells, which are a potential lethal source of bilirubin (Klemperer 1984).

The dental findings are a striking example of prenatal dental dysplasia associated with erythroblastosis fetalis (Forrester and Miller 1955). It is not unexpected that similar enamel defects have been reported in 22% of premature children, and 58% of children with Rh(D) (Perlstein and Massler 1956). The site of the developmental defect of enamel corresponds to the time in utero when the maternal antibody titer was rising (26–28th weeks in utero), and the premature delivery (Kraus and Jordan 1965). The defects are present from the incisal edges to the neonatal line of Rushton (Rushton 1933). The neonatal line represents the more pronounced lines of Reitzus where the ameloblasts were disturbed; thus, the enamel formation is thin or incomplete (Stein 1947). The more normal enamel has formed in the post-

transfusion period (McMillan and Kashgarian 1961). The ring of hypoplasia present on the maxillary canines has been referred to as the "Rh hump," since it is present in that form of erythroblastosis fetalis (Watson 1955). This patient also presented with a complete ring of hypoplasia, since the clinical effect of the hemolytic disease is indistinguishable from the cause.

The discoloration of his teeth was limited to yellow, was only noted on his incisors, and perhaps was due to the thinning of the enamel rather than incorporation of the by-products of the jaundice. Although this patient had severe anemia and jaundice, he was treated by a blood transfusion when he was 1 week old. The levels of bilirubin were controlled, and the duration of the jaundice was short. Most cases of green tooth discoloration are the result of prolonged, untreated jaundice (Thursfield 1912; Gibson and Conchie 1964).

The child's previous dentist had diagnosed the child as having nursing caries syndrome, because the child was breast fed until he was 2 years old, and the enamel appeared chipped and yellow. Careful evaluation would have revealed the different quality of the pre- and postnatally formed enamel; the postnatally formed enamel was normal in color, texture, and quantity. The hypoplasia did not result in softer teeth, nor did the child present with any clinical caries. The child's parent was alerted to the possibility of an increased caries risk.

Physicians have been warned to be alert to the presence of irregular antibodies in their pregnant patients, with regard to the proper management of problems caused by the isoimmunization (Dornan 1982). Pediatric dentists should be aware of these rare causes of erythroblastosis fetalis, and the dental implications.

## Summary

An unusual case of erythroblastosis fetalis due to immunization by the Kell blood group is presented. The developmental enamel defects correlated with the time of the rise of antibody titer in utero due to this severe hemolytic disease. The "ring" of hypoplasia on the maxillary primary canine is characteristic of erythroblastosis fetalis.

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