Kernicterus in Otherwise Healthy, Breast-fed Term Newborns

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ABSTRACT. *Objective.* **To document the occurrence of classical kernicterus in full-term, otherwise healthy, breast-fed infants.**

Methods. **We reviewed the files of 22 cases referred to us by attorneys throughout the United States during a period of 18 years, in which neonatal hyperbilirubinemia was alleged to be responsible for brain damage in apparently healthy, nonimmunized, full-term infants. To qualify for inclusion, these infants had to be born at 37 or more weeks' gestation, manifest the classic signs of acute bilirubin encephalopathy, and have the typical neurologic sequelae.**

Results. **Six infants, born between 1979 and 1991, met the criteria for inclusion. Their peak recorded bilirubin levels occurred 4 to 10 days after birth and ranged from 39.0 to 49.7 mg/dL. All had one or more exchange transfusions. One infant had an elevated reticulocyte count (9%) but no other evidence of hemolysis. The other infants had no evidence of hemolysis, and no cause was found for the hyperbilirubinemia (other than breast-feeding).**

Conclusions. **Although very rare, classic kernicterus can occur in apparently healthy, full-term, breast-fed newborns who do not have hemolytic disease or any other discernible cause for their jaundice. Such extreme elevations of bilirubin are rare, and we do not know how often infants with similar serum bilirubin levels escape harm. We also have no reliable method for identifying these infants early in the neonatal period. Closer follow-up after birth and discharge from the hospital might have prevented some of these outcomes, but rare, sporadic cases of kernicterus might not be preventable unless we adopt an approach to follow-up and surveillance of the newborn that is significantly more rigorous than has been practiced. The feasibility, risks, costs, and benefits of this type of intervention need to be determined.** *Pediatrics* **1995;96:730–733;** ***jaundice, hyperbilirubinemia, kernicterus, breast-feeding, newborn, medicolegal, litigation.***

ABBREVIATION. G6PD, glucose-6-phosphate dehydrogenase.

There is considerable debate regarding the potential dangers of hyperbilirubinemia in full-term newborns who do not have isoimmune or other types of hemolytic disease.[1–14] Whether hyperbilirubinemia in these infants causes mild neurodevelopmental or intellectual handicaps, there is no doubt that frank kernicterus in this population is exceptionally rare. Few pediatricians have ever seen a case, and there is a widespread belief that kernicterus does not occur in otherwise healthy, breast-feeding infants, although some cases have been described.[15] Because frank kernicterus is now such a rare event, even investigators and clinicians with a special interest in neonatal jaundice are unlikely to have seen a case. The medicolegal system, however, provides a unique opportunity for the study of rare events. As pediatricians and neonatologists with an interest in neonatal jaundice are consulted by attorneys for plaintiffs or defendants when neonatal hyperbilirubinemia is alleged to be the cause of brain damage, these consultations allow us to gather data that otherwise would be very difficult, or impossible, to obtain.

We reviewed the files of 22 cases referred to either of us by attorneys throughout the United States during a period of approximately 18 years, in which neonatal hyperbilirubinemia was alleged to be responsible for brain damage in full-term infants. We did not see or evaluate any of these infants, but we were able to review the complete medical records in detail.

METHODS

To qualify for inclusion, infants had to be born at 37 or more weeks' gestation and meet the following criteria: (1) manifest the classic signs of acute bilirubin encephalopathy (Table 1); (2) manifest the typical clinical features of chronic bilirubin encephalopathy on follow-up (if available) (Table 1); (3) have a normal perinatal and neonatal course and seem healthy at the time of discharge; (4) have no clinical or laboratory evidence of a hemolytic condition; and (5) have no diagnosis of sepsis or other known cause for hyperbilirubinemia (other than breast-feeding).

Sixteen infants where excluded for the following reasons: (1) clinical features not consistent with classical kernicterus (n = 8); (2) diagnosis of glucose-6-phosphate dehydrogenase (G6PD) deficiency (n = 3); (3) B-O hemolytic disease (n = 1); (4) sepsis (n = 2); and (5) adrenal hemorrhage (n = 2). Six infants met the criteria for inclusion. They were born between 1979 and 1991 in Georgia, Illinois, Massachusetts, New York, Texas, and Wisconsin.

RESULTS

Clinical data for the infants are shown in Tables 2 and 3. All where white and breast-fed. Although the mean birth weight was 3574 g, four of six infants were born at only 37 weeks' gestation, and none was born at 40 weeks or more. Three of six seemed to have excessive weight loss, and one had mild hypernatremic dehydration. All but one (born at home) had been discharged from hospitals and were readmitted with hyperbilirubinemia, the measured peak

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TABLE 1. Clinical Features of Bilirubin Encephalopathy (Kernicterus)

Acute	Chronic
Poor feeding	Motor delay
Lethargy	Extrapyramidal disturbance
High-pitched cry	Sensorineural hearing loss
Increased tone	Gaze palsy
Opisthotonus	Dental dysplasia
Seizures	
Sensorineural hearing loss	

bilirubin level occurring between ages 4 and 10 days. All infants had the same blood type as their mothers, thus eliminating hemolytic disease attributable to Rh or ABO incompatibility as a possible cause of hyperbilirubinemia. None of these infants was anemic, and none was jaundiced in the first 24 hours. Case 5 had a reticulocyte count of 9% but detailed hematologic investigations revealed no evidence of hemolytic disease, no abnormalities of red blood cell morphology, and no enzyme defects. Two infants (cases 3 and 5) had measurements of G6PD activity, which were normal, and none had blood smears suggesting hemolysis.

DISCUSSION

These anecdotal observations must be taken in context; these infants represent a very small fraction of newborns at the outer limits of the spectrum of neonatal jaundice. Nevertheless, they do serve to remind us that kernicterus, with its devastating consequences, is not extinct. Although it seems clear that extremely high bilirubin levels, such as those we reported, are both very rare and likely to be hazardous, we do not know how often infants with similar bilirubin levels escape harm or how many additional infants with kernicterus are not brought to the attention of attorneys. In addition, for obvious reasons, bilirubin experts do not hear about healthy infants who had very high bilirubin levels or about brain-damaged infants who had normal bilirubin levels.

It seems likely that the infants we describe had clinical bilirubin encephalopathy, because our criteria for making that diagnosis were stringent. Nevertheless, it is important to note that most children who are deaf or have athetoid cerebral palsy did not have bilirubin encephalopathy. In the Collaborative Perinatal Project, of 61 children with athetosis at 7 years of age, 57 had peak bilirubin levels less than 10 mg/dL, and none had bilirubin levels of 20 mg/dL or more.[3] Two of these children, both with peak bilirubin levels less than 10 mg/dL, also had sensorineural hearing loss (M. Klebanoff, personal communication, 1995).

Could these problems have been anticipated or prevented? Although all but infant 4 were jaundiced at the time of discharge, none of the infants was jaundiced in the first 24 hours, and the only risk factors for hyperbilirubinemia were slightly shortened gestation (four of six were born at 37 weeks' gestation) and breast-feeding (in all). Yet these hardly can be considered risks for such extreme hyperbilirubinemia. The reticulocyte count of 9% in case 5 is outside of most reference ranges but could

TABLE 2. Clinical Data on Full-term Healthy Newborns, Without Hemolysis Who Had Kernicterus

Case	Year of Birth	Race	Sex	Gestation (wk)	Birth weight (g)	Apgar 1′ 5′ 10′	Blood Type		Direct Coombs	Feeding	Age at Discharge From Hospital	Max Weight Loss (%)	Peak Serum Bilirubin (mg/dL)*		Age at Peak Bilirubin (d)	Other Laboratory Data		
							Mother	Infant					Total	Direct		Hgb (g/dL)	Hct (%)	Retic (%)
1	1979	W	M	37	2820	7,9	O+	O+	Negative	Breast	75h	11	49.7	1.1	7	16.2	49.5	2.0
2	1985	W	M	37	3771	8,9	A+	A+	Negative	Breast	3d	22	39.0	1.8	5	24.0	69.7	3.4
3	1989	W	M	39	4280	9,9	O+	O–	Negative	Breast	66h	1.3	40.3	0.8	10	15.8	48.7	0.6
4	1990	W	F	37	4026	4,6,8	B+	B+	Negative	Breast	+	20	44.7	3.4	7	18.4	54.1	3.1
5	1991	W	F	38	3374	9,8	O+	O+	Negative	Breast	36h	?	44.7	0.0	4	17.8	52.0	9.0
6	1987	W	M	37	3175	8,9	A–	A–	Negative	Breast	52h	17.9	41.4	0.6	6	19.5	59.2	?
Mean ± SD				37.5 ± 0.84	3574 ± 549							14.4 ± 8.4	43.3 ± 3.9	1.3 ± 1.2	6.5 ± 2.1	18.6 ± 3.0	55.5 ± 7.9	3.6 ± 3.2

* Highest level recorded.
† Born at home, seen by midwife on day 2.